Specific Antisocial and Borderline Personality Disorder Criteria and General Substance Use : A Twin Study

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Abstract

Antisocial (ASPD) and Borderline (BPD) personality disorders (PDs) are associated with increased risk for substance use. They are "specific" risk factors among PDs in that they withstand adjusting for the other PDs, whereas the reverse does not hold. Specificity is a classic sign of causation. This empirical work addresses three further problems that can undermine causal inferences in personality and substance-use research: hierarchical nature of etiologic factors in psychiatry, imperfectly operationalized PD criteria, and possible genetic or environmental confounding, as seen in lack of 'etiologic continuity'. We used exploratory structural equation bifactor modeling and biometric models to mitigate these problems. The participants were Norwegian adult twins of ages 19–36 years (N = 2801). Criteria for DSM-5 PDs were assessed using a structured interview. General substance-use risk was indicated by WHO Composite International Diagnostic Interviewed alcohol use disorder and illicit drug use, and by self-reported regular smoking. A general risk factor for all criteria of both ASPD and BPD was the strongest individual correlate of general substance use and showed etiologic continuity, though just three specific PD criteria could predict substance use the same. The findings indicate that a broad latent factor for both ASPD and BPD may be a specific and a genetically and environmentally unconfounded risk factor for substance use. Substance-use treatment research might benefit from attending to transdiagnostic models of ASPD, BPD, and related behavioral disinhibition.

Introduction

Personality disorders (PDs) inflict a huge burden on society and on individuals suffering from them. In Nordic countries, for example, PDs were associated with 13–22 year's reduction in life expectancy (Nordentoft et al., 2013). Risky behaviors, such as substance use and misuse, are one of the likely mechanisms through which PDs increase mortality and disability (Kuo et al., 2018; Lenzenweger et al., 2007). Most PDs are associated with alcohol and substance use disorders (Gillespie, Aggen, Gentry, et al., 2018; Gillespie, Aggen, Neale, et al., 2018; Long et al., 2017; Trull et al., 2010). PDs are highly comorbid, however, and studies that control one PD for the presence of other PDs have found that only antisocial (ASPD) and borderline (BPD) PDs independently and robustly predict substance use (Compton et al., 2007; Gillespie, Aggen, Gentry, et al., 2018; Gillespie, Aggen, Neale, et al., 2018; Hasin et al., 2007; Long et al., 2017). These findings appear not to be substance-specific, but rather implicate ASPD and BPD as specific PD-related risk factors for substance use in general.

In general, adverse life outcomes associated with substance use disorders are not specific to use of a given substance. Instead, a recent large study found that a one-factor model explained well intercorrelations among different substance use disorders (Franco et al., 2019). The same factor was the main predictor of their association with other adverse outcomes. The authors concluded that future work should examine the mechanisms underlying the latent factor for substance use and its relation to adverse life outcomes. In this study, we investigate specific criteria of ASPD and BPD as such potential mechanisms because they may mediate relationship between life events and substance use (e.g., Rosenström et al., 2019). Franco and colleagues (2019) did not find much specificity in associations between substance use disorders and adverse outcomes, but this does not necessarily hold for personality disorder traits (Rosenström, Torvik, et al., 2018). "Specificity" of an association is considered an important sign of causation (A. B. Hill, 1965), whereas understanding causation facilitates treatment and has been called for psychological treatments (Cuijpers et al., 2019).

ASPD and BPD constructs aggregate etiologically complex symptoms (Kendler et al., 2012; Reichborn-Kjennerud et al., 2013; Rosenström et al., 2017), meaning that the aggregate constructs could dilute what is central to substance use risk in them, as suggested by some predictive models (Rosenström, Torvik, et al., 2018). Therefore, here we strive to model the full structure of ASPD and BPD criteria to disentangle specific effects in ASPD and BPD from general dispositions. Here we further consider three important insights from recent literature on psychiatric nosology, listed in this Introduction section and further expanded throughout the paper.

First, nearly all psychiatric disorders appear to share some underlying common risk with each other, as discussed in the literature on "general psychopathology factor" or "p factor" (Caspi & Moffitt, 2018; Lahey et al., 2017). In addition, normative and pathological personality traits may partly reflect the same general psychopathology factor (Oltmanns et al., 2018; Rosenström, Gjerde, et al., 2018). Genetic overlap among PDs and other psychiatric disorders is pervasive (Kendler et al., 2011) and major ongoing efforts aim to organize all psychiatric disorders into a hierarchy of successively more specific etiologic factors (Kotov et al., 2017). This suggests that one should ask "what proportion of substance-use risk is attributable to specific *versus* non-specific factors of PDs" rather than "are there specific factors". An argument against the use of the general psychopathology factor has been that it is not of interest because it may reflect general impairment rather than a common cause (Oltmanns et al., 2018). However, a 'measurement-invariant' general factor has been detected in onsets and recoveries of psychiatric disorders (Gluschkoff et al., 2019) and a general factor also fits with genetic and brain correlates of psychopathology (e.g., Elliott et al., 2018; Goodkind et al., 2015; McTeague et al., 2017; Neumann et al., 2016; Wang et al., 2017) as well as responses to psychosocial treatment (Constantinou et al., 2019). Requiring more indicators of validity for a psychometrically derived construct than this would mean having to discount many constructs studied in clinical and personality psychology. Furthermore, neglecting possibility of shared general factors could lead to serious misinterpretations of specific traits (Caspi & Moffitt, 2018). For example, without a general factor the specific traits can act as continuous confounders for each other in multivariate analyses—a situation where both categorical measurement and measurement errors can

induce statistical errors and bias (Austin & Brunner, 2004; Brunner & Austin, 2009). Here, we chose to explicitly take into account a general factor, whatever its underlying substantive interpretations might be, and consider how different levels of a hierarchy of ASPD and BPD risk factors relate to substance use risk. Bifactor models are typically used to extract a general factor but have been criticized for their high 'fitting-propensity' in comparison to classic factor models (Markon, 2019). That discussion pertains to confirmatory frameworks which are not used in this study (see below paragraph). Exploratory bifactor analysis model has the exact same fit as the exploratory factor analysis model; in fact, the models are indistinguishable on statistical grounds only (Jennrich & Bentler, 2011, 2012).

Second insight in recent literature is that the DSM-5 symptoms that make up the ASPD and BPD diagnoses may be viewed as currently best accepted but imperfect operationalizations for the PDs. They are lay language representations subject to semantic drift (changing meaning in different time periods) and multiple possible interpretations (Zandersen et al., 2019). As one example, Zandersen et al. (2019) discuss the BPD criterion "chronic feelings of emptiness", noting that the only additional remark DSM-5 provides in terms of defining how this criterion characterizes individuals is: "Easily bored, they [individuals with BPD] may constantly seek something to do" (American Psychiatric Association, 2013, p. 664). This definition is general enough that it could describe addictive cravings as well as antisocial urges, among other things, whereas historically "chronic feelings of emptiness" have been associated with basic identity and a fragile sense of self-presence, characteristic of schizophrenia and other 'self-disorders' (Zandersen et al., 2019). Exploratory structural equation models (ESEMs) have been developed in an attempt to mitigate consequences of fallible, non-pure, indicator variables—PD symptoms in this case—that may simultaneously reflect several latent constructs (Asparouhov & Muthén, 2009; Morin et al., 2016). Typical inferences based on the classic, confirmatory, approach to SEM are biased if e.g. "chronic feelings of emptiness" reflect both a latent factor for ASPD and another for BPD. ESEMs remove such bias, while retaining much of the flexibility of SEMs. Here, we combine ESEMs with hierarchical models of ASPD and BPD as substance-use risk factors.

Third, after putting our data to the above frameworks, we assess whether our main findings conform to "*etiologic continuity*" in having congruent multivariate findings for genetic and environmental variance in the observed phenotypes (Kendler et al., 2019). That is, we say PDs are etiologically continuous with risk of using various substances if the indicators of the PDs and the substances are "correlated primarily because they share etiologic influences (as opposed to genetic and environmental forces working in distinct ways on each indicator)" (Mullins-Sweatt et al., 2019). Technically, etiologic continuity is assessed via "common pathway biometric model", further explained in the Methods section (Franić et al., 2013; Kendler et al., 1987; Livesley, 2005; Neale & Cardon, 1992). Etiologic continuity provides evidence for specificity and causation because it supports attributing an association to observed phenotypes instead of genetic or environmental confounders "working in distinct ways on each indicator" (Briley et al., 2019; Rosenström et al., 2019).

The existing evidence on ASPD, BPD, and substance use suggests that efforts should be taken to implement the above three considerations in empirical works. For example, the etiologic factors of ASPD and BPD appear to form a hierarchy of highest, intermediate, and lowest level of generality, as expressed in bifactor models (Figure 1a). Diagnoses of ASPD and BPD share genetic etiology with each other and with other related PDs, but they also have independent genetic influences (Chun et al., 2017; Reichborn-Kjennerud et al., 2015; Torgersen et al., 2008). Specific criteria for ASPD (resp. BPD) share many genetic influences, but also they have specific (i.e., *criterion*-specific) genetic and environmental influences (Kendler et al., 2012; Reichborn-Kjennerud et al., 2013; Rosenström et al., 2017).

While ASPD and BPD are known to share genetic influences with substance use risk (Gillespie, Aggen, Gentry, et al., 2018; Gillespie, Aggen, Neale, et al., 2018; Long et al., 2017), it is unclear where substance use is situated within the hierarchy of etiologic factors for these PDs. Many researchers argue that a broad and continuous dimension of externalizing psychopathology, or that of general liability to all psychopathology, is the key trait behind ASPD, BPD, and all substance use (Caspi & Moffitt, 2018; Kotov et al., 2017; Krueger et al., 2007; Rosenström, Gjerde, et al., 2018; Soe-Agnie et al., 2018). Yet, there

are also findings on the lowest level of risk-factor hierarchy—a level of explanation that has been frequently overlooked in personality research for technical reasons (Ashton et al., 2014). Using modern tools that mitigate technical problems e.g. due to overfitting, we previously found that three specific PD criteria independently increased alcoholism risk over and above all the other PD criteria (80 altogether) and diagnoses (10 altogether): "failure to conform to social norms with respect to lawful behavior", "childhood conduct disorder" (ASPD criteria #1 and #8), and "self-damaging impulsivity" (BPD criterion #4) (Rosenström, Torvik, et al., 2018). It remains unclear whether those 'independent' effects derive from the criterias' central role in the etiology of the PDs or from their own specific etiologies, but such questions can be addressed using bifactor ESEMs.

(Bifactor) modeling of the hierarchy of etiologic factors behind ASPD and BPD does not itself solve the problem of impurely operationalized criteria (Morin et al., 2016). In addition to the problems of semantic drift and multiple interpretations discussed by Zandersen et al. (2019), one could note that PD criteria like "self-damaging impulsivity" and "conduct disorder" are themselves complex phenotypes (Aggen et al., 2009; Dick et al., 2010; Kendler et al., 2013). Most likely, it is unrealistic to assume that the DSM-5 criteria for ASPD and/or BPD are 'pure' indicators of single unidimensional constructs that will have factor cross-loadings of zero on any closely related constructs (Morin et al., 2016). Fortunately, the "exploratory" version of bifactor model relaxes the pure-indicator assumption (Morin et al., 2016) of the more restricted, confirmatory bifactor models (Eid et al., 2017; e.g., Gibbons & Hedeker, 1992).

When it comes to etiologic continuity *vs*. confounding, mediational relationships between stressful life events, BPD, and alcohol use disorder (AUD) may be subject to genetic and/or environmental confounding (Bornovalova et al., 2013; Rosenström et al., 2019). Whatever predominant substance-use risk factor emerges from hierarchical modeling of ASPD and BPD criteria, it should ideally be subjected to a test of etiologic continuity. After all, a better understanding of etiology helps in design of prevention strategies and treatment programs. Questions could be answered regarding choice of therapies specifically for substance use *versus* more unified protocols covering wider sets of psychopathologies, as well as those

regarding treatments directed towards overarching personality pathologies *versus* specific thoughts and behaviors indicated by individual diagnostic criteria.

The Current Study

Whereas many previous studies have found evidence that ASPD and BPD have strong links with general substance use risk, the exact etiology behind the link remains unclear. We know ASPD and BPD are constructs with partly overlapping etiologies that aggregate over criteria with partly distinct etiologies, which calls for a criterion-level re-assessment of the findings. We know that the plausible existence of a continuous general factor can bias the typical regression-based epidemiology on categorical disorders. We know that confirmatory bifactor models, although useful and appropriate in certain applications, can lead to overfitting data, whereas the less often used explorative bifactor models are rotations with the exact same fit as for the classic factor model, reducing the reliance on the assumption of pure indicators. We suspect that few indicators are "pure" in the sense that they are completely unique in identifying a particular PD, which implies a degree of bias or interpretational confounding when fitting typical confirmatory models. And, we know that bifactor ESEMs can partly eliminate biases due to non-pure indicators, categorical formulations, measurement errors, and confirmatory bifactor modeling. What we know less about is what happens when attempts are made to reduce the effects of these known sources of bias: what kind of etiologic constructs arise from data then and how do they associate with substance use risk? This is the question this paper aims to clarify.

This study aims to clarify the etiology of substance use in relation to its risk PDs, while addressing the above discussed three complicating factors (i.e., hierarchical nature of etiologic factors in psychiatry, imperfectly operationalized PD criteria, and genetic and/or environmental confounding). To that end, we take an exploratory structural equation modeling approach. First, we assessed the joint phenotypic hierarchical structure of the ASPD and BPD criteria. Second, we investigated how the structure relates to substance use risk when minimizing the introduced modeling pitfalls (i.e., determined which levels of the

hierarchy captured the predominant risk factor for general substance use). Third, we determined what genetic and environmental etiology pertains to the PD-related substance use risk (i.e., determined how genetic and environmental influences on the predominant risk factor were related to general substance use risk). Because the structural equation models used here to address the above-discussed complicating factors typically make more assumptions than many regression models and suffer more from computational and data-related bottlenecks (e.g., VanderWeele, 2012; Zahery et al., 2017), we concentrate only on the core constructs of ASPD, BPD and substance use, leaving other psychiatric comorbidities for future research.

Methods

Sample

The participants, 2801 Norwegian twins, were drawn from the Norwegian Institute of Public Health's Twin Panel (Harris et al., 2002; Tambs et al., 2009). The zygosity of the twins was determined by a combination of questionnaire items and genotyping. The sampling targeted twins born between 1967 and 1979, capturing 43.5% of those eligible. Their mean age was 28.2 years (range 19-36 years). Their DSM-IV Axis I and Axis II psychiatric disorders were assessed in an interview between 1999 and 2004. Although 2284 of the twins were re-interviewed again in between 2010 and 2011 and they completed a self-report questionnaire in 2017-18, here we concentrate on the first wave of data collection because recording of substance use has differed across the three waves, and because genetic etiology of substance use differs by age and peaks in young adults (e.g., E. M. Hill & Chow, 2002; Torvik et al., 2017). Approval for this study was received from The Norwegian Data Inspectorate and the Regional Committee for Medical and Health Research Ethics, and written informed consent was obtained from all participants.

Procedures

PDs within past 5 years were assessed using a Norwegian version of the Structured Interview for DSM-IV Personality (Pfohl et al., 1995), a comprehensive semi-structured interview of all DSM-IV Axis II diagnoses that produced an ordinal rating of the specific DSM-IV criteria (0 = not present or limited to rare isolated examples, 1 = subthreshold, 2 = present, 3 = strongly present (e.g., Reichborn-Kjennerud et al., 2015; Rosenström, Torvik, et al., 2018 for more detail)). PD diagnoses are identical in DSM-5 and -IV (American Psychiatric Association, 2013).

We studied general risk of substance use rather than risks for specific substances, since previous research has indicated that ASPD and BPD are non-specific predictors of substance use and since use disorders of different substances reflect a single dimension of risks and outcomes (Franco et al., 2019). Specifically, an underlying risk factor was modeled using three available *indicators* of general substance use: AUD, illicit drug use, and smoking. The indicators for AUD and drug use were assessed using the computerized Norwegian version of World Health Organization's Composite International Diagnostic Interview (CIDI) (Wittchen & Pfister, 1997), whereas smoking status was assessed in a separate mailed questionnaire. Lifetime AUD was indicated by either alcohol abuse (F10.1 in ICD-10) or dependence (F10.2). Because specific drug use disorders are rare outcomes, we combined illicit drug use into an ordinal variable with value 0 indicating no serious use, value 1 indicating having used illegal (non-prescribed) drugs more than ten times, and value 2 indicating a disorder or dependency for opioids, cannabis, sedative, cocaine, amphetamine, hallucinogens, or inhalants (as in F11–16 and F18). Smoking was indicated as the status of current regular smoking (yes/no). See previous studies for more details on the procedures (Harris et al., 2002; e.g., Reichborn-Kjennerud et al., 2015; Tambs et al., 2009). Note that smoking reflects further health hazards (e.g. lung cancer) besides its strong association with general substance use risks (Franco et al., 2019), but here we are primarily interested in shared behavioral antecedents of substance use.

Statistics

Exploratory structural equation models (ESEM) were fit to underlying liabilities for the binary and ordinal-valued indicator variables using liability-threshold modeling (Asparouhov & Muthén, 2009; Falconer, 1965; Morin et al., 2016; Neale & Cardon, 1992). Liability-threshold models estimate an underlying normally distributed continuum of risk behind each crude categorical observation item to remove the bias in ESEMs that would otherwise result from the low (i.e., ordinal) measurement precision. All the ESEM models were fitted using mean- and variance adjusted weighted least squares estimator of Mplus software. Because members of twin pairs are more similar to each other than to the other twins, they represent clusters of dependent observations. Sandwich estimators were therefore used to correct the ESEM estimates for the dependent observations (Asparouhov, 2005; Højsgaard et al., 2006). The underlying heritability patterns behind the phenotypes were studied using the "Open Mx" R package, "ACE" twin design, and full-information maximum likelihood estimation (Neale et al., 2016; Neale & Cardon, 1992). The twin design uses the average 100% genetic similarity of monozygotic twins and 50% similarity of dizygotic twins to estimate heritability and correlations of genetic and (shared and non-shared) environmental influences for given variables. Regarding, specific study questions, the following logic was applied.

To assess the hierarchical structure of ASPD and BPD (research question *i*), "parallel analysis criterion" was used to determine the optimal number of underlying factors for modeling of covariance among the ASPD and BPD criteria, because previous studies support the strategy (Garrido et al., 2013, 2016; Hayashi et al., 2007; Rosenström et al., 2017). Parallel analysis sorts (Mplus estimates of) eigenvalues of the polychoric correlation matrix in descending order, and then compares them to average descending eigenvalues from 1000 simulated datasets of the same size but with no underlying factors; the estimated factor number corresponds to those eigenvalues that exceed the average sampling noise in the simulated values. Given the number of factors, the estimated bifactor loadings and their stability were investigated to interpret the underlying factors. A bifactor rotation does not affect factor number nor model fit (Jennrich & Bentler, 2011, 2012), and its robustness (Mansolf & Reise, 2016) was verified in our online supplement by re-rotating from 1000 distinct randomly generated starting rotations (Mezzadri, 2007).

To assess which levels in the hierarchical model of ASPD and BPD criteria best predict general substance use risk (research question *ii*), an ESEM described by the path diagram of Figure 1b was fit to the data (Morin et al., 2016). This model assumes a hierarchy of general, specific, and criterion-specific influences in ASPD and BPD items. It does not fix factor loadings *a priori* before using the members of the factorial hierarchy to predict a general substance use factor (controlling sex). Instead, all the parameters are estimated simultaneously. In a direct analogy with usual regression models, however, the ESEM model can be used to test which predictors are needed (statistically significant). The factor loadings are estimated jointly with the other model structure using an exploratory bi-factor (an orthogonal 'bi-quartimin') rotation (Jennrich & Bentler, 2011, 2012) that rotates the solution as close to a hierarchical pattern as possible (cf. Figure 1a). The ASPD criteria #1 (failure to conform to social norms) and #8 (childhood conduct disorder) and the BPD criterion #4 (self-damaging impulsivity) are treated similarly to the other PD criteria in the factor analysis part of the model, but are only illustrated in the middle of Figure 1b because they are also directly used in the regression part of the model, based on their previously shown independent associations with AUD (Rosenström, Torvik, et al., 2018).

To explore continuity of etiologic factors behind ASPD, BPD, and substance use (research question *iii*), multivariate twin models were estimated. Specifically, we tested whether the pertinent dimensions of risk reflected common *vs.* independent genetic and environmental pathways (cf. Figure 1c) (Franić et al., 2013; Kendler et al., 1987; Neale & Cardon, 1992; Rosenström et al., 2017). The most parsimonious path model was then used to partition variance to shared *vs*. specific components, which were further partitioned to genetic *vs.* environmental components. We used a different software (Open Mx) to assess etiologic continuity than for bifactor modeling (Mplus) because it has been developed specifically for such questions. We concentrated only on core variables (discussed below) because pertinent biometric models failed to converge for all the variables. Even when they do so, achieving convergence for single models of this many variables takes several weeks and does not always provide reliable results (Kendler et al., 2019; Zahery et al., 2017).

Results

Bifactor structure of borderline and antisocial personality disorder criteria

According to the parallel analysis criterion, a three-factor solution was sufficient to capture the correlations between the PD criteria (Figure 1d). Although that analysis left room to argue also for a two-factor solution, we used a three-factor solution because over-factoring is generally considered less detrimental than under-factoring (Hayashi et al., 2007) and because three factors was favored also by the RMSEA fit index (RMSEA = 0.019 with 90% CI = 0.015–0.023 vs. RMSEA = 0.030 with CI= 0.027–0.033). According to a bi-factor rotation (Table 1), the three factors could be interpreted as (*i*) a general risk factor for both antisocial and borderline personality disorder (titled G), (*ii*) a specific factor distinguishing affective BPD criteria from remorseless antisocial behaviors (S1), and (*iii*) a specific factor for aggression (S2). While all ASPD and BPD criteria loaded strongly on the general-risk factor (G in Table 1), the pre-selected three PD criteria had much more variance (more endorsements of non-zero categories) than the other criteria (Table 1), meaning they were relatively well-suited for measuring a wide range of G-factor values (i.e., suffered less from 'range restriction' than most PD criteria). The orthogonal bifactor rotation was preferred for this study because it was able to differentiate between hierarchies of risk factors, but, see online supplement for alternative classic rotations and for our sensitivity analysis suggesting the bifactor solution was robust.

Factor structure of general substance use

Loadings of AUD, illicit drug use, and smoking on the general substance use factor were 0.694, 0.826, and 0.396, respectively (Table 2). This means that the general factor explained 48%, 68%, and 16% of variance in the liabilities to endorse AUD, drug use, and smoking, respectively. Thus, smoking was clearly related to the general liability to substance use, but less so than AUD and illicit drug use.

Which level of personality pathology best captures general risk for substance use?

We then investigated the model described in Figure 1b (Model I) and its versions where regression coefficients of substance use on the pre-selected criteria (Model II) or those on the latent factors (Model III) were constrained to zero. Both the latent factors ($\chi 2 = 22.537$, d.f. = 3, $p < 0.001$) and the pre-selected risk criteria ($\chi 2 = 19.381$, d.f. = 3, $p < 0.001$) were independently associated with the general substance use factor (i.e., constrained versions of Model I were rejected). However, all three models had practically equal fit to data (Table 3; see also supplementary analysis of residuals following Maudeu-Olivares, 2017), whereas a model using only sex as a predictor had a significantly worse fit (e.g., RMSEA = 0.082 with CI = 0.079–0.084).

The criterion-level and the factor-level predictors of general substance use appeared near-multicollinear in the sense that the full-hierarchy model (Model I) had rather different pattern of regression coefficient compared to the higher- and lower-level predictive models (Model II and III, respectively). To sum, while all levels of personality hierarchy were associated with general risk for substance use, the effects of factor vs. criteria were largely exchangeable (i.e., traded predictive variance), with G being the dominant predictor (cf. Model II).

Etiologic continuity in inheritance patterns

Both the above phenotypic analyses and a supplementary biometric analysis of factor scores (supplementary Fig. S3) suggested that mainly the general PD factor played a role in associations between the PDs and the general substance use risk. According to the phenotypic factor rotation (Table 1), the criteria that loaded primarily only on the general factor were ASPD criteria #2, #5, and #8 and BPD criteria #4, #5, and #9. We used a count of these criteria (full or sub-threshold) to explore the multivariate genetic and environmental structure of the general PD factor and the different substances (i.e., the orthogonal residual PD factors were excluded for the sake of clarity and computational feasibility).

We started from the most general model, which modeled independent genetic (A) and shared- (C) and non-shared (E) environmental factors for both the overlapping and the specific variance in the variables, as well as sex-specific factor loadings and ordinal thresholds. Although this "independent pathway model" slightly differed from a "common pathway model" (χ^2 = 23.71, d.f. = 23, p = 0.022; cf. Fig. 1c), both Akaike's and Bayesian Information Criteria suggested that a common pathway model was more parsimonious interpretation of the data (i.e., a common pathway model was favored by ΔAIC = -0.29 and ΔBIC = -83.53). A previous simulation study suggested that one should rely on BIC in this model comparison (Markon & Krueger, 2004). The shared environmental influences (C parts) in the model were non-significant and were therefore not further interpreted or modeled (χ^2 = 3.77, *d.f.* = 10, *p* = 0.957). The model could be further simplified by constraining factor loadings (but not thresholds) across the sexes (χ^2 = 6.37, *d.f.* = 14, *p* = 0.956). Figure 2 summarizes the biometric relationships between the substances and the general liability to ASPD and BPD.

From Figure 2, we see that a common-pathway general factor explained roughly 42% (i.e., $100\% \times 0.668^2$), 67%, 41%, and 18% of variance in the (proxy of) general PD factor, illicit drug use, AUD, and smoking, respectively. Of these influences, 89% (i.e., $100\% \times 0.943^2$) were of additive-genetic origin. However, also specific genetic variance existed in the variables (χ^2 = 91.25, *d.f.* = 4, *p* < 0.001; Figure 2), in addition to the etiologically continuous latent factor of shared risks.

A sensitivity analysis of content overlap

In interpreting findings like herein, one is often concerned that the specific criteria may contain a degree of content overlap with substance use outcomes. Our previous research and Supplementary Figure S3 indicate that simple content overlap is an unlikely explanation of our findings (e.g., Gillespie, Aggen, Gentry, et al., 2018; Long et al., 2017; Rosenström, Torvik, et al., 2018).

Discussion

The current study demonstrates that a single shared underlying dimension of risk for both ASPD and BPD criteria largely explains the associations between the PD criteria and substance use. Three simple PD criteria were efficient clinical proxies for this latent dimension: social-norm violations (ASPD criterion #1), conduct disorder (ASPD #8), and self-damaging impulsivity (BPD #4). The latent dimension of general risk for ASPD, BPD, and substance use reflected primarily heritable population variance (89% with 95% CI = 77–99%), but also environmental influences were detected (11% with CI = 1–22%). It showed evidence of etiologic continuity, or lack of genetic and/or environmental confounding. Our findings suggest that ASPD and BPD traits largely fall on the same shared dimension of risk factors with substance use disorders and a wide range of adverse outcomes (Franco et al., 2019).

A previous study on the joint structure of ASPD and BPD criteria suggested that an overarching general dimension of risk for all the criteria plus other psychopathology exists (Chun et al., 2017). Similarly, our investigation underscored the importance of such an overarching dimension of risk. Unlike previous studies, we did not assume a factor loading pattern *a priori*, but instead used an exploratory approach (Morin et al., 2016) to address concerns about operationalization of PD criteria (e.g., Zandersen et al., 2019). The exploration revealed a general factor of liability for all the criteria of both ASPD and BPD (“G factor”), a specific (residual) factor capturing tendency to manifest affective instability instead of norm violations and lack of remorse (“factor S1”), and a specific factor capturing anger proneness (“factor S2”; sign inverted). We do not enter further speculation on the specific factors here, as they were less relevant to substance use than the general factor. However, they may suggest interesting targets for future research.

Our current findings using ESEM analysis framework found that ASPD and BPD criteria were not specific in predicting substance use and thus seemingly depart from our previous report that found three specific criteria as best predictors of AUD using a modern regression analysis framework (Rosenström, Torvik, et al., 2018). However, current methods focused on etiology whereas the previous

ones focused on prediction. Even though our present findings suggest a strong etiologic role for factors affecting both ASPD and BPD, they do not necessarily suggest using these diagnostic constructs in clinical predictions of substance-use risk. ASPD and BPD diagnoses poorly predict AUD, for example, because they are so rare in the population in comparison to AUD (Rosenström, Torvik, et al., 2018). Similarly, many of their specific criteria have relatively little variance (Table 1). Simply formulated and well-predicting criteria can have a high clinical utility, while different models are needed to understand their etiologic role (Briley et al., 2019). Indeed, our present *predictive* analysis was in line with the previous one in that three specific PD criteria were sufficient for predicting AUD (Rosenström, Torvik, et al., 2018).

Regarding understanding etiology, we found that the latent dimension of risk for ASPD, BPD, and substance use reflect a "common pathway" rather than independent genetic and environmental influences. Such etiologic continuity appears consistent with previous findings on ASPD, BPD, drug abuse, AUD, externalizing spectrum, and adverse outcomes (Franco et al., 2019; Kendler et al., 2016; Reichborn-Kjennerud et al., 2013; Rosenström et al., 2017, 2019), although it may not generalize to all personality domains (Franić et al., 2013; Kendler et al., 2019).

Although our present analysis does not directly inform what could give rise to an etiologically continuous latent factor associated with ASPD and BPD criteria and substance use, it may be worthwhile to speculate upon certain patterns found in literature. The PD criteria tapping to this factor appeared to lie on a causal pathway from stressful childhood environment to AUD in an earlier paper (Rosenström et al., 2019). They are also related to "disinhibition", which has been suggested as a unifying construct in understanding how personality disposition undergird psychopathology (Mullins-Sweatt et al., 2019): "the construct of disinhibition (*versus* constraint) is a broad personality trait that refers to individual differences in the ability to self-regulate or control one's behavior". Such ability would presumably develop worse in worse environmental conditions, explaining why environmental enrichment reduce risk of PDs (Raine et al., 2003), and why personality-targeted interventions may lead to long-term reductions in substance-use behaviors (Conrod et al., 2011). Thus, the general PD and substance use risk factor we found could

represent or overlap with the construct of disinhibition. In contrast, reverse causation from substance use to PD pathology seems less likely. ASPD and BPD tend to temporally precede non-PD psychopathologies, including substance use (Defoe et al., 2019; Gunderson et al., 2004; Young et al., 2008), often exhausting PD-related genetic risk factors (e.g., Gillespie, Aggen, Gentry, et al., 2018; Reichborn-Kjennerud et al., 2010; Rosenström, Torvik, et al., 2018). A recent review of BPD and substance use concluded that substance use may exacerbate PD symptomatology, but "because common genetic, personality, and early influences predate overt substance use, it seems unlikely that PDs are simply secondary to substance use" (Trull et al., 2018). Normative personality traits also primarily precede e.g. episodes of depression, with only very small reverse effects at the most (Klein et al., 2011; Rosenström et al., 2014, 2015), although their interaction with alcohol and substance use appears more complex (Hakulinen & Jokela, 2019; Kendler et al., 2014).

Recent studies that included many psychiatric disorders and indicators of personality have reported a very broad underlying dimension of risk that encompasses both personality pathology and other psychopathology (Kotov et al., 2017; Krueger et al., 2007; Oltmanns et al., 2018; Rosenström, Gjerde, et al., 2018). This study concurs in showing that the key personality pathologies in substance use risk can be interpreted as reflecting a broad continuum of risk. Findings on etiologic overlap among the broad dimensional constructs appear solid, but accurate estimates of the full extent of overlap may turn out elusive for practical reasons. Accurate analysis of increasingly complex models may require increasingly large data [although exceptions exist (Rosenström et al., 2019; Schmitz et al., 1998)]. At the same time, accurate estimation of structural equations on ordinal variables requires repeated numeric integration of multivariate normal distribution. Therefore, complex models with many variables may become prohibitively slow to compute or they may require different methods than problems involving less variables (Gibbons & Hedeker, 1992; Zahery et al., 2017; Gassmann et al., 2002; Kendler et al., 2019).

The present findings should be interpreted in the light of important limitations. First, the sample is subject to moderate selection towards good health (Tambs et al., 2009). Ideally the findings should be replicated in a more disabled population; however, care must be taken if the population has

been selected based on aggregate measures of ASPD, BPD, or substance use, because that may distort factor structures (Muthén, 1989). Second, a more comprehensive analysis with more substances might reveal further effects. Third, it should be kept in mind that modeling of latent liabilities does not directly translate to ability to predict new observations (but see our previous paper for some cross-validated predictions (Rosenström, Torvik, et al., 2018)). Fourth, we had self-report and interview data on substance use, but no objective biomarkers that could eliminate risk of dishonest reporting. Nevertheless, our findings suggest that treatments and theories targeting a wider set of behavioral problems than just substance use could be more efficient long-term solutions than those targeting substance-use behaviors only (Bateman et al., 2015; Conrod et al., 2011; Newton-Howes & Foulds, 2018). Transdiagnostic models of ASPD and BPD could be useful for addiction research.

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References

455 Aggen, S. H., Neale, M. C., Røysamb, E., Reichborn-Kjennerud, T., & Kendler, K. S. (2009). A psychometric
456 evaluation of the DSM-IV borderline personality disorder criteria: Age and sex moderation of
457 criterion functioning. *Psychological Medicine*, *39*(12), 1967–1978.
458 https://doi.org/10.1017/S0033291709005807
459 American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders, Fifth*
460 *Edition*. American Psychiatric Association.
461 Ashton, M. C., Paunonen, S. V., & Lee, K. (2014). On the validity of narrow and broad personality traits: A
462 response to Salgado, Moscoso, and Berges (2013). *Personality and Individual Differences*, *56*, 24–
463 28. https://doi.org/10.1016/j.paid.2013.08.019
464 Asparouhov, T. (2005). Sampling weights in latent variable modeling. *Structural Equation Modeling*, *12*(3),
465 411–434. https://doi.org/10.1207/s15328007sem1203_4
466 Asparouhov, T., & Muthén, B. (2009). Exploratory structural equation modeling. *Structural Equation*
467 *Modeling: A Multidisciplinary Journal*, *16*(3), 397–438.
468 https://doi.org/10.1080/10705510903008204
469 Austin, P. C., & Brunner, L. J. (2004). Inflation of the type I error rate when a continuous confounding
470 variable is categorized in logistic regression analyses. *Statistics in Medicine*, *23*(7), 1159–1178.
471 https://doi.org/10.1002/sim.1687
472 Bateman, A. W., Gunderson, J., & Mulder, R. (2015). Treatment of personality disorder. *The Lancet*,
473 *385*(9969), 735–743. https://doi.org/10.1016/S0140-6736(14)61394-5
474 Bornovalova, M. A., Huibregtse, B. M., Hicks, B. M., Keyes, M., McGue, M., & Iacono, W. (2013). Tests of a
475 direct effect of childhood abuse on adult borderline personality disorder traits: A longitudinal
476 discordant twin design. *Journal of Abnormal Psychology*, *122*(1), 180–194.
477 https://doi.org/10.1037/a0028328
478 Briley, D. A., Livengood, J., Derringer, J., Tucker-Drob, E. M., Fraley, R. C., & Roberts, B. W. (2019).
479 Interpreting behavior genetic models: Seven developmental processes to understand. *Behavior*
480 *Genetics*, *49*(2), 196–210. https://doi.org/10.1007/s10519-018-9939-6

Brunner, J., & Austin, P. C. (2009). Inflation of Type I error rate in multiple regression when independent variables are measured with error. *Canadian Journal of Statistics*, *37*(1), 33–46.

Caspi, A., & Moffitt, T. E. (2018). All for one and one for all: Mental disorders in one dimension. *The American Journal of Psychiatry*, *175*(9), 831–844. https://doi.org/10.1176/appi.ajp.2018.17121383

Chun, S., Harris, A., Carrion, M., Rojas, E., Stark, S., Lejuez, C., Lechner, W. V., & Bornovalova, M. A. (2017). A psychometric investigation of gender differences and common processes across borderline and antisocial personality disorders. *Journal of Abnormal Psychology*, *126*(1), 76–88. https://doi.org/10.1037/abn0000220

Compton, W. M., Thomas, Y. F., Stinson, F. S., & Grant, B. F. (2007). Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States: Results from the national epidemiologic survey on alcohol and related conditions. *Archives of General Psychiatry*, *64*(5), 566–576. https://doi.org/10.1001/archpsyc.64.5.566

Conrod, P. J., Castellanos-Ryan, N., & Mackie, C. (2011). Long-term effects of a personality-targeted intervention to reduce alcohol use in adolescents. *Journal of Consulting and Clinical Psychology*, *79*(3), 296–306. https://doi.org/10.1037/a0022997

Constantinou, M. P., Goodyer, I. M., Eisler, I., Butler, S., Kraam, A., Scott, S., Pilling, S., Simes, E., Ellison, R., Allison, E., & Fonagy, P. (2019). Changes in general and specific psychopathology factors over a psychosocial intervention. *Journal of the American Academy of Child and Adolescent Psychiatry*, *58*(8), 776–786. https://doi.org/10.1016/j.jaac.2018.11.011

Cuijpers, P., Reijnders, M., & Huibers, M. J. H. (2019). The role of common factors in psychotherapy outcomes. *Annual Review of Clinical Psychology*, *15*, 207–231. https://doi.org/10.1146/annurev-clinpsy-050718-095424

Defoe, I. N., Khurana, A., Betancourt, L. M., Hurt, H., & Romer, D. (2019). Disentangling longitudinal relations between youth cannabis use, peer cannabis use, and conduct problems: Developmental cascading links to cannabis use disorder. *Addiction*, *114*(3), 485–493. https://doi.org/10.1111/add.14456

Dick, D. M., Smith, G., Olausson, P., Mitchell, S. H., Leeman, R. F., O'Malley, S. S., & Sher, K. (2010). Understanding the construct of impulsivity and its relationship to alcohol use disorders. *Addiction Biology*, *15*(2), 217–226. https://doi.org/10.1111/j.1369-1600.2009.00190.x

Eid, M., Geiser, C., Koch, T., & Heene, M. (2017). Anomalous results in G-factor models: Explanations and alternatives. *Psychological Methods*, *22*(3), 541–562. https://doi.org/10.1037/met0000083

Elliott, M. L., Romer, A., Knodt, A. R., & Hariri, A. R. (2018). A connectome-wide functional signature of transdiagnostic risk for mental illness. *Biological Psychiatry*, *84*(6), 452–459. https://doi.org/10.1016/j.biopsych.2018.03.012

Falconer, D. S. (1965). The inheritance of liability to certain diseases, estimated from the incidence among relatives. *Annals of Human Genetics*, *29*(1), 51–76. https://doi.org/10.1111/j.1469-1809.1965.tb00500.x

Franco, S., Olfson, M., Wall, M. M., Wang, S., Hoertel, N., & Blanco, C. (2019). Shared and specific associations of substance use disorders on adverse outcomes: A national prospective study. *Drug and Alcohol Dependence*, *201*, 212–219. https://doi.org/10.1016/j.drugalcdep.2019.03.003

Franić, S., Dolan, C. V., Borsboom, D., Hudziak, J. J., van Beijsterveldt, C. E. M., & Boomsma, D. I. (2013). Can genetics help psychometrics? Improving dimensionality assessment through genetic factor modeling. *Psychological Methods*, *18*(3), 406–433. https://doi.org/10.1037/a0032755

Garrido, L. E., Abad, F. J., & Ponsoda, V. (2013). A new look at Horn's parallel analysis with ordinal variables. *Psychological Methods*, *18*(4), 454–474. https://doi.org/10.1037/a0030005

Garrido, L. E., Abad, F. J., & Ponsoda, V. (2016). Are fit indices really fit to estimate the number of factors with categorical variables? Some cautionary findings via Monte Carlo simulation. *Psychological Methods*, *21*(1), 93–111. https://doi.org/10.1037/met0000064

Gassmann, H. I., Deák, I., & Szántai, T. (2002). Computing multivariate normal probabilities: A new look. *Journal of Computational and Graphical Statistics*, *11*(4), 920–949. https://doi.org/10.1198/106186002385

Gibbons, R. D., & Hedeker, D. R. (1992). Full-information item bi-factor analysis. *Psychometrika*, *57*(3), 423–436. https://doi.org/10.1007/BF02295430

Gillespie, N. A., Aggen, S. H., Gentry, A. E., Neale, M. C., Knudsen, G. P., Krueger, R. F., South, S. C., Czajkowski, N., Nesvåg, R., Ystrom, E., Rosenström, T. H., Torvik, F. A., Reichborn-Kjennerud, T., & Kendler, K. S. (2018). Testing genetic and environmental associations between personality disorders and cocaine use: A population-based twin study. *Twin Research and Human Genetics*, *21*(1), 24–32. https://doi.org/10.1017/thg.2017.73

Gillespie, N. A., Aggen, S. H., Neale, M. C., Knudsen, G. P., Krueger, R. F., South, S. C., Czajkowski, N., Nesvåg, R., Ystrom, E., Kendler, K. S., & Reichborn-Kjennerud, T. (2018). Associations between personality disorders and cannabis use and cannabis use disorder: A population-based twin study. *Addiction*, *113*(8), 1488–1498. https://doi.org/10.1111/add.14209

Gluschkoff, K., Jokela, M., & Rosenström, T. (2019). The general psychopathology factor: Structural stability and generalizability to within-individual changes. *Frontiers in Psychiatry*, *10*, 594. https://doi.org/10.3389/fpsyt.2019.00594

Goodkind, M., Eickhoff, S. B., Oathes, D. J., Jiang, Y., Chang, A., Jones-Hagata, L. B., Ortega, B. N., Zaiko, Y. V., Roach, E. L., Korgaonkar, M. S., Grieve, S. M., Galatzer-Levy, I., Fox, P. T., & Etkin, A. (2015). Identification of a common neurobiological substrate for mental illness. *JAMA Psychiatry*, *72*(4), 305–315. https://doi.org/10.1001/jamapsychiatry.2014.2206

Gunderson, J., Morey, L., Stout, R., Skodol, A., Shea, M., McGlashan, T., Zanarini, M., Grilo, C., Sanislow, C., Yen, S., Daversa, M., & Bender, D. (2004). Major depressive disorder and borderline personality disorder revisited: Longitudinal interactions. *Journal of Clinical Psychiatry*, *65*(8), 1049–1056.

Hakulinen, C., & Jokela, M. (2019). Alcohol use and personality trait change: Pooled analysis of six cohort studies. *Psychological Medicine*, *49*(2), 224–231. https://doi.org/10.1017/S0033291718000636

Harris, J. R., Magnus, P., & Tambs, K. (2002). The Norwegian Institute of Public Health Twin Panel: A description of the sample and program of research. *Twin Research*, *5*(5), 415–423. https://doi.org/10.1375/136905202320906192

Hasin, D. S., Stinson, F. S., Ogburn, E., & Grant, B. F. (2007). Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry*, *64*(7), 830–842. https://doi.org/10.1001/archpsyc.64.7.830

Hayashi, K., Bentler, P. M., & Yuan, K.-H. (2007). On the likelihood ratio test for the number of factors in exploratory factor analysis. *Structural Equation Modeling*, *14*(3), 505–526. https://doi.org/10.1080/10705510701301891

Hill, A. B. (1965). The environment and disease: Association or causation? *Proceedings of the Royal Society of Medicine*, *58*(5), 295–300.

Hill, E. M., & Chow, K. (2002). Life-history theory and risky drinking. *Addiction*, *97*(4), 401–413. https://doi.org/10.1046/j.1360-0443.2002.00020.x

Højsgaard, S., Halekoh, U., & Yan, J. (2006). The R Package geepack for Generalized Estimating Equations. *Journal of Statistical Software*, *15*(2), 1–11. https://doi.org/10.18637/jss.v015.i02

Jennrich, R. I., & Bentler, P. M. (2011). Exploratory bi-factor analysis. *Psychometrika*, *76*(4), 537–549. https://doi.org/10.1007/s11336-011-9218-4

Jennrich, R. I., & Bentler, P. M. (2012). Exploratory bi-factor analysis: The oblique case. *Psychometrika*, *77*(3), 442–454. https://doi.org/10.1007/s11336-012-9269-1

Kendler, K. S., Heath, A. C., Martin, N. G., & Eaves, L. J. (1987). Symptoms of anxiety and symptoms of depression. Same genes, different environments? *Archives of General Psychiatry*, *44*(5), 451–457. https://doi.org/10.1001/archpsyc.1987.01800170073010

Kendler, K. S., Aggen, S. H., Gillespie, N., Krueger, R. F., Czajkowski, N., Ystrom, E., & Reichborn-Kjennerud, T. (2019). The structure of genetic and environmental influences on normative personality, abnormal personality traits, and personality disorder symptoms. *Psychological Medicine*, *49*(8), 1392–1399. https://doi.org/10.1017/S0033291719000047

Kendler, K. S., Aggen, S. H., Knudsen, G. P., Røysamb, E., Neale, M. C., & Reichborn-Kjennerud, T. (2011). The structure of genetic and environmental risk factors for syndromal and subsyndromal common

584 DSM-IV axis I and all axis II disorders. *The American Journal of Psychiatry*, *168*(1), 29–39.
585 https://doi.org/10.1176/appi.ajp.2010.10030340
586 Kendler, K. S., Aggen, S. H., & Patrick, C. J. (2012). A multivariate twin study of the DSM-IV criteria for
587 Antisocial Personality Disorder. *Biological Psychiatry*, *71*(3), 247–253.
588 https://doi.org/10.1016/j.biopsych.2011.05.019
589 Kendler, K. S., Lönn, S. L., Maes, H. H., Lichtenstein, P., Sundquist, J., & Sundquist, K. (2016). A Swedish
590 population-based multivariate twin study of externalizing disorders. *Behavior Genetics*, *46*(2), 183–
591 192. https://doi.org/10.1007/s10519-015-9741-7
592 Kendler, K. S., Ohlsson, H., Sundquist, K., & Sundquist, J. (2014). Peer deviance, parental divorce, and
593 genetic risk in the prediction of drug abuse in a nationwide Swedish sample: Evidence of
594 environment-environment and gene-environment interaction. *JAMA Psychiatry*, *71*(4), 439–445.
595 https://doi.org/10.1001/jamapsychiatry.2013.4166
596 Kendler, K. S., Aggen, S. H., & Patrick, C. J. (2013). Familial influences on conduct disorder reflect 2 genetic
597 factors and 1 shared environmental factor. *JAMA Psychiatry*, *70*(1), 78–86.
598 https://doi.org/10.1001/jamapsychiatry.2013.267
599 Klein, D. N., Kotov, R., & Bufferd, S. J. (2011). Personality and depression: Explanatory models and review of
600 evidence. *Annual Review of Clinical Psychology*, *7*, 269–295. https://doi.org/10.1146/annurev-
601 clinpsy-032210-104540
602 Kotov, R., Krueger, R. F., Watson, D., Achenbach, T. M., Althoff, R. R., Bagby, R. M., Brown, T. A., Carpenter,
603 W. T., Caspi, A., Clark, L. A., Eaton, N. R., Forbes, M. K., Forbush, K. T., Goldberg, D., Hasin, D.,
604 Hyman, S. E., Ivanova, M. Y., Lynam, D. R., Markon, K., … Zimmerman, M. (2017). The Hierarchical
605 Taxonomy of Psychopathology (HiTOP): A dimensional alternative to traditional nosologies. *Journal*
606 *of Abnormal Psychology*, *126*(4), 454–477. https://doi.org/10.1037/abn0000258
607 Krueger, R. F., Markon, K. E., Patrick, C. J., Benning, S. D., & Kramer, M. D. (2007). Linking antisocial
608 behavior, substance use, and personality: An integrative quantitative model of the adult

externalizing spectrum. *Journal of Abnormal Psychology*, *116*(4), 645–666. https://doi.org/10.1037/0021-843X.116.4.645

Kuo, C.-J., Chen, W.-Y., Tsai, S.-Y., Chen, P.-H., Ko, K.-T., & Chen, C.-C. (2018). Excessive mortality and causes of death among patients with personality disorder with comorbid psychiatric disorders. *Social Psychiatry and Psychiatric Epidemiology*, *[Epub ahead of print]*. https://doi.org/10.1007/s00127-018-1587-x

Lahey, B. B., Krueger, R. F., Rathouz, P. J., Waldman, I. D., & Zald, D. H. (2017). Validity and utility of the general factor of psychopathology. *World Psychiatry*, *16*(2), 142–144. https://doi.org/10.1002/wps.20410

Lenzenweger, M. F., Lane, M. C., Loranger, A. W., & Kessler, R. C. (2007). DSM-IV personality disorders in the National Comorbidity Survey Replication. *Biological Psychiatry*, *62*(6), 553–564. https://doi.org/10.1016/j.biopsych.2006.09.019

Livesley, W. J. (2005). Behavioral and molecular genetic contributions to a dimensional classification of personality disorder. *Journal of Personality Disorders*, *19*(2), 131–155. https://doi.org/10.1521/pedi.19.2.131.62631

Long, E. C., Aggen, S. H., Neale, M. C., Knudsen, G. P., Krueger, R. F., South, S. C., Czajkowski, N., Nesvåg, R., Ystrom, E., Torvik, F. A., Kendler, K. S., Gillespie, N. A., & Reichborn-Kjennerud, T. (2017). The association between personality disorders with alcohol use and misuse: A population-based twin study. *Drug and Alcohol Dependence*, *174*, 171–180. https://doi.org/10.1016/j.drugalcdep.2017.01.022

Mansolf, M., & Reise, S. P. (2016). Exploratory Bifactor Analysis: The Schmid-Leiman Orthogonalization and Jennrich-Bentler Analytic Rotations. *Multivariate Behavioral Research*, *51*(5), 698–717. https://doi.org/10.1080/00273171.2016.1215898

Markon, K. E. (2019). Bifactor and hierarchical models: Specification, inference, and interpretation. *Annual Review of Clinical Psychology*, *15*, 51–69. https://doi.org/10.1146/annurev-clinpsy-050718-095522

634 Markon, K. E., & Krueger, R. F. (2004). An empirical comparison of information-theoretic selection criteria
635 for multivariate behavior genetic models. *Behavior Genetics*, *34*(6), 593–610.
636 https://doi.org/10.1007/s10519-004-5587-0
637 Maydeu-Olivares, A. (2017). Assessing the size of model misfit in structural equation models.
638 *Psychometrika, 82*(3), 533–558. https://doi.org/10.1007/s11336-016-9552-7
639 McTeague, L. M., Huemer, J., Carreon, D. M., Jiang, Y., Eickhoff, S. B., & Etkin, A. (2017). Identification of
640 common neural circuit disruptions in cognitive control across psychiatric disorders. *The American*
641 *Journal of Psychiatry*, *174*(7), 676–685. https://doi.org/10.1176/appi.ajp.2017.16040400
642 Mezzadri, F. (2007). How to generate random matrices from the classical compact groups. *NOTICES of the*
643 *AMS, 54*, 592–604.
644 Morin, A. J. S., Arens, A. K., & Marsh, H. W. (2016). A bifactor exploratory structural equation modeling
645 framework for the identification of distinct sources of construct-relevant psychometric
646 multidimensionality. *Structural Equation Modeling: A Multidisciplinary Journal*, *23*(1), 116–139.
647 https://doi.org/10.1080/10705511.2014.961800
648 Mullins-Sweatt, S. N., DeShong, H. L., Lengel, G. J., Helle, A. C., & Krueger, R. F. (2019). Disinhibition as a
649 unifying construct in understanding how personality dispositions undergird psychopathology.
650 *Journal of Research in Personality*, *80*, 55–61. https://doi.org/10.1016/j.jrp.2019.04.006
651 Muthén, B. O. (1989). Factor structure in groups selected on observed scores. *British Journal of*
652 *Mathematical and Statistical Psychology*, *42*(1), 81–90. https://doi.org/10.1111/j.2044-
653 8317.1989.tb01116.x
654 Neale, M. C., & Cardon, L. R. (1992). *Methodology for Genetic Studies of Twins and Families*. Kluwer
655 Academic Publishers.
656 Neale, M. C., Hunter, M. D., Pritikin, J. N., Zahery, M., Brick, T. R., Kirkpatrick, R. M., Estabrook, R., Bates, T.
657 C., Maes, H. H., & Boker, S. M. (2016). OpenMx 2.0: Extended structural equation and statistical
658 modeling. *Psychometrika*, *81*(2), 535–549. https://doi.org/10.1007/s11336-014-9435-8

659 Neumann, A., Pappa, I., Lahey, B. B., Verhulst, F. C., Medina-Gomez, C., Jaddoe, V. W., Bakermans-
660 Kranenburg, M. J., Moffitt, T. E., van IJzendoorn, M. H., & Tiemeier, H. (2016). Single nucleotide
661 polymorphism heritability of a general psychopathology factor in children. *Journal of the American*
662 *Academy of Child and Adolescent Psychiatry*, *55*(12), 1038-1045.e4.
663 https://doi.org/10.1016/j.jaac.2016.09.498
664 Newton-Howes, G., & Foulds, J. (2018). Personality disorder and alcohol use disorder: An overview.
665 *Psychopathology*, *51*(2), 130–136. https://doi.org/10.1159/000486602
666 Nordentoft, M., Wahlbeck, K., Hällgren, J., Westman, J., Osby, U., Alinaghizadeh, H., Gissler, M., & Laursen,
667 T. M. (2013). Excess mortality, causes of death and life expectancy in 270,770 patients with recent
668 onset of mental disorders in Denmark, Finland and Sweden. *PLoS One*, *8*(1), e55176.
669 https://doi.org/10.1371/journal.pone.0055176
670 Oltmanns, J. R., Smith, G. T., Oltmanns, T. F., & Widiger, T. A. (2018). General factors of psychopathology,
671 personality, and personality disorder: Across domain comparisons. *Clinical Psychological Science*,
672 *6*(4), 581–589. https://doi.org/10.1177/2167702617750150
673 Pfohl, B., Blum, N., & Zimmerman, M. (1995). *Structured Interview for DSM-IV Personality (SIDP-IV)*.
674 University of Iowa, Department of Psychiatry.
675 Raine, A., Mellingen, K., Liu, J., Venables, P., & Mednick, S. A. (2003). Effects of environmental enrichment
676 at ages 3-5 years on schizotypal personality and antisocial behavior at ages 17 and 23 years. *The*
677 *American Journal of Psychiatry*, *160*(9), 1627–1635. https://doi.org/10.1176/appi.ajp.160.9.1627
678 Reichborn-Kjennerud, T., Czajkowski, N., Røysamb, E., Ørstavik, R. E., Neale, M. C., Torgersen, S., & Kendler,
679 K. S. (2010). Major depression and dimensional representations of DSM-IV personality disorders: A
680 population-based twin study. *Psychological Medicine*, *40*(9), 1475–1484.
681 https://doi.org/10.1017/S0033291709991954
682 Reichborn-Kjennerud, T., Czajkowski, N., Ystrøm, E., Ørstavik, R., Aggen, S. H., Tambs, K., Torgersen, S.,
683 Neale, M. C., Røysamb, E., Krueger, R. F., Knudsen, G. P., & Kendler, K. S. (2015). A longitudinal twin

study of borderline and antisocial personality disorder traits in early to middle adulthood. *Psychological Medicine*, *45*(14), 3121–3131. https://doi.org/10.1017/S0033291715001117

Reichborn-Kjennerud, T., Ystrom, E., Neale, M. C., Aggen, S. H., Mazzeo, S. E., Knudsen, G. P., Tambs, K., Czaijkowski, N. O., & Kendler, K. S. (2013). Structure of genetic and environmental risk factors for symptoms of DSM-IV Borderline Personality Disorder. *JAMA Psychiatry*, *70*(11), 1206–1214. https://doi.org/10.1001/jamapsychiatry.2013.1944

Rosenström, T., Czajkowski, N. O., Ystrom, E., Krueger, R. F., Aggen, S. H., Gillespie, N. A., Eilertsen, E., Reichborn-Kjennerud, T., & Torvik, F. A. (2019). Genetically informative mediation modeling applied to stressors and personality-disorder traits in etiology of alcohol use disorder. *Behavior Genetics*, *49*(1), 11–23. https://doi.org/10.1007/s10519-018-9941-z

Rosenström, T., Gjerde, L. C., Krueger, R. F., Aggen, S. H., Czajkowski, N. O., Gillespie, N. A., Kendler, K. S., Reichborn-Kjennerud, T., Torvik, F. A., & Ystrom, E. (2018). Joint factorial structure of psychopathology and personality. *Psychological Medicine*, *49*(13), 2158-2167. https://doi.org/10.1017/S0033291718002982

Rosenström, T., Jylhä, P., Cloninger, C. R., Hintsanen, M., Elovainio, M., Mantere, O., Pulkki-Råback, L., Riihimäki, K., Vuorilehto, M., Keltikangas-Järvinen, L., & Isometsä, E. (2014). Temperament and character traits predict future burden of depression. *Journal of Affective Disorders*, *158*, 139–147. https://doi.org/10.1016/j.jad.2014.01.017

Rosenström, T., Jylhä, P., Pulkki-Råback, L., Holma, M., Raitakari, O. T., Isometsä, E., & Keltikangas-Järvinen, L. (2015). Long-term personality changes and predictive adaptive responses after depressive episodes. *Evolution and Human Behavior*, *36*(5), 337–344. https://doi.org/10.1016/j.evolhumbehav.2015.01.005

Rosenström, T., Torvik, F. A., Ystrom, E., Czajkowski, N. O., Gillespie, N. A., Aggen, S. H., Krueger, R. F., Kendler, K. S., & Reichborn-Kjennerud, T. (2018). Prediction of alcohol use disorder using personality disorder traits: A twin study. *Addiction*, *113*(1), 15–24. https://doi.org/10.1111/add.13951

710 Rosenström, T., Ystrom, E., Torvik, F. A., Czaijkowski, N. O., Gillespie, N. A., Aggen, S. H., Krueger, R. F.,
711 Kendler, K. S., & Reichborn-Kjennerud, T. (2017). Genetic and environmental structure of DSM-IV
712 criteria for Antisocial Personality Disorder: A twin study. *Behavior Genetics*, *47*(3), 265–277.
713 https://doi.org/10.1007/s10519-016-9833-z
714 Schmitz, S., Cherny, S. S., & Fulker, D. W. (1998). Increase in power through multivariate analyses. *Behavior*
715 *Genetics*, *28*(5), 357–363.
716 Soe-Agnie, S. E., Paap, M. C. S., VanDerNagel, J. E. L., Nijman, H. J. M., & de Jong, C. A. J. (2018). The
717 generalizability of the structure of substance abuse and antisocial behavioral syndromes: A
718 systematic review. *Psychiatry Research*, *259*, 412–421.
719 https://doi.org/10.1016/j.psychres.2017.11.007
720 Tambs, K., Rønning, T., Prescott, C. A., Kendler, K. S., Reichborn-Kjennerud, T., Torgersen, S., & Harris, J. R.
721 (2009). The Norwegian Institute of Public Health twin study of mental health: Examining
722 recruitment and attrition bias. *Twin Research and Human Genetics*, *12*(2), 158–168.
723 https://doi.org/10.1375/twin.12.2.158
724 Torgersen, S., Czajkowski, N., Jacobson, K., Reichborn-Kjennerud, T., Røysamb, E., Neale, M. C., & Kendler,
725 K. S. (2008). Dimensional representations of DSM-IV cluster B personality disorders in a population-
726 based sample of Norwegian twins: A multivariate study. *Psychological Medicine*, *38*(11), 1617–
727 1625. https://doi.org/10.1017/S0033291708002924
728 Torvik, F. A., Rosenström, T. H., Ystrom, E., Tambs, K., Røysamb, E., Czajkowski, N., Gillespie, N. A., Knudsen,
729 G. P., Kendler, K. S., & Reichborn-Kjennerud, T. (2017). Stability and change in etiological factors for
730 alcohol use disorder and major depression. *Journal of Abnormal Psychology*, *126*(6), 812–822.
731 https://doi.org/10.1037/abn0000280
732 Trull, T. J., Freeman, L. K., Vebares, T. J., Choate, A. M., Helle, A. C., & Wycoff, A. M. (2018). Borderline
733 personality disorder and substance use disorders: An updated review. *Borderline Personality*
734 *Disorder and Emotion Dysregulation*, *5*, 15. https://doi.org/10.1186/s40479-018-0093-9

735 Trull, T. J., Jahng, S., Tomko, R. L., Wood, P. K., & Sher, K. J. (2010). Revised NESARC personality disorder
736 diagnoses: Gender, prevalence, and comorbidity with substance dependence disorders. *Journal of*
737 *Personality Disorders*, *24*(4), 412–426. https://doi.org/10.1521/pedi.2010.24.4.412
738 VanderWeele, T. J. (2012). Invited commentary: Structural equation models and epidemiologic analysis.
739 *American Journal of Epidemiology*, *176*(7), 608–612. https://doi.org/10.1093/aje/kws213
740 Wang, K., Gaitsch, H., Poon, H., Cox, N. J., & Rzhetsky, A. (2017). Classification of common human diseases
741 derived from shared genetic and environmental determinants. *Nature Genetics*, *49*(9), 1319–1325.
742 https://doi.org/10.1038/ng.3931
743 Wittchen, H. U., & Pfister, H. (1997). *DIA-X Interview (M-CIDI)*. Swets & Zeitlinger.
744 Young, R., Sweeting, H., & West, P. (2008). A longitudinal study of alcohol use and antisocial behaviour in
745 young people. *Alcohol and Alcoholism*, *43*(2), 204–214. https://doi.org/10.1093/alcalc/agm147
746 Zahery, M., Maes, H. H., & Neale, M. C. (2017). CSOLNP: Numerical Optimization Engine for Solving Non-
747 linearly Constrained Problems. *Twin Research and Human Genetics*, *20*(4), 290–297.
748 https://doi.org/10.1017/thg.2017.28
749 Zandersen, M., Henriksen, M. G., & Parnas, J. (2019). A recurrent question: What is borderline? *Journal of*
750 *Personality Disorders*, *33*(3), 341–369. https://doi.org/10.1521/pedi_2018_32_348
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Tables

Table 1. Exploratory bifactor loadings for antisocial and borderline personality disorder criteria

		Factor loadings (Λ)			Observed variance
		G: General	S1: BPD vs ASPD	S2: Aggression	
ASPD1	Not conforming	**0.762**	**-0.463**	0.136	0.159
ASPD2	Deceitfulness	**0.565**	-0.157	0.015	0.070
ASPD3	Impulsivity or failure to plan	**0.697**	0.090	**0.328**	0.063
ASPD4	Irritability/repeated fights	**0.849**	-0.270	**-0.353**	0.034
ASPD5	Reckless disregard	**0.507**	-0.296	0.111	0.072
ASPD6	Irresponsibility	**0.716**	-0.028	**0.407**	0.090
ASPD7	Lack of remorse	**0.760**	**-0.451**	-0.014	0.037
ASPD8	Conduct disorder	**0.663**	-0.260	0.181	0.280
BPD1	Avoid abandonment	**0.533**	**0.362**	0.028	0.140
BPD2	Unstable relationships	**0.633**	**0.424**	-0.027	0.227
BPD3	Identity disturbance	**0.607**	**0.411**	0.113	0.032
BPD4	Self-damaging impulsivity	**0.738**	-0.195	0.264	0.317
BPD5	Suicidality or self-mutilation	**0.612**	0.302	0.037	0.135
BPD6	Affective instability	**0.605**	**0.496**	-0.172	0.369
BPD7	Feelings of emptiness	**0.488**	**0.510**	-0.028	0.213
BPD8	Inappropriate. intense anger	**0.650**	0.139	**-0.626**	0.256
BPD9	Stress-related paranoia	**0.604**	0.309	0.063	0.079

Note: Loadings above √0.1 are highlighted. The last column shows raw observed variance per criterion to demonstrate the large differences in endorsement rates of the criteria. These numbers characterize potentially informative variance and its relationship to a latent factor. However, factor loadings were estimated using liability-threshold modeling, i.e., an underlying continuum was modeled instead of direct modeling of ordinal data. Abbreviations: "ASPD" = Antisocial personality disorder criterion/trait, "BPD" = Borderline personality disorder criterion/trait.

Table 2. Prevalence of substance use and loadings on a general substance use factor

	Observed frequency			Model estimate
Substance use variable	**Not present**	**>10 times**	**Present**	**Factor loading**
Alcohol use disorder (AUD)	2528	-	264	0.694
Illicit drug use	2586	133	54	0.826
Smoking	1174	-	492	0.396

Note: ">10 times" refers to having used illicit drugs more than 10 times; such intermediate category was not recorded for AUD and smoking. Factor loadings were estimated using liability-threshold modeling, i.e., an underlying continuum was modeled instead of direct modeling of ordinal data.

Table 3. Exploratory structural equation regression models predicting substance use risk with a hierarchy of general, specific (S), and criterion-level (crit.) personality pathology

	Model I			Model II			Model III		
Predictor	***β***	**SE(*β*)**	***p***	***β***	**SE(*β*)**	***p***	***β***	**SE(*β*)**	***p***
Male sex	0.421	0.083	0.000	0.420	0.083	0.000	0.419	0.083	0.000
General PD factor	-0.136	0.214	0.526	0.764	0.085	0.000	-	-	-
S1 (BPD vs. ASPD)	0.334	0.135	0.013	-0.148	0.176	0.402	-	-	-
S2 (Aggression)	-0.051	0.078	0.509	-0.292	0.079	0.000	-	-	-
ASPD crit. #1	0.365	0.090	0.000	-	-	-	0.230	0.042	0.000
ASPD crit. #8	0.109	0.054	0.044	-	-	-	0.111	0.041	0.006
BPD crit. #4	0.177	0.061	0.004	-	-	-	0.243	0.046	0.000
Fit index	**Value**	**90% CI**	**P(RMSEA<0.05)**	**Value**	**90% CI**	**P(RMSEA<0.05)**	**Value**	**90% CI**	**P(RMSEA<0.05)**
RMSEA	0.038	0.036–0.041	1.000	0.039	0.036–0.041	1.000	0.039	0.036–0.041	1.000
CFI	0.927	-	-	0.925	-	-	0.925	-	-
TLI	0.899	-	-	0.899	-	-	0.899	-	-
AASRC	0.037	-	-	0.039	-	-	0.041	-	-

Note: Because the specific-aggression factor (S2) was inverted, the negative coefficient implies that high aggression is associated with substance use. Abbreviations: ASPD = Antisocial personality disorder criterion/trait; BPD = Borderline personality disorder criterion/trait; RMSEA = Root of mean squared error of approximation; CFI = Comparative fit index; TLI = Tucker-Lewis index. AASRC = Average absolute sample residual correlation. AASRC is just a mean absolute difference between model-predicted and observed correlations, which provides intuition on effect size for model misfit.

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791 **Figures**

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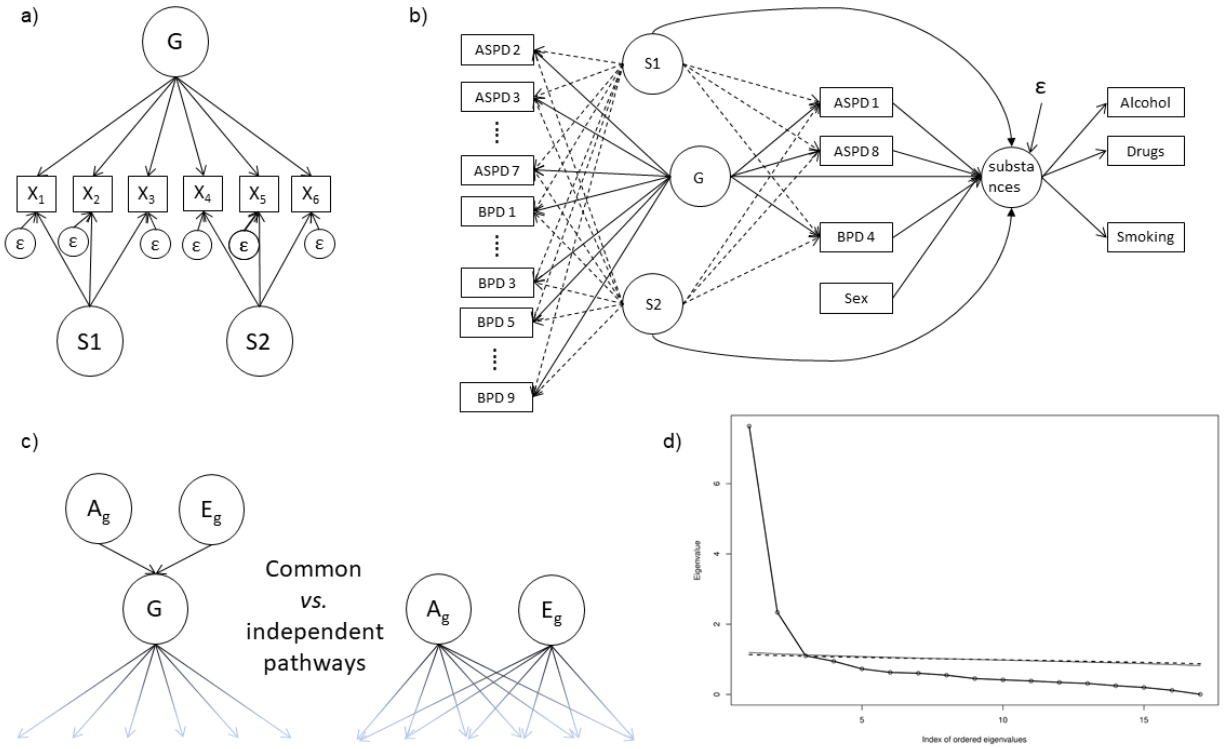

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794 *Figure 1. Path modeling.* ***a)*** *A bifactor model captures a hierarchy of successively more specific unobserved*
795 *etiologic factors (circles) underlying the observed variables (X; boxes): the general factor (G) affects*
796 *everything, the specific factors (S1 and S2) affect sub-groups of variables, and the unique variances affect*
797 *just one variable (ε; these are always modeled, but often not drawn to path diagrams).* ***b)*** *In exploratory*
798 *bifactor models also the specific factors (S1 and S2) can 'cross-load' on every variable (cf. dashed lines) but*
799 *they are rotated to load maximally on just one specific factor. In our exploratory structural equation model*
800 *(ESEM), both the latent factors and three observed personality criteria are allowed to predict the substance*
801 *use factor.* ***c)*** *Additive genetic (A_g) and environmental (E_g) factors can influence variables through a common*
802 *phenotypic pathway (G; left-hand side) or the phenotype may be 'illusory' in that the genes and*
803 *environments exert their effects through independent pathways, as in right-hand side* (ref. Rosenström et
804 al., 2017 for more examples)*. A common-pathway model is 'nested' within independent pathway model,*
805 *allowing statistical null-hypothesis testing of the common-pathway model.* ***d)*** *A parallel analysis plot,*
806 *suggesting 3 phenotypic factors.*

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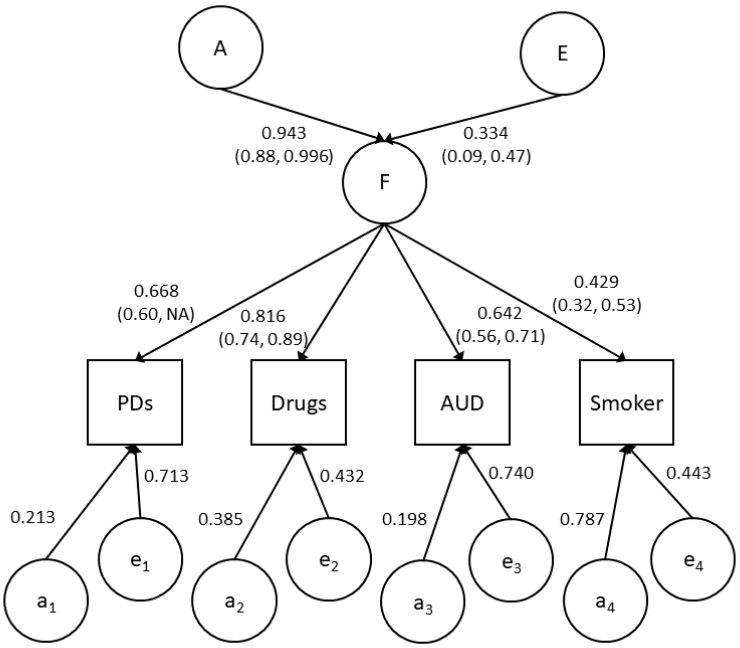

Figure 2. A path diagram of the final multivariate twin model. A biometric common pathway model of general antisocial-borderline personality (PDs), illicit drug use (Drugs), alcohol use disorder (AUD), and regular smoking (Smoker). The model partitions the covariance structure of the variables into a "common-pathway" trait (F), its genetic (A) and environmental (E) influences, and to variable-specific 'residual' genetic (a_i) and environmental (e_i) influences (i = 1, ..., 4). Variances are standardized to unity (i.e., square of a path coefficient indicates proportion of explained variance). Parentheses give 95% likelihood-profile confidence intervals for the path coefficients. Value "NA" was substituted for the upper interval-limit without a convergent estimator, and significance of genetic residuals was only collectively tested for similar reasons. The variable "PDs" stands for a liability-threshold model for a count of subthreshold or full endorsements of ASPD criteria #2, #5, and #8 and BPD criteria #4, #5, and #9, as they had strong loadings exclusively on the general PD factor in Table 1.