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Personality Disorders and the Persistence of Substance Use Disorders: A Reanalysis of Published NESARC Findings

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Abstract

The purpose of this study was to examine whether published findings regarding the association of personality disorders (PDs) with the persistence of substance use disorders (SUDs) are attributable to an artifact due to time of assessment of the PD. Two previous studies analyzed data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) and found that Antisocial PD, Schizotypal PD, and Borderline PD are unique predictors of SUDs. However, a design limitation in NESARC (assessment of PDs at different waves) can potentially compromise these findings. To assess the influence of time of assessment of PDs and to identify associations that might be robust to time of assessment, we compared the association of PDs with two estimates of SUD persistence that were based on different populations at risk: 1) among those who were diagnosed with SUD at baseline, the proportion who continued to meet full criteria at follow-up ("prediction"), and 2) among those who were diagnosed with SUD at follow-up, the proportion who met full criteria at baseline ("postdiction"). Differences between prediction and postdiction revealed a robust pattern of higher odds ratios for postdiction among PDs assessed at baseline, and lower odds ratios for postdiction among PDs assessed at follow-up. All published significant

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associations between PDs and persistence of SUDs became non-significant in the postdiction analyses, with the exception of Obsessive-Compulsive PD predicting Nicotine Dependence persistence. The present results raise serious doubts about the validity of published findings on PDs and SUD persistence from the NESARC. Design limitations in NESARC preclude a direct comparison among PDs measured at different waves.

Keywords

personality disorders; substance use disorders; NESARC

The importance of personality disorder (PD) comorbidity in the assessment and treatment of substance use disorders (SUDs) has been repeatedly recognized in the literature (e.g., Lenzenweger, Lane, Loranger, & Kessler, 2007; Marlowe, Kirby, Festinger, Husband, & Platt, 1997; McGlashan et al., 2000; Oldham et al., 1995; Trull, Sher, Minks-Brown, Durbin, & Burr, 2000; Zanarini, Frankenburg, Hennen, Reich, & Silk, 2004; Zimmerman, & Coryell, 1989; Zimmerman, Rothschild, & Chleminski, 2005). However, until recently there were no large epidemiological studies investigating the prospective association between PDs and SUDs. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) was designed, in part, to fill this gap in the literature. The NESARC is a nationally representative study conducted over two waves of data collection separated by three years. It included assessment of SUDs and all ten DSM-IV PDs (Grant & Kaplan, 2005; Grant, Moore, & Kaplan, 2003). This provides a unique opportunity to establish the association of each PD with the persistence of SUDs adjusting for the presence of all other PDs.

The investigation of SUDs persistence is particularly important for empirically determining the degree of chronicity of these disorders. Moreover, distinguishing cases that persist over time from those that remit might help better delineate the essential features of SUDs. Kahlbaum (1863) is credited (see Angst & Gamma, 2008) with distinguishing “limited psychological disorders” (i.e., vecordia) with good prognosis from “total psychological disorders” (i.e., “vesania”) with more morbid courses, a distinction that influenced Kraepelin’s distinction between manic-depressive illnesses and dementia praecox (schizophrenia) on the basis of course, and the larger intellectual contribution of the recognition of prognosis in guiding diagnosis. In addition, the study of SUDs persistence is relevant for both assessment and treatment. By assessing known predictors of a chronic course, clinicians can refer or counsel patients to a higher level of care even in the absence of high levels of consumption or high severity as implied by criteria counts (e.g., O'Brien & McLellan, 1996). Clinicians could also evaluate the utility of targeting comorbid conditions that can be contributory to a persistent course.

More specifically, the identification of PDs that uniquely predict (i.e., adjusting for all other PDs) SUD persistence in a nationally-representative sample might have significant theoretical and clinical implications. First, it can help refine our understanding of the comorbidity among PDs and SUDs beyond the contemporaneous co-occurrence that is typically addressed in the epidemiological literature, which can then facilitate inferences

regarding how this comorbidity affects the course of SUDs over time. Second, it can guide research to further investigate the mechanisms that lead to SUD chronicity. Third, it can provide guidelines for clinical assessment and prognosis of SUDs that are based on data from the general population, as opposed to specific clinical samples that can vary on a host of other variables (e.g., health care coverage, medical and psychiatric comorbidities, referral source), and consequently confound observed associations.

Two recent papers (Fenton et al., 2012; Hasin et al., 2011) took advantage of the design characteristics of the NESARC to investigate the association of PDs with the persistence of different SUDs (i.e., alcohol dependence [AD], nicotine dependence [ND], cannabis use disorder [CUD], and drug use disorder [DUD]). Hasin et al. (2011) found that Antisocial PD, Borderline PD, and Schizotypal PD were significantly associated with the persistence of AD, ND, and CUD, adjusting for all other PDs, Axis I disorders, and several other covariates. In addition, Obsessive-Compulsive and Schizoid PDs were associated with the persistence of ND only, and Narcissistic PD was associated with the persistence of AD only. Similarly, Fenton et al. (2012) showed that Antisocial PD, Borderline PD, and Schizotypal PD were significantly associated with the persistence of DUD (that included CUD) across models that progressively adjusted for more covariates (including all other PDs). Narcissistic PD was also associated with DUD persistence in initial models, but became non-significant when adjusting for all other PDs. Overall, these findings suggest that some PDs uniquely predict the persistence of SUDs. Although the consistent association of Antisocial PD and SUDs is expected given the robust comorbidity among these externalizing disorders (e.g., Compton, Conway, Stinson, Colliver, & Grant, 2005; Krueger et al., 2002), the associations involving Borderline PD and Schizotypal PD are somewhat less obvious. Borderline PD has been found to be associated with both internalizing (e.g., Gunderson et al., 2004; Gunderson et al., 2008; Koenigsberg et al., 1999; Luca, Luca, & Calandra, 2012) and externalizing disorders (e.g., Røysamb et al., 2011; Stepp, Trull, & Sher, 2005). Consequently, although it is not purely an externalizing disorder, Borderline PD can be considered “multifactorial” in its associations with other disorders (Eaton et al., 2011; Røysamb et al., 2011) and might hence uniquely predict the course of externalizing pathology. With regard to Schizotypal PD, its consistent association with the persistence of SUDs is somewhat surprising, given the relative scarcity of research suggesting a unique association between these disorders.

Results from these studies have been included in recent reviews of the literature (Baigent, 2012; Hasin & Kilcoyne, 2012; Szerman et al., 2013) which highlight the unique associations found between certain PDs and SUD persistence. For instance, commenting on the associations involving Schizotypal PD, Baigent concludes that “Clinicians should be vigilant for odd thoughts and behaviours as a marker for poorer outcomes in substance use problems” (p. 204). Similarly, the need to expand the range of PDs beyond Antisocial PD to include Borderline and Schizotypal PDs in research investigating the course of SUDs is one of the key points highlighted by Hasin & Kilcoyne in their review of NESARC findings regarding comorbidity.

Despite the potential importance of these findings, in our own research using this valuable dataset we have identified a design limitation that can potentially compromise the validity of

the observed associations (Trull, Vergés, Wood, Jahng, & Sher, 2012; see also, Trull, Vergés, Wood, & Sher, 2013). Specifically, the ten DSM-IV PDs were not all assessed at the same time. Seven PDs were assessed at Wave 1, and three PDs (i.e., Borderline, Narcissistic, and Schizotypal PDs) were assessed at Wave 2 (Adult Antisocial Behavior [AAB] was also assessed at Wave 2, so that the two papers mentioned used a combined variable including information from both waves for Antisocial PD). The decision to assess PDs at different waves appears to have been made under the assumption that wave of assessment would not affect the patterns of associations because PDs are highly stable constructs (Fenton et al., 2012). However, several studies have found that PDs can exhibit substantial change over time (Durbin & Klein, 2006; Gunderson et al., 2011; Lenzenweger, Johnson, & Willett, 2004), making time-of-measurement effects a relevant concern. In particular, the difference in wave of assessment of PDs makes it possible for PDs assessed at Wave 2 to have stronger associations with the persistence of SUDs than PDs assessed at Wave 1, due to common measurement error that occurs when both constructs are assessed at the same occasion (here, Wave 2). In fact, both papers reported that PDs measured at Wave 2 (i.e., Antisocial, Borderline, and Schizotypal PDs) were the most consistent predictors of SUD persistence (Fenton et al., 2012; Hasin et al., 2011). This was also the case in two papers examining the association of PDs and major depressive disorder persistence (Skodol, Grilo et al., 2011) and anxiety disorder persistence (Skodol, Geier, Grant, & Hasin, in press), and a recent paper addressing transitions in illicit drug use (Compton, Dawson, Conway, Brodsky, & Grant, 2013; see also Goodwin, Pagura, Spiwak, Lemeshow, & Sareen, 2011; Grant et al., 2009; Harrington, Robinson, Bolton, Sareen, & Bolton, 2011; Maclean, Xu, French, & Ettner, 2014, for other analyses of NESARC data in which the same issue might partially explain the results).

In a recent study on anxiety disorder persistence (Vergés et al., 2014), we investigated the possibility of such a time-of-measurement effect by comparing two ways of defining persistence. The traditional definition evaluates persistence in terms of “prediction”, that is, estimating the prevalence of a disorder at Wave 2 among participants diagnosed with the disorder at Wave 1. However, persistence can also be defined in terms of “postdiction”, that is, estimating the prevalence of a disorder at Wave 1 among participants diagnosed with the disorder at Wave 2. This method of inference, also referred to as backward prediction or retrodiction, is often used in perception, neural network, and machine learning models, and has been shown to give converging estimates compared to prediction when the temporal process of interest is stationary (e.g., Benesty, Chen, & Huang, 2008). Therefore, if the association between PDs and SUDs is independent of the time of assessment, then “postdicting” Wave 1 disorders among participants affected at Wave 2 should yield similar patterns of results to those using the other definition. While there could be non-artifactual reasons to observe asymmetry in prediction versus postdiction (e.g., if the association is age-graded such that personality pathology is more strongly associated with substance use disorders in older individuals), this seems unlikely. This is because both SUDs and PDs tend to be observed more in younger adults compared to older adults (Grant, 1996; Grant, 1997; Grant et al., 2004; Jackson & Burgess, 2000; Vergés et al., 2012; Vergés et al., 2013; Warner, Kessler, Hughes, Anthony, & Nelson, 1995) and, indeed, influential subtyping of substance use tends to link personality disordered forms with earlier onset of consumption

(e.g., Babor et al., 1992; Cloninger, 1987; Zucker, 1987). In contrast, an artifact due to time of assessment would lead to increased postdiction associations for PDs measured at Wave 1 and decreased associations for PDs measured at Wave 2 in comparison to the forward predictions estimated in the published literature (see Vergés et al., 2014, for more details about the logic of this approach).[1]

Given this potentially serious design limitation, demonstrating robustness of findings across both strategies would lend credibility to the results previously reported. Alternatively, if findings are only significant when the "dependent variable" is contemporaneously associated with the covariate, the results become simply another cross-sectional association with no unique "lagged" effects.[2] More critically, if the relative strength of postdictive and predictive relationships were found to vary as a function of the time of assessment of the covariate (i.e., the specific personality disorder), then the previously reported findings must be seriously questioned. Such qualifying findings would be important in the context of the larger corpus of research linking PDs and SUDs given that the two papers under question were published in two of the highest impact journals in the field and have already been cited more than 50 times between the two. Furthermore, the research team responsible for both papers has been highly influential in the field, producing multiple other impactful papers using this dataset in particular. It is not our intention to impugn their high quality work, but to highlight an important design nuance that may challenge the validity of causal inference when using this data set and drawing conclusions about PDs' and SUDs' temporal associations. Thus, the goal of the current paper was to explore the degree to which the findings of previously published papers may be interpreted as a time-of-measurement effect and to identify PDs that show a robust (i.e., significant both in prediction and postdiction) association with the persistence of substance use disorders. In particular, we were interested in examining the robustness of associations involving Borderline PD and Schizotypal PD, given the significant theoretical implications of the relatively unexpected associations found in previously published papers.

Method

Sample

The NESARC is a nationally representative study of civilians 18 years and older of the non-institutionalized United States population. The survey oversampled Blacks and Hispanics and young adults between 18 and 24 years. An initial wave of face-to-face interviews was conducted during 2001–2002 and includes 43,093 respondents (Grant, Moore, & Kaplan, 2003). A follow-up second wave of face-to-face interviews was performed during 2004–

[1]To the extent that earlier onset disorders are likely to be more severe, then persistence defined prospectively might be more associated with comorbidity than persistence defined retrospectively. Similarly, if there are cumulative effects of personality pathology, then persistence defined retrospectively might be more associated with comorbidity than persistence defined prospectively. However, either effect would lead to an overall difference between prediction and postdiction as opposed to an interaction between prediction/postdiction and Wave of assessment of PDs.

[2]Note that differences between prediction and postdiction are driven by participants who have a diagnosis only at Wave 1 or only at Wave 2. Consistent diagnosis (either diagnosed or not diagnosed at both Waves) is the same for prediction and postdiction. We used these different groups for statistical significance testing (see Statistical Significance of Difference between Associations in the Results section).

2005 and contains 34,653 of the same respondents (Grant & Kaplan, 2005). The dataset is weighted to approximate the general population of the United States.

Measures

Substance Use Disorders—The NESARC used the Alcohol Use Disorders and Associated Disabilities Interview Schedule-DSM-IV version (AUDADIS-IV) to assess DSM-IV Axis I and II disorders (Grant, Dawson, & Hasin, 2001). A number of studies have provided evidence of the reliability of the substance use disorders diagnoses as measured by the AUDADIS-IV (e.g., Grant, Harford, Dawson, Chou, & Pickering, 1995; Hasin, Carpenter, McCloud, Smith, & Grant, 1997). Hasin et al. (2011) used NESARC variables coding for DSM-IV AD and ND, but created a new CUD variable that included cannabis withdrawal that is not available for public use. The same definition of CUD was used by Fenton et al. (2012) to create their measure of DUD. In the absence of specific coding instructions for cannabis withdrawal, we attempted to replicate the diagnosis, and came reasonably close as evidenced by similar sample size and odds ratios for CUD and DUD displayed in Tables 2 and 3 (we include results from the original articles in all tables to facilitate comparison with our prediction analyses).

In addition, we note that Hasin et al. (2011) used different coding schemes for prior-to-past-12-month AD versus ND (used at Wave 2 to assess persistence of disorder across the 3-year interval between waves). In particular, prior-to-past-12-month AD required the endorsement of clustering items to ensure that AD symptoms occurred during the same 12-month period. However, prior-to-past-12-month ND did not have the clustering requirement, leading to higher rates of ND persistence compared to AD persistence. We used the same code so as to optimize comparability.

Personality Disorders—PD diagnoses from the AUDADIS-IV are reliable according to NESARC reports (e.g., Grant, Dawson et al., 2003; Ruan et al., 2008). The NESARC assessed Avoidant, Dependent, Paranoid, Obsessive-Compulsive, Schizoid, and Histrionic PDs at Wave 1, and Borderline, Narcissistic, and Schizotypal PDs at Wave 2. Antisocial PD, including assessment of conduct disorder before age 15, was assessed at Wave 1, with AAB reassessed at Wave 2. As for other NESARC constructs, the code for AAB is not available, requiring development of our own algorithm that remained faithful to the criteria in DSM-IV. Our code failed to closely approximate published results (see Results section), so our findings regarding Antisocial PD need to be taken with caution.[3] In addition, models in which Antisocial PD was entered as a covariate yielded results that were less close to those published than models in which Antisocial PD was not included.

Statistical analyses

Following the published results, we constructed a definition of persistence that was defined as continuous diagnosis across the 3-year interval between Wave 1 and Wave 2 (i.e.,

[3]As we do not have a clear hypothesis of what to expect for a PD measured at both waves in the case of an artifact effect, this is not necessarily a limitation. We present the Antisocial PD results for the sake of completeness, but we do not focus on these results. Nevertheless, given the theoretical importance of Antisocial PD, we conducted additional analyses using Wave 1 Antisocial PD (which is available in the NESARC dataset), even though this variable was not used in the previous studies.

participants had to meet criteria for past-12-month diagnosis at Wave 1, and for both past-12-month diagnosis at Wave 2 and in the 24 month interval from Wave 1 to Wave 2). Those findings were then compared to results from postdiction of Wave 1 disorders among participants diagnosed at Wave 2 (including the interval from Wave 1 to Wave 2). As done in a previous report (Vergés et al., 2014), we tested the statistical significance of a pattern of findings suggesting a time-of-measurement effect using the probability under the binomial distribution of finding greater than or equal to the number of associations consistent with this effect (i.e., higher associations for postdiction among PDs assessed at Wave 1, and lower associations for postdiction among PDs assessed at Wave 2), using robust standard errors within a Generalized Estimating Equations framework (Liang & Zeger, 1986) to account for the non-independence between the contrasts.

The analytic strategy used in Fenton et al. (2012) involved a sequence of models that progressively adjusted for more covariates (see Footnote to Table 3). Due to limited space, only the first and last models from that paper are presented. All analyses used SUDAAN (Research Triangle Institute, 2004) in order to adjust for the sampling weights in the calculation of standard errors of parameter estimates.

Results

Persistence of Substance Use Disorders

A comparison of estimates from the original publications and our predictive and postdictive estimates of persistence is shown in Table 1. As can be seen, our predictive estimates are identical to those previously reported for AD and ND, and only slightly discrepant for CUD and DUD, as expected from the differences in algorithms used. Estimates are similar across the two definitions using prediction and postdiction, with the exception of AD, for which persistence defined as postdiction (47.7%) is considerably higher than persistence defined as prediction (30.1%), presumably due to the difference in number of participants who meet AD diagnosis at Wave 1 versus follow-up.

Alcohol Dependence, Nicotine Dependence, and Cannabis Use Disorder

Table 2 shows the results of logistic regressions predicting persistence in AD, ND, and CUD, adjusting for the covariates mentioned in Hasin et al. (2011; see Table note). Our forward-prediction results were very similar to those previously reported. The only exception to this is Antisocial PD at both Waves, for which our odds ratio estimates were considerably lower, but still significantly elevated, for AD and ND. Moreover, as expected, owing to uncertainty regarding coding of withdrawal, our results for CUD slightly diverged from those reported.

Differences between prediction and postdiction showed a robust pattern of higher odds ratios for postdiction among PDs assessed at Wave 1, and lower odds ratios for postdiction among PDs assessed at Wave 2. In particular, of the 18 pairs of analyses comparing predictive and postdictive ORs for PDs assessed at Wave 1, 15 (83%) were larger in the postdictive than in the predictive models. In addition, all 9 pairs of analyses comparing predictive and postdictive ORs for PDs assessed at Wave 2, were larger in the predictive

models. Taken together, 24 out of 27 pairs of analyses were consistent with a time-of-measurement effect, a pattern that is statistically significant, even when adjusting for the non-independence of estimates ($\chi^2(1) = 11.53$, $p < .001$).

Moreover, significant results reported in Hasin et al. (2011) became non-significant for the postdicted persistence. In particular, Borderline and Schizotypal PDs, which were significantly associated with all three outcomes in the prediction, became non-significant in the postdiction. The same occurred with Narcissistic PD (which was significantly associated with AD in the prediction), and Schizoid PD (which was significantly associated with ND in the prediction, although in this case the odds ratio remained similar). The exception to this was OCPD, which significantly elevated the likelihood of ND persistence under both predicted and postdicted definitions. Also, compared to predicted ND persistence, Avoidant/Dependent PD significantly elevated, while Narcissistic PD significantly reduced, the likelihood of postdicted ND persistence.

Drug Use Disorders

Table 3 shows the results from Models 1 and 3 reported by Fenton et al. (2012). As can be seen, our results in the forward prediction were very similar to those reported by Fenton et al., especially for Model 1. Further, there was again a pattern suggestive of an effect of time of measurement, with higher odds ratios for postdiction among disorders measured at Wave 1 and lower odds ratios among disorders measured at Wave 2. The pattern of results revealing a time-of-measurement effect is particularly evident here when we consider two disorders that were measured at both waves, AD and ND, as we could compare predictions and postdictions for the same disorder measured at different times. As seen in Table 3, AD and ND measured at Wave 1 had higher odds ratios in the postdiction, whereas AD and ND measured at Wave 2 had lower odds ratios in the postdiction, with the pattern of significance completely reversed for AD (i.e., significant only in postdiction when measured at Wave 1 and only in prediction when measured at Wave 2). Overall, of the 17 pairs of analyses comparing predictive and postdictive ORs for PDs assessed at Wave 1, 14 (82%) were larger in the postdictive than in the predictive models. In addition, all 8 pairs of analyses comparing predictive and postdictive ORs for PDs assessed at Wave 2, were larger in the predictive models. Taken together, 22 out of 25 pairs of analyses were consistent with a time-of-measurement effect, a pattern that is statistically significant, even when adjusting for the non-independence of estimates ($\chi^2(1) = 12.41$, $p < .001$).

Fenton et al. (2012) found that Borderline, Schizotypal, and Narcissistic (the latter in Model 1 only) PDs were associated with the persistence of DUDs. These associations became non-significant in the postdiction (but note that Borderline PD was not significant in our forward analysis in Model 3). Moreover, in Model 1 four Wave 1 PDs that were not associated with persistent DUDs in Fenton et al. were observed to have significant associations in our postdiction analyses (i.e., Avoidant/Dependent, OCPD, Paranoid, and Histrionic).

Bivariate Associations and Comparison with Demographic Variables

Results from our analyses suggest that there is in fact a strong time-of-assessment effect in the association of PDs with the persistence of SUDs. This raises questions as to why PD, a

supposedly stable construct, can be affected by time in this way. To shed some light on this issue, we replicated our models using three variables that have minimal measurement error and maximal stability: sex, age, and ethnicity. Results from bivariate associations (i.e., not including covariates) are shown in Table 4 for these three variables and for the PDs, for the sake of comparison. Some change in the association with persistence of SUDs is observed for these three variables, but with lower magnitude and less consistency than for PDs. Consistent with our prior (multivariate) findings, bivariate postdictive associations show a remarkably systematic pattern (with no exceptions) of higher odds ratios for PDs measured at Wave 1 and lower odds ratios for PDs measured at Wave 2. In contrast, sex, age, and ethnicity (measured at Wave 1) exhibit postdictive associations that are sometimes higher, sometimes lower, and sometimes almost identical to predictive associations ($\chi^2(1) = .01$, $p = .999$), suggesting that their changes in association with persistence of SUDs are due to measurement error of the disorders rather than a systematic effect of predictive versus postdictive models.

Statistical Significance of Difference between Associations

Although the pattern of predictive and postdictive associations shown in previous sections strongly suggests a time-of-measurement effect, we could have greater confidence in our findings if we had a direct statistical test of the difference between predictive and postdictive odds ratios. This is a limitation within our approach because the samples involved in prediction and postdiction are partially overlapping, making direct statistical tests of differences in parameter estimates challenging. However, it is possible to obtain a significance test by slightly altering the statistical model used thus far. Instead of looking at persistence defined as prediction or postdiction, an alternative model can be used in which all participants diagnosed at both waves are compared with participants diagnosed only at Wave 1 (akin to predicting whether diagnosis was maintained at Wave 2), participants diagnosed only at Wave 2 (akin to postdicting whether diagnosis had been present at Wave 1), and participants who do not have a diagnosis at either Wave. Including these four groups as levels of the dependent variable, we conducted a series of multinomial logistic regressions with PD as predictor, with those diagnosed at both waves as the reference group. As can be seen in Table 5, the pattern of associations is comparable with the one reported in Table 4, revealing stronger associations (i.e., odds ratios further from one) for PDs measured at Wave 1 with Wave-2-only substance use diagnoses (i.e., postdiction of Wave 1), and for PDs measured at Wave 2 with Wave-1-only substance use diagnoses (i.e., prediction of Wave 2) in all cases. *Note that these estimates are reversed in direction compared to findings presented in previous tables because the group characterized by diagnosis at both times* [i.e., *persistent*] *serves as the reference group for these comparisons. This is in contrast to the prior analyses where non-persistent groups served as the reference group*. Then, to test the hypothesis that prediction and postdiction would be similar, the odds ratios for participants diagnosed only at Wave 1 and participants diagnosed only at Wave 2 were constrained to be equal, and a chi-square difference test based on loglikelihood values and scaling correction factors (Satorra & Bentler, 2001) was used to determine if model fit was significantly worse when this constraint was applied. These supplementary analyses were conducted in Mplus (Muthén & Muthén, 1998–2012), and the results are shown in Table 5. For the large majority of findings (83%, not considering Antisocial PD which was based on

measures collected at both Waves) the time-of-measurement effect was significant, adding further support to the thesis of a major methodological confound.[4]

Discussion

The current reanalysis showed that previously published associations between PDs and SUDs are likely attributable to an artifact due to time of measurement. Because of the NESARC design, those findings that were reported to be significant in the original papers (Fenton et al., 2012; Hasin et al., 2011) are best viewed as cross-sectional rather than true prospective findings (i.e., associations tended to be significantly elevated only for disorders and PDs assessed at the same time). Compared with prediction, postdiction tended to be higher for PDs measured at Wave 1 and lower for PDs measured at Wave 2. This was true for all PDs and for all SUDs in bivariate associations (see Table 4). Although some exceptions to this trend occurred when including covariates in the analyses (particularly in more complex models including all PDs simultaneously where multicollinearity is high), the general picture suggests that the time-of-measurement effect is pervasive and should be taken into account when drawing conclusions regarding putative prospective associations with PDs using the NESARC dataset.[5]

In fact, the conclusions regarding which PDs are consistently associated with the persistence of substance use disorders change significantly when considering the time-of-measurement effect. In particular, both Hasin et al. (2011) and Fenton et al. (2012) reported that Borderline and Schizotypal PDs were associated with persistence of AD, ND, CUD, and DUD. All eight associations became non-significant in the postdiction analyses. The only exception to this pattern was Obsessive-Compulsive PD with the persistence of ND (reported by Hasin et al.; also reported in cross-sectional analyses using NESARC: Grant, Mooney, & Kushner, 2012; Pulay et al., 2010; Trull, Jahng, Tomko, Wood, & Sher, 2010). However, a recent study using a population-based sample in Spain found an association of Obsessive-Compulsive PD with cigarette smoking only among non-dependent participants (Becoña, del Río, López-Durán, Piñeiro, & Martínez, 2012). It is possible that the association with ND persistence might be stronger than the association with current diagnosis, given the rigidity that is characteristic of individuals with Obsessive-Compulsive PD. Indeed, supplementary analyses at the symptom level showed that only one symptom of Obsessive-Compulsive PD, “rigidity and stubbornness”, is associated with ND persistence in both prediction and postdiction (results available upon request).[6] With regard to Antisocial PD, which was found to be associated with the persistence of substance use disorders in Hasin et al. and Fenton et al., our analytic strategy does not provide clear evidence that these findings are due to the same artifact. Nevertheless, analyses involving

[4]Note that this approach for significance testing is useful only for bivariate associations. When more predictors are included in the model, the equality constraint does not yield a sensitive test for significant changes in model fit, even when the original odds ratios were very different in magnitude, because changes in other parameters can compensate for potential model misfit caused by inappropriate constraints.

[5]As mentioned, the differential pattern observed between prediction and postdiction results could be due to non-artifactual factors such as age grading. To investigate this possibility we split individuals into 3-year bins corresponding to the period of time between Wave 1 and Wave 2, and examined the bivariate associations between PDs and SUDs (diagnosed at Wave 1 and Wave 2) across matched age groups. When associations across matched age groups were compared, a robust time-of-measurement effect continued to be present, with 268 of 396 (11 matchable age groups × 4 SUDs × 9 PDs) age-matched pairs in the predicted direction ($p < 10^{-10}$). This suggests that the observed effects are at least not due to cohort effects.

Wave 1 Antisocial PD did not yield significant associations in the predictive analyses, suggesting that the associations found in previous studies might be due to the definition that incorporates data from both waves. Finally, the fact that Schizotypal PD was not shown to be robustly associated with the persistence of substance use disorders is more in line with the overall literature showing that Schizotypal PD is not a particularly strong correlate of problematic substance use (e.g., McGlashan et al., 2000; Pulay et al., 2009).

Although Fenton et al. (2012) argue that PDs are stable and enduring, and therefore not subject to a time-of-assessment effect, our analyses appear to refute this finding, and are in line with studies reporting change in PDs over time (Durbin & Klein, 2006; Gunderson et al., 2011; Lenzenweger, Johnson, & Willett, 2004). In fact, PDs measured by the AUDADIS do not behave as do other stable covariates like sex, age, and ethnicity (see Table 4). Moreover, additional analyses that examined differences in the association of PDs across four groups constructed on the basis of presence or absence of Wave 1 and Wave 2 diagnoses showed that this time-of-measurement effect yielded statistically significant differences between the group of participants diagnosed at Wave 1 versus the group of participants diagnosed at Wave 2 in the majority of the associations with PDs (see Table 5).

As mentioned in the introduction, the time-of-measurement effect likely explains at least some of the findings from other papers that were not analyzed here (Compton et al., 2013; Goodwin et al., 2011; Grant et al., 2009; Harrington et al., 2011; Maclean et al., 2014; Skodol, Geier, et al., in press; Skodol, Grilo et al., 2011).[7] Given the richness of the NESARC dataset, it is likely that researchers will continue using it to explore associations involving PDs. We hope the present findings will help the research community to better appreciate the implications of the difference in wave of assessment of PDs in NESARC. Also, the problems found with the NESARC design should motivate researchers to consider alternative research strategies (such as missing-by-design; Graham, Taylor, Olchowski, & Cumsille, 2006) to minimize response burden in a way that does not introduce potentially serious biases such as measuring different constructs at different times in longitudinal studies. Researchers should also take care in assessing and analyzing constructs as time-varying covariates when those constructs are expected (based on prior or burgeoning literature) to change over time. Moreover, we have introduced a novel methodological framework that can be useful for determining the extent to which the time-of-measurement effect underlies some associations.

While the present analyses lead to our skepticism about the published claims of unique prospective relationships between PDs and persistence of SUDs, we would not argue that

[6]For analyses at the symptom level, clinically significant impairment or distress was included by requiring endorsement of a given symptom plus impairment or distress in *any* symptom of Obsessive-Compulsive PD. This strategy was used to maintain comparability with coding for the disorder. However, when impairment or distress for the specific symptom endorsed was required, a different symptom, “unable to discard worn-out or worthless objects even when they have no sentimental value” was robustly associated with ND persistence. Notably, symptom level analyses did not show that one symptom was significantly more correlated with ND persistence than other symptoms, but rather that a given symptom was associated with ND persistence in both prediction and postdiction.

[7]Although the current analyses focused on substance use disorder persistence, the same time-of-measurement effect has been shown for the association of PDs and anxiety disorder persistence (Vergés et al., 2014; cf. Skodol, Geier, et al., in press). In addition, although we were not able to replicate results published by Skodol, Grilo, et al (2011), similar analyses to those conducted here revealed that a time-of-measurement effect might also underlie associations between PDs and major depressive disorder persistence.

there is no effect of personality pathology on persistence of substance use and other disorders. Rather, the design limitations in NESARC preclude a direct comparison among PDs measured at different waves and represent a lost opportunity to systematically address this important question in a nationally-representative sample. Indeed, although it would be desirable to develop a method to quantify the time-of-measurement effect in order to create a correction that allows for accurate persistence estimates, to the best of our knowledge this is not possible given that no PD was fully measured at both waves. Moreover, as assessed in NESARC and in other studies (e.g., The Collaborative Longitudinal Personality Disorders Study; Skodol et al., 2005), the exceptionally high comorbidity among PDs (Widiger & Trull, 2007) makes the demonstration of unique effects exceedingly difficult. Additionally, the presumption that PDs are highly stable constructs is undermined by the fact that current measures like those used in NESARC show significant levels of change over time. We note that the initial version of DSM-5 retains the current definitions of PDs but that this will likely change in the future given that the entire conceptual structure of personality pathology is undergoing revision (Bender, Morey, & Skodol, 2011; Skodol, Bender et al., 2011; Skodol, Clark et al., 2011). With this in mind it is likely that as the terrain of personality pathology is mapped more validly, we will be better able to characterize relationships between what is now termed personality pathology and the course of other psychiatric conditions.

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Table 1

Persistence of Axis I Disorders Defined by Prediction and Postdiction

	Estimation								
	Original[a]			Prediction[b]			Postdiction[c]		
Disorder	N subpopulation	%	SE	N subpopulation	%	SE	N subpopulation	%	SE
AD	1172	30.1	NR	1172	30.1	1.8	753	47.7	2.4
ND	4017	56.6	NR	4017	56.6	1.0	3879	58.8	1.2
CUD	454	30.8	NR	456	30.9	2.5	428	32.9	2.7
DUD	613	30.9	2.2	612	30.8	2.2	605	30.5	2.2

Note. AD = Alcohol Dependence; ND = Nicotine Dependence; CUD = Cannabis Use Disorder; DUD = Drug Use Disorder; NR = Not reported.

[a] Results published in the original reports (Hasin et al., 2011; Fenton et al., 2012).

[b] Prevalence of disorder at Wave 2 among those diagnosed at Wave 1.

[c] Prevalence of disorder at Wave 1 among those diagnosed at Wave 2.

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Table 2

Prediction and Postdiction (Adjusted Odds Ratios and 95% Confidence Intervals) by Personality Disorders in the Persistence of Alcohol Dependence, Nicotine Dependence, and Cannabis Use Disorder

	Alcohol Dependence						Nicotine Dependence						Cannabis Use Disorder					
	Hasin et al. W1→W2 (N = 1172)		Prediction W1→W2 (N =1172)		Postdiction W2→W1 (N =753)		Hasin et al. W1→W2 (N = 4017)		Prediction W1→W2 (N = 4017)		Postdiction W2→W1 (N = 3879)		Hasin et al. W1→W2 (N = 454)		Prediction W1→W2 (N = 456)		Postdiction W2→W1 (N = 428)	
Predictor	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Measured at Wave 1																		
Antisocial			1.07	0.69–1.67	0.74	0.38–1.43			1.14	0.84–1.56	1.34	0.73–2.46			1.33	0.70–2.52	0.45	0.19–1.09
Avoid/Depend	0.92	0.49–1.74	0.92	0.48–1.75	1.10	0.43–2.81	1.02	0.69–1.51	0.98	0.65–1.47	4.59	1.03–20.56	0.73	0.29–1.83	0.67	0.26–1.68	1.40	0.30–6.52
OCPD	0.89	0.57–1.38	0.89	0.57–1.40	0.56	0.25–1.24	1.40	1.06–1.85	1.40	1.05–1.87	1.90	1.06–3.42	0.91	0.44–1.87	0.80	0.36–1.76	2.58	0.97–6.87
Paranoid	1.18	0.72–1.95	1.14	0.68–1.90	2.21	0.90–5.43	0.99	0.73–1.35	0.96	0.70–1.33	2.01	0.89–4.55	0.83	0.40–1.73	0.80	0.39–1.65	0.91	0.33–2.49
Schizoid	1.10	0.59–2.06	1.08	0.56–2.06	1.13	0.43–2.98	1.47	1.08–2.01	1.46	1.06–2.01	1.51	0.70–3.25	0.80	0.33–1.97	0.71	0.28–1.80	0.77	0.25–2.34
Histrionic	0.96	0.57–1.60	0.90	0.53–1.54	1.07	0.30–3.85	1.10	0.76–1.59	1.07	0.74–1.56	4.02	0.97–16.59	1.10	0.46–2.65	0.99	0.43–2.30	1.01	0.34–2.99
Measured at Wave 2																		
Borderline	2.52	1.64–3.85	2.52	1.64–3.86	1.05	0.52–2.10	2.04	1.56–2.68	2.05	1.57–2.69	1.12	0.61–2.05	2.78	1.40–5.50	2.46	1.27–4.77	1.12	0.50–2.50
Narcissistic	1.96	1.32–2.91	1.94	1.29–2.91	1.18	0.55–2.53	1.22	0.92–1.61	1.20	0.91–1.58	0.53	0.30–0.91	1.32	0.63–2.74	1.26	0.61–2.57	0.93	0.38–2.25
Schizotypal	3.36	1.98–5.72	3.46	2.01–5.96	1.05	0.50–2.22	1.65	1.19–2.28	1.62	1.16–2.27	1.28	0.61–2.71	5.90	2.68–13.00	6.49	2.79–15.1	1.46	0.53–4.04
At both Waves																		
Antisocial[a]	3.51	1.74–7.08	2.49	1.07–5.82	0.11	0.03–0.42	3.19	1.64–6.18	2.18	1.06–4.49	2.60	0.34–19.94	2.46	1.05–5.73	2.38	1.01–5.66	1.78	0.50–6.32

Note. Models adjusted for demographics, Axis I disorders, other personality disorders, family history of alcohol or drug problems, current alcohol or drug treatment, and baseline duration of longest or only use disorder. Avoid/Depend = Avoidant or Dependent Personality Disorder; OCPD = Obsessive-Compulsive Personality Disorder.

[a]Antisocial PD at Wave 1 and AAB at Wave 2.

Table 3

Prediction and Postdiction (Adjusted Odds Ratios and 95% Confidence Intervals) by Personality Disorders in the Persistence of Drug Use Disorders

	Model 1[a]						Model 3[b]					
	Fenton et al. W1→W2 (N = 613)		Prediction W1→W2 (N = 612)		Postdiction W2→W1 (N = 605)		Fenton et al. W1→W2 (N = 613)		Prediction W1→W2 (N = 612)		Prediction W2→W1 (N = 605)	
Predictor	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Measured at Wave 1												
Alcohol Dependence	1.07	0.67–1.73	1.08	0.67–1.73	3.92	2.30–6.69		-		-		-
Nicotine Dependence	1.08	0.71–1.66	1.07	0.70–1.63	3.16	2.14–4.66		-		-		-
Unipolar	1.43	0.83–2.49	1.38	0.79–2.42	1.37	0.72–2.60		-		-		-
Bipolar	1.55	0.80–3.00	1.29	0.69–2.40	3.13	1.66–5.92		-		-		-
Anxiety	1.61	0.98–2.66	1.39	0.85–2.27	3.02	1.79–5.10		-		-		-
Antisocial			1.30	0.81–2.07	2.79	1.71–4.52			1.15	0.66–2.00	0.89	0.66–1.19
Avoid/Depend	1.05	0.52–2.14	1.02	0.50–2.07	2.32	1.09–4.93	0.75	0.37–1.52	0.77	0.35–1.70	0.96	0.62–1.47
OCPD	1.35	0.74–2.47	1.35	0.73–2.49	2.65	1.30–5.39	1.05	0.54–2.03	1.01	0.48–2.13	1.35	0.89–2.02
Paranoid	1.23	0.71–2.14	1.20	0.68–2.11	3.13	1.56–6.27	0.86	0.48–1.56	0.88	0.43–1.78	0.68	0.46–1.02
Schizoid	0.82	0.40–1.70	0.83	0.40–1.70	1.32	0.61–2.86	0.60	0.28–1.29	0.58	0.27–1.25	0.94	0.61–1.47
Histrionic	1.47	0.79–2.72	1.46	0.79–2.71	3.65	1.75–7.62	1.10	0.58–2.07	0.93	0.43–2.03	1.31	0.85–2.03
Measured at Wave 2												
Alcohol Dependence		-	2.27	1.51–3.43	1.08	0.70–1.68		-		-		-
Nicotine Dependence		-	2.34	1.44–3.80	1.46	1.00–2.14		-		-		-
Borderline	2.32	1.34–4.01	2.26	1.31–3.88	1.04	0.65–1.67	1.91	1.06–3.45	1.26	0.67–2.38	1.03	0.77–1.38
Narcissistic	2.08	1.16–3.70	2.06	1.15–3.71	1.19	0.68–2.08	1.55	0.84–2.84	1.35	0.69–2.67	1.04	0.76–1.43
Schizotypal	3.20	1.69–6.08	3.22	1.68–6.16	1.56	0.90–2.71	2.77	1.42–5.39	2.78	1.34–5.74	1.05	0.77–1.44
At both Waves												
Antisocial[c]	3.30	1.53–7.11	2.75	1.18–6.41	4.42	1.86–10.51	2.75	1.27–5.99	2.50	1.01–6.22	1.24	0.77–1.99

Note. Avoid/Depend = Avoidant or Dependent Personality Disorder; OCPD = Obsessive-Compulsive Personality Disorder.

[a] Adjusting for demographics: age, race/ethnicity, sex and education.

[b] Adjusting for demographics, Axis I disorders, all other Axis II disorders, family history of alcohol or drug problems, treatment, and number of baseline drug use disorders.

[c] Antisocial PD at Wave 1 and AAB at Wave 2.

Table 4

Bivariate Prediction and Postdiction (Unadjusted Odds Ratios and 95% Confidence Intervals) by Personality Disorders in the Persistence of Substance Use Disorders

	AD				ND				CUD				DUD			
	Prediction W1→W2 (N = 1172)		Postdiction W2→W1 (N = 753)		Prediction W1→W2 (N = 4017)		Postdiction W2→W1 (N = 3879)		Prediction W1→W2 (N = 456)		Postdiction W2→W1 (N = 428)		Prediction W1→W2 (N = 612)		Postdiction W2→W1 (N = 605)	
Predictor	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**
Measured at Wave 1																
Sex[a]	0.60	0.43–0.83	0.73	0.52–1.04	1.15	0.98–1.36	1.30	1.11–1.53	0.78	0.48–1.28	1.00	0.55–1.83	0.76	0.48–1.18	0.84	0.52–1.38
Age[b]	1.48	1.10–1.99	0.94	0.66–1.35	1.71	1.45–2.01	1.10	0.91–1.33	1.17	0.71–1.92	0.64	0.37–1.11	0.89	0.58–1.36	0.62	0.38–1.01
Race[c]	0.73	0.53–1.02	0.71	0.50–1.01	0.85	0.71–1.03	0.64	0.54–0.77	0.71	0.41–1.21	0.84	0.46–1.55	0.71	0.45–1.10	0.93	0.56–1.54
Antisocial	1.77	1.20–2.61	2.81	1.69–4.70	1.34	1.01–1.77	3.51	2.51–4.89	1.22	0.69–2.13	2.47	1.36–4.50	1.30	0.81–2.07	2.80	1.71–4.59
Avoid/Depend	1.33	0.73–2.41	2.48	1.18–5.23	1.46	0.98–2.16	5.16	3.10–8.61	1.22	0.51–2.97	3.44	1.22–9.67	1.07	0.53–2.16	2.30	1.08–4.92
OCPD	1.36	0.90–2.06	1.57	0.91–2.69	1.83	1.40–2.39	3.70	2.76–4.95	1.43	0.69–2.96	4.37	1.94–9.86	1.33	0.72–2.45	2.54	1.23–5.26
Paranoid	1.64	1.07–2.50	3.66	2.17–6.18	1.44	1.09–1.92	3.29	2.27–4.76	1.17	0.59–2.31	3.27	1.40–7.60	1.13	0.66–1.93	3.11	1.57–6.15
Schizoid	1.62	0.93–2.80	2.02	1.02–3.99	1.96	1.45–2.65	3.69	2.39–5.70	1.31	0.56–3.06	2.82	1.05–7.61	0.87	0.42–1.79	1.26	0.56–2.83
Histrionic	1.41	0.86–2.30	3.54	1.79–6.99	1.37	0.98–1.93	4.38	2.49–7.71	1.38	0.68–2.81	3.84	1.46–10.13	1.51	0.79–2.87	3.96	1.82–8.64
Measured at Wave 2																
Borderline	3.09	2.08–4.60	1.25	0.84–1.87	2.36	1.87–3.00	1.58	1.26–1.97	2.12	1.22–3.70	1.19	0.70–2.02	2.15	1.27–3.62	1.07	0.67–1.72
Narcissistic	2.66	1.83–3.86	1.29	0.84–1.99	1.43	1.10–1.86	0.97	0.76–1.22	1.62	0.88–2.98	1.43	0.77–2.64	2.06	1.13–3.74	1.21	0.69–2.13
Schizotypal	4.35	2.70–7.02	1.34	0.82–2.19	2.18	1.61–2.96	1.89	1.39–2.56	3.75	1.85–7.60	2.08	1.12–3.87	3.22	1.71–6.05	1.50	0.85–2.64
At both Waves																
Antisocial[d]	3.27	1.53–7.01	1.17	0.52–2.67	2.39	1.19–4.81	5.21	2.37–11.48	2.92	1.16–7.35	4.03	1.61–10.12	3.03	1.29–7.13	4.70	1.99–11.10

Note. AD = Alcohol Dependence; ND = Nicotine Dependence; CUD = Cannabis Use Disorder; DUD = Drug Use Disorder; Avoid/Depend = Avoidant or Dependent Personality Disorder; OCPD = Obsessive-Compulsive Personality Disorder.

[a] Male is reference group.

[b] 18 to 29 is reference group.

[c] White, Non-Hispanic is reference group.

[d] Antisocial PD at Wave 1 and AAB at Wave 2.

Table 5

Odds Ratios from Multinomial Logistic Regression predicting Diagnosis only at Wave 1 or only at Wave 2 (with Diagnosis at both Waves as Reference Group), and Significance Tests of Equality of the Odds Ratios

	Non-Persistent AD			Non-Persistent ND			Non-Persistent CUD			Non-Persistent DUD		
Predictor	**W1 only**	**W2 only**	**χ^2**	**W1 only**	**W2 only**	**χ^2**	**W1 only**	**W2 only**	**χ^2**	**W1 only**	**W2 only**	**χ^2**
Measured at Wave 1												
Antisocial	0.57*	0.36*	3.85*	0.75*	0.29*	30.20*	0.82	0.41*	7.87*	0.77	0.36*	12.64*
Avoid/Depend	0.75	0.40*	4.66*	0.69	0.19*	24.36*	0.82	0.29*	7.64*	0.94	0.43*	7.21*
OCPD	0.74	0.64	0.4	0.55*	0.27*	22.82*	0.70	0.23*	14.57*	0.75	0.39*	6.65*
Paranoid	0.61*	0.27*	13.47*	0.69*	0.30*	24.12*	0.86	0.31*	9.35*	0.89	0.32*	16.08*
Schizoid	0.62	0.50*	0.68	0.51*	0.27*	8.32*	0.76	0.35*	4.4*	1.15	0.79	1.62
Histrionic	0.71	0.28*	12.09*	0.73	0.23*	18.84*	0.73	0.26*	7.15*	0.66	0.25*	10.05*
Measured at Wave 2												
Borderline	0.32*	0.80	25.87*	0.42*	0.63*	7.41*	0.47*	0.84	5.27*	0.47*	0.93	11.05*
Narcissistic	0.38*	0.77	14.68*	0.70*	1.04	7.93*	0.62	0.70	0.2	0.49*	0.83	5.37*
Schizotypal	0.23*	0.75	23.2*	0.46*	0.53*	0.58	0.27*	0.48*	3.39	0.31*	0.67	9.67*
At both Waves												
Antisocial[a]	0.31*	0.85	7.11*	0.42*	0.19*	3.41	0.34*	0.25*	0.63	0.33*	0.21*	1.25

Note. Participants diagnosed at both waves constitute the reference group, so these estimates are reversed from those of previous tables. AD = Alcohol Dependence; ND = Nicotine Dependence; CUD = Cannabis Use Disorder; DUD = Drug Use Disorder; Avoid/Depend = Avoidant or Dependent Personality Disorder; OCPD = Obsessive-Compulsive Personality Disorder;

* $p < .05$.

[a] Antisocial PD at Wave 1 and AAB at Wave 2.