International Journal of Mental Health and Addiction
https://doi.org/10.1007/s11469-020-00299-9

ORIGINAL ARTICLE

Examining Relations Between Obsessive-Compulsive Features, Substance-Use Disorders, and Antisocial Personality Disorder in the Vietnam Era Twin Cohort

Molly Williams[1] · Arielle R. Baskin-Sommers[1,2] · Hong Xian[3] · Lorinette Wirth[3] · Jeffrey F. Scherrer[4] · Rachel A. Volberg[5] · Wendy S. Slutske[6] · Shane W. Kraus[7] · Seth A. Eisen[8] · Marc N. Potenza[2,9,10,11]

Published online: 13 May 2020

Abstract
Classes of obsessive-compulsive features differing both quantitatively and qualitatively have been linked to gambling disorder. This secondary data analysis sought to extend this line of investigation to examine the extent to which previously reported latent obsessive-compulsive classes may relate to externalizing conditions in a sample of 1675 twin male veterans recruited and surveyed for studies of gambling behaviors/disorder. Using latent class analysis and multivariate regression, we found that participants who reported the highest levels of obsessive-compulsive features were more likely to meet criteria for cannabis abuse and dependence and antisocial personality disorder. When adjusting for co-occurring disorders, the relationship with antisocial personality disorder remained significant whereas those for cannabis use disorders did not. These results highlight the potential utility of considering obsessive-compulsive features within a transdiagnostic framework and suggest that specific externalizing disorders have important links to obsessive-compulsive features. Future research is needed to extend these findings to other samples.

Keywords Obsessive-compulsive features · Impulsivity · Compulsivity · Transdiagnostic

In recent years, a focus on transdiagnostic frameworks of mental disorders has become increasingly prevalent, leading to development of the Research Domain Criteria (RDoC) framework (Insel et al. 2010), ROAMER project (Schumann et al. 2014), and PhenX catalog (RTI International 2017). Whereas some traditional frameworks consider specific psychopathologies as discrete diagnostic entities (World Health Organization 1992; American Psychiatric Association 2013), a transdiagnostic conceptualization of psychopathology suggests that specific features of different disorders cross diagnostic boundaries and may link

✉ Marc N. Potenza
marc.potenza@yale.edu

Extended author information available on the last page of the article

more closely to biological underpinnings of behavior (Gottesman and Gould 2003; Insel et al. 2010; Krueger and Eaton 2015).

Obsessive-compulsive disorder is characterized by intrusive obsessive thoughts and compulsive, ritualized behaviors performed to dispel or alleviate the thoughts. Obsessive-compulsive disorder has been conceptualized historically as an anxiety disorder, but more recently has been reclassified in DSM-5 within the category of "Obsessive-Compulsive and Related Disorders." However, obsessive-compulsive disorder may be a heterogeneous construct that may be fractionated into obsessive-compulsive features that may span multiple psychopathologies (Insel et al. 2010). Additionally, compulsivity may link to multiple disorders in a transdiagnostic fashion and possibly in a distinct fashion from obsessive-compulsive disorder (Fineberg et al. 2014). On the other hand, impulsivity is described as a "predisposition towards rapid, unplanned reactions to internal or external stimuli with diminished regard to the negative consequences" (Moeller et al. 2001). Understanding the interplay between impulsivity and compulsivity has direct implications for treatment efforts for addictive behaviors.

Consistent with the relevance of transdiagnostic obsessive-compulsive constructs, a data-driven approach (latent class analysis) recently identified four classes of obsessive-compulsive features differing both quantitatively (two classes with low and high endorsements of features, respectively) and qualitatively (two classes with high endorsements of ordering/symmetry and germs/contamination fears, respectively, with both classes also having high likelihoods of endorsing rituals) in a sample of 1675 male twins from the Vietnam Era Twin (VET) cohort (Scherrer et al. 2015). The specific endorsement frequencies of each OC domain within each OC class can be seen in Table 1 of Scherrer et al. (2015). In this article, Scherrer et al. (2015) found that gambling disorder was associated with the three classes with elevated obsessive-compulsive features. Because gambling disorder is currently classified together with substance-use disorders within the "Substance-Related and Addictive Disorders" category in DSM-5, the findings raise questions regarding the extent to which other addictive disorders might relate to these previously identified obsessive-compulsive classes. Additionally, given that antisocial personality disorder shows high rates of co-occurrence with substance use disorders (National Institute on Alcohol Abuse and Alcoholism 2005) and with gambling disorder and has been considered within an externalizing family of disorders (Robbins et al. 2012), a question regarding the extent to which antisocial personality disorder relates to obsessive-compulsive features is raised.

Using Latent Gold 4.0 program (Vermont and Magidson 2005), Scherrer et al. (2015) performed latent class analysis to identify classes of obsessive-compulsive features, using the Bayesian information criterion to select the best-fitting model. The best-fitting model included four classes of obsessive-compulsive features that differed in quality and severity—these are utilized in the present study. The latent classes were based on ten obsessive-compulsive items that were adapted from the NIMH Obsessive-Compulsive Disorder Collaborative Genetics Study (for additional details see: https://www.nimhgenetics.org/resources/clinical-instruments). Class 1 included individuals who had low likelihoods of endorsing any obsessive-compulsive symptoms; class 2 included individuals with higher likelihoods of endorsing obsessive-compulsive features relating to symmetry, ordering, and rituals; class 3 included individuals with higher likelihoods of endorsing obsessive-compulsive features relating to germs, contamination fears and rituals; and the fourth class was comprised of people who had high likelihoods of endorsing all obsessive-compulsive symptoms (Scherrer et al. 2015). Additional details on the procedures and steps taken to conduct the latent class analysis can be found in Scherrer et al. 2015.

Table 1 Sample characteristics

	Frequency	Percent
Highest completed education		
< high school degree	56	3.34%
High school degree	598	35.70%
> high school degree	525	31.34%
College degree	496	29.61%
Marital status		
Married or cohabiting	1296	77.37%
Widowed or divorced	287	17.13%
Never married	92	5.49%
Race		
Black	104	6.23%
Other	70	4.19%
White	1495	89.57%
Antisocial personality disorder		
Yes	53	3.16%
No	1622	96.84%
Cannabis use disorders		
Yes	121	7.24%
No	1551	92.76%
Generalized anxiety disorder		
Yes	43	2.57%
No	1631	97.43%
Posttraumatic stress disorder		
Yes	169	10.14%
No	1498	89.86%
Major depression		
Yes	185	11.04%
No	1490	88.96%
Panic disorder		
Yes	25	1.49%
No	1649	98.51%
Nicotine dependence		
Yes	813	48.54%
No	862	51.46%
Gambling disorder*		
Yes	78	4.66%
No	1597	95.34%
Alcohol use disorders		
Yes	956	57.25%
No	714	42.75%
Amphetamine use disorders		
Yes	50	2.99%
No	1621	97.01%
Cocaine disorders		
Yes	52	3.11%
No	1619	96.89%
Stimulant use disorders		
Yes	90	5.37%
No	1585	94.63

*We rescored the previous data for pathological gambling using DSM-5 criteria for gambling disorder. The substance use disorders reflect abuse/dependence as described in the methods

Information about the racial demographics of six participants was missing

Using the four obsessive compulsive classes established by Scherrer et al. (2015), the present study examined the relationships between obsessive-compulsive features and substance use disorders and antisocial personality disorder in VET participants. We hypothesized that based on relationships between obsessive-compulsive classes and gambling disorder, we would identify relationships between obsessive-compulsive classes and both substance use disorders and antisocial personality disorder.

Methods

Participants

The present study used data from the VET Registry (see https://www.seattle.eric.research.va.gov/VETR/Home.asp for additional details). These data include information collected via telephone from male monozygotic and dizygotic twin pairs born from 1939 to 1955, all of whom served on active duty during the Vietnam War.[1] The full registry included 7375 twin pairs and has been described elsewhere (Eisen et al. 1987; Goldberg et al. 2002). In 1992, these twin pairs were invited to participate in a telephone diagnostic interview, and diagnoses of Axis I psychiatric disorders were assessed based on DSM-III-R criteria after the participants gave informed consent for the study (Robins et al. 1988). All diagnostic variables for measures that were not obsessive-compulsive features were dichotomous (Krueger 1999; Kendler et al. 2003; Desai and Potenza 2008). Ten years later, in 2002, 1200 twin pairs were invited to participate in an additional phone interview that oversampled for individuals with features of pathological gambling (Scherrer et al. 2015). This interview also assessed obsessive-compulsive features, with information regarding selection and re-contacting of individuals described previously (Scherrer et al. 2015). Of the 2400 individuals who were eligible, 252 were not contacted because they were deceased, not located, unavailable, on active military duty, or incapacitated. Of the 2148 participants who could be reached by phone, 1675 (78.0% response rate) were interviewed from March 2002 through November 2003 (Scherrer et al. 2015) (see Table 1 for sample characteristics).

Gambling Disorder Definitions

As reported in Scherrer et al. (2015), we rescored veterans' data assessing symptoms of pathological gambling to determine how many individuals met full criteria for DSM-5 gambling disorder. This retrospective approach has been previously applied to other studies to yield more accurate (and current) prevalence data on gambling disorder (Grant et al. 2017a; Medeiros et al. 2015).

Analytic Plan

Chi-square tests of association were performed to examine relationships between obsessive-compulsive features and multiple variables including alcohol abuse/dependence, nicotine

[1] Twin studies provide a great opportunity for genetic analysis; however, due to low base rates of disorders, there was insufficient power to perform genetic analysis related to antisocial personality disorder and substance use disorders as they relate to the overlap with obsessive-compulsive features.

dependence, antisocial personality disorder, cannabis abuse/dependence, illicit drug dependence, amphetamine abuse/dependence, cocaine abuse/dependence, and stimulant dependence (that is, a variable measuring disordered use of either cocaine or amphetamines). Univariate and multivariate logistic regression analyses were then performed to clarify and establish the relationships between each obsessive-compulsive class and each externalizing disorder, and then to determine whether the relationships previously established were influenced by socio-demographic factors (multivariate model 1) and socio-demographics and psychiatric disorders (multivariate model 2). All univariate and multivariate models were adjusted for oversampling for gambling disorder (formerly pathological gambling in DSM-IV) as described previously (Scherrer et al. 2015).

Results

Obsessive-Compulsive Features, Substance-Use Disorders, and Antisocial Personality Disorder

There were significant associations between obsessive-compulsive class and antisocial personality disorder ($X^2(3) = 8.6631$, $p = 0.0341$), obsessive-compulsive class and cannabis dependence ($X^2(3) = 10.7330$, $p = 0.0133$), and obsessive-compulsive class and cannabis abuse/dependence ($X^2(3) = 9.7953$, $p = 0.0204$). Individuals with obsessive-compulsive features (classes 2, 3, and 4) compared with those without (obsessive-compulsive class 1) were more likely to meet criteria for antisocial personality disorder, cannabis abuse, and cannabis dependence. No other relationships between obsessive-compulsive class and psychopathology were significant (obsessive-compulsive -alcohol: $p = .0928$; OC-amphetamine: $p = 0.1911$; obsessive-compulsive -cocaine abuse/dependence: $p = 0.9092$; obsessive-compulsive -nicotine: $p = 0.0750$; obsessive-compulsive -stimulant use disorders: $p = 0.6534$; obsessive-compulsive-illicit drug dependence: $p = 0.1039$).

Obsessive-Compulsive Classes, Cannabis Use Disorders, and Antisocial Personality Disorder

Univariate and multivariate logistic regression including socio-demographic measures were conducted to determine the association between specific obsessive-compulsive classes and cannabis use disorders and specific obsessive-compulsive classes and antisocial personality disorder. Significant relationships were observed for obsessive-compulsive class 2 (characterized by high rates of symmetry/ordering/rituals) and antisocial personality disorder (see Table 2) and obsessive-compulsive class 2 and cannabis abuse/dependence (see Table 3), and these differences withstood correction for socio-demographic differences. When adjusting for co-occurring disorders, the findings for antisocial personality disorder remained similar whereas those for cannabis abuse/dependence were no longer statistically significant.

Discussion

Partially consistent with our a priori hypotheses, we observed significant relationships between obsessive-compulsive classes and both substance use disorders and antisocial personality

Table 2 Obsessive compulsive class and antisocial personality disorder for univariate (unadjusted) and multivariate (adjusted) logistic regression

	Odds ratio	*p* value	95% Wald confidence interval
Univariate			
Class 2 (symmetry/rituals)	2.433	0.0177	[1.167, 5.071]
Class 3 (germs/fears/rituals)	2.339	0.1107	[0.823, 6.645]
Class 4 (all features)	2.741	0.0718	[0.914, 8.214]
Multivariate 1			
Class 2 (symmetry/rituals)	2.694	0.0136	[1.227, 5.917]
Class 3 (germs/fears/rituals)	2.466	0.0843	[0.885, 6.871]
Class 4 (all features)	2.291	0.1045	[0.842, 6.232]
Multivariate 2			
Class 2 (rituals/symmetry/rituals)	3.056	0.0144	[1.250, 7.474]
Class 3 (germs/fears/rituals)	2.715	0.0620	[0.951, 73,752]
Class 4 (all features)	2.211	0.2326	[0.617, 7.301]

Reference group class 1 (low OC features). For multivariate analysis 1, race, age, education level, and marital status were included as covariates. For multivariate analysis 2, covariates included sociodemographic factors in multivariate 1 and psychiatric diagnoses of gambling disorder, cannabis use disorders, generalized anxiety disorder, nicotine dependence, depression, alcohol use disorders, panic disorder, stimulant use disorders, and posttraumatic stress disorder

disorder. However, these relationships were limited to cannabis abuse and dependence and antisocial personality disorder and were related specifically to a latent obsessive-compulsive class characterized by high likelihood of endorsement of obsessive-compulsive features relating to symmetry, ordering, and rituals. Furthermore, the relationship between obsessive-compulsive features and cannabis use disorders seemed related to demographic features and co-occurring disorders, and particularly the latter. Interestingly, these findings appear to differ from the findings relating to gambling disorder, in which relationships with all three obsessive-compulsive classes with elevated symptomatology were observed. Implications are discussed below.

Table 3 OC class and cannabis abuse/dependence for univariate (unadjusted) and multivariate (adjusted) logistic regression

	Odds ratio	*p* value	95% Wald confidence interval
Univariate			
Class 2 (symmetry/rituals)	1.693	0.0409	[1.022, 2.806]
Class 3 (germs/fears/rituals)	1.596	0.2252	[0.750, 3.398]
Class 4 (all features)	1.588	0.2783	[0.688, 3.663]
Multivariate 1			
Class 2 (symmetry/rituals)	1.697	0.0466	[1.008, 2.857]
Class 3 (germs/fears/rituals)	1.552	0.2644	[0.717, 3.359]
Class 4 (all features)	1.530	0.3227	[0.658, 3.559]
Multivariate 2			
Class 2 (symmetry/rituals)	1.610	0.1027	[0.908, 2.853]
Class 3 (germs/fears/rituals)	1.563	0.2956	[0.675, 3.612]
Class 4 (all features)	1.892	0.1720	[0.757, 4.725]

Reference group class 1 (low OC features). For multivariate analysis 1, race, age, education level, and marital status were included as covariates. For multivariate analysis 2, covariates included sociodemographic factors in multivariate 1 and psychiatric diagnoses of gambling disorder, antisocial personality disorder, generalized anxiety disorder, nicotine dependence, depression, alcohol use disorders, panic disorder, stimulant use disorders, and posttraumatic stress disorder

Cannabis use has been previously linked to obsessive-compulsive disorder in populations of multiple ages. Individuals who use cannabis and people with obsessive-compulsive disorder have been found to display similar deficits on neuropsychological tasks. For example, adolescents who use cannabis heavily regularly display higher than average rates of perseverative responses on tasks such as the Wisconsin Card Sorting Test; those with obsessive-compulsive disorder also exhibit perseveration in response to certain tasks requiring cognitive set-shifting (Douglass et al. 1995; Buckner et al. 2007). Additionally, certain patterns of behavior that can arise within chronic cannabis use (e.g., cannabinoid hyperemesis, which is characterized by vomiting and compulsive bathing behaviors) may appear like obsessive-compulsive disorder to the extent that they may be misdiagnosed (Sanz et al. 2001; Lane et al. 2007; Scholes and Martin-Iverson 2009). Some data suggest that obsessive-compulsive disorder symptoms may arise after cannabis use in certain populations, or that cannabis use may potentiate preexisting vulnerabilities to obsessive-compulsive disorder (Wallace et al. 2007). The current findings suggest that specific obsessive-compulsive features may link particularly closely to cannabis use disorders, and that these may relate importantly to other co-occurring disorders.

Previous research has also linked antisocial personality disorder and obsessive-compulsive features. Williams and Ching (2016) suggested that antisocial personality disorder and obsessive-compulsive disorder fall on opposite sides of a continuum expressed in part within the orbito-fronto-striato-pallidal system, with antisocial personality disorder representing hypo-moralism and obsessive-compulsive disorder representing hyper-moralism. Additionally, one theory about the etiology of antisocial personality disorder, a theory of dysfunction of the frontal lobe, posits that antisocial personality disorder involves impairment in executive functioning, which manifests itself through neuropsychological symptoms such as cognitive inflexibility (Braun et al. 2008). Obsessive-compulsive disorder has been linked to cognitive inflexibility and may be reflected in the ritualistic behaviors in the latent class associated with antisocial personality disorder in the present study. Such cognitive inflexibility has been linked to brain functions involving dorsal and ventral fronto-striatal circuits (Fitzgerald and Demakis 2007), with such circuits implicated in obsessive-compulsive disorder and antisocial personality disorder. Such an overlap in cognitive impairment suggests a broader relationship between antisocial personality disorder and specific obsessive-compulsive features, whereby the impulsive behavior commonly displayed by individuals with antisocial personality disorder may paradoxically be rooted in a perseverative, compulsive focus on cue aligning with antisocial goals. Such a possibility, although currently speculative, warrants further investigation.

Several limitations of the present study should be noted. First, the cross-sectional design of the study does not allow insight into possible causation or the directionality of relationships between obsessive-compulsive features, cannabis use disorders, and antisocial personality disorder. Second, as obsessive-compulsive features, antisocial personality disorder, and substance use disorders were measured at a single point in time and not again over the course of the study, it is unclear whether these features remain constant over time. Future longitudinal studies would be helpful in investigating the temporal natures of these relationships and their stability over time. Third, the study was not sufficiently powered to model genetic and environmental contributions to the obsessive-compulsive classes and externalizing disorders. In the future, a larger twin study investigating overlap between obsessive-compulsive features and substance use disorders and antisocial personality disorder should be conducted. Additional work is needed to examine genetic markers associated with gambling disorder among

vulnerable individuals such as military veterans, a group noted for high rates of co-occurring mental health conditions (Grant et al. 2017b; Shirk et al. 2018).

Fourth, the study population was male, middle-aged, and predominantly white, which limits the generalizability of the present findings to other populations, including women, adolescents, and racial minority groups. Fifth, the present study focused solely on one transdiagnostic domain (namely, obsessive-compulsive features). Future research may consider other transdiagnostic features. For example, impulsivity has been linked to substance use disorders and antisocial personality disorder, and warrants further investigation with respect to relationships with obsessive-compulsive features and externalizing disorders. Sixth, as a subset of the original cohort participated in the current study, potential effects of participation bias cannot be excluded. Seventh, views towards and legality and availability of cannabis have changed over time. Thus, the extent to which the observed relationships exist in the current cannabis environments warrants investigation. Such studies should be conducted prospectively with aims to identify relationships both cross-sectionally and longitudinally. Eighth, military samples like the VET cohort typically have high rates of psychiatric disorders (e.g., posttraumatic stress disorder) that may be related to military exposure. The extent to which the findings may generalize to other samples (e.g., non-twin community samples) warrants additional study. Ninth, the interviews were conducted via the telephone and it is possible that underreporting occurred. Tenth, as data were collected at multiple time intervals and diagnostic criteria have changed over time, there exists a limitation if using diagnostic criteria from different editions of the DSM, thus potentially introducing errors and biases. Eleventh, multiple analytic approaches were employed (latent class analysis, chi-square and logistic regression). It is possible that errors or biases from one analytic step may have been propagated to other steps. Despite these limitations, the results of this study have important implications for our understanding of the relationships between obsessive-compulsive features and externalizing disorders.

The present study provides evidence for a model in which specific externalizing disorders may relate importantly to specific obsessive-compulsive features. Future studies should also investigate the extent to which these findings may extend to other populations and the extent to which identifying and targeting specific obsessive-compulsive features in prevention and treatment settings may help individuals with or at elevated risk for developing cannabis use disorders or antisocial personality disorder.

Acknowledgments The US Department of Defense, National Personnel Records Center, National Archives and Records Administration, Internal Revenue Service, National Opinion Research Center, National Research Council, National Academy of Sciences, and Institute for Survey Research provided invaluable assistance in the conduct of this study. Most importantly, the members of the VET Registry and their families provided continued cooperation and participation, without which this research would not have been possible.

Role of the Funder/Sponsor The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Funding Information This study was supported by grant MH60426 (Pathological Gambling: Courses, Consequences and Causes) from the Health Services Research and Development Service of the VA and National Institute of Mental Health, Yale and University of Missouri Center of Excellence in Gambling Research grants from the National Center for Responsible Gaming and by the National Center on Addiction and Substance Abuse, the Connecticut Mental Health Center, the Connecticut Department of Mental Health and Addiction Services, and the Connecticut Council on Problem Gambling. The US VA has provided financial support for the development and maintenance of the VET Registry.

Compliance with Ethical Standards

Conflict of Interest The authors report no conflicts of interest. Dr. Potenza has consulted for and advised Game Day Data, the Addiction Policy Forum, AXA, and Opiant/Lakelight Therapeutics; received research support from the Mohegan Sun Casino and the National Center for Responsible Gaming (now the International Center for Responsible Gaming); participated in surveys, mailings, or telephone consultations related to drug addiction, impulse-control disorders, or other health topics; consulted for legal and gambling entities on issues related to impulse-control and addictive disorders; provided clinical care in the Connecticut Department of Mental Health and Addiction Services Problem Gambling Services Program; performed grant reviews for the National Institutes of Health and other agencies; edited journals and journal sections; given academic lectures in grand rounds, CME events, and other clinical/scientific venues; and generated books or chapters for publishers of mental health texts. The other authors report no disclosures. The views presented in this manuscript represent those of the authors and not necessarily those of the funding agencies.

Ethical Approval The original and current study was approved by the institutional review boards of the St Louis Veterans Affairs Medical Center and the Washington University School of Medicine. All participants provided verbal informed consent.

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders*. Arlington: American Psychiatric Publishing.

Braun, C., Léveillé, C., & Guimond, A. (2008). An orbitofrontostriatopallidal pathway for morality: evidence from postlesion antisocial and obsessive-compulsive disorder. *Cognitive Neuropsychiatry, 13*, 296–337.

Buckner, J., Bonn-Miller, M., Zvolensky, M., & Schmidt, N. (2007). Marijuana use motives and social anxiety among marijuana-using young adults. *Addictive Behaviors, 32*, 2238–2252.

Desai, R., & Potenza, M. (2008). Gender differences in the associations between past-year gambling problems and psychiatric disorders. *Social Psychiatry and Psychiatric Epidemiology, 43*, 173–183.

Douglass, H., Moffitt, T., Dar, R., McGee, R., & Silva, P. (1995). Obsessive-compulsive disorder in a birth cohort of 18-year-olds: prevalence and predictors. *Journal of the American Academy of Child and Adolescent Psychiatry, 34*, 1424–1431.

Eisen, S., True, W., Goldberg, J., Henderson, W., & Robinette, C. D. (1987). The Vietnam Era Twin (VET) Registry: method of construction. *Acta Geneticae Medicae et Gemellologiae, 36*, 61–66.

Fineberg, N., Chamberlain, S., Goudriaan, A., Stein, D., Vanderschuren, L., Gillian, C., Shekar, S., Gorwood, P., Voon, V., Morein-Zamir, S., Denys, D., Sahakian, B., Moeller, F., Robbins, T., & Potenza, M. (2014). New developments in human neurocognition: clinical, genetic and brain imaging correlates of impulsivity and compulsivity. *CNS Spectrums, 19*, 69–89.

Fitzgerald, K., & Demakis, G. (2007). The neuropsychology of antisocial personality disorder. *Disease-a-Month, 53*, 177–183.

Goldberg, J., Curran, B., Vitek, M., Henderson, W., & Boyko, E. (2002). The Vietnam Era Twin Registry. *Twin Research, 5*, 476–481.

Gottesman, I., & Gould, T. (2003). The endophenotype concept in psychiatry: etymology and strategic intentions. *The American Journal of Psychiatry, 160*, 636–645.

Grant, J. E., Odlaug, B. L., & Chamberlain, S. R. (2017a). Gambling disorder, DSM-5 criteria and symptom severity. *Comprehensive Psychiatry, 75*, 1–5.

Grant, J. E., Potenza, M. N., Kraus, S. W., & Petrakis, I. L. (2017b). Naltrexone and disulfiram treatment response in veterans with alcohol dependence and co-occurring problem-gambling features. *The Journal of Clinical Psychiatry, 78*(9), e1299–e1306.

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D., Quinn, K., Sanislow, C., & Wang, P. (2010). Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. *The American Journal of Psychiatry, 167*, 748–751.

Kendler, K., Prescott, C., Myers, J., & Neale, M. (2003). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Archives of General Psychiatry, 60*, 929–937.

Krueger, R. (1999). The structure of common mental disorders. *Archives of General Psychiatry, 56*, 921–926.

Krueger, R., & Eaton, N. (2015). Transdiagnostic factors of mental disorders. *World Psychiatry, 14*, 27–29.

Lane, S., Cherek, D., Tcheremissine, O., Steinberg, J., & Sharon, J. (2007). Response perseveration and adaptation in heavy marijuana-smoking adolescents. *Addictive Behaviors, 32*, 977–990.

Medeiros, G. C., Leppink, E. W., Yaemi, A., Mariani, M., Tavares, H., & Grant, J. E. (2015). Electronic gaming machines and gambling disorder: a cross-cultural comparison between treatment-seeking subjects from Brazil and the United States. *Psychiatry Research, 230*(2), 430–435.

Moeller, F. G., Barratt, E. S., Dougherty, D. M., Schmitz, J. M., & Swann, A. C. (2001). Psychiatric aspects of impulsivity. *AmJ Psychiatry., 158*(11), 1783–1793.

National Institute on Alcohol Abuse and Alcoholism, (2005). *National epidemiologic survey on alcohol and related conditions-III*.

Robbins, T., Gillan, C., Smith, D., de Wit, S., & Ersche, K. (2012). Neurocognitive endophenotypes of impulsivity and compulsivity: towards dimensional psychiatry. *Trends in Cognitive Sciences, 16*, 81–91.

Robins, L., Helzer, J., Cottler, L., & Goldring, E. (1988). *NIMH diagnostic interview schedule, version III, revised, Dept of Psychiatry,Washington University School of Medicine*. St Louis.

RTI International, (2017). PhenX toolkit. Retrieved February 9 2017.

Sanz, M., Molina, V., Calcedo, A., Martin-Loeches, M., & Rubia, F. (2001). The Wisconsin Card Sorting Test and the assessment of frontal function in obsessive-compulsive patients: an event-related potential study. *Cognitive Neuropsychiatry, 6*, 109–129.

Scherrer, J., Xian, H., Slutske, W., Eisen, S., & Potenza, M. (2015). Associations between obsessive-compulsive classes and pathological gambling in a national cohort of male twins. *JAMA Psychiatry, 72*, 342–349.

Scholes, K., & Martin-Iverson, M. (2009). Cannabis use and neuropsychological performance in healthy individuals and patients with schizophrenia. *Psychological Medicine, 40*, 1635–1646.

Schumann, G., Binder, E., Holte, A., de Kloet, E., Oedegaard, K., Robbins, T., Walker-Tilley, T., Bitter, I., Brown, V., Buitelaar, J., Ciccocioppo, R., Cools, R., Escera, C., Fleischhacker, W., Flor, H., Frith, C., Heinz, A., Johnsen, E., Kirschbaum, C., Klingberg, T., Lesch, K., Lewis, S., Maier, W., Mann, K., Martinot, J., Meyer-Lindenberg, A., Müller, C., Müller, W., Nutt, D., Persico, A., Perugi, G., Pessiglione, M., Preuss, U., Roiser, J., Rossini, P., Rybakowski, J., Sandi, C., Stephan, K., Undurraga, J., Vieta, E., van der Wee, N., Wykes, T., Haro, J., & Wittchen, H. (2014). Stratified medicine for mental disorders. *European Neuropsychopharmacology, 24*, 5–50.

Shirk, S. D., Kelly, M. M., Kraus, S. W., Potenza, M. N., Pugh, K., Waltrous, C., Federman, E., Krebs, C., & Drebing, C. E. (2018). Gambling-related cognitive distortions predict level of function among US veterans seeking treatment for gambling disorders. *The American Journal on Addictions, 27*(2), 108–115.

Vermont, J. K., & Magidson, J. (2005). *Latent Gold 4.0 User'sGuide*. Belmont: Statistical Innovations Inc.

Wallace, D., Martin, A., & Park, B. (2007). Cannabinoid hyperemesis: marijuana puts patients in hot water. *Australasian Psychiatry, 15*, 156–158.

Williams, M., & Ching, T. (2016). Transgender identity, cultural issues, and cannabis in obsessive-compulsive disorder. *AACE Clinical Case Reports, 2*, 276–277.

World Health Organization, 1992. The ICD-10 classification of mental and behavioral disorders: clinical descriptions and diagnostic guidelines. Geneva.

Affiliations

Molly Williams[1] · Arielle R. Baskin-Sommers[1,2] · Hong Xian[3] · Lorinette Wirth[3] · Jeffrey F. Scherrer[4] · Rachel A. Volberg[5] · Wendy S. Slutske[6] · Shane W. Kraus[7] · Seth A. Eisen[8] · Marc N. Potenza[2,9,10,11]

1 Department of Psychology, Yale University, New Haven, CT, USA

2 Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06519, USA

3 Department of Biostatistics, Saint Louis University, Saint Louis, MO, USA

4 Department of Family and Community Medicine, Saint Louis University School of Medicine, St. Louis, MO, USA

5 School of Public Health and Health Sciences, University of Massachusetts Amherst, Amherst, MA, USA

6 Department of Psychological Sciences, University of Missouri, Columbia, MO, USA

7 Department of Psychology, University of Nevada, Las Vegas, NV, USA

8 Department of Medicine, Washington University School of Medicine, St. Louis, MO, USA

9 Department of Neuroscience and Child Study Center, Yale University School of Medicine, New Haven, CT, USA

10 The Connecticut Mental Health Center, New Haven, CT, USA

11 The Connecticut Council on Problem Gambling, Wethersfield, CT, USA