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Comorbidity of psychiatric and substance use disorders in the United States: current issues and findings from the NESARC

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Abstract

Purpose of review—The comorbidity between psychiatric and substance use disorders remains an important phenomenon to understand, and an active area of investigation. The purpose of this review is to highlight key 2011 issues and novel findings on psychiatric and substance disorders comorbidity from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a large national survey of the US general population.

Recent findings—Topics of active investigation included the internalizing/externalizing meta-structure of common mental disorders; the 10 Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) personality disorders; the 3-year incidence and persistence of disorders; treatment of major depression; and many other topics not as easily categorized.

Summary—Meta-structure may increasingly offer a parsimonious way of addressing comorbidity, although adding new disorders adds complexity and the value of etiologic analyses utilizing broad dimensions of psychopathology rather than individual disorders is not yet fully known. Expanding the range of personality disorders beyond antisocial personality disorder appears essential in understanding the incidence and persistence of substance use disorders. Substance use disorders have low rates of treatment relative to major depression, but increase the likelihood of depression treatment among comorbid cases, a phenomenon that needs to be understood. These comorbidity studies provide much novel information, and indicate many potentially fruitful directions for new research.

Keywords

alcohol; comorbidity; drug; epidemiology; psychiatric; substance

INTRODUCTION

Early studies of the comorbidity between substance use and psychiatric disorders were primarily clinical [1,2]. However, the US Epidemiologic Catchment Area (ECA) study [3] of psychiatric disorders conducted in the early 1980s brought widespread attention to the high degree of association between psychiatric and substance use disorders in the general population [4]. This comorbidity has generated much scientific interest and an extensive

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Conflicts of interest

There are no conflicts of interest.

literature. Research on comorbidity offers avenues to better understand etiology, natural history, treatment utilization, and, ultimately, more effective treatment and prevention efforts for substance and psychiatric disorders.

Epidemiologic research on the comorbidity of psychiatric and substance use disorders in the US is greatly facilitated by the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) [5,6]. The NESARC, conducted in 2001–2002, confirmed that substance use and psychiatric disorders remain comorbid [7,8]. NESARC features facilitating comorbidity research include:

1. A sample size ($N = 43\,093$) large enough to examine the co-occurrence of rare and common disorders, and detailed features of these disorders.
2. Complete assessment of all Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) alcohol abuse and dependence criteria among drinkers, and 10 categories of illicit and prescription drugs among users of those drugs [9], ensuring complete coverage of substance-specific DSM-IV criteria and no loss of information due to potentially biasing screening procedures [10,11].
3. A prospective follow-up re-interview study of 34 653 of the original wave 1 participants (86.7%) in 2004–2005 [12], when the axis I disorders whose lifetime and 12-month prevalence were assessed at wave 1 were re-evaluated, providing information on onset, persistence and remission in the 3-year interval.
4. Disorder-specific assessment of a wide variety of treatments.
5. Assessment of early and proximal risk factors.

The NESARC has led to over 500 publications. The present study reviews 2011 NESARC research on the comorbidity of substance use and psychiatric disorders. Studies were identified by searching Pubmed for 2011 publications with the following: 'National Epidemiologic Survey on Alcohol and Related Conditions', NESARC, 43 093, or 34 653, along with alcohol, drug, substance or comorbidity. We organized this material as follows: metastructure of mental disorders; personality disorders; incidence and persistence; and treatment of major depression. In addition, less easily categorized studies were tabled for easy reference.

META-STRUCTURE OF MENTAL DISORDERS

Seminal work on the underlying meta-structure of comorbidity among common mental disorders [13] indicated that many common mental disorders can be considered indicators of latent dimensional propensities to experience two types of psychopathology: internalizing or externalizing. The externalizing dimension is characterized by antisocial personality disorder and alcohol, nicotine, and drug dependence. The internalizing dimension is often divided into two sub-dimensions, one involving distress (major depression, dysthymia, generalized anxiety) and the other involving fear (panic, social phobia, specific phobia). This meta-structure has been replicated numerous times. New 2011 NESARC studies expanded our understanding of the metastructure by examining whether the association of risk factors with individual psychiatric disorders could be better expressed in terms of the latent internalizing/externalizing dimensions, and whether cross-dimension associations between disorders could be better expressed in terms of the internalizing/externalizing dimensions, and expanded the range of disorders analyzed in the meta-structure.

Risk factors and the meta-structure

Five types of child maltreatment (emotional neglect, physical neglect, emotional abuse, physical abuse and sexual abuse) were investigated for their relationship to the internalizing

and externalizing dimensions [14]. Results showed that the association between child maltreatment and individual psychiatric disorders was fully mediated through the latent internalizing and externalizing dimensions. With regard to gender, the internalizing and externalizing meta-structure was shown to be consistent in men and women [15], with gender differences in prevalence rates of individual disorders originating from women's higher mean standing on the underlying internalizing dimension and men's higher mean standing on the externalizing dimension.

Cross-dimension associations

Alcohol dependence is clearly part of the externalizing dimension. However, a wide range of studies have shown that alcohol dependence is associated with individual internalizing disorders when these disorders are considered separately [7]. New findings showed that, once the general internalizing psychopathology dimension is accounted for, knowing whether a particular internalizing disorder is present or absent provides little additional information regarding the risk for alcohol dependence. These findings suggest that the components of internalizing psychopathology associated with alcohol dependence are shared and cumulative among common anxiety and depressive disorders [16].

New disorders considered in the meta-structure: borderline personality disorder and pathological gambling

Borderline personality disorder was shown to load on both the distress sub-factor of the internalizing dimension and the externalizing dimension [17]. Since borderline personality disorder was unidimensional in terms of its symptoms, different borderline symptoms loading on different dimensions do not explain the relationship of this personality disorder to both the internalizing and externalizing dimensions, suggesting a complex etiology. Pathological gambling loaded onto the externalizing dimension for men and women [18]. However, in women, the best model fit was obtained when pathological gambling was also allowed to load on an internalizing factor composed primarily of mood disorders.

Summary and implications

The consistency of the 2011 studies on the metastructure underlying the comorbidity of substance use and psychiatric disorders argues for investigation of etiological factors underlying the dimensions rather than the individual disorders. At the same time, adding new disorders to the analyses does not always produce the cleanly divided internalizing/externalizing structure found previously. Finally, the fact remains that some individuals manifest symptoms of one disorder but not another within a dimension. A better understanding of the reasons for these different clinical presentations within a dimension should advance our understanding of the etiology and treatment.

PERSONALITY DISORDERS

In DSM-IV, a personality disorder is defined as an enduring pattern of inner experience and behavior manifested in cognition, affectivity, interpersonal functioning, or impulse control that is inflexible and enduring and that leads to clinically significant distress or impairment [19]. Whereas the assumption of lifetime persistent course for personality disorders is challenged by studies showing symptomatic remission after several years [20,21], such remissions may occur more slowly than axis I disorders, and impairment often persists long after symptoms remit [20,21]. Therefore, personality disorders have considerable public health and clinical significance. DSM-IV includes 10 personality disorders: antisocial, avoidant, borderline, dependent, histrionic, narcissistic, obsessive-compulsive, paranoid, schizoid, and schizotypal. The NESARC included seven personality disorders at wave 1 (antisocial, avoidant, dependent, histrionic, obsessivecompulsive, paranoid, schizoid) and

three at wave 2 (borderline, narcissistic, and schizotypal) with antisocial personality disorder assessed at both waves 1 and 2. NESARC studies prior to 2011 showed considerable disability and comorbidity of substance use disorders associated across the range of DSM-IV personality disorders [5,22]. NESARC 2011 studies addressed the influence of personality disorders on the course of axis I disorders, and aspects of the cross-sectional associations of personality disorders with axis I disorders.

Influence of personality disorders on the course of substance use disorders

The 3-year persistence of alcohol, cannabis and nicotine disorders was studied among those with current diagnoses of these disorders at wave 1 [23]. Antisocial, borderline and schizotypal personality disorders consistently predicted persistent course of all three disorders. A similar design addressed the persistence of any drug disorder (cannabis, other illicit substances, and/or nonmedical use of prescription drugs) [24]. Antisocial, borderline and schizotypal personality disorders also predicted the persistence of this outcome. The course of nicotine dependence was studied by examining current nicotine dependence diagnosis at wave 2 among those with wave 1 lifetime nicotine dependence [25]. A combined personality disorder category representing the personality disorders assessed at wave 1 predicted current nicotine dependence at wave 2.

Cross-sectional associations

Antisocial personality disorder was associated with smoking with or without nicotine dependence, whereas other personality disorders were only associated with smoking accompanied by nicotine dependence [26]. The risk for most axis I psychiatric disorders, including drug and nicotine disorders, was elevated among individuals with obsessivecompulsive personality disorder [27]. A factor analytic study indicated that a general personality disorder factor and a factor representing the DSM-IV 'Cluster B' personality disorders (antisocial, borderline, histrionic and narcissistic) accounted for the covariation among personality disorders [28], and that the general personality disorder factor accounted for much of the comorbidity of personality and substance disorders.

Summary and implications

In addition to the strong cross-sectional associations of numerous personality disorders with axis I disorders shown prior to 2011, personality disorders also predict poor course of axis I disorders when comorbid (also see next section). In the area of alcohol and drug studies, a focus on antisocial personality disorder has been traditional. NESARC 2011 studies are consistent with an increasing literature indicating that consideration only of antisocial personality disorder in the study of substance use disorders is overly limited, and that a broader range of personality disorders must be addressed to better understand the etiology and course of substance use disorders.

INCIDENCE AND PERSISTENCE OF DISORDERS

Wave 2 data enabled investigators to examine the effects of comorbidity prospectively, providing clear information on the direction of effect. The first NESARC incidence study, from 2009 [12], indicated that mood (major depressive disorder, bipolar I) and anxiety disorders (panic, generalized anxiety) were significant predictors of incident alcohol and drug disorders before controlling for comorbidity, but not after. Incident substance use *per se* was not examined. Among incident mood and anxiety disorders, only alcohol dependence predicted bipolar I disorder, and this was prior to but not after comorbidity control [12]. These important findings left many questions open.

Predicting incident mood or anxiety disorders

Four 2011 studies addressed substance use, abuse or dependence as predictors of incident mood or anxiety disorders. Considering only NESARC respondents aged at least 60, substance use disorders did not predict incident mood or anxiety disorders [29]. Remaining studies considered all age groups. When alcohol dependence was operationalized dimensionally (number of positive criteria), wave 1 alcohol dependence at higher severity levels predicted incident major depression [30]. Past-year but not lifetime nonmedical use of psychoactive prescription drugs predicted incident major depression, bipolar disorder and any anxiety disorder [31]. Focusing specifically on wave 1 lifetime nonmedical opioid use, abuse and dependence, these all predicted incident major depression and generalized anxiety disorders at wave 2 [32].

Predicting incident substance use or substance use disorders

Lifetime affective and generalized anxiety predicted incident nonmedical opioid use, and lifetime panic and generalized anxiety disorders predicted incident nonmedical opioid abuse or dependence [32]. Wave 1 mood and personality disorders predicted incident drug use (cannabis and/or nonmedical use of sedatives and opioids [33]). Lifetime panic attacks, *per se*, did not predict incident alcohol or drug disorders [34]. Among NESARC respondents aged at least 60, mood and anxiety disorders did not predict incident substance disorders [29]. Wave 1 overweight or obesity predicted incident major depression, but was inversely related to the risk for incident substance use disorders [35].

Predicting persistent disorders

Studies of persistent substance use disorders are described above [23, 24]. Two 2011 studies addressed the persistence of internalizing disorders, that is, social anxiety disorder [36] and major depressive disorder [37]. Substance use disorders did not predict the persistence of either disorder.

Summary and implications

Initial 2008 findings [12] that substance use disorders were not important predictors of incident mood and anxiety disorders may have resulted from the broad categories examined. More refined measures of severity and more specific substance categories provided informative results about incident mood and anxiety disorders, suggesting utility in applying similar methods to additional substances. The consistency in two studies that mood disorders predict incident substance use (opioids used nonmedically, and a combined substance category) suggests further studies to understand this relationship better. Psychopathological predictors of incident adolescent drug use have been studied extensively, but less is known about these predictors in young and middle-aged adults. Finally, the findings that wave 1 substance use disorders did not predict the persistence of depressive or anxiety disorders at wave 2 may indicate that substance disorders are not important to the course of affective or anxiety disorders, but may also indicate that additional information about the time-varying course of the substance disorders during the follow-up needs to be taken into account. Finally, the inverse relationships between wave 1 overweight/ obesity and incident substance use disorders invite research to explain this effect at the epidemiologic, clinical or biological level. Incorporating eating disorder diagnoses, including the DSM-5 binge eating disorder diagnosis [46], may be helpful in this regard.

TREATMENT UTILIZATION FOR DEPRESSIVE DISORDERS

Improving treatment utilization for substance and psychiatric disorders is an important public health priority. Comorbidity can indicate additional need for treatment. Several 2011 studies addressed comorbidity and treatment utilization for depressive disorders.

Cross-sectional studies

Lifetime treatment for major depression was received by 61.3% of those with the disorder, higher treatment rates than those for alcohol and drug disorders [7,8]. Drug disorders were related to treatment for major depression [47]. Among those with major depression, those with 'atypical' depressive symptoms (increased sleep, eating) were more likely than others to have substance use disorders and to receive treatment for depression [48].

Prospective studies

Among those with wave 1 never-treated major depression that persisted to wave 2 [49], incident treatment for depression was associated with comorbid substance use disorders.

Summary

Treatment rates for major depression are double those for alcohol and drug dependence [7,8]. Given these treatment disparities, understanding the role of substance disorders in receiving treatment for major depression, and the role that affective and anxiety disorders may play in receiving treatment for alcohol and drug use disorders, is a high priority for further investigation.

Other 2011 findings on comorbidity

Additional 2011 NESARC comorbidity studies are summarized in Table 1. Attention deficit hyperactivity disorder, first assessed at wave 2, was associated with alcohol but not drug disorders [38]. Two studies showed associations of gambling and substance disorders [39,40]. A study showed that men were more likely than women to self-medicate for social anxiety symptoms with alcohol or drugs [41]. Post-traumatic stress disorder, also first assessed at wave 2, was associated with lifetime substance use disorders [42]. Association of trauma exposure and alcohol disorders regardless of post-traumatic stress disorder suggested that the latter did not mediate the relationship between trauma exposure and alcohol disorders [43]. Psychiatric disorders were associated with substance use and also substance disorders among users [44], suggesting that comorbidity was not mediated entirely through use. Finally, drinking circumstances (at home, to self-medicate mood) were related to alcohol and depression comorbidity [45]. A theme from many of these studies is that the field has moved beyond simple association studies, and sought more original designs to understand potential mediators and mechanisms.

CONCLUSION

The breadth of NESARC 2011 studies on substance use and psychiatric disorders illustrates continuing interest in understanding the implications of comorbidity in terms of etiology, course and treatment. Findings on personality disorder indicate the importance of addressing a broader range than just antisocial personality disorder. Work that expands our understanding of meta-structure by including new disorders into the analyses is important, as is understanding whether studies of propensities to broad dimensions of psychopathology can be informative about genetic and environmental risk factors. NESARC studies on incidence and persistence have started to utilize this unique source of information about prospectively studied natural history. The 2011 NESARC work on substance use and psychiatric comorbidity points to numerous directions for future research.

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of special interest

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KEY POINTS

- Utilizing knowledge of the meta-structure of common mental disorders, that is, broad internalizing and externalizing dimensions of psychopathology, appears to offer a parsimonious way of addressing comorbidity, although adding new disorders (e.g. borderline personality disorder; pathological gambling) adds complexity.
- Expanding the range of personality disorders beyond antisocial personality disorder to disorders such as borderline and schizotypal personality disorders appears essential to understanding the incidence and persistence of substance use disorders.
- Although treatment rates for substance disorders are only half those of major depression, cases of major depression are more likely to be treated if they have comorbid substance use disorders, a phenomenon that merits further investigation.
- Studies utilizing the two waves of the NESARC 3 years apart are beginning to be published, but much more could be done with this unique source of prospective information from a national sample.

Table 1

Additional 2011 NESARC reports on the comorbidity of psychiatric and substance use disorders

First author	Condition predicted	Predictors	Results	Subgroups included
Bernardi 2011 [38]	Substance use disorders	Attention deficit hyperactivity disorder	Attention deficit hyperactivity disorder was associated with lifetime and 12-month alcohol dependence but not other substance disorders after control for sociodemographic factors and other psychiatric disorders	All individuals participating in both waves 1 and 2
Barry 2011 [39]	Substance use disorders	Three levels of gambling disorders no gambling or low-frequency gambling, low-risk or at-risk gambling, or problem or pathologic gambling	Drug abuse or dependence and the full range of gambling severity were associated among white but not Hispanic respondents. Sub clinical gambling problems and substance use disorders were associated at a higher level among Hispanics than whites	White and Hispanic participants in wave 1
Chou 2011 [40]	Substance use disorders	Disordered (pathologic or problem) gambling	Disordered gambling was significantly associated with alcohol use disorders and alcohol dependence	All individuals participating in both waves 1 and 2
Xu 2012 [41]	Social anxiety disorder	Gender	Men were more likely to use alcohol and illicit drugs to relieve social anxiety disorder symptoms	Persons with lifetime social anxiety disorder diagnosis at wave 1
Pietrzak 2011 [42]	Substance use disorders	Post-traumatic stress disorder	Full and partial post-traumatic stress disorder was associated with lifetime alcohol and drug abuse/dependence and nicotine dependence	All individuals with full or partial post-traumatic stress disorder and trauma controls participating in both waves 1 and 2
Fetzner 2011 [43]	Alcohol abuse/dependence	Post-traumatic stress disorder, traumatic life events	Exposure to traumatic events was associated with alcohol use disorders at a similar magnitude regardless of post-traumatic stress disorder comorbidity	All individuals participating in both waves 1 and 2
Martins 2011 [44]	Substance disorders among substance users	Mood or anxiety disorder or schizophrenia	Mood and anxiety disorders were associated with substance use and also with substance use disorders among users	All individuals participating in wave 1 only
Cranford 2011 [45]	Comorbid alcohol and major depressive disorders	Drinking circumstances	Among individuals with alcohol use disorders, major depression was associated with drinking at home among men and with drinking to self-medicate depressed mood among women and men	All individuals participating in wave 1 only