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Psychiatric Comorbidity as a Function of Severity: DSM-5 Alcohol Use Disorder and HiTOP Classification of Mental Disorders

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Abstract

Background: Understanding the comorbidity of alcohol use disorder (AUD) and other psychiatric diagnoses has been a long-standing interest of researchers and mental health professionals. Comorbidity is often examined via the diagnostic co-occurrence of discrete, categorical diagnoses, which is incongruent with increasingly supported dimensional approaches of psychiatric classification and diagnosis, and for AUD more specifically. The present study examined associations between DSM-5 AUD and psychiatric symptoms of other DSM-IV and DSM-5 disorders categorically, and dimensionally organized according to the Hierarchical Taxonomy of Psychopathology (HiTOP) spectra (e.g., Internalizing, Disinhibited Externalizing).

Method: The comorbidity of AUD with other psychological disorders were examined in two independent nationally-representative samples of past-year drinkers via an initial examination in the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) Wave 2 and replicated in NESARC-III.

Results: Analyses focusing on psychopathology symptom counts organized by spectra demonstrated that greater AUD severity was associated with a higher number of symptoms across HiTOP spectra. Traditional categorical analyses also demonstrated increasing prevalence as a monotonic function of DSM-5 AUD severity gradients.

Conclusions: This study indicates that AUD and other psychiatric disorder comorbidity implies increased presence of multiple forms of psychopathology with a corresponding increased number of symptoms across hierarchical spectra. Greater AUD severity increases the likelihood of other psychopathology and, when present, “more severe” presentations. That is, on average, a given disorder (e.g., depression) is more severe when co-presenting with an AUD, and increases in severity along with the AUD.

Keywords

alcohol use disorder; comorbidity; psychopathology; dimensional models

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A large body of research has examined the relationships between alcohol use disorder (AUD) and other psychiatric conditions. This literature has demonstrated a high degree of co-occurrence between AUD and other mental disorders, with a particularly strong association between AUD/substance use disorders (SUD) and other externalizing disorders (e.g., antisocial personality; see Kessler, 2004 for review). From a clinical and public health perspective, the impact of comorbid conditions on individual outcomes is substantial (e.g., Cohen et al., 2007; Grant et al., 2015; Plana-Ripoll et al., 2019), yet relatively little research has examined the *severity* of comorbid psychiatric disorders across psychopathology domains (e.g., externalizing, internalizing) with AUD. The ability to assess the extent to which the comorbid disorders (e.g., symptom count, severity) covary with AUD is limited given that most studies examining comorbidity rely on categorical representations of the disorders, consistent with the diagnostic systems that were in place at the time of the research (e.g., previous versions of the DSM). That is, the traditional dichotomous, categorical approach to comorbid diagnoses obscures simple but clinically important questions related to severity. For example, is "freestanding" depression more or less severe than depression comorbid with an AUD, and is depression accompanying more severe AUD more severe than depression accompanying milder forms of AUD? These limitations may be addressed with dimensional representations of both AUD and related psychopathology.

Comorbidity of AUD with Psychiatric Disorders

There are a few primary findings from extant AUD comorbidity research. First, there is an increased likelihood of having AUD (yes/no) given the presence of another categorical disorder, and vice versa (e.g., Regier et al., 1990). Next, an increased number of categorical disorders are endorsed in the context of alcohol abuse and dependence (e.g., Merikangas et al., 1998). Additionally, there is considerable comorbidity between AUD/SUD and personality disorders (PDs; Trull et al., 2010). Finally, certain classes of psychopathology are associated with increased risk for AUD, such as anxiety and mood disorders (e.g., Kessler et al., 2003; Swendsen et al., 1998) and externalizing disorders (e.g., Kessler et al., 2004). Of mood disorders, bipolar disorder in particular demonstrates an increased risk for AUD (e.g., Kessler, 2004; Swendsen & Merikangas, 2000). Of psychiatric conditions, AUD's comorbidity with externalizing psychopathology is perhaps most robust (e.g., Kessler et al., 2003, 2004). This comorbidity may be due, in part, to shared features among AUD and other forms of externalizing, such as common personality correlates (Trull & Sher, 1994), shared genetic etiology (e.g., Kendler et al., 2012; Krueger et al., 2000; Slutske et al., 2000), bidirectional associations of AUD and other psychopathology (e.g., Sher, 1991; White et al., 2011), and other alcohol-related processes, such as niche-picking (Park et al., 2009).

Severity in the Context of Comorbidity.

As described earlier, establishing comorbidity in research studies and/or clinical settings generally considers the presence (v. absence) of a discrete, dichotomous AUD diagnosis with another discrete disorder. Although categorical diagnoses are a reasonable starting point to establish comorbidity, using categories to characterize the covariation of these constructs can be limiting if the constructs themselves are graded or dimensional. Examining the

associations between AUD and other psychiatric disorders dimensionally can provide valuable information regarding the severity of the disorders. One way to begin exploring this is through investigations of comorbidity at a more granular level (e.g., signs/symptoms, severity).

Although not limited to AUD, severity-graded conceptualizations of alcohol use have been included in comorbidity investigations. A cross-cultural epidemiological study of alcohol and substance use (including abuse and dependence categories from the Diagnostic and Statistical Manual, third edition-revised [DSM-III-R]) found that the likelihood of being diagnosed with a categorical psychiatric disorder (e.g., mood, antisocial) increased linearly as alcohol involvement progressed, using the following spectra for alcohol use (ranging from least to most severe): lifetime history of alcohol use, alcohol problems (defined as one or more symptoms of DSM alcohol abuse), and DSM alcohol dependence (Merikangas et al., 1998). Other substance use followed this same pattern. Further, although 'worsening' groups were associated with a greater *number* of other psychiatric disorders, this effect was relatively small for alcohol, at least compared with other substance use (Merikangas et al., 1998). Other large-scale studies have identified the higher likelihood of mood and anxiety disorders for those with alcohol dependence than alcohol abuse (Grant & Harford, 1995; Grant et al., 2004), which appears to be due to a greater number of symptoms required for alcohol dependence than for alcohol abuse as opposed to the different criteria sets for dependence versus abuse (Vergés et al., 2010).

More recent work (Grant et al., 2015) has examined DSM-5 AUD comorbidity using a severity-graded perspective (i.e., mild, moderate, severe) for AUD and categorical representations of other psychiatric disorders (e.g., presence or absence of disorder). AUD diagnoses and severity were associated with higher odds for some categorical DSM-5 disorders (e.g., drug use disorder, BPD), and showed no effect (e.g., agoraphobia) or more modest or mixed effects for other disorders (e.g., anxiety) across AUD severity levels and timeframes (i.e., lifetime, past year AUD; Grant et al., 2015). Given that the other psychiatric disorders were represented categorically, limited information about the severity of those co-occurring disorders was provided. Collectively, these studies demonstrate the importance of examining AUD dimensionally to reveal associations obscured by categorical representations of AUD. There is increased clarity regarding comorbidity, such that at a more 'severe' place along the AUD spectrum (e.g., dependence v. abuse), the odds increase for having another categorical psychiatric disorder.

What is often missing from these studies of comorbidity that consider alcohol-related pathology from a dimensional perspective is a corresponding dimensional perspective of co-occurring psychopathology, which may mask the degree of covariation among conditions. For example, persons who do not meet the threshold for a diagnosis (e.g., borderline personality disorder) may still endorse features (e.g., impulsivity) that are highly relevant to comorbidity given shared features or potential impact on AUD, or vice versa. Expanding such investigations to include a more nuanced perspective (e.g., severity gradients, symptom counts regardless of diagnosis) can improve our understanding of these complex relationships. Using categorical diagnoses, previous comorbidity investigations have identified that although comorbidity of AUD with other disorders was common, the

associations were attenuated when accounting for other psychiatric disorders, pointing to both unique and shared factors across disorders that may provide incremental information to explain these associations (Hasin et al., 2007). Continued work focused on the dimensionality of psychopathology is pertinent to continuing AUD comorbidity investigations.

Dimensional Psychopathology

The established limitations of categorical classifications of psychiatric disorders (e.g., heterogeneity within diagnostic categories, lack of coverage, arbitrary cut-offs, diagnostic co-occurrence; Krueger et al., 2005; Trull & Durrett, 2005) have contributed to the development of dimensionally-oriented diagnostic classification systems. Dimensional approaches have a strong empirical basis (Krueger et al., 2018) and are increasingly incorporated into diagnostic systems. For instance, DSM-5 (American Psychiatric Association, 2013) has initiated a transition toward dimensional approaches (e.g., autism spectrum disorder, AUD, SUDs), and the International Classification of Disease, Eleventh Revision (ICD-11; World Health Organization, 2018) has incorporated dimensional aspects of classification, such as including severity ratings within disorders (e.g., PDs) and grouping disorders based on common factors (e.g., multiple anxiety disorders clustered together given their commonality of a ‘fear’ component; Reed et al., 2019).

The Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017) is a recently developed psychopathology system spanning spectra of DSM-5 disorders (e.g., internalizing). HiTOP organizes traditionally discrete psychiatric phenomena within an empirically-derived hierarchical framework based on increasing degrees of covariation. This model begins with signs and symptoms (e.g., dysthymia, worry) at the lowest level of the hierarchy, which coalesce into symptom components/maladaptive traits (e.g., negative emotionality), subfactors (e.g., fears, distress), which then coalesce into broader spectra (e.g., internalizing) based on their degree of covariation. In this way, the HiTOP structure organizes psychopathology based on observed commonalities across symptoms (both phenotypic and genetic covariation; Kotov et al., 2017), inherently leveraging long-observed comorbidity among discrete psychiatric conditions.

A specific example of the HiTOP structure is provided here to demonstrate how an individual presentation may fit into the structure of the Disinhibited Externalizing spectrum. At the lowest level (signs and symptoms), an individual may endorse specific features (e.g., blurts out answers, interrupts/intrudes on others, runs away from home), that share in common a broad liability for impulsivity; within the HiTOP model, impulsivity might reflect a broader symptom component/maladaptive trait. Along with other symptom components/ maladaptive traits (e.g., irresponsibility, risk taking, rebelliousness), impulsivity is then subsumed under the broad disinhibited and antagonistic externalizing spectra. Because it reflects the intersection of disinhibition and antagonism, ADHD is subsumed within both disinhibited and antagonistic externalizing, along with ASPD, conduct disorder, oppositional defiant disorder, and the like. Other disorders within disinhibited externalizing only (i.e., not in antagonistic externalizing) include substance-related disorders (including AUD), whereas

the antagonistic externalizing spectrum includes narcissistic, borderline (also in internalizing), histrionic (also in detachment), and paranoid PDs.

Present Study

A renewed and novel examination of AUD's comorbidity with other psychiatric conditions is necessary given the widespread adoption of dimensional conceptualizations of psychiatric conditions, changes to AUD through the transition to DSM-5, and the larger overhaul of our psychiatric classification system. The former, in particular, alters the way we view comorbidity (Forbes et al., 2016). Therefore, the present investigation aimed to examine AUD comorbidity from the lens of more current, dimensional approaches to psychopathology and with a focus on severity (i.e., characterized as symptom count). Broadly, the goals of the present study were to examine the comorbidity of DSM-5 AUD using traditional categorical approaches and current dimensional approaches (i.e., HiTOP-organized psychiatric symptoms; Kotov et al., 2017) to conceptualize other psychiatric disorders in two separate population-wide samples collected via the National Epidemiological Survey on Alcohol and Related Conditions (NESARC Wave 2; NESARC-III).

There were two primary aims of the current study, specifically to examine: (1) AUD and DSM disorder comorbidity from a traditional categorical perspective; (2) AUD comorbidity with HiTOP-organized symptoms of DSM psychopathology represented dimensionally. The first aim of this study was achieved through the examination of the comorbidity of DSM-5 AUD with four single, categorical disorders (one per HiTOP spectra) to first illustrate the baseline categorical associations. This aim also included a snapshot of symptom count patterns of a given categorical disorder (subset on individuals with that disorder), across AUD severity gradients (no AUD, mild, moderate, severe AUD). This aim largely aligns with previous examinations of comorbidity (including those using NESARC, e.g., Hasin et al., 2007; Trull et al., 2010) but expands them to examine the extent of the psychiatric comorbidity with AUD severity. Given this goal and the extant literature examining comorbidity categorically, only one disorder from each spectrum was included to illustrate the categorical associations at a basic level (see Supplemental Materials for all other categorical disorder associations). This aim is included to illustrate the differences of examining AUD comorbidity from a categorical and dimensional approach.

The second aim of the study was to examine the association between HiTOP-organized psychiatric symptoms and AUD severity diagnostic groups. The presence and "severity" of psychiatric diagnosis were represented as symptom counts within the HiTOP spectra, integrating a dimensional approach and leveraging covariation among psychiatric conditions to understand comorbidity. It was hypothesized that increasing AUD severity would be associated with increased "severity" (i.e., larger number of symptoms) of other psychiatric disorders, across spectra.

The inclusion of a categorical and dimensional representation of other psychopathology highlights the incremental utility of a dimensional approach beyond that of strict categorical associations. For example, simply finding that the mean symptom count of associated

diagnoses or spectra increases as a function of AUD severity fails to resolve if this reflects more individuals being affected (e.g., increasing numbers of individuals above a diagnostic threshold), more severe presentations of those above a diagnostic threshold, more individuals experiencing subthreshold symptomatology, or some combination of these. Focusing on only one approach or the other would not allow for distinguishing between the mean symptom level of all individuals affected (e.g., have symptoms but not necessarily a disorder) and those who are "more affected" (e.g., have a categorical disorder, thus, implying they have more symptoms).

Materials and Methods

Samples

The current study used two independent, nationally representative samples (NESARC), which were collected as part of a large initiative by NIAAA. Two independent samples were used in order to test the replication of findings. The NESARC studies were conducted to examine general population characteristics and trends of alcohol use disorder and associated comorbidities (e.g., psychological disorders) and behaviors (e.g., binge drinking). The first sample included data from NESARC Wave 2, and the second sample comprised data from NESARC-III, both of which were sampled to represent a noninstitutionalized, adult population in the United States. Additional information on the sampling strategies and methodologies for the samples can be found in the Source and Accuracy Statements for NESARC Waves 1 and 2 (Grant et al., 2003, 2005) and NESARC-III (Grant et al., 2014).

Participants who endorsed drinking in the past 12 months were retained for the present study analyses; thus, all information included below is specific to "past-year drinkers" (i.e., individuals who endorsed having at least one alcoholic beverage in the past 12 months). Further, given the epidemiological nature of the study, the current study used survey weighting procedures to derive accurate population estimates, based on an accurate representation of the US population. Demographic variables presented here represented weighted estimates.

NESARC Wave 2 (2004–2005; Grant et al., 2004).—NESARC Wave 2 (N = 34,653) is a follow-up for participants that had previously participated in NESARC Wave 1 (2001–2002; N = 43,093) and only those who completed both waves (83% retention from Wave 1) and endorsed past year drinking (22,177; 64%) were included in these analyses. Wave 2 weights, which account for the attrition from Wave 1 to 2, were used in the analyses. NESARC Wave 2 interviews (AUDADIS-IV; see Measures) were collected by the Census Bureau, under the direction of NIAAA (Grant et al., 2005). NESARC Wave 2 symptoms were used with some exceptions (see Measures), in which Wave 1 symptoms were used to capture disorders that were not assessed at Wave 2. NESARC Wave 1 did not include an assessment of AUD craving; therefore, Wave 1 was not included as a sample in order to retain consistent DSM-5 AUD composition across samples in the present study. Weighted estimates of the demographic variables for this sub-sample are as follows: 74.99% White; 10.64% Hispanic; 9.16% Black; 3.22% Asian; 1.99% American Indian/Alaska Native; 52.08% male; ages ranging from 20 to 90 years (M = 45.86 years).

NESARC-III (2012–2013; Grant et al., 2015).—NESARC-III is an independent, cross-sectional sample, with similar original study aims as NESARC Waves 1 and 2. NESARC-III interviews (AUDADIS-5; see Measures) were conducted by trained interviewers (Grant et al., 2014). Of NESARC-III participants (N = 36,309), 71% (N = 25,778) endorsed past-year drinking, and were included in the present study. Weighted estimates of the demographic variables for the subset are as follows: 68.50% White; 14.24% Hispanic; 10.72% Black; 4.90% Asian; 1.58% American Indian/Alaska Native; 50.72% male; ages ranging from 18 to 90 years (M = 43.41 years).

Measures

Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV; Grant et al., 2001).—The AUDADIS-IV (used in NESARC Wave 2) is a structured, computer-assisted interview that assesses alcohol abuse and dependence symptoms, alcohol consumption, a number of DSM-IV psychiatric conditions, and other psychosocial functioning indicators. Although DSM-IV alcohol abuse and dependence were assessed in the AUDADIS-IV, craving was also assessed, allowing for the construction of DSM-5 AUD severity groups that were equivalent (i.e., both samples had the possibility of 11 AUD criteria) to the second sample (NESARC-III).[1] This was also the case for SUDs (i.e., Cannabis Use Disorder and Opioid Use Disorder) included in the substance use subfactor in the composition of the Disinhibited Externalizing spectra. Table 1 includes the disorders whose symptoms were represented within each spectrum (Kotov et al., 2017) in the present study, as well as the respective intervals of assessment. For example, each social phobia symptom counted toward the Internalizing sum if endorsed “since the last interview” (from Wave 1 to 2), whereas each ADHD symptom was counted toward the Disinhibited Externalizing sum if endorsed “prior to age 18”. The Wave 1 AUDADIS-IV was used to pull forward symptoms of ‘lifetime conditions’ assessed at Wave 1, where applicable (e.g., conduct disorder, PDs; see Table 1).

Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5; Grant et al., 2011).—The AUDADIS-5 (used in NESARC-III) is a structured interview that assesses DSM-5 AUD symptoms, alcohol consumption and consequences, DSM-5 psychiatric disorders, and other psychosocial functioning factors. The AUDADIS-5 is similar to AUDADIS-IV, but assesses DSM-5, rather than DSM-IV disorders. Reference Table 1 for disorders included in the composition of each spectrum for the present study.

Construction of HiTOP Spectra and AUD Groups

Criteria counts represent symptom-based DSM criteria, and do not include other exclusionary and/or differential diagnosis criteria (e.g., rule out due to medical condition). In the case of AUD, there are 11 possible criteria, which are, in some cases, calculated based on a number of symptoms. For example, the DSM AUD withdrawal criterion has a number

[1]The craving criterion was similarly assessed across samples. Both samples include a lower threshold item (strong desire or urge) and a higher threshold item (wanted a drink so badly that I couldn’t think of anything else). The lower threshold item in AUDADIS-IV (Wave 2) asked about a “strong desire” whereas the AUDADIS-5 (NESARC-III) asked about a “strong desire *or urge*”.

of possible symptoms (e.g., relief from drinking, restlessness, seizures). If an individual endorsed relief and/or two or more of the other withdrawal symptoms, the withdrawal criterion would count toward the AUD sum. Given that the focus is on AUD severity groups, the 11 criteria were used for the AUD criteria counts across samples. For other psychiatric disorders, the same process for creating criteria counts was applied, such that symptom-based DSM criteria, and not the exclusionary criteria were used toward the count, to represent distinct criteria. When DSM-5 symptoms are grouped, yet distinct (e.g., PTSD intrusion symptoms), the individual symptoms are used in the count. For simplicity, the counts for AUD, spectra, and individual categorical disorders will be referred to as "criteria" and "criteria counts" throughout the manuscript.

AUDADIS psychiatric criteria were organized into spectra based on the HiTOP structure (Kotov et al., 2017). Criteria across all represented disorders within a given spectrum were summed to create an overall spectrum score, which was converted to a standardized z-score. This process was repeated for each spectrum within each sample, resulting in four dependent variables (z-scores) for NESARC Wave 2 (i.e., Internalizing, Disinhibited Externalizing, Antagonistic Externalizing, Detachment), and three for NESARC-III (i.e., Internalizing, Disinhibited Externalizing, Antagonistic Externalizing). There were no PDs assessed in NESARC-III that fell within the Detachment spectrum; thus, Detachment was not included in the NESARC-III replication sample. It should be noted that not all HiTOP disorders within a given spectrum were assessed in NESARC. For example, eating disorders were not assessed in NESARC Wave 2 and thus, are not included in the calculation of the Internalizing spectrum for NESARC Wave 2. Somatoform and Thought Disorder spectra were not included for either sample given the lack of coverage in the AUDADIS.

AUD diagnostic groups were calculated using DSM-5 severity gradients in both samples. AUD severity groups were computed using a conservative strategy that can handle limited missing data and only assigns a severity group for cases in which the missing data for a given criterion does not impact the certainty of severity level assignment (PhenX Toolkit, n.d.). For example, if an individual positively endorsed two of 11 AUD criteria, and were "missing" (i.e., no response recorded) for two other criteria, the AUD severity level would be coded as "missing". This is due to the fact that based on the true and unknown response for the two missing criteria, that individual could be classified as a 'mild' or 'moderate' AUD diagnosis. However, if an individual positively endorsed six of 11 AUD criteria and were missing for two other criteria, the AUD severity level would be coded as "severe", rather than "missing" given that regardless of the true response for the missing items, the severe AUD threshold would be met. The other diagnostic sums (criteria counts) were calculated so that endorsement of each criterion would equate to one point toward the sum, and persons who did not endorse any of the relevant screening items for a given disorder were given a "0" for that disorder sum.

Analytic Strategy

Per the present study aims, single disorder illustrations with one disorder from each spectrum (i.e., generalized anxiety disorder [GAD], ASPD, BPD, avoidant PD) were included to demonstrate the associations between AUD and other disorders. First, a more

traditional examination of comorbidity (i.e., categorical approach) was used to assess the relationship between an AUD diagnosis (diagnose or not) and another psychiatric disorder (diagnose or not) via two measures of association appropriate for use with binary variables (i.e., phi coefficients [r_ϕ], tetrachoric correlations [r_{tet}]).[2] The prevalence of the single disorders within the diagnostic AUD severity groups were also examined. SAS 9.4 (SAS, 2013) PROC FREQ (r_ϕ and r_{tet}) and SURVEYFREQ were used to examine the analyses described thus far. Analysis of Variance (ANOVA) was used to examine the differences in disorder criteria counts between AUD groups (i.e., none, mild, moderate, severe) using the REGRESS procedure in SUDAAN 11.0.03 (SAS 9.4) to derive accurate standard errors (using the Taylor series linearization method) in data with complex survey designs (e.g., accounting for clustering, stratification, and weighting). These categorial disorder analyses were specifically conducted within a subset of the sample that diagnosed with the respective disorder. For example, within each sample, the data were subset on individuals that diagnosed with GAD, and then differences in symptoms of GAD were examined (conditional marginal means, accounting for sex, age, and race) across the four AUD groups (no AUD, mild AUD, moderate AUD, and severe AUD) with the REGRESS procedure. For the dimensional spectra analyses, the REGRESS procedure was used to examine differences in standardized spectra scores (z-score sums of criteria) across AUD diagnostic severity groups. Omnibus, linear, and AUD group effects were examined for each individual disorder and each spectrum. Post hoc pairwise comparisons of AUD groups were examined for single disorder and spectra criteria count means. Age (curvilinear representation), race/ethnicity, and sex were included as covariates in all REGRESS analyses. Wave 2 weights were used in the estimation procedures for the NESARC Wave 1/2 sample (which accounts for attrition across Waves 1 and 2) and NESARC-III weights for the NESARC-III sample.

Results

Categorical and Single Disorder Illustration Analyses (Aim 1)

Four categorical disorders (i.e., one from each spectrum) were included here for illustrative purposes. Measures of association between the binary DSM-5 AUD diagnostic variable and binary diagnostic variables of the single disorder illustrations demonstrated small to moderate effects across samples: AUD with GAD (Wave 2: $r_\phi = 0.07$; $r_{tet} = 0.21$; NESARC-III: $r_\phi = 0.05$; $r_{tet} = 0.12$); AUD with BPD (Wave 2: $r_\phi = 0.17$; $r_{tet} = 0.39$; NESARC-III: $r_\phi = 0.20$; $r_{tet} = 0.39$); AUD with ASPD (Wave 2: $r_\phi = 0.11$; $r_{tet} = 0.28$; NESARC-III: $r_\phi = 0.15$; $r_{tet} = 0.36$); AUD with Avoidant PD: (Wave 2: $r_\phi = 0.05$; $r_{tet} = 0.17$). The NESARC Wave 2 results were largely consistent with the odds ratios in Hasin and colleagues (2007) using past-year DSM-IV AUD. The prevalence of these (and other) categorical disorders within the overall sample, within AUD diagnostic (diagnose/not) and severity groups are included in Supplemental Table 1. In general, increased AUD severity was associated with a higher prevalence of other disorders.

Table 2 displays the mean number of other psychiatric criteria for each categorical disorder illustration across AUD groups, when subset on individuals with the respective disorder.

[2]To the extent that each disorder reflects an underlying continuum, the tetrachoric correlation is a better estimate of the associations; however, if the disorders are truly discrete, the phi coefficient is a better estimate.

There was a significant linear effect of criteria count across AUD groups within each diagnostic group ($p < 0.05$), though the effect was less pronounced for GAD compared to other disorders. Generally, the number of other psychiatric criteria was significantly higher for persons in the severe AUD group compared to the no AUD or mild AUD groups. *Taken together, this suggests that not only were these disorders largely more prevalent in those with severe AUD, but the comorbid conditions were themselves more severe as assessed by criteria count.*

Spectra (Aim 2)

The overall ANOVAs across the AUD diagnostic groups (Table 3) were significant for each HiTOP spectrum. Specifically, the omnibus tests for the Internalizing spectrum were significant in NESARC Wave 2 ($Wald\ F(10,65) = 173.04$, $p < 0.001$; $R^2 = 0.097$) and NESARC-III ($Wald\ F(10,113) = 141.40$, $p < 0.001$; $R^2 = 0.083$); for Disinhibited Externalizing in NESARC Wave 2 ($Wald\ F(10,65) = 253.67$, $p < 0.001$; $R^2 = 0.172$) and NESARC-III ($Wald\ F(10,113) = 351.62$, $p < 0.001$; $R^2 = 0.144$); for Antagonistic Externalizing in NESARC Wave 2 ($Wald\ F(10,65) = 273.18$, $p < 0.001$; $R^2 = 0.160$) and NESARC-III ($Wald\ F(10,113) = 257.99$, $p < 0.001$; $R^2 = 0.132$); and for Detachment in NESARC Wave 2 ($Wald\ F(10,65) = 7.15$, $p < 0.001$; $R^2 = 0.006$).

Internalizing, Disinhibited Externalizing, and Antagonistic Externalizing spectra demonstrated monotonic associations with AUD, such that as AUD severity increased levels, spectra means increased (Table 3). Conditional marginal means and standard errors across all spectra and samples are presented in Table 3 (overall models). Given the potential for sex differences across spectra (e.g., females likely higher in internalizing disorders; e.g., Kessler et al., 1994), a secondary set of analyses examined the models by sex, which demonstrated similar results as the combined samples (Table 4).[3] The overall model, linear effect, and AUD group estimates were significant in all models (combined and by sex) for all spectra, and in both samples (NESARC Wave 2 and NESARC-III), with the exception of the Detachment spectrum in the female sample, in which the overall effect was significant; however, the AUD group and linear effect were not (Table 4).

Post hoc pairwise contrasts for main analyses (Table 3) demonstrated that within the Internalizing, Disinhibited Externalizing, and Antagonistic Externalizing spectra, the spectra means were different at each AUD severity level (none, mild, moderate, severe). Specifically, the means increased as AUD severity levels increased. Models broken down by sex demonstrate a similar pattern, such that the more severe AUD groups are significantly different, in most cases, than the no AUD or less severe AUD groups (Table 4).

[3]We also conducted models examining the AUD severity group by sex interaction (predicting each spectrum separately). Due to the complex survey design, SUDAAN was used to account for singleton clusters. However, SUDAAN does not produce interaction term estimates in these models, therefore, SAS PROC SURVEYREG was used both with and without the “nocollapse” option (default collapses singleton clusters, influencing the denominator degrees of freedom). This option influences the significance tests; however, the simple effects demonstrated the same pattern. For the Internalizing spectrum, sex was a significant moderator in both NESARC Wave 2 and NESARC-III. Females were higher in internalizing for all AUD groups, and this effect was pronounced in the severe AUD group. The Disinhibited Externalizing symptom mean was significantly higher for males at each level, though the interaction term was not significant in either sample (with the exception of the nocollapse option in W2). Sex was a significant moderator in NESARC-III, but not NESARC Wave 2 for Antagonistic Externalizing. In general, males had higher Antagonistic Externalizing mean scores in the no AUD group; though males and females had similar scores in the AUD severity groups (mild, moderate, severe). Sex was not a significant moderator in the models examining the Detachment spectrum.

The Detachment spectrum exhibited a similar, yet slightly different pattern of associations with AUD severity, such that compared to the other spectra, Detachment (assessed in NESARC Wave 2 only) means did not differ significantly across all AUD levels. The overall model was significant, as noted earlier, but the total effect and linear contrast (Table 3) were relatively small (i.e., $R^2 = 0.006$), as were the conditional marginal means for each of the AUD severity gradients. Post hoc pairwise comparisons demonstrated that the spectra means were significantly different across larger gradations of AUD (i.e., no v. severe AUD; mild v. severe AUD), but were not significantly different among adjacent gradations of AUD severity (e.g., no v. mild AUD; moderate v. severe AUD). Models broken down by sex demonstrate that this effect is likely driven largely by males, as these results followed a similar pattern (Table 4). For females, detachment spectrum means did not significantly differ by AUD severity.

Discussion

Across two samples of large epidemiological data (NESARC Wave 2, NESARC-III), there was a positive association between AUD severity gradients and number of psychopathology criteria organized in terms of spectra within the HiTOP system (Kotov et al., 2017), a hierarchical framework of psychopathology. Specifically, a more severe AUD diagnosis was associated with a significantly higher number of psychopathology criteria. This effect was demonstrated for Internalizing, Disinhibited Externalizing, and Antagonistic Eternalizing spectra across two samples, and for the Detachment spectrum in one sample, though the Detachment effect was weaker. Standardized spectra means were the highest for the Disinhibited Externalizing spectrum, followed by Antagonistic Externalizing, Internalizing, and then Detachment spectra. These findings indicate that AUD comorbidity implies increased severity, as evidenced by a greater number of criteria. This was also the case when examined by sex, with few exceptions (e.g., Detachment spectrum). Although males and females demonstrated different mean levels within a spectrum (e.g., females had higher means across AUD groups on Internalizing spectrum; males higher on Disinhibited Externalizing), the patterns were similar given that the number of criteria increased as AUD severity increased.

The same pattern of findings was illustrated with criteria of single disorders, four of which were selected as illustrations of each HiTOP spectra. Specifically, the single disorder illustrations of criteria count demonstrated that within subsets of individuals with a respective psychiatric diagnosis (e.g., BPD), the number of psychiatric criteria endorsed was greater for those with severe AUD compared to other, more mild AUD groups. These findings further highlight the association between a greater number of criteria as AUD severity increases.

Although AUD's comorbidity with other forms of psychopathology is well documented, rarely has the focus been on severity. It is evident that higher AUD severity is associated with greater likelihood of other psychiatric disorders (e.g., Supplemental Table 1), however this type of examination also obscures the dimensional nature of the other psychiatric diagnoses. Investigating the extent of symptomatology (e.g., number of DSM symptoms/criteria) encompassed within a comorbid diagnosis adds incremental information, such that

someone endorsing a fewer number of criteria would be distinguished from someone endorsing a higher number of criteria, and arguably more severe psychopathology.

Most examinations of comorbidity focus on pairings of individual disorders, rather than on a broad array of psychopathology. Although some studies have examined comorbidity among classes of disorders (e.g., mood) with AUD, rarely have studies examined individual criteria or symptoms of single disorders that are then grouped according to similar dimensions of psychopathology (e.g., symptoms across externalizing disorders). An advantage of the present study includes information regarding categorical associations within specific domains of psychopathology, and the inclusion of individual symptoms/criteria that were largely free from categorical restraints (i.e., disorder threshold not necessary) and placed within a common-features hierarchical framework. Therefore, rather than examining only cases above and beyond a certain number of criteria, as with a strict categorical diagnostic system, this study represented individuals across a spectrum: those endorsing a subthreshold number of criteria and those endorsing a more substantial number, both within and across related disorders.

Overall, the current results suggest that an AUD diagnosis not only augurs risk for a range of comorbid conditions, but also for more severe variations of those conditions. That is, our findings suggest that, all other things being equal, the severity of a condition (e.g., represented as symptom criteria counts) when accompanied by AUD tends to be greater than when a condition appears without co-occurring disorders. Although this is not as apparent for every categorical disorder examined (e.g., GAD), the patterns across psychopathology are largely consistent. Further, the extent of severity for the psychiatric diagnosis tends to increase with greater AUD severity. Based on the literature, it is probable that the covariation among AUD severity and HiTOP spectra is likely due to shared etiological mechanisms, directional associations from AUD to the co-occurring condition or the reverse, and transactional associations. Regardless of the causal processes, our findings using cross-sectional samples highlight what is lost by traditional nominal classification, that is the increase in psychiatric symptoms with increasing AUD severity, irrespective of diagnosis.

With respect to clinical implications, studying and using transdiagnostic treatment approaches for substance use and other disorders is becoming more common. Transdiagnostic approaches aim to target key mechanisms (e.g., affect dysregulation) common across disorders, rather than focusing on the treatment of categorical diagnoses per se (e.g., Barlow et al., 2004; Steele et al., 2018). Transdiagnostic approaches are also consistent with literature on shared etiologies and the influence of personality traits (e.g., neuroticism) on the association between AUD and psychopathology and/or psychological distress (e.g., Jackson & Sher, 2003; Kotov et al., 2017). The present study reinforces prior work demonstrating the strength of the associations between forms of psychopathology and AUD, providing further evidence for the potential utility of transdiagnostic-oriented treatments. Increased severity also has important clinical implications, such as the relevance of more intensive interventions for persons diagnosed with comorbid conditions. The current study suggests that the severity of conditions (e.g., higher criteria/symptom counts) other than AUD may be present as well with more severe AUD presentations. Although dimensional models such as HiTOP imply such relations, rarely has this implication been

described and examined. Such a perspective highlights the potential value of considering general psychopathology as dimensional.

The inclusion of both categorical and dimensional approaches allows for a clearer picture of what may be lost when only examining a categorical association between AUD and another disorder. Although it is notable that the prevalence of other disorders (e.g., MDD, BPD) is higher in the presence, rather than absence of AUD, this traditional categorical approach may overlook intricacies of these associations. The additional categorical analyses (e.g., Table 2) and dimensional approaches (Tables 3 and 4) provide a nuanced assessment of these associations, highlighting the relevance of severity of conditions. As in various areas in clinical medicine, establishing a diagnostic threshold for a condition (e.g., diabetes, hypertension) provides useful information for estimating prevalence, determining when treatment is indicated, and establishing treatment goals. However, there is considerable variation in the degree of supra-threshold severity that carries additional information about need for treatment and the probability of complications. Dimensional approaches facilitate this more finely resolved approach to assessing psychopathology.

Limitations

There are a few notable limitations in this examination of comorbidity. First, though in the spirit of a dimensional framework, the construction of the HiTOP spectra variables are simply summations of criteria/symptoms that originated from DSM-IV and DSM-5 categorical diagnoses. Any limitations of these symptoms themselves, or the assessment of them, are then retained in the present study investigation. For example, there is considerable variation in how different diagnostic interviews operationalize diagnostic criteria and a relatively severe (from an item response theory perspective) criterion in one diagnostic interview could be a relatively mild criterion in another (Lane, Steinley, & Sher, 2016).

Therefore, this introduces a potential limitation of the use of diagnostic criteria counts as a proxy for syndrome or spectrum severity in the present study, such that it ignores the severity of individual criteria and/or symptoms. Recent research has addressed similar concerns. For instance, Boness and colleagues (2019) recently demonstrated how individual AUD criteria could be operationalized with multiple items to refine severity at the symptom level which, when aggregate, can refine severity at the syndrome level. Grading the severity of symptoms is common in various areas of clinical medicine such as in evaluating newborn health (e.g., APGAR score) or depth of coma (e.g., Glasgow Coma Scale). Grading symptom severity and comorbid symptomatology may have implications for refining spectrum level assessment.

Related to the previous point (i.e., symptoms included are based on categorical diagnoses), constructing spectra from the perspective of a full dimensional system could produce different results as the ‘input’ (e.g., symptoms, disorder features) may comprise different structures or content than DSM-5. It is worth noting that there are measures (Kotov et al., 2017) that organize psychopathology into broad dimensions (e.g., Inventory for Anxiety and Depression Symptoms; Watson et al., 2012) as opposed to categorical diagnoses. Dimensional measures of extant disorders/symptoms may produce better estimates of the types of associations reported here. Similarly, the inclusion of relevant dimensional

constructs within spectra construction (e.g., neuroticism, impulsivity), would be beneficial in that it would align with dimensional conceptualizations of interest, and not rely on DSM-5 symptoms, but rather focus on broad and robust constructs/traits of each spectra (e.g., Kotov et al., 2017; Widiger et al., 2019). An extension of the present study using that approach may also speak to potential mediating connections of the spectra with AUD (e.g., negative urgency).

Second, the methodological design of NESARC included screening/skip-out items within the diagnostic categories, such that if a person did not endorse initial screening items, the interviewer would not administer the full module. This presumes that some symptoms are at the core of, or necessary for, the disorder being assessed within the categorical system. For example, if an individual did not endorse anhedonia or depressed mood (key symptoms of major depressive episodes [MDE]), that individual would not receive the remainder of the items and therefore, for the purpose of this study, would receive “0” MDE criteria toward the Internalizing spectrum count. Although congruent with the diagnostic structure of DSM MDE, other symptoms or features of the disorder (e.g., fatigue, hypersomnia/insomnia), may have been present, but were entered as absent toward the symptom count. This can limit our ability to garner spectra counts encompassing the features that are often relevant across disorders of similar etiologies (e.g., anxiety and depression), but occur outside of a traditional categorical diagnosis. Further, this may contribute to restriction of range for sum scores (e.g., spectra, individual disorders), thus restricting the overall variance.

Similarly, when drawing conclusions about the spectra overall, caution should be taken in making broad assumptions as not all disorders represented in the original HiTOP spectra were included (e.g., sexual disorders within Internalizing) given lack of coverage in NESARC. It is anticipated that inclusion of additional disorders would enhance the coherence of the dimensions/spectra and therefore, also increase relevant indicators. This would then, in turn, likely increase reliability and strengthen the findings. This is hypothesized given the nature of the HiTOP spectra, in which disorders are grouped based on commonalities. Future research should examine the spectra that were not represented here (e.g., Somatoform, Thought Disorder) and the inclusion of other disorders within spectra that were represented.

Finally, whereas all AUD criteria included (NESARC Wave 2, NESARC-III) were based on past-year endorsement, the time frame of the comorbid symptoms varied across sample. Spectra criteria counts largely represented past two-to-three years (NESARC Wave 2) and lifetime (NESARC-III) endorsement, with some minor exceptions (Table 1). Our confidence in the broad assessment of some symptoms may be dampened by a number of factors, such as the accuracy of retrospective report (e.g., Ben-Zeev & Young, 2010). Further, developmental trajectories and/or other life factors that may play an important role in the presence, absence, or change in symptom presentation are not captured in the present analyses (e.g., Gotham et al., 2006).

Future Directions

Given that AUD is often associated with decreased likelihood of seeking or receiving treatment services utilized compared to other psychiatric disorders, a more detailed

investigation into treatment seeking for comorbid conditions is needed. For instance, research has indicated that the presence of another psychiatric disorder increases the likelihood that someone diagnosed with AUD will seek treatment (Petrakis et al., 2002). On the other hand, the presence of AUD may decrease the likelihood of seeking or receiving treatment for either condition given that persons diagnosed with AUD have low treatment-seeking rates (Cohen et al., 2007; Grant et al., 2015), are more likely to receive mental health treatments than an alcohol-focused treatment (Edlund et al., 2012), and treatment received is often not a substance-specific intervention when comorbid conditions are present (Petrakis et al., 2002). Further, comorbid AUD may influence various aspects of treatment, such as the need for more intensive intervention, diagnostic overshadowing, or negative beliefs held by providers (Van Boekel et al., 2013). Similarly, treatment approaches and availability of services that address similar components across AUD and other disorders (e.g., transdiagnostic factors) simultaneously should be further explored.

Knowledge of the presence of comorbid AUD can be beneficial in many ways, although a more in depth understanding of the relationships between disorders and causal processes may further improve assessment, diagnosis, and treatment. Exploring temporal sequencing within a dimensional framework can speak to the primary, secondary, or concurrent nature of the alcohol use and/or other disorder, as well as the clarify common factors through the investigation of onset, course, duration, and severity. Continued research focused on these complex associations may lend further insight into areas for prevention efforts and moments of increased risk for persons diagnosed with, or who may go on to develop, comorbid conditions. Thus, we can benefit from additional in-depth investigations of these constructions within these complex samples and comorbidities.

Conclusions

The comorbidity of AUD with other psychiatric disorders has been long established and this study demonstrated the associations of timely dimensional models (i.e., hierarchical categorizations of disorders) and DSM-5 AUD severity. AUD severity was associated with a greater number of symptoms across groups of psychiatric disorders (HiTOP Internalizing, Disinhibited Externalizing, Antagonistic Externalizing) within individual categorical disorders across two epidemiological samples (NESARC Wave 2, NESARC-III). This investigation demonstrated that across shared pathology (e.g., Internalizing, Disinhibited Externalizing), psychiatric comorbidity increases as a function of AUD severity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Symptoms Represented Across Samples, Organized by HiTOP Spectra

NESARC Wave 2 (W2) - DSM-IV	Interval	NESARC-III - DSM-5	Interval
Internalizing		**Internalizing**	
Social Phobia (F)	SLI	Bulimia Nervosa (EP)	LIFE
Agoraphobia (F)	SLI	Anorexia Nervosa (EP)	LIFE
Specific Phobia (F)	SLI	Binge-Eating Disorder (EP)	LIFE
Panic Disorder (F)	SLI	Social Anxiety Disorder (F)	LIFE
Major Depressive Disorder (D)	SLI	Agoraphobia (F)	LIFE
Dysthymic Disorder (D)	SLI	Specific Phobia (F)	LIFE
Generalized Anxiety Disorder (D)	SLI	Panic Disorder (F)	LIFE
Posttraumatic Stress Disorder (D)	LIFE	Major Depressive Disorder (D)	LIFE
Borderline Personality Disorder (D)	LIFE	Persistent Depressive Disorder (D)	LIFE
Mania/hypomania[^] (M)	SLI	Generalized Anxiety Disorder (D)	LIFE
		Posttraumatic Stress Disorder (D)	LIFE
		Borderline Personality Disorder (D)	LIFE[‡]
		Mania/hypomania[^] (M)	LIFE
Disinhibited Externalizing		**Disinhibited Externalizing**	
Cannabis Use Disorder (SA)	SLI	Cannabis Use Disorder (SA)	LIFE
Opioid Use Disorder (SA)	SLI	Opioid Use Disorder (SA)	LIFE
Antisocial Personality Disorder (AB)	LIFE/SLI[†]	Antisocial Personality Disorder (AB)	LIFE
Conduct Disorder (AB)	W1 (<15)	Conduct Disorder (AB)	<15
Attention-Deficit/Hyperactivity Disorder (AB)	W2 (<18)		
Antagonistic Externalizing		**Antagonistic Externalizing**	
Antisocial Personality Disorder (AB)	LIFE/SLI[†]	Antisocial Personality Disorder (AB)	LIFE
Conduct Disorder[*] (AB)	W1 (<15)	Conduct Disorder (AB)	<15
Attention-Deficit/Hyperactivity Disorder (AB)	W2 (<18)	Borderline Personality Disorder	LIFE[‡]
Narcissistic Personality Disorder	LIFE		
Histrionic Personality Disorder[*]	LIFE		
Paranoid Personality Disorder[*]	LIFE		
Borderline Personality Disorder	LIFE		
Detachment		**Detachment**	
Schizoid Personality Disorder[*]	LIFE	*N/A*	*N/A*
Avoidant Personality Disorder[*]	LIFE		
Dependent Personality Disorder[*]	LIFE		
(-) Histrionic Personality Disorder[*]	LIFE		

Note. SLI = since last interview (2–3 years); LIFE = lifetime.

[*] Assessed at Wave 1 (W1)

[†] Assessed at W1 (lifetime, >15 years) and SLI for W2, symptoms counted as positive if endorsed at W1 or W2.

[^] Mania/hypomania symptoms were administered based on screening item endorsement, therefore symptoms were only counted toward the sum once. "<" or ">" value indicates age (e.g., Conduct disorder symptoms assessed for "prior to age 15").

[‡] Symptoms "since early adulthood". HiTOP Subfactors: F=Fear; D=Distress; M=Mania; SA=Substance Abuse; AB=Antisocial Behavior; EP=Eating Pathology.

Table 2.

ANOVA results for individual disorder subsets[2]: Criteria counts within disorder subsets, by AUD group

	NESARC Wave 2						NESARC-III					
	EMM (SE)				*Wald F Statistic*[1]		*EMM (SE)*				*Wald F Statistic*[1]	
	AUD Severity Group						AUD Severity Group					
	none	mild	mod	severe	Linear	AUD grp	none	mild	mod	severe	Linear	AUD grp
Generalized Anxiety Disorder subset (n = 996)					df = 1,38	df = 3,38	(n = 1995)				df = 1,109	df = 3,109
symptoms	6.87_{a} (0.05)	6.80_{a} (0.12)	7.25_{b} (0.14)	7.08_{ab} (0.14)	4.56 *	2.54	6.96_{a} (0.03)	6.89_{ab} (0.09)	7.11_{ac} (0.09)	7.27_{c} (0.08)	17.76 ***	6.06 ***
Borderline PD subset (n =1541)					df = 1,49	df = 3,49	(n = 3236)				df = 1,113	df = 3,113
symptoms	5.72_{a} (0.06)	5.80_{ab} (0.09)	5.77_{ac} (0.13)	6.30_{d} (0.14)	12.95 ***	4.73 **	5.13_{ac} (0.05)	4.97_{ab} (0.10)	5.36_{c} (0.12)	5.99_{d} (0.12)	57.11 ***	20.76 ***
Antisocial PD subset† (n = 927)					df = 1,35	df = 3,35	(n = 1278)				df = 1,103	df = 3,103
symptoms	5.26_{a} (0.07)	5.35_{ab} (0.16)	5.63_{ac} (0.20)	6.21_{d} (0.14)	34.70 ***	12.41 ***	5.16_{a} (0.09)	5.09_{ab} (0.13)	5.36_{ac} (0.18)	5.72_{c} (0.13)	20.30 ***	7.52 ***
Avoidant PD subset (n = 522)						df = 1,20	df = 3,20					
symptoms	4.98_{a} (0.06)	4.78_{ab} (0.16)	5.02_{ac} (0.18)	5.61_{d} (0.20)	11.41 ***	4.24 *	-	-	-	-	-	-

Note. EMM(SE) = conditional marginal means and standard errors, accounting for age, sex, and race/ethnicity.

[1] Represents *Wald F*(df) for overall test and for AUD severity levels ("AUD Grp").

[2] Disorder subsets represent subsets of the larger sample, conditioned on a categorical diagnosis of the respective disorder (e.g., major depressive disorder).

† ASPD symptoms include the presence of conduct disorder as one criterion and other adult antisocial behaviors, consistent with DSM-5.

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$. Pairwise comparisons represented with subscripts: i.e., EMMs (within sample) that do not share a subscript are significantly different ($p < 0.05$).

Table 3.

Spectra ANOVA results of AUD group conditional marginal means (standard errors), by sample

	NESARC Wave 2						NESARC-III					
Spectrum	***EMM (SE)***				***Wald Statistic*[1]**		***EMM (SE)***				***Wald Statistic*[1]**	
	AUD Severity Group				**Linear *F*(1,65)**	**AUD grp *F*(3,65)**	**AUD Severity Group**				**Linear *F*(1,113)**	**AUD grp *F*(3,113)**
	none	**mild**	**mod**	**severe**			**none**	**mild**	**mod**	**severe**		
Internalizing	-0.11_{a} (0.01)	0.16_{b} (0.03)	0.45_{c} (0.06)	1.25_{d} (0.10)	190.83***	96.50***	-0.10_{a} (0.01)	0.17_{b} (0.02)	0.35_{c} (0.04)	0.83_{d} (0.06)	257.91***	121.33***
Disinhibited Externalizing	-0.10_{a} (0.01)	0.32_{b} (0.03)	0.77_{c} (0.09)	1.89_{d} (0.18)	133.51***	108.46***	-0.14_{a} (0.01)	0.21_{b} (0.03)	0.58_{c} (0.04)	1.16_{d} (0.06)	441.82***	245.40***
Antagonistic Externalizing	-0.15_{a} (0.01)	0.30_{b} (0.03)	0.67_{c} (0.05)	1.26_{d} (0.07)	438.07***	249.45***	-0.16_{a} (0.01)	0.22_{b} (0.03)	0.55_{c} (0.04)	1.10_{d} (0.06)	608.10***	318.69***
Detachment	-0.03_{a} (0.01)	-0.01_{a} (0.03)	0.10_{ab} (0.06)	0.24_{bc} (0.09)	9.48**	3.69*	-	-	-	-	-	-
Ns	*18422–18598*	*2200–2244*	*731–753*	*461–516*	*21651–22111*	*21651–22111*	*20594*	*2603*	*1173*	*1259*	*25629*	*25629*

Note. EMM(SE) = conditional marginal means and standard errors, accounting for age, sex, and race/ethnicity.

[1] Represents *Wald F*(df) for linear contrast ("linear") and for AUD severity levels ("AUD grp").

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$. Pairwise comparisons represented with subscripts: i.e., EMMs (within sample) that do not share a subscript are significantly different ($p < 0.05$).

Table 4.

Spectra ANOVA results of AUD group conditional marginal means (standard errors), by sex and sample

	NESARC Wave 2						NESARC-III					
Spectrum	***EMM (SE)***				***Wald Statistic*[1]**		***EMM (SE)***				***Wald Statistic*[1]**	
	AUD Severity Group				**Linear *F*(1,65)**	**AUD grp *F*(3,65)**	**AUD Severity Group**				**Linear *F*(1,113)**	**AUD grp *F*(3,113)**
	none	**mild**	**mod**	**severe**			**none**	**mild**	**mod**	**severe**		
Internalizing												
Male	-0.26_a (0.01)	-0.03_b (0.03)	0.29_c (0.07)	0.85_d (0.11)	121.08***	66.24***	-0.26_a (0.01)	0.01_b (0.03)	0.10_{bc} (0.04)	0.51_d (0.07)	129.37***	69.76***
Female	0.05_a (0.01)	0.39_b (0.05)	0.64_c (0.09)	1.98_d (0.20)	101.76***	52.54***	0.07_a (0.02)	0.33_b (0.03)	0.65_c (0.08)	1.28_d (0.10)	155.52***	79.25***
Disinhibited Externalizing												
Male	-0.01_a (0.02)	0.40_b (0.04)	0.93_c (0.11)	2.03_d (0.24)	83.13***	70.13***	-0.03_a (0.02)	0.30_b (0.04)	0.71_c (0.06)	1.19_d (0.08)	247.00***	126.12***
Female	-0.20_a (0.01)	0.25_b (0.06)	0.49_{bc} (0.11)	1.70_d (0.31)	40.28***	43.98***	-0.24_a (0.01)	0.11_b (0.04)	0.43_c (0.06)	1.19_d (0.11)	190.35***	130.05***
Antagonistic Externalizing												
Male	-0.11_a (0.02)	0.35_b (0.03)	0.74_c (0.06)	1.30_d (0.09)	268.45***	155.72***	-0.11_a (0.02)	0.26_b (0.04)	0.56_c (0.05)	1.06_d (0.07)	340.33***	156.50***
Female	-0.20_a (0.01)	0.26_b (0.04)	0.56_c (0.08)	1.23_d (0.11)	177.28***	110.77***	-0.22_a (0.01)	0.19_b (0.04)	0.55_c (0.06)	1.21_d (0.08)	316.14***	190.96***
Detachment												
Male	-0.06_a (0.01)	-0.02_{ab} (0.03)	0.10_{bc} (0.08)	0.17_{bd} (0.10)	7.06**	3.04*	-	-	-	-	-	-
Female	0.01_a (0.01)	0.00_a (0.05)	0.06_a (0.09)	0.37_a (0.19)	3.79	1.28	-	-	-	-	-	-
Ns (male, female)	*8145 10453*	*1355 889*	*508 245*	*345 171*	*10353 11785*	*10353 11785*	*9010 11584*	*1457 1146*	*673 500*	*772 387*	*11912 13717*	*11912 13717*

Note. EMM(SE) = conditional marginal means and standard errors, accounting for age and race/ethnicity.

[1] Represents *Wald F*(df) for linear contrast ("linear") and for AUD severity levels ("AUD grp").

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$. Pairwise comparisons represented with subscripts: i.e., EMMs (within sample) that do not share a subscript are significantly different ($p < 0.05$).