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INVITED REVIEWS

Transdiagnostic factors of psychopathology and substance use disorders: a review

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Abstract
Purpose Research on the structure of mental disorders and comorbidity indicates that many forms of psychopathology and substance use disorders are manifestations of relatively few transdiagnostic latent factors. These factors have important consequences for mental disorder research and applied practice.
Methods We provide an overview of the transdiagnostic factor literature, with particular focus on recent advances.
Results Internalizing and externalizing transdiagnostic factors have been well characterized in terms of their structures, links with disorders, stability, and statistical properties (e.g., invariance and distributions). Research on additional transdiagnostic factors, such as thought disorder, is quickly advancing latent structural models, as are integrations of transdiagnostic constructs with personality traits. Genetically informed analyses continue to clarify the origins of transdiagnostic factor levels, and links between these factors and important environmental exposures provide promising new avenues of inquiry.
Conclusions Transdiagnostic factors account for the development and continuity of disorders and comorbidity over time, function as the primary links between disorders and important outcomes such as suicide, mediate associations between environmental exposures and disorders, provide an empirically supported classification system, and serve as foci for efficient, broadband intervention approaches. Overall, transdiagnostic factor research indicates the paramount importance of understanding these constructs and, thereby, broadening our understanding of mental disorder in general.

Keywords Transdiagnostic · Comorbidity · Internalizing · Externalizing · Psychopathology

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Introduction

Mental disorders are typically conceptualized as categorical entities by official nosologies, such as the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*; [1]) and the *International Classification of Diseases, Tenth Edition* (*ICD-10*; [2]). In such systems, diagnoses of psychopathology and substance use disorders (SUDs) are typically defined as dichotomous. In other words, a disorder is either present or absent, determined by whether or not a certain numerical threshold of polythetic diagnostic criteria is met. These systems outline a very large (and growing) number of disorders, which have become foundational for many assessment, prevention, and intervention efforts; they also have guided mental health research in psychiatry, psychology, and related fields for much of the past several decades. In short, these classifications have been, and continue to be, hugely impactful, and the question of how best to define mental disorders is of critical importance.

Unfortunately, as we will discuss, there are myriad conceptual problems with disorders as outlined by current classification systems. These limitations have led researchers to search for alternative means by which to

conceptualize psychopathology and SUDs—approaches that reflect empirical findings, data-driven conclusions, and overall higher congruence between the theoretical classification model and the observed disorder data. Such alternative approaches to nosology have gained traction and scientific support over the past few decades, while traditional approaches have simultaneously experienced a loss of favor by practitioners and scholars alike. Although multiple approaches to classification are possible, and several have been proposed, the current report reviews what appears to be the best-supported alternative system to date: transdiagnostic factor models.

Transdiagnostic factor models of psychopathology, SUDs, and multivariate comorbidity patterns have emerged as a leading contender in the search for an empirically supported classification system. As we shall discuss, these models have a long history, but only relatively recently have they found widespread use and become the focus of inquiry. Indeed, two previous reviews have been written on the topic, focusing almost exclusively on two transdiagnostic factors, internalizing and externalizing, taking narrative [3, 4] and meta-analytic [5] approaches. However, in the ensuing years, transdiagnostic factor research has experienced tremendous growth, with new, competing models being proposed, expanded, and directly tested in a variety of innovative ways. Rather than belaboring the original scholarship covered by previous reviews of the internalizing–externalizing model, we limit our historical discussion to the most foundational studies and theoretical developments, referring the reader to previous reviews for more detail about early transdiagnostic factor research. This allows us to focus the current review primarily on "big picture" issues, innovations, elaborations, and recent developments. To supplement this review, a companion report deals with implications and future directions of transdiagnostic approaches to mental disorder classification [6].

Problems with traditional classification systems

Although they pervade nearly all domains of mental health research and practice, studies have identified marked limitations of traditional classification systems, paving the way for reconceptualization of how mental disorders are best defined. We outline two such limitations. First, traditional classification approaches using dichotomous diagnoses truncate potentially important disorder variance. Two individuals who fail to meet the diagnostic threshold receive the same non-diagnosis (i.e., the disorder is absent), even if person A did not endorse any of the criteria and person B experienced many, but not quite enough to reach the threshold. Similarly, persons C and D may both receive the same diagnosis, even if the former meets the minimum diagnostic threshold while the latter far exceeds it. For instance, the *DSM-5* categorical diagnosis of borderline personality disorder (BPD) requires at least five of nine diagnostic criteria to be present. Person A endorsed no diagnostic criteria, person B endorsed four potentially highly distressing and impairing criteria (e.g., unstable relationships, recurrent suicidal behavior, affective instability, and intense, inappropriate anger), person C endorsed five criteria (e.g., those of person B as well as chronic feelings of emptiness), and person D endorsed all nine criteria. The prima facie organization of these individuals would likely be that person A had "no BPD," persons B and C had "largely similar BPD," and person D had "severe BPD." Such an assessment would be rational, given the similarity between persons B and C, and that group's apparent dissimilarity with persons A and D, who differ from each other in the extreme. This, however, is not how dichotomous diagnoses function. *DSM-5* would treat persons A and B the same ("no BPD diagnosis") and persons C and D the same ("BPD diagnosis"), and thus lose important clinical variation. This results in heterogeneous diagnostic groups and groups of undiagnosed individuals with significant, subthreshold psychopathology [7].

Second, traditional classification systems frame the various mental disorder diagnoses as independent entities, but this fails to take into account high rates of observed comorbidity. Although grouped under rationally derived headings such as "anxiety disorders" or "mood disorders" [8], the organization of psychopathology and SUDs into putatively distinct, non-overlapping diagnoses suggests that they should occur independently of one another. Thus, their co-occurrence, referred to as comorbidity (but see [9]), should theoretically be a simple probability calculation reflecting the product of the prevalence rates of each disorder. In practice, however, this assumption of independence is commonly rejected. As an illustration, Eaton, South, and Krueger [3] examined prevalence data from the Midlife Development in the United States survey (MIDUS; 10]) for major depressive disorder (MDD) and generalized anxiety disorder (GAD), finding that the disorders by chance alone (i.e., no systematic comorbidity or correlation between the disorders) should co-occur in fewer than four individuals per 1,000. In actuality, this co-occurrence pattern was observed in more than 17 individuals per 1,000—nearly 400 % of the rate predicted if the disorders were truly independent.

Epidemiological studies have demonstrated that comorbidity is the rule rather than the exception. Among individuals receiving a past 12-month mental disorder diagnosis in the National Comorbidity Survey Replication (NCS-R), nearly half received one (22 %) or more (23 %) additional diagnoses [11]. In terms of lifetime prevalence,

approximately 50 % of individuals in the National Comorbidity Survey (NCS) received at least one mental disorder diagnosis, and more than half of all lifetime disorders were diagnosed in the 14 % of the population with a history of three or more comorbid disorders [12]. This pattern of diffuse, generalized comorbidity across disorders also holds for particular disorders. For instance, among individuals who received a past 12-month diagnosis of major depressive disorder in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), 36 % had a comorbid 12-month anxiety disorder, 38 % had a comorbid personality disorder, 14 % had an alcohol use disorder, and 5 % had a drug use disorder. Thus, the implied independence of dichotomous disorder diagnoses is not empirically tenable, and psychopathology and SUDs show both high rates, and diffuse patterns, of comorbidity [13].

The emergence of the internalizing–externalizing transdiagnostic factor model

How can we account for the high and heterogeneous comorbidity observed among various psychopathology and SUD diagnoses? We must first seriously question the independence of putatively distinct mental disorders that is implied by the dichotomous diagnoses in modern classification systems. A compelling alternative to the current independent disorders structure is based on Thurstone's [14] common factor model, which informs psychometric techniques such as factor analysis. In that model, the reason that diagnoses are comorbid at higher-than-chance levels is that they are not actually independent parsings of mental disorder into meaningful groups; rather, comorbidity is a reflection of multiple disorders being manifestations of fewer core, undifferentiated latent constructs that cut across diagnostic boundaries. According to this approach, each person would have some standing on these constructs, and all diagnoses associated with a particular construct would move in tandem with one another—this would be observed as comorbidity. We approximate these constructs statistically as latent variables, which we refer to as transdiagnostic factors (or, alternatively, "comorbidity factors," "spectra," "dimensions," or "liabilities"), and they represent the common (shared) variance among disorders. For a more in-depth discussion of how the common factor model is used to frame comorbidity, see Eaton, South, and Krueger [3].

The early history of transdiagnostic factor research illustrates the technical discussion of common factors well. Much early research applying the common factor to mental disorder was conducted in child populations, examining how various psychopathological signs and symptoms, and problem behaviors, might relate to one another (for reviews, see [15, 16]). Among the most seminal events in transdiagnostic factor research, Achenbach submitted a variety of such items to factor analytic approaches, and determined that this diverse set of indicators could be reduced meaningfully into two groups: internalizing and externalizing. Internalizing problems included sadness, anxiety, and related issues, while externalizing problems included impulsivity, rule breaking, and aggressiveness. Achenbach noted that these two broad latent factors accounted for a good deal of the variance of each item, and they additionally accounted for the covariance (i.e., item-level "comorbidity") among items. In common factor model terms, we would say that internalizing and externalizing are latent factors, akin to personality traits in their structure, and each child's higher or lower factor levels were manifested as higher or lower levels of observed problem symptoms and behaviors. Thus, it was not that a child experienced high levels of sadness and anxiety independently of one another—this child had a high standing on the latent internalizing factor, and this was manifested as observed sadness and anxiety, as well as any other items that were related to the internalizing factor. These sorts of studies laid the foundation for the current transdiagnostic factor approach, and internalizing and externalizing factors have been at the heart of this research area ever since.

Another early contribution to transdiagnostic factor research was made by Wolf and colleagues [17], who conducted exploratory factor analysis of seven "Feighner criteria" (i.e., a Washington University in St. Louis research diagnostic nosology; [18]) in a sample of 205 adult psychiatric inpatients. The authors identified a three-factor solution, wherein diagnoses of primary depression and primary mania loaded highly on one factor; alcoholism, drug dependence, and antisocial personality disorder loaded highly on another factor; and schizophrenia loaded highly on a third factor. These first two transdiagnostic factors, therefore, formed what would later be referred to as internalizing and externalizing, respectively. The identification of the third transdiagnostic factor, relating to psychosis, was a finding ahead of its time. As we will see, although internalizing–externalizing model replications would proliferate in the adult literature around a decade later, it would be around 20 years before researchers began studying this third, psychosis-related transdiagnostic factor in earnest.

Beginning in the late 1990s, a series of studies were published by independent groups, using diverse data and diagnoses, examining the transdiagnostic factors that accounted for comorbidity among the common mental disorders (i.e., primarily various mood and anxiety disorders, SUDs, and antisocial personality disorder). Among

the first of those studies was conducted by Krueger et al. [19], who compared various competing models of psychopathology, including models representing *DSM*-inspired structures (e.g., "mood disorders" vs. "anxiety disorders"). Results indicated that a two-factor internalizing–externalizing model was optimal in two waves (ages 18 and 21) of psychopathology data from a birth cohort in New Zealand. The internalizing transdiagnostic factor accounted for comorbidity among major depressive episodes, dysthymia, GAD, agoraphobia, social phobia, simple phobia, and obsessive–compulsive disorder. The externalizing transdiagnostic factor accounted for comorbidity among conduct disorder, marijuana dependence, and alcohol dependence. In addition to the identification of these two key transdiagnostic factors, this study produced two other notable findings relevant to this review. First, it was noted that the transdiagnostic were significantly correlated (rs = 0.45 at age 18 and 0.42 at age 21). Second, these factors were relatively stable between assessments. When each age 21 factor was regressed on its age 18 counterpart, both internalizing ($\beta = 0.69$) and externalizing ($\beta = 0.86$) were notably stable, with externalizing being significantly more stable than internalizing. Importantly, most autocorrelations among disorders (i.e., disorder-specific correlated residuals across waves) were nonsignificant, and cross-lagged paths between factors (i.e., age 18 internalizing predicting age 21 externalizing, age 18 externalizing predicting age 21 internalizing) were nonsignificant. These findings indicated that (a) the continuity of psychopathology and SUDs over time was almost solely through the transdiagnostic factors, (b) the transdiagnostic factors themselves were quite stable over time, and (c) the transdiagnostic factors, although correlated, represented two unique pathways of disorder continuity over time.

The study by Krueger et al. [19] was seminal and ignited a flurry of subsequent investigations. The next major advance in the study of transdiagnostic factors was the identification of two potential sub-factors of internalizing. In this model, a higher-order internalizing factor subsumed two lower-order transdiagnostic factors of distress (or anxious-misery) and fear. Distress was identified by such variables as major depressive episode, dysthymia, and GAD, while fear was identified by such variables as panic disorder and various phobias. Replicated in various countries [5, 20–25], these distress and fear sub-factors appear to be somewhat robust. See Fig. 1.

There has been subsequent general agreement in the published literature of some sort of internalizing–externalizing structure of common mental disorders. The internalizing–externalizing structure has been identified in unique datasets from countries including Australia, Brazil, Chile, China, France, Germany, Greece, India, Italy, Japan, the Netherlands, New Zealand, Nigeria, Turkey, the United Kingdom, and the United States [24–26]. In terms of failed replications, we are aware of one study that failed to replicate this structure in multi-wave data from Germany [27], although another investigation of those data indicated a distress-fear-externalizing structure was present [20]. There is less agreement about the structure of internalizing itself. Whether the bifurcated internalizing–externalizing model (i.e., including distress and fear sub-factors) is superior to the unitary internalizing–externalizing model (i.e., not including distress and fear sub-factors) remains an open question, with some studies producing equivocal results [28] and others favoring the bifurcated model [22, 25]. In general, distress and fear show a very high correlation, and thus, their identification involves statistical issues (i.e., testing whether their correlation is at or below unity) and indicator diagnoses available. We now turn our attention to more recent developments, expanding the foundational finding of a robust internalizing–externalizing structure to common mental disorders.

Recent developments in the internalizing–externalizing model

The internalizing–externalizing model has been elaborated in recent years in several ways. First, studies have begun modeling the stability of these transdiagnostic factors over time, which has notable implications for the development and stability of mental disorders and comorbidity across the lifespan. Second, researchers have investigated two key conceptual questions about these factors: factorial invariance and distributional qualities. Third, the internalizing–externalizing model has been expanded via investigating links with new disorders and personality.

Stability

Insofar as transdiagnostic factors represent core psychiatric phenomena that saturate multiple forms of psychopathology and SUDs, developing an understanding of their stability over time will inform investigations about the etiology, onset, persistence, remittance, recurrence, and temporal development of mental disorders as well as their comorbidity. To the extent that these factors are relatively stable over time, like personality traits, they may have utility for screening and prediction of the development of future disorders given individuals' latent transdiagnostic factor levels. Thus, stable transdiagnostic factors could inform developmental psychopathology research in early childhood and adolescence [29, 30] up to empirical questions of successful aging in later life [31, 32].

Few studies have examined internalizing stability over time, and fewer still have examined externalizing stability.

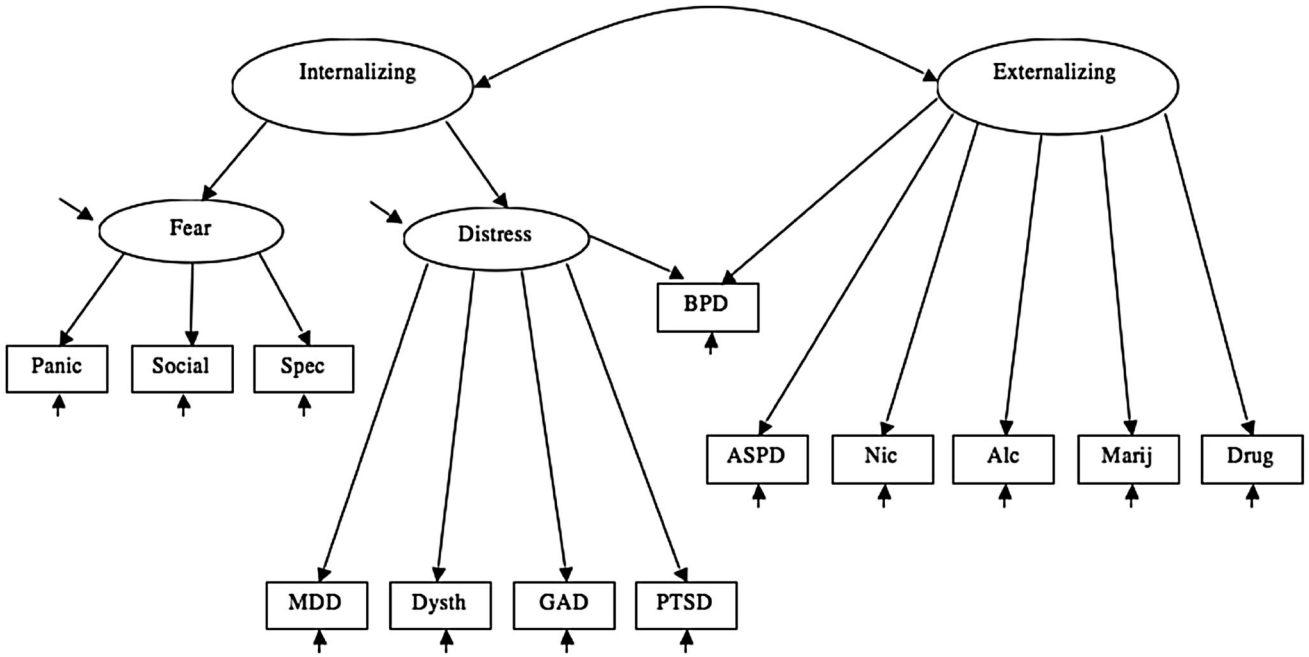

Fig. 1 An internalizing–externalizing transdiagnostic factor model of common mental disorder comorbidity, with distress and fear sub-factors of internalizing. *Panic* panic disorder with agoraphobia. *Social* social phobia. *Spec* specific phobia. *MDD* major depressive disorder. *Dysth* dysthymic disorder. *GAD* generalized anxiety disorder. *PTSD* post-traumatic stress disorder. *BPD* borderline PD. *ASPD* antisocial PD. *Nic* nicotine dependence. *Alc* alcohol dependence. *Marij* marijuana dependence. *Drug* other drug dependence. Adapted from [69]

Overall, though, a reasonable understanding of stability is emerging in the literature. The first investigations of stability focused on relatively short time intervals, finding high levels of stability. Krueger et al. [19] correlated internalizing and externalizing factors at age 18 with those at age 21. For internalizing, the resulting correlation was 0.69; for externalizing, the resulting correlation was 0.86. Thus, over approximately 3 years, both of these transdiagnostic factors were generally stable, and that around 48 % (0.69^2) of internalizing and 74 % (0.86^2) of externalizing variance were shared across assessment time points. Vollebergh et al. [25] extended this research by examining the one-year stability of the distress and fear sub-factors of internalizing, as well as the externalizing factor. Externalizing was highly stable ($r = 0.96$), and significantly more stable than either distress (0.85) or fear (0.89). Taken together, these studies indicated that internalizing and its sub-factors, as well as externalizing, are highly stable over short periods of time. As the temporal distance between assessment time points increased, the level of stability of externalizing was understandably attenuated.

Although the stability of internalizing and externalizing remains a question for further study, more recent investigations have helped to clarify several aspects of this topic. In terms of long-term stability, one study examined the stability of internalizing over approximately a decade, finding strong evidence of stability ($r = 0.74$; [32]). The long-term stability of externalizing remains a less studied question, although Hicks and colleagues [33], for instance, found a rank-order stability of 0.69 between externalizing factors at age 17 and 24.

Additionally, researchers have examined whether the stability of transdiagnostic factors that occurs at the between-domain level (i.e., $\text{internalizing}_{T1}$ predicting $\text{externalizing}_{T2}$; $\text{externalizing}_{T1}$ predicting $\text{internalizing}_{T2}$) is similar in magnitude to the within-domain level (i.e., $\text{internalizing}_{T1}$ predicting $\text{internalizing}_{T2}$; $\text{externalizing}_{T1}$ predicting $\text{externalizing}_{T2}$). The resolution of these questions of between-domain stability is critical, particularly the adjudication of whether internalizing and externalizing represents stable and distinct pathways of comorbidity development over time. In a time-lagged survival analysis of first onset disorders, Kessler and colleagues [34, 35] found significant between-domain relationships over time. This was perhaps unsurprising given that internalizing and externalizing transdiagnostic factors are correlated [3, 5], although within-domain relations were larger in magnitude. Another study, investigating stability of the distress and fear sub-factors, however, found relatively high levels of within-domain stability for distress and fear, but low levels of between-domain stability, suggesting that distress and

fear are stable and distinct pathways of comorbidity continuity and development [22], even if very highly correlated.

Factorial invariance

The issue of the factorial invariance of the internalizing–externalizing model is a question of similarity: Do common mental disorders show similar latent comorbidity structures across groups? Here, the issue of similarity is adjudicated by factorial invariance analyses, which test the formal statistical "sameness" of model parameters that are estimated in data from various groups of individuals, such as those defined by age, gender, and race/ethnicity. There are various degrees of factorial invariance, with each permitting different interpretations [36, 37]. Given that transdiagnostic factors are typically indicated by categorical variables (i.e., diagnoses), alternative analytic methods may be required [38].

In general, the internalizing and externalizing transdiagnostic factors show notable invariance across reported comparison groups. Configural invariance of disorders—similar factors across groups—has been established in highly diverse samples, including mental health data from Australia, Brazil, Chile, China, France, Germany, Greece, India, Italy, Japan, the Netherlands, New Zealand, Nigeria, Turkey, the United Kingdom, and the United States [24, 26]. To make meaningful comparisons across groups, however, more stringent levels of invariance must be established. In particular, strong invariance (the same factor loadings and intercepts across groups) is necessary to compare latent factor means across groups (e.g., "Do women have a higher level of internalizing than men?") [37, 39, 40]. Further, strong invariance indicates differences between groups in disorder prevalence rates reflect group differences in the latent factor level.

Studies suggest the internalizing–externalizing model is statistically robust across population sub-groups such as age, gender, race/ethnicity, and sexual orientation. Invariance has been established across age groups. Configurally, these two transdiagnostic factors appear in data from young children [15, 41] as well as in data from individuals ranging from ages 15 to over 98 [23, 32, 42]. One study of a higher-order factor structure resembling internalizing was found to be age invariant [43], and subsequent research established the internalizing factor showed strong invariance across younger, middle-aged, and older adult cohorts as well as within individuals as they aged [32]. In terms of gender, analyses have again established invariance across women and men [22, 33, 44–47]. The establishment of strong gender invariance can be interpreted to mean that elevated prevalence rates of mood and anxiety disorders in women reflect women's significantly higher average standing on internalizing, whereas elevated rates of SUDs and antisociality-related disorders in men reflect men's significantly higher average level of externalizing [45]. In comparison of race/ethnicity groups, two studies—both using United States data—have demonstrated invariance of transdiagnostic factors across various race/ethnic groups [21, 46]. Finally, invariance has been established between sexual minority (lesbian, gay, and bisexual) and heterosexual individuals in a large United States sample [48].

Distributional qualities

Although transdiagnostic factors are often assumed to be continuous, this is not necessarily the case. For instance, person-centered research suggests that individuals may be distributed into various psychopathology classes rather than along one or more dimensions [49]. Other distributional possibilities exist, including severity dimensions within classes, for instance. Such analytic possibilities have led researchers to compare class and dimension models for particular disorders such as mania [50], personality and eating disorders [51], and related phenomena such as magical thinking [52]. Recently, studies have applied tests of these alternative distributional models to the transdiagnostic factors themselves, indicating that internalizing, distress, fear, and externalizing are best modeled as dimensional [22, 44, 53–56]. Thus, rather than representing comorbidity/liability classes or hybrid class-dimensions, transdiagnostic factors appear to be continuous latent variables.

Links with new disorders and personality

Typically, a relatively similar set of disorders—those available in psychiatric epidemiological studies—is used as indicators for transdiagnostic factors. For instance, major depression and generalized anxiety are almost invariably included as indicators of internalizing, and the SUDs and antisociality-related disorders are included as indicators of externalizing. Ongoing research is identifying how other disorders fit into the internalizing–externalizing model. For instance, Forbush et al. [57, 58] found that bulimia nervosa, anorexia nervosa, and binge eating disorder could all be subsumed under the internalizing factor, highlighting that internalizing is more than simply mood and anxiety psychopathology. Sexual problems appear to relate to internalizing in women but not men [59]. Similarly, externalizing has been expanded to include non-illicit substances, such as abuse of prescription medications [60], as well as relational aggression [61]. Examination of substance abuse versus substance dependence may yield different multivariate comorbidity associations, with abuse showing secondary associations with distress [62]. The

extent to which these and other newly included disorders can and should be folded into the internalizing–externalizing model, or whether they would instead better be conceptualized as indicators of other transdiagnostic factors, is a critical question for further study. As discussed below, while there is some evidence that thought disorder relates to internalizing [63], there is competing evidence that it may be better conceptualized as a unique transdiagnostic factor.

One area of particular advance in the past decade has been the incorporation of personality with transdiagnostic factors [64–66]. This integration has taken several forms. First, personality disorders have been modeled alongside more commonly modeled disorders in a multivariate context. Although antisocial personality disorder is commonly included as an indicator of externalizing, the full complement of 10 *DSM-IV* personality disorders has now been modeled simultaneously with the standard diagnostic indicators. These investigations indicate that personality disorders are associated with internalizing and externalizing latent factors to some degree, although their versions of these transdiagnostic factors may be separable from those of other disorders [67], and they may require additional factors to account for their comorbidity structure [68]. An alternative approach to this broadband study of all personality disorders and other disorders simultaneously is to focus on the location of a single personality disorder within the internalizing–externalizing framework. For instance, direct examinations of the location of BPD within a transdiagnostic factor model indicated the disorder reflects both internalizing/distress and externalizing [69–71], accounting for its high and heterogeneous comorbidity patterns (see Fig. 1). Such analyses indicate transdiagnostic factor models can help clarify within-diagnosis heterogeneity patterns—by demonstrating that certain diagnoses are confluences of multiple underlying phenomena. Third, researchers have found latent structures reflecting internalizing–externalizing in personality disorder measures, such as the personality inventory for *DSM-5* [72, 73] and the personality assessment inventory [46]. Finally, researchers have examined the zero-order relationships among personality traits and transdiagnostic factors, finding that internalizing and neuroticism have a nearly perfect correlation [74]. Externalizing has been linked to neuroticism as well as disinhibition, disagreeableness, and novelty seeking [5, 75, 76].

Alternative transdiagnostic models

The internalizing–externalizing model is the most studied, and best-characterized, transdiagnostic comorbidity model to date. However, alternative models have appeared in the literature of late. We discuss two types of alternative models: modified internalizing–externalizing models and models with new transdiagnostic factors.

Modified internalizing–externalizing models

There is some disagreement about the optimal structure of internalizing, concerning whether or not distress and fear sub-factors should be included. There is similarly some evidence that externalizing may have lower-order factors as well. For instance, the general externalizing factor can be thought of as a higher-order factor, subsuming sub-factors such as SUDs, aggression, impulsivity, and so on [61, 76, 77]. Other studies, however, present evidence suggesting the optimality of a one-factor model for broad externalizing behaviors [53]. The structure of externalizing thus remains an open question in the literature and will depend on the number and type of indicator disorders modeled.

An increasingly impactful modification to the internalizing–externalizing model has been the inclusion of a general psychopathology factor. In general, this sort of general psychopathology factor is evaluated in a bifactor model, meaning that all diagnoses are linked to this general factor (*p*), which accounts for the generalized shared variance across them, and internalizing and externalizing factors are used to account for additional shared variance within groups of disorders. These models are gaining increasing empirical traction in the adult literature [78–82], but have been particularly influential in the child and adolescent literature [29, 30, 41, 61, 83–85]. These bifactor approaches are a compelling means to model, reduce, and understand the correlation between internalizing and externalizing.

New transdiagnostic factors

Although it has been known for decades that transdiagnostic factors beyond internalizing and externalizing are required to capture important disorder variance and comorbidity [17], only recently have these factors become a primary focus of structural modeling. The factor with perhaps the strongest literature to date captures psychosis, or thought disorder, and it subsumes psychotic experiences such as schizophrenia and schizotypal personality disorder. Evidence for such a psychosis-related factor has emerged in various studies [56, 78, 86–88]. Such a factor can guide research on these related disorders, particularly given a growing understanding that they may represent points along a spectrum [89]. Other transdiagnostic factors have emerged as well, including eating disorders [58], sexual problems [59], pathological introversion [68, 88], antagonism and detachment [73, 90], and cognitive-relational

disturbances [68]. At this level, the transdiagnostic domains of psychopathology, SUDs, and normal and maladaptive personality appear to converge [91].

Overall, it is unlikely to be the case that a single structure will fit diagnostic data if disorders are sampled broadly. Further, it appears there is no "correct" level of analysis. For instance, *p* might be beneficial in some contexts, internalizing and externalizing in others, and distress-fear-externalizing in others; these questions will likely depend on the question of interest [28], the granularity of assessment desired, the statistical balance of fit and model parsimony, among other considerations. Although there is no single optimal structure for all purposes, an informative perspective here can be found by examining multiple possible transdiagnostic factor solutions. By looking across levels, it is possible to model how disorders are organized into interpretable hierarchies [90, 92]. For instance, one recent study [73] found that extracting two factors from personality disorder data produced an internalizing–externalizing model. When extracting three factors, the internalizing factor bifurcated into negative affect and detachment factors. When extracting four factors, the externalizing factor then bifurcated into antagonism and disinhibition. At a five-factor level, a negative affect–detachment–antagonism–disinhibition–psychoticism solution emerged. These findings and others [88, 93] suggest that hierarchical models hold promise for understanding the transdiagnostic latent structure of mental disorders at varying levels of analysis, from undifferentiated *p* to more fine-grained constructs such as distress and fear.

The origins and impacts of transdiagnostic factors

At least two fundamental questions remain regarding transdiagnostic factors: Where do they come from? What do they do? With regard to the origins of transdiagnostic factor levels, a number of genetically informed studies have indicated that transdiagnostic factors appear, in large part, to reflect genetic effects, while unique (non-shared) variance of each disorder tends to reflect environmental effects (as well as measurement error; [29, 67, 68, 79, 94]). Although the majority of their variance is genetic, environmental exposures also have an impact on transdiagnostic factor levels. For instance, adverse childhood events such as maltreatment and neglect are prospectively associated with increased levels of internalizing and externalizing [42], as are discriminatory experiences faced by sexual minority individuals [48, 95]. Understanding how environmental exposures modulate latent factor levels is an important area for future research.

The second question—what transdiagnostic factors do beyond characterizing comorbidity—is receiving increased attention, and results indicate that these factors play a critical role in understanding mental disorders, their comorbidity, and their associations with important outcomes. First, they have clinical descriptive utility, as evidenced by these sorts of transdiagnostic organizations framing the meta-structure of the *DSM-5* nosology [96, 97]. Second, they account for the continuity of disorders, and the development of comorbidity, over time; across studies, few, if any, disorders show continuity patterns not accounted for by the latent factors [22, 32, 34, 35, 98]. Third, they appear to serve as potent targets of efficient transdiagnostic interventions [99, 100], and they help clarify why many psychotherapeutic [101] and pharmacological [102, 103] interventions have diffuse impacts on multiple disorders. Fourth, environmental exposures, such as adverse childhood events and discrimination, appear to impact these factors rather than individual disorders directly [42, 48]. Fifth, transdiagnostic factors account for important links between distinct disorders and outcomes, such as suicide [22, 104, 105]. Finally, it appears that transdiagnostic factors may relate more closely to neurobiological substrates of behavior [78, 106, 107], making them prime candidates for integrating biological and phenomenological investigations and for framing investigations compliant with the Research Domain Criteria (RDoC). For further discussion of these sorts of issues, please see our companion report [6].

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