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INVITED REVIEWS

Disorders without borders: current and future directions in the meta-structure of mental disorders

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Abstract
Purpose Classification is the cornerstone of clinical diagnostic practice and research. However, the extant psychiatric classification systems are not well supported by research evidence. In particular, extensive comorbidity among putatively distinct disorders flags an urgent need for fundamental changes in how we conceptualize psychopathology. Over the past decade, research has coalesced on an empirically based model that suggests many common mental disorders are structured according to two correlated latent dimensions: internalizing and externalizing.
Methods We review and discuss the development of a dimensional-spectrum model which organizes mental disorders in an empirically based manner. We also touch upon changes in the DSM-5 and put forward recommendations for future research endeavors.
Results Our review highlights substantial empirical support for the empirically based internalizing–externalizing model of psychopathology, which provides a parsimonious means of addressing comorbidity.
Conclusions As future research goals, we suggest that the field would benefit from: expanding the meta-structure of psychopathology to include additional disorders, development of empirically based thresholds, inclusion of a developmental perspective, and intertwining genomic and neuroscience dimensions with the empirical structure of psychopathology.

Keywords Internalizing · Externalizing · Meta-structure · Psychopathology · DSM

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Introduction

Classification is fundamental to the quantitative study of psychiatric phenomena. Just as a building requires a solid foundation to support its framework and remain upright, in mental health, a valid classification system provides the fundamental building block of diagnosis, assessment, intervention, and research. In psychiatry, the two leading classification systems are the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD). The release of the DSM-III in 1980 and ICD-10 in 1992 heralded a major advance for the psychiatric field by providing standardized diagnostic criteria for the first time [1].

The DSM and ICD facilitate communication across users (e.g., clinicians, researchers, judicial systems, and insurance companies) [2]. From a clinical perspective, they promote consistent descriptions and reliable diagnostic assessment. From a research point-of-view, they facilitate comparative analyses, systematic recording, and analysis and interpretation of data from different countries. From an educational perspective, they provide a means of delivering standardized training. With such a wide range of applications, it is critical that our classification systems reflect an accurate description of mental illness. Empirical research from clinical and community

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populations, however, highlights significant flaws in assumptions underlying the DSM and ICD. Crucially, extensive comorbidity among putatively distinct disorders has challenged the traditional view that disorders are discrete entities. Comorbidity patterns are considered to reflect the underlying structure of psychopathology; accordingly, over the last decade extensive structural investigations have been conducted to elucidate the natural classification of mental disorders.

Our companion report [3] provides a comprehensive review of the transdiagnostic factor literature that has emerged in the search for an empirically based nosology. This review outlines future directions and implications of transdiagnostic approaches to mental disorder classification. Due to space restrictions, we focus on the DSM, although the issues are equally pertinent to the ICD, which shares a similar structure [4].

Flaws in the DSM rubric

Historically, the DSM was developed on the basis of consensus among clinicians appointed to specific workgroups, and mental disorders were conceptualized as polythetic, categorical concepts. Polythetic means that disorders are defined by multiple symptoms, but not all symptoms are required to meet a diagnostic threshold. Categorical means that disorders are considered to be absent or present.

In the 30 years following the release of DSM-III, major scientific advances have been made. Large genetic and community studies have been conducted and longitudinal studies, beginning in the 1970s and 1980s, have matured. New statistical techniques have emerged, providing important insights into patterns of disorders, natural history, and trajectories over time, ultimately advancing our understanding of the nature of mental illness. As its architects concede, this work has increasingly cast the spotlight on problems inherent in the assumptions underlying the DSM [5].

First, a polythetic-categorical approach gives rise to significant heterogeneity within diagnostic groupings as it does not account for differences in clinical presentation (e.g., symptoms, age-of-onset, and stage of illness) [6–8].

Second, the categorical system is often criticized for being rigid and reductionist in practice, leading to frustration among clinicians, poor application of diagnostic guidelines, and limited clinical utility [9]. By placing an over-emphasis on reliability, highly specific, and narrow criteria have been identified that fail to cover the spectrum of symptoms. Consequently, many patients are classified under the vague 'not otherwise-specified' category [10, 11].

Third, valuable clinical information is lost when adhering to a categorical, diagnostic threshold. This contrasts with clinical medicine where the clinical significance of subthreshold symptoms is well recognized. For example, 'undifferentiated connective tissue disease' refers to patients who are in the early stages but do not meet diagnostic criteria for a well-defined connective tissue disease (e.g., rheumatoid arthritis) [12]. Revolutionizing psychiatric classification to include dimensions would align the field with other medicine areas [13].

Fourth and the focus of this review, converging lines of research indicate that disorders co-occur more often than expected by chance, challenging the DSM conceptualization that disorders are discrete entities. Dimensionality also exists between disorders, reflecting shared underlying genetic and environmental liabilities. Based on this evidence, and recognition of the benefits of dimensions, widespread international calls have been made to restructure nomenclature in light of scientific evidence [14].

A quantitative nosology: disorders without borders

To better understand why multiple diagnoses share common risk factors and clinical correlates, latent variable modeling techniques have been applied to diagnostic data. Seminal work by Krueger [15], examining the underlying structure of common mental disorders, indicates that relations between disorders reflect two genetic and environmental dimensions: internalizing and externalizing (see Fig. 1). Internalizing reflects a propensity to experience distress inwards. Internalizing may be conceptualized as a unitary dimension [16, 17], but some research suggests it may also have meaningful subcomponents [4, 18–20], bifurcating into two lower-order sub-dimensions: (1) distress (or anxious-misery), including disorders such as major depression, dysthymia, and generalized anxiety disorder, and (2) fear, including disorders such as panic, social phobia, and specific phobia. Externalizing indicates a tendency to experience distress outwards, and includes substance use disorders (e.g., alcohol, nicotine, cannabis, and drug abuse/dependence) and behavioral problems (e.g., conduct disorder, oppositional defiant disorder, and antisocial personality disorder). For a more in-depth discussion of these latent transdiagnostic dimensions, and those underlying the comorbidity among less common disorders, see our companion review [3] and previous reviews [20, 21]. Overall, the implicit assumption underlying this quantitative, organizational meta-structure of psychopathology is that certain disorders are reflections of a few core psychopathological dimensions. Thus, disorders indicating a particular latent dimension are more likely to be closely related in clinical presentation, likelihood of co-

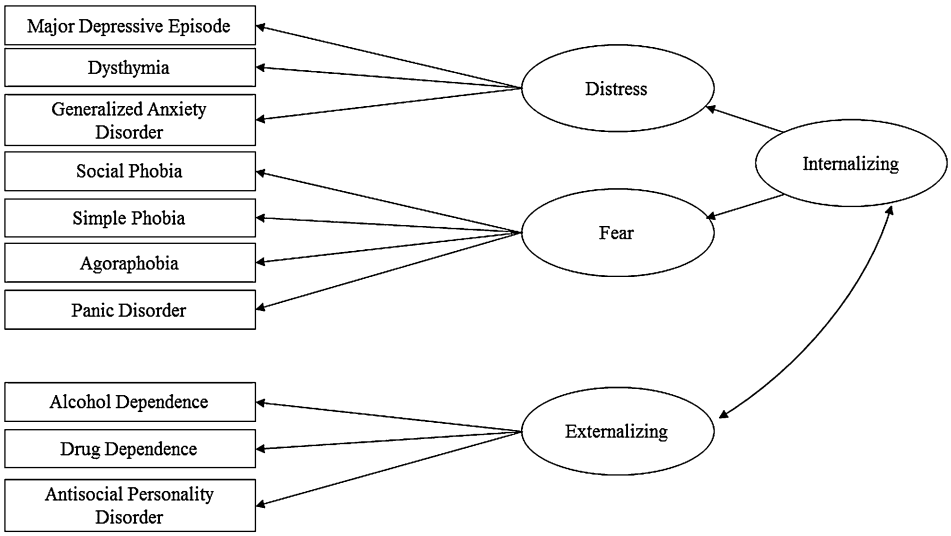

Fig. 1 The internalizing–externalizing model of psychopathology

occurrence, shared variance, etiology, and treatment response [22].

DSM syndrome comorbidity has revealed a structure similar to what was already known in Achenbach's work with young people. Early research on transdiagnostic comorbidity factors in children [23, 24] and adults [18, 25] was seminal in developing a dimensional-spectrum model. Today, the internalizing–externalizing model has accumulated robust, independent support. It has demonstrated invariance across cultures [4, 16–18, 26, 27], gender [28], ethnicity [29], age [30], sexual orientation [31], and time [18, 26, 30, 32]. The model also provides insight into how key psychopathological processes map onto unique components of individual disorders versus shared pathology [33–35]. Furthermore, genetic and environmental risk factors for experiencing psychopathology are parsimoniously accounted for in this model, and internalizing–externalizing mediate the likelihood of developing additional related diagnoses across the lifespan [17, 36–39]. Indeed, Lahey and colleagues [40] found evidence for widespread heterotypic continuity of mental disorders during adulthood, indicating that mental disorders are not fixed, independent entities. Rather, disorders are robustly related to one another in a correlational structure that is manifested both concurrently and across time. This literature has important clinical relevance; rather than focusing on individual disorders, consideration of underlying liabilities may be a useful avenue for identifying appropriate treatment approaches.

While the majority of published structural psychopathology research supports the internalizing–externalizing model, one study failed to replicate this structure. Wittchen et al. [41] failed to replicate the bifurcated internalizing–externalizing model, or any structure, across their age cohorts, concluding that "psychopathology cannot be reduced to any simple structure" (p. 189). In the same year, this research group re-evaluated their findings, finding evidence of a three-factor (distress-fear-externalizing) model, but not for a higher order internalizing factor [42]. Further, Seeley et al. [42] found that while the bifurcated internalizing model fitted their data well, it did not fit notably better than a single-factor or DSM-IV-based model.

A dimensional nosology of mental disorders

Behavior genetic modeling of comorbidity

Findings from behavior genetic modeling of comorbidity suggest that the internalizing–externalizing spectra are etiologically coherent, providing further support for a liability-spectrum model. Kendler and colleagues [36–38, 43, 44] have conducted the most comprehensive multivariate behavior genetic studies to date. This research provides support for a genetic basis underlying the internalizing–externalizing spectra, in addition to a genetic basis for the distress and fear subdimensions. It also supports a hierarchical structure of comorbidity as a number of individual disorders (e.g., alcohol dependence)—though linked to broad liability dimensions—was also characterized by genetic factors unique to each disorder.

Relatedly, disorders, and traits which optimally reflect the underlying genetic risk of externalizing and internalizing psychopathology appear to differ by gender [36] and mothers appear to confer a general propensity to transit internalizing disorders to their offspring, rather than risk for a specific disorder [45].

The role of personality in dimensional spectra

One key question concerns the underlying psychological reasons that psychopathology spectra have a particular structure. For example, why are antisocial problems and substance use problems so closely connected? Evidence suggests that psychopathology spectra derive their organization from the role personality plays in conveying risk for psychopathology in a coherent, psychologically meaningful manner. For example, externalizing derives its coherence from the role disinhibitory personality traits play in seemingly diverse antisocial and substance use behaviors [46]. Similarly, internalizing derives its coherence from the role negative affect (also termed neuroticism) plays in diverse disorders involving mood and anxiety disturbances [36]. Indeed, negative affect is relevant to most forms of psychopathology, such that it increases risk for both internalizing and externalizing disorders, thereby providing the psychological basis for the general factor that ties these spectra together [47]. Conversely, disinhibition is linked to risk for externalizing rather than internalizing syndromes [46]. This helps explain why the structure of psychopathology has reliable hierarchical features, involving an overarching general factor that bifurcates into internalizing–externalizing and further into more even more specific aspects.

Additional higher order aspects of psychopathology structure

Recently, it has been speculated that the meta-structure may encompass an overarching, general factor [48]. This stems from observations that disorders and the internalizing–externalizing spectra are substantially correlated. Capsi et al. [49] labeled this dimension the '*p* factor', suggesting it can be best understood as a general factor—analogous to the g factor of general intelligence—which summarizes individuals' propensity to develop any and all forms of common psychopathologies. The authors suggest the *p* factor may account for the difficultly in identifying causes, consequences, biomarkers, and treatments with specificity to individual disorders. Research by Lahey and colleagues exploring the etiologic structure of child, adolescent [39], and adult [48] psychopathology provides evidence for a broad general factor (a bifactor in factor analytic terms), with higher order internalizing and externalizing factors reflecting additional shared variance in symptoms.

Caveats of dimensions

While dimensions overcome many problems associated with categories, they also have caveats. First, dimensions are less familiar than categories in mental health settings and may therefore be more difficult to use, at least initially, leading to concerns about difficulties in clinical communication and user acceptability [50]. Second, no single dimensional model has achieved universal acceptance. Third, given a historical emphasis on categories, there is only a nascent literature demonstrating the clinical utility of dimensions [5, 51].

Interim summary: a point of reorientation and look toward the future

The internalizing–externalizing model can accommodate comorbidity. It is robustly supported and offers a promising avenue for better understanding etiology, natural history, treatment use, and developing targeted treatment and prevention approaches. From a practical perspective, however, work remains to derive a valid, empirically based psychiatric classification system. In the following section, we discuss challenges and future research directions.

Contemporary and newer directions for the future

Categorical vs. continuous vs. hybrid models

To date, researchers have largely made a priori assumptions about the latent structure of psychopathology. Studies have characterized internalizing as a unidimensional structure [18, 30, 52], two-dimensional structure [4, 15, 26, 28], and set of distinct classes [53, 54]. To our knowledge, limited studies have directly compared continuous, categorical, and hybrid models [55–59].

Continuous (latent trait) models account for patterns of co-occurrence among disorders with reference to a dimension(s). Using factor analytic techniques, individuals are arrayed along a continuum of mild, moderate, and severe pathology. Theoretically, a continuous conceptualization is plausible if the underlying etiologies of the externalizing/internalizing disorders reflect a mixture of genetic polymorphisms and environmental stressors.

Conversely, categorical models—investigated using latent class analysis—account for observed patterns of comorbidity by reference to a finite number of mutually exclusive classes. This approach presumes that individuals within a given class have the same probability of experiencing the disorders. Theoretically, a categorical conceptualization of externalizing and internalizing liabilities is plausible if the underlying etiologies are discrete in nature. Along these lines, for example, specific genetic polymorphisms (distinct forms of genes) may be related to externalizing liability, leading to discrete classes of individuals

who experience externalizing behaviors and those who do not.

Alternatively, the latent structure may compose continuous and categorical components—investigated using factor mixture modeling. Hybrid models are categorical insofar as they group individuals into categories. They are also dimensional because once individuals are assigned to liability classes, differences in severity between classes are modeled through continuous latent variables [60]. Hybrid models facilitate meaningful distinctions between homogeneous groups while allowing for different levels of severity.

Although successful, the majority of structural analyses have focused on syndromal-level indicators, which are often heterogeneous. Since symptoms are more homogeneous, extending the existing framework to incorporate symptoms could help delineate lower levels of the hierarchy. Indeed, Markon's [61] symptom-level analysis replicated the internalizing–externalizing meta-structure and found novel thought disorder and pathological introversion spectra. It is possible that such analyses could produce a proliferation of multiple fine-grained constructs, and it is critical to focus not only on construct identification but also on how these constructs can be incorporated into overarching hierarchical structures and embedded in broader nomological networks.

Relatedly, most research to date has relied on latent variable mixture modeling, taxometric procedures, and model-based clustering. These methods differ in their assumptions and selection should be empirically guided [62]. Future research should explore other analytic options, such as network analysis [63, 64].

Lumping versus splitting

Designing an optimal nosology will be challenging and associated with advantages and disadvantages [65]. The meta-structure provides a succinct means of grouping disorders according to shared commonalities and has given rise to transdiagnostic treatment approaches, offering efficient means of addressing multiple problems in a single framework. Division of disorders could be argued to result in unnecessary complexity and splitting. That being said, the unique features of some disorders, which have a corresponding need for differential treatment, highlights instances where it may be useful to assign labels to reflect heterogeneity [65]. Indeed, while DSM-5 incorporates the internalizing–externalizing meta-structure it also comprises meaningful subtyping distinctions, including a dissociative subtype of PTSD.

Expanding the meta-structure

Much of the research to date has focused on common disorders. To increase utility, it is important to include additional and severe types of mental illness (e.g., schizophrenia, schizoaffective disorder, and autism). As highlighted below, some researchers have begun this process.

Additional spectra

The inclusion of more extreme forms of psychopathology has highlighted novel dimensions spectra. For example, Keyes et al. [66] investigated the location of disorders characterized by detachment and/or psychoticism (i.e., schizotypal, schizoid, avoidant and paranoid personality disorder, manic episodes, and bipolar disorder) in the meta-structure. They found that detachment and psychoticism represented a unique subdimension of internalizing (labeled 'thought disorder'). Additionally, manic episodes and bipolar disorder demonstrated substantial associations with the distress subdimension and thought disorder dimension. Caspi et al. [49] also found evidence for a thought disorder spectrum, which—together with internalizing and externalizing—was best captured by a general psychopathology dimension (discussed earlier).

The inclusion of schizophrenia and schizotypal personality disorder led Kotov et al. [67] to identify internalizing, externalizing, and psychosis dimensions. In a separate study [68], these authors integrated personality pathology into the model and identified additional dimensions, including thought disorder (e.g., mania, schizotypal personality disorder), somatoform (e.g., hypochondriasis) and antagonism (e.g., histrionic and narcissistic personality disorders) spectra. Markon [61] identified novel thought disorder and pathological introversion dimensions. Finally, Røysamb et al. [27] identified two novel spectra: cognitive-relational disturbance (e.g., histrionic, narcissistic, paranoid, schizotypal, obsessive–compulsive, and borderline personality disorders) and anhedonic introversion (e.g., avoidant and dependent personality disorders, schizoid personality disorder, depressive personality disorder, and dysthymia). Finally, Noordhof et al. [69] found support for a bi-factor model, including one non-specific factor and four specific factors, including two novel spectra—internalizing, externalizing, attention and orientation, and autism spectrum problems.

Bipolar pathology

Evidence for the location of bipolar pathology—conceptualized as a disorder [70], manic episodes [25, 68], or manic symptoms [61]—within the meta-structure has suggested a number of possibilities, consistent with the way in which these phenomena have internalizing and psychotic aspects (i.e., are interstitial). Research indicates that bipolar pathology loads onto internalizing [17, 25, 28,

70] and psychosis [68]. Others suggest that irritability facet loads onto internalizing to a much stronger extent than the expansive mood facet of mania [56].

While some disorders such as bipolar disorder are distinguished on the basis of episodic course, this does not invalidate the basic observations underlying this review that the close relationships between disorders are meaningful. That is, course information is incorporated in the DSM diagnoses that are the focus of meta-structure research, by definition. Indeed, Eaton et al. [55] found that almost 50 % of bipolar's diagnostic variance were accounted for by internalizing liability which predicted for future internalizing disorders, suicide attempts, angina, and ulcers.

ADHD

Attention deficit hyperactivity disorder (ADHD) [57] has been found to load on externalizing for men and women. The observation that externalizing liability encompasses childhood ADHD provides support for a degree of developmental continuity such that a childhood diagnosis of ADHD predicts the later development of other externalizing disorders in adulthood.

Gambling

Pathological gambling has been found to load onto externalizing for men and women. However, among women, pathological gambling demonstrated best fit when loading on externalizing and the distress subdimension of internalizing [71].

Sexual dysfunction

Forbes and Schniering [72] found that sexual problems represent an additional subfactor of internalizing amongst females. However, no models including sexual problems provided an adequate fit to males.

PTSD

Post-traumatic stress disorder (PTSD) is less often included in structural investigations. Cox et al. [73] found PTSD loaded on the distress factor, and Wolf et al. [74] found that while PTSD covaried strongly with internalizing it also demonstrated a significant, more modest relationship with externalizing.

Borderline personality disorder

BPD appears to be interstitial, loading on internalizing and externalizing [19, 27, 68, 75]. Eaton et al. [19] found that, across males and females, BPD loaded on the distress subdimension of internalizing and externalizing. James and Taylor [75] observed the same finding among males, however, among females this model and an alternative model—in which BPD only loaded on the distress subdimension of internalizing—fit equally well. Sharp and colleagues [76] found that adolescent BPD loaded on internalizing and externalizing across males and females. However, divergent from Eaton et al. [19] and James and Taylor [75] (who both found that BPD demonstrated higher factor loadings on internalizing compared to externalizing in adults) [19, 75], Sharp et al. [76] reported opposite results for adolescents. The authors suggest this indicates a pattern of heterotypic continuity in the development of BPD. Finally, Hudson and colleagues [77] found that familial internalizing and externalizing liabilities were associated with BPD, which may help explain the pattern of comorbidity between BPD and internalizing and externalizing disorders.

Eating disorders

The location of eating disorders in the meta-structure has been recently investigated. Forbush et al. [78] demonstrated that, amongst females, eating pathology represents a distinct subdimension of internalizing. This finding was replicated by Forbush and Watson [70] using data from both males and females. Overall, the authors found evidence of five subdimensions within internalizing: distress, fear, eating pathology, dysphoria, and bipolar. Further, impulse control disorders loaded onto externalizing; and factor analytically derived personality disorder scales split between the internalizing–externalizing spectra. Conversely, Mitchell et al. [79] found that, across genders, anorexia nervosa, bulimia nervosa, and binge eating disorder load on the distress subdimension of internalizing.

OCD

Only a small number of structural studies have included obsessive–compulsive disorder (OCD). Overall, Krueger et al. [18] found that OCD loaded on internalizing. For the bifurcated internalizing–externalizing model, OCD has been found to load onto the fear subdimension [4] and distress subdimension [80] of internalizing.

Somatic disorders

Somatic disorders/symptoms have received some attention. Krueger et al. [16] found that somatization, hypochondriasis, and neurasthenia load on internalizing, an observation that was robust across 14 countries. Simms and colleagues [81] found that somatic symptoms loaded

onto internalizing, with specific factors also present for somatic symptoms, reflecting symptoms that are independent of internalizing. As mentioned earlier, somatoform disorders have been found to represent a distinct dimension [68].

Other disorders

Research suggests that relational aggression [82] represents a distinct subdimension of externalizing. Nonmedical prescription drug use has been found to load on externalizing and, to a small extent, on the fear subdimension of internalizing, across men and women [83].

DSM-5

The most recent iteration of the DSM [5] included a number of evidence-based changes. Of relevance to this review, the axial system was removed and disorders were re-organized, with externalizing disorders placed next to one another and internalizing disorders adjacent to one another. The new structure reflects recognition of the utility of common underlying liabilities (or transdiagnostic dimensions) in explaining differences within and communalities between diagnostic categories. This is explicitly documented in the manual's Preface [5]. Further, Section III of the DSM-5—entitled "emerging models and measures"—includes a maladaptive personality trait model, which can be assessed with the Personality Inventory for DSM-5 (PID-5) [5, 84]. This is the first empirical model of personality in the pathological range included in the DSM. The PID-5 was developed by the DSM-5 Personality and Personality Disorder Workgroup to address criticisms of personality pathology in previous iterations. In this hybrid model, functional impairment criteria and dimensional personality traits map onto one of six categorical personality disorders, and a seventh diagnosis (Personality Disorder-Trait Specified) replaces Personality Disorder Not Otherwise Specified. The PID-5 trait domains can be broadly conceptualized as maladaptive variants of the Five-Factor Model traits [85] and characterized by an overarching personality factor which subsumes internalizing and externalizing [86]. These observations highlight continuity between personality and psychopathology.

The PID-5 is copyrighted by the American Psychiatric Association and freely available (http://www.psychiatry.org/practice/dsm/dsm5/online-assessment-measures#Personality). In this way, it provides a formal bridge for potential scaffolding in future meta-structure endeavors and a vehicle for steering the DSM further away from categorical diagnoses—based on political processes and clinical authority—toward an empirically based dimensional model of personality and psychopathology [87].

Identification of empirically based thresholds

As highlighted above, a wealth of literature has identified continua underlying psychopathology. While a dimensional-spectrum approach offers a number of benefits, it is important to consider practical utility and feasibility. The categorical system has occupied a central position in our knowledge base for over 30 years. It frames training textbooks in the mental health professions, treatment guidelines, epidemiological surveys, service use, and medical economic data [51]. Therefore, a complete shift from a strictly categorical to strictly dimensional system would disrupt the activities of a range of professionals and require significant retraining. It would also warrant revisions of research assessment tools; complicate research involving diagnostic groupings across studies and diagnostic change over time; and create administrative barriers to medical record keeping and collection of vital statistics [51]. Categories also offer ease of communication.

We suggest that the combined goals of validity and utility could be best served by combining dimensions with categories. This hybrid approach holds promise for overcoming inherent limitations in the DSM, while achieving a balance between including new components urgently called for by the field (e.g., scientific foundation, dimensions). Ultimately, by preserving continuity with the extant system and using an intuitive, user-friendly format with minimal disruption, a hybrid approach would be more likely to be adopted in practice [14]. In fact, a categorical-dimensional psychiatric classification would draw closer parallels to practice in other medicine areas. For example, a diagnosis of hypertension is accompanied by systolic and diastolic blood pressure reading and a diagnosis of breast cancer is augmented by noting the Stage and/or Karnofsky score [13].

A dimensional classification system with the flexibility to set different diagnostic cut-points is likely to be more useful than the current system and satisfy different users' needs [88]. For example, cut-points on the basis of symptom severity could be identified; e.g., a patient might be described as experiencing a moderate level of depressive symptomatology and a severe level of anxiety symptoms. The use of severity labels serves as a subtle reminder that we are not dealing with natural categories [14]. Further, severity cut-points explicitly acknowledge dimensions and move away from traditional single disorder models and treatment silos. While the architects of DSM-5 have—conservatively—retained the categorical diagnostic structure, they have introduced a severity component for some disorders. In the case of alcohol use disorder (AUD), a tri-categorized severity scale distinguishes mild (2–3 AUD symptoms), moderate (4–5 symptoms), and severe (6 + symptoms) dependence [5].

Additionally, a single, evidence-based diagnostic threshold—indicating absence or presence of a disorder—could be identified. This cut-point, likely to lie somewhere between the moderate and severe cut-points, could be identified for each disorder. Suggested guidelines informing the derivation of empirically based cut-points are provided elsewhere [50].

Both types of thresholds would mark significant advances over DSM thresholds and dimensional scales elsewhere in the literature as they would be empirically derived and underpinned by theoretical constructs and a conceptual rationale. This has particular relevance to clinical practice as relating pathology to a theoretically meaningful framework improves clinical utility [89].

A developmental perspective

Much of the structural research on the internalizing–externalizing model has been confined to adults. This work is not developmentally informed as the meaning, age-of-onset, and expression of mental disorders differ for children, adolescents, young adults, and older adults [90, 91]. Surprisingly, although the terms 'internalizing' and 'externalizing' originate from the child and adolescence literature [23, 24], comparatively less attention has focused on structural investigations of DSM disorders in youth [92]. Of those studies that have been conducted, most have relied on epidemiological samples from the United States [39, 41, 59, 90, 92–98].

The importance of incorporating a developmental perspective in diagnoses was reflected in the research agenda and priorities of the DSM-5 workgroups [99, 100]. Indeed, extending structural accounts of psychopathology to youth is important for several reasons. First, adolescence and young adulthood are periods of major neurobiological, psychosocial, and hormonal changes [101, 102], and mark first onset of the majority of high-prevalence mental and substance use disorders. For instance, 31.9 % of US adolescents aged 13–18 years have anxiety disorders, 14.3 % have mood disorders, and 11.4 % have substance use disorders. Moreover, 40 % of adolescents with one class of mental disorder meet criteria for another disorder class. Median age of onset is 6 years for anxiety disorders, 13 years for mood disorders, and 15 years for substance use disorders [103]. The presence of psychopathology during adolescence and young adulthood may portend persistence of symptoms in adulthood. Indeed, longitudinal research indicates that 50 % of adults with a mental disorder had a diagnosable disorder at age 11–15, and 75 % had a first diagnosis before age 18 [104].

Second and relatedly, given that the phenotypic expression of mental disorders changes in both nature and intensity across development [105], the etiology of comorbid mental disorders may be unique during different age periods. For instance, a large developmental twin study examining anxiety and depressive symptoms from childhood to early adulthood highlighted that genetic risk factors play a developmentally dynamic role, varying across early adolescence, late adolescence, and early adulthood [106]. In particular, with the onset of substance abuse problems during adolescence, the phenotypic expression of psychopathology is likely to alter [18]. Increased understanding of the etiology underlying adult psychopathology has informed the development of evidence-based pharmacological and psychological intervention programs to effectively treat symptoms already present. It follows that a more thorough understanding of the internalizing–externalizing liabilities among youth holds promise for developing approaches designed to prevent initial symptom presentation [93]. Further, understanding causal pathways among disorders, and potentially reciprocal causation, over time will be a key future direction, and time-sensitive designs will be critical [17].

It is also critical to examine psychiatric classification in older adults. Given that current nosological systems show age bias in many diagnostic criteria [107], it is important to expand evidence-based classification systems across the lifespan. Little research has examined this issue, although evidence suggests potential invariance of internalizing across age cohorts and within individuals as they age [22]. Understanding relatively undifferentiated, core phenomena, such as personality traits and these latent psychopathology dimensions, has been identified as an important avenue for future studies of successful aging and later life development [108].

Biomarkers

A promising avenue of future research involves incorporating genetic, neuroimaging and neurophysiology research findings into psychopathology structural accounts [109, 110]. Identifying the genetic underpinnings of disorders holds much promise for improving our understanding of biological mechanisms linked with disorders. The Research Domain Criteria Project (RDoC) emerged out of recognition for the need for alternative approaches to psychiatric classification and aims to develop new approaches to classifying mental disorders on the basis of dimensions of observable behavior and neurobiological measures [111, 112]. At present, the search for biomarkers remains in its infancy and laboratory tests of the genetic and molecular signatures of mental disorders have not yet emerged. The internalizing–externalizing model provides an empirical, coherent framework for integrating biological findings, to accommodate comorbidity and improve ecological validity [113].

Conclusion

Our review indicates that the internalizing–externalizing model offers a parsimonious framework for accommodating comorbidity and can provide a better understanding of etiology and natural history. In this way, the meta-structure holds much promise for informing the development of more targeted and effective treatment and prevention approaches based on a solid empirical foundation. These benefits were recognized—at least in part—in DSM-5, with the introduction of a new organizational structure reflecting internalizing–externalizing liabilities.

Unlike its predecessors, DSM-5 is intended to be a living document, incorporating changes to reflect advances in research and knowledge. Thus, as psychopathology classification continues to evolve, we hope that its development and refinement relies on the accumulation of empirical research evidence, rather than clinical authority, to derive a system that is more valid, reliable, better suited to research biological underpinnings, and better reflects how psychopathology is structured in nature.

Conflict of interest None declared.

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