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Beyond comorbidity: Toward a dimensional and hierarchal approach to understanding psychopathology across the lifespan

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Abstract

In this review, we propose a novel developmentally informed framework to push research beyond a focus on comorbidity between discrete diagnostic categories, and to move towards research based on the well-validated dimensional and hierarchical structure of psychopathology. For example, a large body of research speaks to the validity and utility of the Internalizing and Externalizing (IE) spectra as organizing constructs for research on common forms of psychopathology. The IE spectra act as powerful explanatory variables that channel the psychopathological effects of genetic and environmental risk factors, predict adaptive functioning, and account for the likelihood of disorder-level manifestations of psychopathology. As such, our proposed theoretical framework uses the IE spectra as central constructs to guide future psychopathology research across the lifespan. The framework is particularly flexible, as any of the facets or factors from the dimensional and hierarchical structure of psychopathology can form the focus of research. We describe the utility and strengths of this framework for developmental psychopathology in particular, and explore avenues for future research.

In this review, we propose that it is time to leave behind research that focuses on the comorbidity between discrete diagnostic categories, and move towards a developmentally informed model based on the well-validated dimensional and hierarchical structure of psychopathology. The review has three parts. Part 1 makes a case for moving away from research that focuses on specific patterns of comorbidity between individual diagnoses, and proposes that empirically validated elements of the hierarchical structure of psychopathology offer better constructs for research. In fact, child psychopathology research acts as a working model that shows how this approach can be successful. In Part 2 we propose a novel theoretical framework to facilitate this move, which uses elements from the hierarchical structure of psychopathology to conceptualize psychopathology across the lifespan. We describe key processes in this framework, and review the evidence for each of them, with a particular focus on behavioural genetic evidence to reflect the structure of etiologic factors that underlie manifest symptoms. Part 3 explores the applications and

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advantages of this framework for developmental psychopathology across the lifespan, as well as how it can be used to integrate developmental research with interdisciplinary psychopathology research more broadly (e.g., with clinical and neurobiological psychopathology research). We also explore avenues for future research deriving from the proposed framework.

Part 1: The Case for Moving Beyond Comorbidity as a Focus in Research

In order to understand psychopathology across the lifespan, we need to move beyond research that focuses on "comorbidity" (i.e., the simultaneous presentation of two putatively distinct diseases or disorders; In Merriam-Webster Online Dictionary, 2015; In Oxford Dictionaries, 2015). By breaking down this definition into parts, it becomes clear that the notion of comorbidity is inherently incompatible with the nature of psychopathology, as revealed in recent research. At a conceptual level, comorbidity is intertwined with the neo-Kraepelinian model, which implies that mental disorders are distinct forms of psychopathology. However, no single mental disorder has been established as a distinct entity (e.g., Haslam, Holland, & Kuppens, 2012). This highlights a fundamental flaw in the application of the classic comorbidity concept to psychopathology and suggests a potentially more generative question to frame our understanding. Specifically, how might the lack of discrete boundaries between disorders be better conceptualized? Further issues arise in the application of classic comorbidity concepts to mental disorders, as they tend to co-occur in varied combinations —rather than in prototypical pairs— and in groups of three or more disorders. For example, Caspi et al. (2014) refer to the 'rule of 50%' in overlap among mental disorders: approximately half of the people who meet criteria for one mental disorder will also meet criteria for a second at the same time; half of those people who meet criteria for two disorders will meet criteria for a third; a significant minority will meet criteria for four or more disorders (Kessler, Chiu, Demler, Merikangas, & Walters, 2005; Newman, Moffitt, Caspi, & Silva, 1998). These rates of co-occurrence are far beyond the levels we would expect by chance (i.e., if the disorders were indeed distinct and independent of one another; Boyd et al., 1984). Further, a focus on the simultaneous presentation of disorders obscures the sequential patterns of continuity and change in disorder presentation, which are central to a developmental psychopathology approach (Kessler, Ormel, et al., 2011; Rutter & Sroufe, 2000; Sroufe & Rutter, 1984). In short, the comorbidity among mental disorders is largely artifactual[1]. This suggests that our diagnostic systems are incompatible with the nature of psychopathology (Krueger & Piasecki, 2002; Watson, 2005).

Despite conceptual issues inherent in the use of the term "comorbidity" to understand psychopathology, research focusing on "comorbidity" has been foundational in helping us to understand the structure of psychopathology. The systematic pattern of correlation among mental disorders highlights their lack of distinction as diagnostic categories, and indicates

[1]Artifactual comorbidity is a result of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) and the *International Classification of Diseases* (ICD) splitting single disease entities into artificial subdivisions (Beauchaine & McNulty, 2013). GAD and depression are a good example of artifactual comorbidity, as they share genotypic and phenotypic variance, and their subdivision is largely an artificial separation of alternate forms of the same underlying liability (cf. Caron & Rutter, 1991; Goldberg, 2015; Watson, 2005). In contrast, true comorbidity is the co-occurrence of clinically and etiologically distinct entities. For example, a person with schizophrenia and peptic ulceration can reasonably be considered to have two comorbid disorders (Goldberg 2015), as these disorders are etiologically distinct.

that they instead represent varied manifestations of underlying psychopathological constructs that cut across traditional diagnostic boundaries (Eaton, Rodriguez-Seijas, Carragher, & Krueger, 2015; Eaton, South, & Krueger, 2010). Through this lens, DSM disorders can be re-conceptualised as reified syndromes that are in fact indicators of latent transdiagnostic spectra, rather than discrete types (Carragher, Krueger, Eaton, & Slade, 2015; Goldberg, 2015). Consistent with this, statistical modelling of the correlations among mental disorders and their criteria has uncovered an extensive hierarchical structure of psychopathology that bridges personality and psychopathology (Achenbach & Edelbrock, 1978, 1984; S. C. Kushner, Quilty, Tackett, & Bagby, 2011; Markon, 2010; Wright & Simms, 2015). Based on this body of research, currently defined symptoms of psychopathology comprise at least three core spectra: Internalizing, Externalizing, and Thought Disorder. Our current understanding of the hierarchical taxonomy of psychopathology incorporates 12 of the 18 classes of mental disorders in the DSM-5 (Kotov et al, in press; Noordhof, Krueger, Ormel, Oldehinkel, & Hartman, 2015), but additional research is needed to determine whether this model applies to all forms of psychopathology. The Internalizing and Externalizing (IE) spectra are the most widely studied factors in the structure, reflect the most common forms of psychopathology in the population, and are clearly relevant throughout development, so they are the focus of this review.

The Internalizing and Externalizing Spectra

In seminal work, Achenbach and Edelbrock (1978, 1984) posited that two factors could account for the systematic patterns of co-occurrence among common psychopathological syndromes in children. This work uncovered the IE spectra, and laid the foundation for future research (Eaton et al., 2015). Others subsequently identified these constructs in adult psychopathology (Krueger, 1999; Krueger, Caspi, Moffitt, & Silva, 1998; Wolf, Schubert, Patterson, Grande, Brocco, & Pendleton, 1988), and the IE spectra have been front and centre in transdiagnostic psychopathology research ever since. The IE constructs will be familiar to many readers: Internalizing comprises depression, anxiety, and other pathologies characterised by prominent negative affect and distress; Externalizing comprises substance use syndromes and antisocial behaviour, where disinhibition and behavioural dyscontrol is prominent. The focus of much of Part 1 is to illustrate that the IE spectra are much more than just descriptive labels for groups of mental disorders; they are also powerful predictive variables. For example, estimates of IE reliably predict disorder onset, course, and treatment response (e.g., Eaton et al., 2015; Kessler, Ormel, et al., 2011; Kim & Eaton, in press; Krueger & Eaton, 2015; Lahey, Zald, Hakes, Krueger, & Rathouz, 2014). Furthermore, these aspects of psychopathology (onset, course, and treatment response) are better accounted for by the IE spectra as opposed to individual disorders (i.e., after accounting for the role of IE, individual disorders no longer predict these variables). We can consequently conceptualise IE as channels for the core aspects of psychopathology; this idea is explored in more detail in Part 2.

The Hierarchical Structure of IE—A summary of our current understanding of the hierarchical structure of IE is presented in Figure 1. Lower levels of the hierarchy represent increasingly specific facets and syndromes of psychopathology. At the highest level there is a general psychopathology factor, which has been found in children, adolescents, and adults

(Caspi et al., 2014; Lahey, Van Hulle, Singh, Waldman, & Rathouz, 2011; Laceulle, Vollebergh, & Ormel, 2015). This general factor is typically characterised by negative affect, and acts as an indicator of severity (e.g., Caspi et al., 2014; Kotov et al., in press; Lahey et al., 2011; Tackett et al., 2013). It correspondingly captures the tendency to experience multiple persistent syndromes of psychopathology. We have used a hierarchical model to describe the structure of IE here (cf. Kim & Eaton, in press; Kotov et al., in press), as it allows us to conceptualise how the structure unfolds at increasingly detailed levels of resolution. For example, the general factor bifurcates into the IE spectra, with Externalizing distinguished from Internalizing by the role of disinhibition in Externalizing (but not Internalizing) syndromes (Krueger & South, 2009); Internalizing subsequently splits into Fear and Distress facets in many structural studies (Doyle, Murphy, & Sheylin, 2016; Gomez, Vance, & Gomez, 2014; Kim & Eaton, in press; Kotov, Perlman, Gamez, & Watson, 2015; Watson, 2005). Symptom-level analyses of Externalizing have also uncovered lower-level facets of Oppositional or Antisocial Behaviour, and Substance Use (Achenbach & Rescorla, 2001a; Kotov et al., in press; Krueger & South, 2009; Krueger & Tackett, 2014; Lahey et al., 2004).

The structure of psychopathology is undoubtedly more complex than Figure 1 depicts (e.g., conduct disorder and attention deficit hyperactivity disorder have facets that are not characterised by Oppositional or Antisocial Behaviour), but the figure offers a broad overview of the literature. While we have argued above that DSM disorders are not psychometrically valid constructs by themselves, the shared variance of multiple DSM disorders can reliably indicate the IE spectra. However, the cross-loadings in Figure 1 (e.g., panic disorder indicates Fear *and* Distress) also highlight that the structure of psychopathology is more nuanced than just IE; DSM disorders are too broad to identify the specific facets. Finer-grained (e.g., symptom-level) analyses will allow us to learn about the lower levels of the hierarchy, which could ultimately be split into progressively more specific facets until we have individual signs and symptoms (e.g., the approach taken in developing the Externalizing spectrum inventory [ESI]; Krueger, Markon, Patrick, Benning, & Kramer, 2007). All levels of the empirically-derived hierarchy offer valid constructs to be used in future psychopathology research, but the IE spectra are currently the most well-validated for understanding psychopathology in a large-scale individual differences framework. We return to our focus on IE here.

Evidence for the Validity of the IE Spectra

Evidence for the validity of the spectra comes from a vast body of interdisciplinary research across the lifespan. This evidence has been reviewed in detail elsewhere (e.g., Beauchaine & McNulty, 2013; Carragher et al., 2015; Eaton et al., 2015); we provide a brief overview of the phenotypic and genotypic research below.

Phenotypic Evidence—The spectra emerge across a large variety of child and adult populations around the world (Krueger, Chentsova-Dutton, Markon, Goldberg, & Ormel, 2003; Slade & Watson, 2006), including across different religions and ethnicities (Eaton, Keyes, et al., 2013; Guttmannova, Szanyi, & Cali, 2008; Yarnell et al., 2013), sexual orientations (Eaton, 2014), and genders (Eaton et al., 2012; Kramer, Krueger, & Hicks,

2008; Lahey et al., 2004; Lahey et al., 2008). The IE spectra also transcend measurement and analytic methods. For example, the spectra have been found in research using continuous and categorical measures of disorders (e.g., Krueger, 1999; Markon, 2010); for lifetime, 12-month, and current disorder diagnoses (e.g., Krueger, 1999; Krueger et al., 2003; Vollebergh et al., 2001); and also using sub-threshold and symptom-level measures (e.g., Kendler et al., 2011; Kotov et al., 2015; Markon, 2010). Phenotypic research has also converged on IE using reports from multiple informants (Lahey et al., 2008), and in variable-centred and person-centred analytic approaches (e.g., latent class and confirmatory factor analyses; Krueger, 1999; Vaidyanathan, Patrick, & Iacono, 2011). The variations in these methods act as a sort of sensitivity analysis, and their convergence on IE offers robust evidence for the structural validity of these constructs.

Genotypic Evidence—Genetically informed studies (e.g., twin and adoption studies) indicate that IE reflect distinct underlying genetic vulnerabilities to develop Internalizing or Externalizing psychopathology (Kendler et al., 2011; Kendler, Prescott, Myers, & Neale, 2003). Genetic influences on IE most likely operate through many genes that pleiotropically influence risk for all Internalizing or all Externalizing psychopathology (Gizer, Otto, & Ellingson, 2015; Kendler, Prescott, et al., 2003; Lahey et al., 2011), rather than through individual candidate genes (e.g., Iacono, Vaidyanathan, Vrieze, & Malone, 2014). The IE spectra also represent the main paths of genetic risk transmission (Krueger et al., 2002; Lahey et al., 2011; Starr, Conway, Hammen, & Brennan, 2014), which suggests that disorders that fall on the same spectra have a shared etiology (Kendler et al., 2011; Krueger et al., 2014).

In short, there is strong evidence for IE as empirically validated constructs. These constructs reflect the natural and genetically based organisation of psychopathology, and consequently represent compelling constructs to act as the focus of future research.

Moving Towards Empirically Validated Constructs as a Focus in Research

The easiest way to immediately integrate IE into research is to use the ubiquitous DSM disorders as indicators of IE. Figure 1 reflects the tendency —in adult research in particular — to use “Internalizing” and “Externalizing” to refer to groups of DSM disorders. In fact, the IE spectra are normally distributed and continuous dimensions of risk for psychopathology that are indicated by manifest phenotypes (e.g., Krueger et al., 2007; see Figure 2). Individually, DSM diagnoses correspond to different severity levels of IE (e.g., Krueger & Finger, 2001; Markon & Krueger, 2005), but when multiple disorders are combined to estimate Internalizing or Externalizing, their shared variance allows us to estimate where an individual sits on the continuous dimensions of risk. As shown in Figure 2, a position at the low end of the spectrum represents a low risk for manifest psychopathology, and a position at the high end represents a high risk for multiple forms of persistent psychopathology. In this sense, multimorbidity (i.e., the simultaneous presentation of multiple disorders) is an indicator of underlying severity. These ideas are explored in more detail in Part 2.

The IE spectra could also be measured using continuous symptom-level measures (e.g., the Interview for Mood and Anxiety Symptoms [IMAS], the Child and Adolescent Psychopathology Scale [CAPS], or the ESI; Kotov et al., 2015; Krueger et al., 2007; Lahey et al., 2008), or using the IE facets from the Achenbach System of Empirically Based Assessment (ASEBA; Achenbach, 2009). The symptom-level measures offer a more detailed assessment of the hierarchy, and can facilitate our understanding of the finer-grained dimensions of psychopathology across the lifespan. When estimating an individual's position on the Internalizing or Externalizing spectra, the inclusion of more indicators (e.g., four or more DSM disorders) will strengthen the reliability and validity of the measurement; if a single disorder forms the focus of a study, researchers are basing their conclusions on a comparatively less reliable measure of the underlying spectrum.

Using the IE Spectra as Central Constructs in Developmental Psychopathology—The IE spectra are particularly well suited to examining the role of development in psychopathology because they emerge as orienting dispositions across the lifespan, from infancy to the oldest old. For example, Carter, Briggs-Gowan, Jones, and Little (2003) found that IE emerged as coherent patterns in parent-rated problem behaviours in children as young as 12 months old. The IE spectra have also been found to characterise related but distinct types of psychopathology in school-age children and adolescents (Carter et al., 2003; Lahey et al., 2008; Lahey et al., 2011), and in adults from 18 to 98 years of age (Hoertel et al., 2015). These studies relied on a variety of indicators to operationalise IE, including parent-reported problems in social-emotional and competency development (Carter et al., 2003), a symptom-level analysis of DSM-IV and ICD-10 disorders that are common in children and adolescents (Lahey et al., 2008), and DSM-IV diagnoses rated as present or absent in adults (Hoertel et al., 2015). As such, it is remarkable to find their emergence across the lifespan. These findings suggest that manifest psychopathology across the lifespan does not merely reflect developmental change, but continuity in shared ontogenic psychological and biological processes underlying IE (Hoertel et al., 2015).

Developmental Change in IE—While the factor structures of the IE spectra have been found to be largely invariant across development (e.g., Carter et al., 2003; Hoertel et al., 2015), there is also evidence that the mean levels of IE may fluctuate throughout development. For example, studies that have examined developmental change in the mean levels of Externalizing suggest that it has a peak in toddlerhood (Wiggins, Mitchell, Hyde, & Monk, 2015), decreases over childhood (Leve, Kim, & Pears, 2005; Miner & Clarke-Stewart, 2008), increases in adolescence before peaking again in early adulthood, and then makes a steady decline throughout later adulthood (Jackson, Sher, & Wood, 2000; Kessler, Berglund, et al., 2005; Krueger & South, 2009). Within this trajectory, impulse disorders tend to have an earlier age of onset than substance use disorders (Krueger & South, 2009). Childhood Externalizing tends to manifest as physical aggression and oppositionality, with behaviours like delinquency, substance use, and risky sexual behaviour emerging in adolescence and adulthood (Krueger et al., 2014). These changes are probably broadly related to cognitive function (Wiggins et al., 2015). For example, as toddlers develop verbally, they can communicate their needs rather than acting out. The increase in Externalizing in adolescence and early adulthood may be due to elevated levels of sensation

seeking and reward sensitivity preceding the development of adult levels of self-control and inhibition (Steinberg, Albert, Cauffman, Banich, Graham, & Woolard, 2008).

Internalizing has a different developmental trajectory: it is relatively stable throughout childhood (Sterba, Prinstein, & Cox, 2007), increasing sharply during adolescence (Achenbach, Howell, & Quay, 1991) —for girls in particular (Leve et al., 2005)— and may decline in old age (Eaton, Krueger, & Oltmanns, 2011; Sunderland, Slade, Carragher, Batterham, & Buchan, 2013). Within this trajectory, anxiety disorders tend to emerge in childhood, while mood disorders emerge during the heightened period of vulnerability in adolescence (Kessler, Berglund, et al., 2005). Other domains of psychopathology that may form part of the Internalizing spectrum —such as eating disorders and sexual dysfunction (Forbes, Baillie, & Schniering, 2015; Forbes & Schniering, 2013; Forbush & Watson, 2013; Forbush et al., 2013; Forbes papers)— also emerge during adolescence (Laumann, Paik, & Rosen, 1999; Swanson, Crow, Le Grange, Swendsen, & Merikangas, 2011). The drop in Internalizing in old age may be due to greater emotional regulation or maturity (Eaton et al., 2011).

Eaton et al. (2011) concluded that although individual disorders may remit and recur over time, the underlying liability to develop and continue to express these disorders remains relatively stable across age. In other words, an individual's position on the dimensions of IE (cf. Figure 2) does not vary substantially over time. In keeping with this, studies that have examined IE over time have found them to have marked temporal stability over retest intervals as long as nine years (Eaton et al., 2011; Eaton et al., 2015; Krueger, 1999; Sunderland et al., 2013; Vollebergh et al., 2001). This suggests that the genetic processes that underpin IE have continuity across the lifespan (Hoertel et al., 2015). Combined with the continuous nature of the spectra, this stability is a valuable characteristic for developmental research, as it provides sensitive measurement for tracking the level and extent of IE behaviours across the lifespan (Krueger et al., 2014).

It is Time to Move Beyond our Focus on DSM disorders as Discrete Entities

Taken together, there is strong evidence that factors like IE offer valuable constructs to frame the focus of psychopathology research. In contrast, DSM disorders have low construct and structural validity (Krueger & Eaton, 2012); while they are somewhat reliable, they are potentially invalid constructs, as they are neither distinct nor independent from one another (Rodriguez-Seijas, Eaton, & Krueger, 2015). DSM disorder diagnoses are particularly poor measurement indicators for psychopathology because they discard valuable information by collapsing signs and symptoms into dichotomous variables deemed present or absent (Krueger & DeYoung, in press). This precludes the possibility that broader, narrower, or different syndromes might offer better representations of the symptom clusters (Goldberg, 2015), which consequently obscures our understanding of the lower-level structure of psychopathology. Statistically, the dichotomous nature (i.e., present versus absent) of DSM diagnoses also means that they will often yield misleading results (e.g., spurious main effects may occur, and nonlinear effects could be overlooked; MacCallum, Zhang, Preacher, & Rucker, 2002). Finally, from a developmental perspective, DSM disorders do not offer a developmentally sensitive framework to understand psychopathology across the lifespan,

and the DSM tradition of separating child and adult syndromes places barriers to identifying and understanding developmentally coherent processes. By these accounts, DSM disorders appear to be a poor and misguided focus for psychopathology research.

Despite this, the bulk of psychopathology research is still conducted on specific manifestations of comorbidity, or on specific disorders in isolation, as if they are etiologically and pathophysiologically unique (Caspi et al., 2014; Lahey et al., 2011). If this were the case, every possible disorder pairing would also be unique, and would require its own comorbidity model (M. G. Kushner, 2014). However, analyses of the correlations among DSM disorders have taught us that, empirically, these disorders are best conceptualised as indicators of the IE spectra. As mentioned earlier, this means that researchers using single disorders as the focus of their research are missing out on a lot of valuable information. DSM disorders were a good place to start developing our understanding of the nature of psychopathology, but they are not a good place to stop. Instead, it is time to move beyond our focus on DSM disorders as discrete entities that co-occur, and to move toward a focus on the empirically derived constructs in the hierarchical structure of psychopathology.

Evidence for the Utility of this Approach—Child and developmental psychopathology research have led the way in adopting this quantitative approach, with considerable success. In contrast to the prominence of the DSM's categorical models in the classification of adult psychopathology, dimensional models have enjoyed long success in child research (Caspi et al., 2014). Achenbach and Edelbrock's early work (1978, 1984) gave child research a 20 year head start in utilising dimensional IE models, and developmental researchers have consequently been ahead of the curve using IE as the framing constructs in their research, rather than DSM disorders (e.g., Connell & Goodman, 2002; Gilliom & Shaw, 2004; Jaffee, Moffitt, Caspi, Taylor, & Arseneault, 2002; Lansford et al., 2006; Leve et al., 2005; Moilanen, Shaw, & Maxwell, 2010; Propper, Willoughby, Halpern, Carbone, & Cox, 2007; Tackett, 2010; van Lier & Koot, 2010). This reflects the broad focus of developmental psychopathology on the whole child, rather than on specific psychiatric diagnoses (Pollak, 2015).

In fact, research that uses ASEBA (Achenbach, 2009) incorporates many of the proposals in this paper: a focus on symptom/syndrome-level analyses, an understanding of developmentally coherent processes (rather than different nosologies separated into child and adult camps), and a focus on the IE spectra as constructs of interest. ASEBA has already highlighted some syndromes that are developmentally coherent from preschool through to adulthood (i.e., withdrawn, anxious/depressed, somatic complaints, attention problems, and aggressive behaviour; Achenbach, 2009). These sorts of findings can be integrated into the IE structure, and future finer-grained research could seek parallels between these syndromes and empirically derived lower-level facets in the IE structure. Taken together, child psychopathology research methods act as a working model suggesting that a framework built around the IE spectra and lower-level facets of psychopathology could guide developmental psychopathology research across the lifespan.

Part 2: A Developmentally Informed Approach Based on the Empirically Validated Structure of Psychopathology

In this section we propose a developmentally informed approach to frame future psychopathology research (see Figure 3). It is not new to suggest that IE should be the focus of research (e.g., Carragher et al., 2015; Eaton et al., 2015; Kessler, Ormel, et al., 2011; Kim & Eaton, in press; Lahey et al., 2011); others already use this approach to frame their research —as mentioned above and described in more detail below. We formalise it here specifically to encourage the integration of measures of empirically derived constructs from the hierarchical structure of psychopathology as central constructs in future research. The framework is nested in a diathesis-stress framework where IE form heritable vulnerabilities that are activated or triggered by environmental stressors (cf. Ormel et al., 2013). This approach draws on the developmental model of Externalizing psychopathology that Beauchaine and McNulty (2013) proposed, and extends it to include Internalizing —and more broadly to include factors and facets from all levels of the hierarchical structure of psychopathology. Of all the components in this structure, the IE spectra have been the focus of the largest body of research, so we will continue to focus on them here to describe the processes in our theoretical model below. However, we note again that all levels of the hierarchy offer potentially strong and valid variables for future research. As such, any of these constructs can be used as the central constructs in our proposed approach.

The framework is shown in Figure 3. It describes three primary processes:

1. Cumulative risk influences mean levels of IE;
2. The IE spectra predict adaptive functioning; and
3. Manifest symptoms and syndromes across the lifespan are broadly determined via IE.

We draw readers' attention to the fact that cumulative risk does not directly influence manifest syndromes, and manifest syndromes do not directly account for adaptive functioning. This is a core characteristic of the framework. Drawing on Busseri, Willoughby and Chalmers' (2006) theoretical model, cumulative risk is represented as a latent risk factor that influences the levels of IE. In our framework, the IE spectra act as channels for the effects of cumulative risk on manifest syndromes and adaptive functioning outcomes. The three core processes in the framework are based on evidence from studies that have used the IE spectra as central constructs. We now turn to review the evidence for each of these processes in greater detail with a continued focus on behavioural genetic processes to reflect the etiologic factors underlying manifest syndromes.

Process 1: Cumulative risk influences levels of IE

While it may not be apparent at first, this first process is the most elaborate in the framework. In Figure 3, cumulative risk represents the combined effects of genetic and environmental vulnerabilities and protective factors, as well as the complex interplay between these factors (cf. Busseri et al., 2006). As we emphasised above, cumulative risk influences the mean levels of the IE spectra —which subsequently account for the likelihood

of manifest psychopathology in Process 3 (*Manifest syndromes across the lifespan are broadly determined via IE*)— but it does not directly affect manifest syndromes. Instead, the effects of cumulative risk 'flow through' the channels of IE. While this profoundly complex series of relationships is presented reductively in the framework, there is a variety of evidence that supports this conceptualisation of IE as channels for the effects of cumulative risk on adaptive functioning outcomes and manifest syndromes (e.g., Jaffee et al., 2002; Lahey et al., 2014; Vachon, Krueger, Rogosch, & Cicchetti, 2015). We give an overview of this research below, and describe how the roles of genes and environment might change throughout development.

The Effects of Genes and Environment—As mentioned earlier, IE are heritable vulnerabilities that tend to remain relatively stable over time (e.g., Eaton et al., 2011). Levels of IE are largely determined by their genetic component; for example, Krueger et al. (2002) found that the Externalizing spectrum is 81% heritable. However, environmental risks have also been found to increase the mean levels of IE in an additive fashion (Busseri et al., 2006; Krueger & South, 2009). Early adversity in particular has been found to effect mean level changes in IE: experiencing early life stress in the forms of child maltreatment and neglect (Lansford et al., 2006; Vachon et al., 2015) or domestic violence (Jaffee et al., 2002) impact IE in a coherent way. Exposure to trauma later in life also has this effect (Meyers et al., 2015). Other adverse environmental factors have also been found to predict levels of IE, such as discrimination (Eaton, 2014; Rodriguez-Seijas, Stohl, Hasin, & Eaton, 2015), difficulties in peer relationships (van Lier & Koot, 2010), harsh parenting (Leve et al., 2005; Wiggins et al., 2015), parents' marital conflict (Obradovic, Bush, & Boyce, 2011), and socioeconomic disadvantage (e.g., Moffitt, 1993). Religiosity appears to act as a protective factor for levels of IE (Kendler, Liu, et al., 2003). In contrast to genetic factors, environmental influences do not show a clear IE structure (Kendler et al., 2011), so it is likely that their influences on IE are through their impact on coherent underlying genetic predispositions.

The Interactions between Genes and Environment—The interactions between genes and environment have a particularly influential role on mean levels of IE because environmental stressors can activate genetic vulnerabilities. For example, high-risk environments (e.g., low socioeconomic status or urban environments) have been found to amplify genetic predispositions to Externalizing behaviours (Hamdi, Krueger, & South, 2015; Legrand, Keyes, McGue, Iacono, & Krueger, 2008), whereas environments that limit choice (e.g., rural environments or high parental monitoring) attenuate genetic influences on Externalizing (Dick et al., 2007; Rose, Dick, Viken, & Kaprio, 2001). Beyond these diathesis-stress mechanisms, there are also some preliminary findings that suggest specific genes and biological mechanisms may increase individuals' sensitivity to the influence of positive or negative environments (e.g., Caspi et al., 2002; Keiley, Howe, Dodge, Bates, & Petti, 2001; Obradovic et al., 2011). This literature is beyond the scope of our review, but offers preliminary evidence that some individuals may be predisposed to develop psychopathology in high adversity circumstances, and more likely to thrive in low adversity circumstances.

The Changing Roles of Genes and Environment over Development—Genetic and environmental influences have changing roles in cumulative risk across development. In general, environmental influences —particularly environmental influences shared within families— appear to have more of an impact on levels of IE earlier in development, whereas the impact of genes increases with age (Bergen, Gardner, & Kendler, 2007; Gjone & Stevenson, 1997; Waszczuk, Zavos, Gregory, & Eley, 2014). Bergen et al. (2007) posited that this may be the result of increasingly active genotype-environment correlations (i.e., a propensity to seek out environments as a result of genetic influence), an increase in gene expression, or proportional decreases in environmental variance. Substance use disorders appear to be a unique case where environmental factors (e.g., exposure to different drugs of abuse) have a greater role in adolescence and early adulthood, while genetic influence declines (Vrieze, Hicks, Iacono, & McGue, 2012).

Summary—The influences of genes and environment are multifactorial and complex, and they differ for Internalizing and Externalizing, as well as across developmental stages. Regardless of developmental stage, the impact of any risk factor depends on the levels of other risk factors (Gilliom & Shaw, 2004), and past and present life experiences interact with genetic vulnerabilities to amplify risk in an ongoing loop. While these relationships are undeniably complex, our point here is to emphasise that the strongest effects of cumulative risk are through changes in the mean levels of IE, rather than by affecting manifest syndromes directly (see Figure 3). In support of this, studies have found that adverse environments effect change in the mean levels of IE, rather than affecting specific syndromes (e.g., Jaffee et al., 2002; Lahey et al., 2014; Vachon et al., 2015). These changes in IE subsequently account for the likelihood, severity, and persistence of psychopathology (see Figure 2, and Process 3 below).

Process 2: The IE spectra account for adaptive functioning

The second process in the framework is much simpler: the IE spectra —rather than manifest syndromes— account for adaptive functioning (i.e., the ability to effectively navigate the demands of our environments). The spectra have been found to predict indicators of severe functional impairment such as suicide attempts, hospitalisations, disability days, use of welfare, violence convictions, and physical health (e.g., Caspi et al., 2014; Eaton, Krueger, et al., 2013; Sunderland & Slade, 2015). IE also account more broadly for adaptive functioning in the form of marital distress (South, Krueger, & Iacono, 2011), peer relationship difficulties (van Lier & Koot, 2010), academic functioning (Moilanen et al., 2010), and social competence (Lansford et al., 2006). Essentially, higher levels of IE are related to greater functional impairment, and this can be roughly operationalised by the number of syndromes for which an individual meets diagnostic criteria. For example, Krueger and Finger (2001) found that people who met criteria for six or seven Internalizing disorders had twice the number of disability days and hospital stays compared to people who met criteria for five or less disorders.

Similar to the literature on Process 1 (*Cumulative risk influences levels of IE*), studies that have compared the predictive validity of individual syndromes with the predictive validity of the IE spectra have found that IE account for nearly all of the variance in adaptive

functioning, while the role of individual syndromes is small and usually non-significant (e.g., Eaton, Krueger, et al., 2013; South et al., 2011). This is depicted in Figure 3 where there are no direct paths from manifest syndromes to adaptive functioning. Instead, IE continue to act as the channels for important developmental processes.

Process 3: Manifest syndromes across the lifespan are broadly determined via IE

The third primary process in the framework depicts manifest syndromes as multiply determined by the severity level of IE interacting with mediating and moderating contextual factors, as well as through ongoing transactional feedback loops with adaptive functioning and manifest syndromes. As we mentioned in Part 1, the likelihood of manifest syndromes is broadly determined by the mean level —or severity— of IE. For example, Krueger and Finger (2001) found that the diagnostic thresholds for major depression, dysthymia, agoraphobia, social anxiety, specific phobias, generalised anxiety, and panic disorders corresponded to different severity levels on the upper half of the Internalizing continuum. This suggests that individuals with Internalizing severity in the lower half of the spectrum may not have any Internalizing syndromes that exceed DSM diagnostic thresholds. More specifically, Krueger and Finger (2001) found that the DSM disorders corresponded with different levels of severity: Specific phobias indicated comparatively lower levels of Internalizing, while panic disorder and generalised anxiety disorder represented more severe indicators. A similar study that focused on Externalizing syndromes found that licit substance dependences (e.g., nicotine or alcohol) indicated comparatively lower levels of Externalizing, while antisocial personality disorder (ASPD) and illicit substance dependences (e.g., cocaine or opioids) represented more severe indicators (Markon & Krueger, 2005).

While specific syndromes correspond broadly with varying severity levels of IE, the mechanisms that determine the manifestation of one syndrome over another (e.g., the development of a substance dependence instead of oppositional behaviour) are less clear, potentially due to the complexity of these processes. In Figure 3, specific manifest syndromes are determined by contextual mediators and moderators interacting with IE to alter their expression. This is based on research that suggests that manifest syndromes are driven largely by environmental effects, and the context in which development takes place (Kendler et al., 2011). For example, if genetic vulnerabilities create a predisposition for a given level of IE, the environmental stressors can be conceptualised as potential mediating or moderating factors; as such, the contextual mediators and moderators in Figure 3 have substantial overlap with the factors that comprise cumulative risk. Using the Externalizing examples described in Process 1, (*Cumulative risk influences levels of IE*), the genetically driven mean levels of risk may be amplified by some environments (e.g., low SES, or urban environments), and dampened by other environments that limit choice (e.g., parental control, rural environments). Other environmental influences like peer and sibling influences, or exposure to drugs of abuse, may also guide the manifestation of specific syndromes, and biological mechanisms are likely to have a role too (e.g., altered or abnormal alcohol metabolism may affect whether someone high on the Externalizing continuum develops problems with alcohol use, or turns to other drugs of abuse instead; cf. Irons, Iacono, Oetting, & McGue, 2012).

Other Processes in the Framework

The recursive arrows in Figure 3 signify that early patterns of adaptation influence later adaptation, but not necessarily in a simple linear manner (Sroufe & Rutter, 1984). These cyclical relationships are closely related to the manifestation of syndromes across the lifespan. The arrows depict the interaction of past and present experiences with changing environments and genetic vulnerabilities, which form an ongoing transactional loop with manifest syndromes and adaptive functioning. For example, early life environmental stressors can have dynamic impacts on adaptive functioning across multiple domains that go on to influence later adaptation and psychopathology via cumulative risk (Burnette & Cicchetti, 2012). This loop can lead to increasingly severe forms of psychopathology over development if maladaptive pathways continue to be supported (Beauchaine & McNulty, 2013; Pollak, 2015).

More broadly, the framework as a whole represents an ontogenic process, which is reflected by the light grey cyclical arrows in Figure 3. The processes and the manifest syndromes in the framework may change across development, but it can be used as a guide for psychopathological research at any developmental stage after infancy. This allows us to conceptualise psychopathology in a developmentally coherent way: manifest syndromes may vary throughout the lifespan, but they do not follow individual idiosyncratic trajectories; they change in concert as variations in IE severity interact with complex developmental processes (Eaton et al., 2010; Krueger & South, 2009).

Part 3: How this Structural Approach Enhances Developmental Psychopathology Research

With these processes combined, the framework provides a developmentally informed approach to understanding psychopathology. Its characteristics make this approach ideal to frame research on the three central concepts of developmental psychopathology, as outlined by Rutter and Sroufe (2000):

1. Understanding causal processes that determine multifinal and equifinal outcomes;
2. Delineating the mechanisms that give rise to continuity and change over time; and
3. Examining the role of development in psychopathology.

Understanding Multifinal and Equifinal Outcomes—The causal processes that lead to different outcomes in manifest psychopathology and adaptive functioning can be understood in the context of our approach. For example, research based in the framework of Process 2 (*The IE spectra account for adaptive functioning*) can be used to examine how broad domains of psychopathology (e.g., the IE spectra) impact adaptive functioning, and how IE mediate or moderate the influence of genes and environment on functional impairment across multiple domains over the lifespan (cf. Burnette & Cicchetti, 2012; Cicchetti & Natsuaki, 2014). Similarly, the framework can account for a multitude of

outcomes through the mean levels of IE interacting with mediating and moderating environmental influences, combined with the feedback loops with adaptive functioning and manifest syndromes. The complex interactions of direct and indirect developmental pathways in the framework mean that a single risk factor may have diverse consequences for different individuals, and any given outcome may also arise from a variety of paths. In developmental terms, these processes account for multifinalilty (i.e., similar pathways resulting in different outcomes) and equifinality (i.e., different pathways that converge on similar outcomes).

Delineating the Mechanisms that Give Rise to Continuity and Change—The whole framework is geared towards understanding the mechanisms that affect change across development. For example, the IE spectra represent the primary pathways of syndrome continuity and change, and act as liabilities for the development of other syndromes (e.g., Eaton, Krueger, et al., 2013; Eaton et al., 2011). They are thus key drivers in the development of sequential comorbidity (Kessler, Ormel, et al., 2011; Krueger & Eaton, 2015). More specifically, IE predict both homotypic and heterotypic continuity (i.e., the development of disorders that belong to the same spectra, or to other spectra, respectively; Kim & Eaton, in press; Lahey et al., 2014). In our proposed framework, we can understand disorder manifestations as facets from the hierarchical structure of psychopathology that wax and wane over the course of development, rather than conceptualizing disorders as presenting with a relapsing course, or acting as risk factors for one another (cf. Goldberg, Krueger, Andrews, & Hobbs, 2009). This sort of understanding of the coherence in the course of an individual's development is important (Sroufe & Rutter, 1984), but is not possible in the categorical DSM framework per se. Our framework thus offers a unique perspective to understand the mechanisms that give rise to continuity and change over time.

Examining the Role of Development in Psychopathology—Understanding the developmental course of illness is valuable because the persistence of psychopathology over time is a strong indicator of severity (Caspi et al., 2014; Kendler et al., 2011), and is consequently related to more severe and complex manifestations of IE over the life course, as well as later developmental outcomes (Young Mun, Fitzgerald, Von Eye, Puttler, & Zucker, 2001). Our framework is intertwined with the role of development in psychopathology because it represents an ontogenic process, as described in Part 2. By moving beyond the DSM traditions that artificially separate child and adult disorders, the framework is particularly well suited to facilitate sensitive measurement of psychopathology across the lifespan, and to investigate the developmental processes at work.

Other Strengths of this Approach for Developmental Psychopathology

Our framework also meets additional needs of developmental psychopathologists, as it facilitates multi-level analysis, while generating empirically testable research questions (Cicchetti & Blender, 2004). For example, it can facilitate research on how the correlates of psychopathology are organised, as well as how genetic, environmental, psychological, and biological processes affect dynamic individual change within and between situations (and we offer specific examples below). The framework can also be used for research on individual-centred (e.g., symptom trajectories) or variable-centred (e.g., path analysis)

relationships. Two additional strengths —the flexibility of the framework, and the opportunity it presents to integrate interdisciplinary research— are discussed in more detail below.

Simplicity as a Strength—Developmentalists may baulk at the apparent simplicity of our proposed framework; it reduces inherently complex mechanisms into single latent variables (e.g., cumulative risk). However, this simplicity is a strength because it offers flexibility and still facilitates the work of developmental psychopathologists in disentangling the complexity within developmental pathways (Rutter & Sroufe, 2000). Rather than prescribing a specific model with a rigid set of relationships, this approach acts as a flexible theoretical framework within which to form tractable research questions. For example, the framework could be used in research that examines the role of a single risk factor in a developmental cascade with IE; in a twin study that aims to understand how genetic and environmental influences affect the likelihood of suicide risk; or in a longitudinal study that aims to understand the factors that predispose adolescents high on the Externalizing spectrum to manifest one given syndrome over another. As such, this approach can integrate the diverse streams of the developmental psychopathology literature to form a coherent body of research.

Integrating Interdisciplinary Research—Our proposed approach also offers a unifying framework for interdisciplinary psychopathology research more broadly. Increasingly varied fields of research are incorporating the empirically derived factors from the hierarchical structure of psychopathology as central constructs, and this maximises the opportunity to integrate research findings within and between these diverse fields. For example, within a given field of research, the characteristics of the IE spectra can account for apparent diagnostic bias (i.e., systematic differences in the prevalence of mental disorder diagnoses) between different populations; specifically, in older age groups (Hoertel et al., 2015; Sunderland et al., 2013), ethnic minorities (Eaton, Keyes, et al., 2013; Guttmannova et al., 2008), and between genders (Eaton et al., 2012; Kramer et al., 2008). This subsequently facilitates a more robust understanding of psychopathology that generalises across populations. On a larger scale, clinical and neurobiological research represent two of the fields that incorporate factors from the hierarchical structure, so developmental psychopathology research based on our proposed framework will generate results that can be understood easily in the context of these other psychopathology disciplines.

Take the example of clinical research: Transdiagnostic spectra have become a focus, as they offer compelling targets for efficient interventions that aim to reduce the burden of mental disorders by targeting processes at the spectrum level (e.g., the Unified Protocol; Barlow et al., 2010). Given the age invariance and persistence of IE, these types of interventions could potentially be efficacious across the lifespan (Hoertel et al., 2015). The developmental coherence of IE also suggests that the spectra could be used to identify children who are at risk of developing psychopathology, as IE emerge by the preschool years and perhaps as early as 12 months of age (Carter et al., 2003; Young Mun et al., 2001). The early onset of psychopathology is a strong predictor of risk for progression to later disorders (Kessler, Ormel, et al., 2011), so the early emergence of IE highlights the attractive possibility that

primary prevention interventions could be developed and applied with comprehensive benefits from early childhood to mitigate changes in neurobiology that may go on to support maladaptive feedback loops, heightening the long term risk for psychopathology (Beauchaine & McNulty, 2013; Vachon et al., 2015). As we learn more about the factors that interact to form cumulative risk, there is also potential to develop interventions for modifiable risk factors to interrupt this cycle. In short, there is plenty of room for clinical research to expand in our current framework, and to integrate with developmental psychopathology research.

Neurobiology represents another field where factors from the hierarchical structure of psychopathology offer ideal target constructs, as they can integrate biological and phenomenological investigations (Eaton et al., 2015). More specifically, these factors can integrate the Research Domain Criteria (RDoC; i.e., a structured research framework that aims to understand neural systems that influence behaviour and psychology) with syndrome-focused research, and incorporate clinical description in the process (Krueger & DeYoung, in press; Krueger et al., 2014). Insel et al. (2010) proposed RDoC to guide research focusing on the basic biological mechanisms underlying behaviour, and Insel (2013) subsequently suggested that research on DSM disorders should no longer be funded by the National Institute of Mental Health, as they lack validity. However, if psychiatric categories are excluded as phenotypes to guide research, and there is not currently enough information to define clinical phenotypes in molecular genetics and biomarker research (Goldberg, 2015), then we are left to find an alternative. Given the IE spectra are closely related to neurobiological substrates of behaviour (see Eaton et al., 2015; Krueger et al., 2014), they are prime candidates to frame RDoC investigations (Krueger & DeYoung, in press; Gizer et al., 2015). Where narrowly defined phenotypes are of interest, such as individual symptoms or very homogeneous symptom sets (Kozak & Cuthbert, 2016), the finer-grained facets in the lower levels of the hierarchical structure can be used as phenotypes to frame molecular genetic research (Patrick & Hajcak, 2016). Lower levels of the structure can also highlight heterogeneity within phenotypes. For example, major depression comes in melancholic, atypical, and psychotic forms, to name a few (Goldberg, 2011), and the specific polymorphisms that give rise to these discrete groups can be examined in the framework of the hierarchical structure of psychopathology. In short, although RDoC and transdiagnostic psychopathology research approach nosology from different perspectives, they are perfectly positioned to move iteratively towards a unified model (Kotov et al., in press). By using factors from the hierarchical structure as the phenotypes in RDoC research, we are presented with an ideal bridge between the ingrained traditions of DSM disorders and emerging biomarker research (Krueger & DeYoung, in press). We note again that this bridge relies on researchers using multiple DSM disorders to indicate IE to maximise their reliability and validity.

In summary, research framed by our proposed developmental framework will contribute to an interdisciplinary body of research on transdiagnostic factors that can ultimately form a unified and developmentally informed model of psychopathology. In contrast, research that continues to focus on DSM disorders in isolation —or on specific patterns of co-occurrence among disorders— will not.

Directions for Future Research

Further research on the mechanisms described in our framework will strengthen our understanding of psychopathology. As described above, our proposed approach is particularly well suited to frame research with a developmental psychopathology focus. There are also some specific avenues for future research that will extend the capabilities of the framework, and we explore these areas below.

Elucidating Lower Levels of the Structure—While we have focused on IE as the examples throughout this paper, we have also highlighted that all levels of the hierarchy can be used as central constructs in the framework. Given IE do not account for *all* of the variance in comorbidity over time, in genetic influences, or in adaptive functioning outcomes, the lower-level facets in the hierarchical structure are also likely to be influential constructs in future research (e.g., Caspi et al., 2014; Hicks, Krueger, Iacono, McGue, & Patrick, 2004; Kessler, Cox, et al., 2011; Krueger & DeYoung, in press). The flexibility of the hierarchical model of psychopathology is an added strength for our proposed approach, as it allows for lumping or splitting shared and unique variance to identify both general risk and syndrome-specific causal influences (Kim & Eaton, in press). Lahey et al. (2004) described the advantages of this flexibility for child psychopathology research, as it can address the four main points of difference among current taxonomies (i.e., the lumping and splitting of hyperactivity and inattention, nonaggressive and aggressive conduct disorder, anxiety and depression, and multiple domains of anxiety). More broadly, partialling out the shared and unique variance at different levels of the structure allows for flexible analyses, and for understanding specificity and generality in an empirical way. For example, broad biological mechanisms are likely to cause variation in higher-order transdiagnostic factors, whereas other mechanisms might affect specific brain function and cause change in lower-level facets (Krueger & DeYoung, in press). Similarly, factors like IE are a particularly valuable focus for public health where the aim is to effect change in common processes in the population, whereas lower-level facets could offer more detailed information for tailored individual-level interventions (Rodriguez-Seijas, Eaton, et al., 2015). To take advantage of the flexibility of the hierarchy, future research will need to empirically elucidate the fine-grained components of the structure, which remain obscured by the focus of research on DSM disorders to date. As we discussed earlier, the best way forward is to use continuous symptom-level measures of psychopathology (e.g., the ESI, CAPS, and/or IMAS inventories).

Testing Facets for Developmental Coherence—As the hierarchy is refined further by extension downward, each component will need to be tested for developmental coherence. Achenbach and colleagues have already contributed decades of foundational work in this area via ASEBA, uncovering numerous dimensional syndromes that are evident across the lifespan (Achenbach, 2009). These syndromes may prove to be developmentally coherent facets in the hierarchical structure, but the research in this context is limited. For example, at the moment there is robust evidence that IE emerge as orienting dispositions across the lifespan, but further research is needed to determine whether the factor structure remains constant throughout childhood and adolescence. This needs to be established before we can make meaningful comparisons on IE across these developmental stages.

At a lower level of the hierarchy, emerging evidence suggests that Fear and Distress are differentiated from early childhood (Hopwood, Zimmermann, Pincus, & Krueger, 2015; Lahey et al., 2008; Lahey et al., 2011; Trosper, Whitton, Brown, & Pincus, 2012), and they have been explicitly found in confirmatory factor analyses in children and adolescents aged 5–16, 8–10 and 12–18 (Gomez et al., 2014; S. C. Kushner, Tackett, & Bagby, 2012; Doyle et al., 2016). However, one study found genetic and phenotypic correlations among anxiety and depression increased from childhood to early adulthood (Waszczuk et al., 2014). Further, studies that use the Child Behavior Checklist (Achenbach, 1991) cannot differentiate between Fear and Distress because the depression/anxiety facet lumps them together. Overall, the developmental coherence of Fear and Distress requires further research.

Research on Externalizing in children and adults also reveal parallels throughout development at a facet level (e.g. Achenbach & Rescorla, 2001b, 2003; Krueger & South, 2009; Krueger et al., 2014). Conduct disorder is an example that illustrates how facets from the hierarchical structure are more developmentally informative than the DSM model: Conduct disorder is comprised of two facets —aggressive and rule-breaking behaviour— that have distinguishable etiologies (Burt, 2009; Tackett, Krueger, Iacono, & McGue, 2005; Tackett, Krueger, Sawyer, & Graetz, 2003). These facets appear to be developmentally coherent into adulthood, where ASPD comprises aggression and disinhibition facets, which also have distinguishable etiologies (Kendler, Aggen, & Patrick, 2012). Despite this apparent developmental coherence in the facets, conduct disorder is redefined as a different category in adulthood (i.e., as ASPD). By conceptualising conduct disorder symptoms as facets of the Externalizing spectrum developing over time, they make sense, and provide more useful developmental information (Krueger et al., 2007).

Overall, these findings highlight that researchers focusing on disorders run the risk of losing valuable information; any findings that specifically relate to lower-level facets will be diluted or obscured entirely. More broadly, these findings emphasise the importance of using empirically derived constructs from the hierarchical structure of psychopathology to guide future research. Given the empirically derived hierarchical structure reflects the natural organisation of psychopathology, it also offers the most efficient way to discover and understand the mechanisms that give rise to manifest psychopathology across the lifespan. As such, utilising constructs from the structure offers the best way forward for all researchers aiming to understand psychopathology, regardless of whether their focus is on development, or on the roles of environmental risk factors, candidate genes, or endophenotypes.

Conclusions

In this review we have described how IE organise the correlates of psychopathology, act as channels between cumulative risk dimensions and manifest syndromes, and account for the variance in important outcomes. On this basis, we argued that the factors and facets in the hierarchical structure of psychopathology are ideal constructs to integrate interdisciplinary research, and specifically to form the focus of developmental psychopathology research. We encourage researchers to adopt a developmentally informed, structural approach to conceptualizing psychopathology. To facilitate this, we have presented a flexible,

developmentally informed framework structured around these constructs to guide research. Our framework is consistent with existing developmental models (e.g., Beauchaine & McNulty, 2013), and can facilitate a variety of multilevel research. Ultimately, we emphasise the importance of moving beyond a focus on DSM disorders in isolation, or on narrow and specific manifestations of comorbidity, and instead moving towards a dimensional and hierarchical approach to understanding psychopathology across the lifespan. DSM disorders can still be used to indicate the IE spectra, but it is time we move beyond comorbidity.

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References

Achenbach, TM. Manual for the Child Behavior Checklist/4–18 and 1991 profile. Department of Psychiatry, University of Vermont; Burlington, VT: 1991.

Achenbach, TM. The Achenbach System of Empirically Based Assessemnt (ASEBA): Development, Findings, Theory, and Applications. Burlington, VT: University of Vermont Research Center for Children, Youth, & Families; 2009.

Achenbach TM, Edelbrock CS. The classification of child psychopathology: A review and analysis of empirical efforts. Psychological Bulletin. 1978; 85(6):1275–1301. [PubMed: 366649]

Achenbach TM, Edelbrock CS. Psychopathology of Childhood. Annual Review of Psychology. 1984; 35(1):227–256.

Achenbach TM, Howell CT, Quay HC. National survey of problems and competencies among four- to sixteen-year-olds: Parents' reports for normative and clinical samples. Monographs of the Society for Research in Child Development. 1991; 56(3):1–131.

Achenbach, TM.; Rescorla, LA. Manual for the Achenbach system of empirically based assessment school-age forms profiles. Burlington, VT: Aseba; 2001a.

Achenbach, TM.; Rescorla, LA. Child behavior checklist for age 6–18, teacher's report from, youth self-report and integrated system of multi-informant assessment. Burlington, VT: University of Vermont; 2001b. Manual for the ASEBA school-age forms and profiles.

Achenbach, TM.; Rescorla, LA. Manual for the ASEBA adult forms & profiles. Burlington, VT: University of Vermont; 2003.

Barlow, DH.; Farchione, TJ.; Fairholme, CP.; Ellard, KK.; Boisseau, CL.; Allen, LB.; May, JTE. Unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide. Oxford University Press; USA: 2010.

Beauchaine TP, McNulty T. Comorbidities and continuities as ontogenic processes: Toward a developmental spectrum model of externalizing psychopathology. Development and Psychopathology. 2013; 25:1505–1528. [PubMed: 24342853]

Bergen SE, Gardner CO, Kendler KS. Age-related changes in heritability of behavioral phenotypes over adolescence and young adulthood: A meta-analysis. Twin Research and Human Genetics. 2007; 10(3):423–433. [PubMed: 17564500]

Boyd JH, Burke JDJ, Gruenberg E, Holzer CEr, Rae DS, George LK, … Nestadt G. Exclusion criteria of DSM-III: A study of co-occurrence of hierarchy-free syndromes. Archives of General Psychiatry. 1984; 41(10):983–989. [PubMed: 6477056]

Burnette ML, Cicchetti D. Multilevel approaches toward understanding antisocial behavior: Current research and future directions. Development and Psychopathology. 2012; 24(3):703–704. [PubMed: 22781849]

Burt SA. Are there meaningful etiological differences within antisocial behavior? Results of a meta-analysis. Clinical Psychology Review. 2009; 29(2):163–178. [PubMed: 19193479]

Busseri MA, Willoughby T, Chalmers H. A rationale and method for examining reasons for linkages among adolescent risk behaviors. Journal of Youth and Adolescence. 2006; 36(3):279–289. [PubMed: 27519027]

Caron C, Rutter M. Comorbidity in child psychopathology: Concepts, issues and research strategies. Journal of Child Psychology and Psychiatry. 1991; 32(7):1063–1080. [PubMed: 1787137]

Carragher N, Krueger RF, Eaton NR, Slade T. Disorders without borders: Current and future directions in the meta-structure of mental disorders. Social Psychiatry and Psychiatric Epidemiology. 2015; 50(3):339–350. [PubMed: 25557024]

Carter AS, Briggs-Gowan MJ, Jones SM, Little TD. The Infant-Toddler Social and Emotional Assessment (ITSEA): Factor structure, reliability, and validity. Journal of Abnormal Child Psychology. 2003; 31(5):495–514. [PubMed: 14561058]

Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, Israel S, … Moffitt TE. The p Factor: One general psychopathology factor in the structure of psychiatric disorders? Clinical Psychological Science. 2014; 2(2):119–137. [PubMed: 25360393]

Caspi A, McClay J, Moffitt TE, Mill J, Martin J, Craig IW, … Poulton R. Role of genotype in the cycle of violence in maltreated children. Science. 2002; 297(5582):851–854. [PubMed: 12161658]

Cicchetti D, Blender JA. A multiple-levels-of-analysis approach to the study of developmental processes in maltreated children. Proceedings of the National Academy of Sciences of the United States of America. 2004; 101(50):17325–17326. [PubMed: 15583123]

Cicchetti D, Natsuaki MN. Multilevel developmental perspectives toward understanding internalizing psychopathology: Current research and future directions. Development and psychopathology. 2014; 26(4pt2):1189–1190. [PubMed: 25422954]

comorbid. Merriam-Webster Online Dictionary. 2015. Retrieved from http://www.merriam-webster.com/dictionary/comorbid

comorbidity. Oxford Dictionaries. 2015. Retrieved from http://www.oxforddictionaries.com/us/definition/american_english/comorbidity

Connell AM, Goodman SH. The association between psychopathology in fathers versus mothers and children's internalizing and externalizing behavior problems: A meta-analysis. Psychological Bulletin. 2002; 128(5):746–773. [PubMed: 12206193]

Dick DM, Viken RJ, Purcell S, Kaprio J, Pulkkinen L, Rose RJ. Parental monitoring moderates the importance of genetic and environmental influences on adolescent smoking. Journal of Abnormal Psychology. 2007; 116(1):213–218. [PubMed: 17324032]

Doyle MM, Murphy J, Shevlin M. Competing Factor Models of Child and Adolescent Psychopathology. Journal of Abnormal Child Psychology. 2016:1–13. [PubMed: 26687502]

Eaton NR. Transdiagnostic psychopathology factors and sexual minority mental health: Evidence of disparities and associations with minority stressors. Psychology of Sexual Orientation and Gender Diversity. 2014; 1(3):244–254. [PubMed: 25530981]

Eaton NR, Keyes KM, Krueger RF, Balsis S, Skodol AE, Markon KE, … Hasin DS. An invariant dimensional liability model of gender differences in mental disorder prevalence: Evidence from a national sample. Journal of Abnormal Psychology. 2012; 121(1):282–288. [PubMed: 21842958]

Eaton NR, Keyes KM, Krueger RF, Noordhof A, Skodol AE, Markon KE, … Hasin DS. Ethnicity and psychiatric comorbidity in a national sample: Evidence for latent comorbidity factor invariance and connections with disorder prevalence. Social Psychiatry and Psychiatric Epidemiology. 2013; 48(5):701–710. [PubMed: 23052426]

Eaton NR, Krueger RF, Markon KE, Keyes KM, Skodol AE, Wall M, … Grant BF. The structure and predictive validity of the internalizing disorders. Journal of Abnormal Psychology. 2013; 122(1): 86–92. [PubMed: 22905862]

Eaton NR, Krueger RF, Oltmanns TF. Aging and the structure and long-term stability of the internalizing spectrum of personality and psychopathology. Psychology and Aging. 2011; 26(4): 987–993. [PubMed: 21728443]

Eaton NR, Rodriguez-Seijas C, Carragher N, Krueger RF. Transdiagnostic factors of psychopathology and substance use disorders: A review. Social Psychiatry and Psychiatric Epidemiology. 2015; 50(2):171–182. [PubMed: 25563838]

Eaton, NR.; South, SC.; Krueger, RF. The meaning of comorbidity among common mental disorders. In: Millon, T.; Krueger, RF.; Simonsen, E., editors. Contemporary directions in psychopathology: Scientific foundations of the DSM-V and ICD-11. New York, NY, US: Guilford Press; 2010. p. 223-241.

Forbes MK, Baillie AJ, Schniering CA. Where do sexual dysfunctions fit into the meta-structure of psychopathology? A factor mixture analysis. Archives of Sexual Behavior. 2015:1–14. [PubMed: 25408500]

Forbes MK, Schniering CA. Are sexual problems a form of internalizing psychopathology? A structural equation modeling analysis. Archives of Sexual Behavior. 2013; 42(1):23–34. [PubMed: 22562617]

Forbush KT, Watson D. The structure of common and uncommon mental disorders. Psychological Medicine. 2013; 43(01):97–108. [PubMed: 22613885]

Forbush KT, Wildes JE, Pollack LO, Dunbar D, Luo J, Patterson K, … Bright A. Development and validation of the Eating Pathology Symptoms Inventory (EPSI). Psychological Assessment. 2013; 25(3):859. [PubMed: 23815116]

Gilliom M, Shaw DS. Codevelopment of externalizing and internalizing problems in early childhood. Development and Psychopathology. 2004; 16(2):313–333. [PubMed: 15487598]

Gjone H, Stevenson J. The association between internalizing and externalizing behavior in childhood and early adolescence: Genetic or environmental common influences? Journal of Abnormal Child Psychology. 1997; 25(4):277–286. [PubMed: 9304444]

Goldberg DP. The heterogeneity of “major depression. World Psychiatry. 2011; 10(3):226–228. [PubMed: 21991283]

Goldberg DP. Psychopathology and classification in psychiatry. Social Psychiatry and Psychiatric Epidemiology. 2015; 50(1):1–5. [PubMed: 24970576]

Goldberg DP, Krueger RF, Andrews G, Hobbs MJ. Emotional disorders: Cluster 4 of the proposed meta-structure for DSM-V and ICD-11. Psychological Medicine. 2009; 39(12):2043–2059. [PubMed: 19796429]

Gomez R, Vance A, Gomez RM. The factor structure of anxiety and depressive disorders in a sample of clinic-referred adolescents. Journal of Abnormal Child Psychology. 2014; 42(2):321–332. [PubMed: 23942827]

Guttmannova K, Szanyi JM, Cali PW. Internalizing and externalizing behavior problem scores: Cross-ethnic and longitudinal measurement invariance of the Behavior Problem Index. Educational and Psychological Measurement. 2008; 68(4):676–694.

Hamdi NR, Krueger RF, South SC. Socioeconomic status moderates genetic and environmental effects on the amount of alcohol use. Alcoholism: Clinical and Experimental Research. 2015; 39(4):603–610.

Haslam N, Holland E, Kuppens P. Categories versus dimensions in personality and psychopathology: A quantitative review of taxometric research. Psychological Medicine. 2012; 42(5):903–920. [PubMed: 21939592]

Hicks BM, Krueger RF, Iacono WG, McGue M, Patrick CJ. Family transmission and heritability of externalizing disorders: A twin-family study. Archives of General Psychiatry. 2004; 61(9):922–928. [PubMed: 15351771]

Hoertel N, McMahon K, Olfson M, Wall MM, Rodriguez-Fernandez JM, Lemogne C, … Blanco C. A dimensional liability model of age differences in mental disorder prevalence: Evidence from a national sample. Journal of Psychiatric Research. 2015; 64:107–113. [PubMed: 25858414]

Hopwood CJ, Zimmermann J, Pincus AL, Krueger RF. Connecting personality structure and dynamics: Towards a more evidence-based and clinically useful diagnostic scheme. Journal of Personality Disorders. 2015; 29(4):431–448. [PubMed: 26200845]

Iacono WG, Vaidyanathan U, Vrieze SI, Malone SM. Knowns and unknowns for psychophysiological endophenotypes: Integration and response to commentaries. Psychophysiology. 2014; 51(12): 1339–1347. [PubMed: 25387720]

Insel, TR. Director’s Blog: Transforming Diagnosis. 2013. Retrieved from http://www.nimh.nih.gov/about/director/2013/transforming-diagnosis.shtml

Insel TR, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, … Wang P. Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. American Journal of Psychiatry. 2010; 167(7):748–751. [PubMed: 20595427]

Irons DE, Iacono WG, Oetting WS, McGue M. Developmental trajectory and environmental moderation of the effect of ALDH2 polymorphism on alcohol use. Alcoholism: Clinical and Experimental Research. 2012; 36(11):1882–1891.

Jackson KM, Sher KJ, Wood PK. Trajectories of concurrent substance use disorders: A developmental, typological approach to comorbidity. Alcoholism: Clinical and Experimental Research. 2000; 24(6):902–913.

Jaffee SR, Moffitt TE, Caspi A, Taylor A, Arseneault L. Influence of adult domestic violence on children's internalizing and externalizing problems: An environmentally informative twin study. Journal of the American Academy of Child and Adolescent Psychiatry. 2002; 41(9):1095–1103. [PubMed: 12218431]

Keiley MK, Howe TR, Dodge KA, Bates JE, Petti GS. The timing of child physical maltreatment: A cross-domain growth analysis of impact on adolescent externalizing and internalizing problems. Development and Psychopathology. 2001; 13(4):891–912. [PubMed: 11771913]

Kendler KS, Aggen SH, Knudsen GP, Roysamb E, Neale MC, Reichborn-Kjennerud T. The structure of genetic and environmental risk factors for syndromal and subsyndromal common DSM-IV axis I and all axis II disorders. The American Journal of Psychiatry. 2011; 168(1):29–39. [PubMed: 20952461]

Kendler KS, Aggen SH, Patrick CJ. A multivariate twin study of the DSM-IV criteria for antisocial personality disorder. Biological Psychiatry. 2012; 71(3):247–253. [PubMed: 21762879]

Kendler KS, Liu XQ, Gardner CO, McCullough ME, Larson D, Prescott CA. Dimensions of religiosity and their relationship to lifetime psychiatric and substance use disorders. The American Journal of Psychiatry. 2003; 160(3):496–503. [PubMed: 12611831]

Kendler KS, Prescott CA, Myers J, Neale MC. The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. Archives of General Psychiatry. 2003; 60(9):929–937. [PubMed: 12963675]

Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry. 2005; 62(6):593–602. [PubMed: 15939837]

Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry. 2005; 62(6):617–627. [PubMed: 15939839]

Kessler RC, Cox BJ, Green JG, Ormel J, McLaughlin KA, Merikangas KR, … Zaslavsky AM. The effects of latent variables in the development of comorbidity among common mental disorders. Depression and Anxiety. 2011; 28(1):29–39. [PubMed: 21225850]

Kessler RC, Ormel J, Petukhova M, McLaughlin KA, Green JG, Russo LJ, … Ustun TB. Development of lifetime comorbidity in the World Health Organization world mental health surveys. Archives of General Psychiatry. 2011; 68(1):90–100. [PubMed: 21199968]

Kim HK, Eaton NR. The hierarchical structure of common mental disorders: Connecting multiple levels of comorbidity, bifactor models, and predictive validity. Journal of Abnormal Psychology. in press.

Kotov R, Krueger RF, Watson D, Achenbach TM, Althoff RR, Bagby M, … Zimmerman M. The hierarchical taxonomy of psychopathology (HiTOP): A dimensional alternative to traditional nosologies. in press.

Kotov R, Perlman G, Gamez W, Watson D. The structure and short-term stability of the emotional disorders: A dimensional approach. Psychological Medicine. 2015; 45(8):1687–1698. [PubMed: 25499142]

Kozak MJ, Cuthbert BN. The NIMH Research Domain Criteria Initiative: Background, issues, and pragmatics. Psychophysiology. 2016; 53(3):286–297. [PubMed: 26877115]

Kramer MD, Krueger RF, Hicks BM. The role of internalizing and externalizing liability factors in accounting for gender differences in the prevalence of common psychopathological syndromes. Psychological Medicine. 2008; 38(1):51–61. [PubMed: 17892625]

Krueger RF. The structure of common mental disorders. Archives of General Psychiatry. 1999; 56(10): 921–926. [PubMed: 10530634]

Krueger RF, Caspi A, Moffitt TE, Silva PA. The structure and stability of common mental disorders (DSM-III-R): A longitudinal-epidemiological study. Journal of Abnormal Psychology. 1998; 107(2):216. [PubMed: 9604551]

Krueger RF, Chentsova-Dutton YE, Markon KE, Goldberg D, Ormel J. A cross-cultural study of the structure of comorbidity among common psychopathological syndromes in the general health care setting. Journal of Abnormal Psychology. 2003; 112(3):437–447. [PubMed: 12943022]

Krueger RF, DeYoung CD. The RDoC initiative and the structure of psychopathology. Psychophysiology. in press.

Krueger RF, Eaton NR. Structural validity and the classification of mental disorders. Philosophical Issues in Psychiatry II: Nosology. 2012; 2:199.

Krueger RF, Eaton NR. Transdiagnostic factors of mental disorders. World Psychiatry. 2015; 14(1):27–29. [PubMed: 25655146]

Krueger RF, Finger MS. Using item response theory to understand comorbidity among anxiety and unipolar mood disorders. Psychological Assessment. 2001; 13(1):140–151. [PubMed: 11281035]

Krueger RF, Hicks BM, Patrick CJ, Carlson SR, Iacono WG, McGue M. Etiologic connections among substance dependence, antisocial behavior and personality: Modeling the externalizing spectrum. Journal of Abnormal Psychology. 2002; 111(3):411. [PubMed: 12150417]

Krueger RF, Markon KE, Patrick CJ, Benning SD, Kramer MD. Linking antisocial behavior, substance use, and personality: An integrative quantitative model of the adult externalizing spectrum. Journal of Abnormal Psychology. 2007; 116(4):645–666. [PubMed: 18020714]

Krueger RF, Piasecki TM. Toward a dimensional and psychometrically-informed approach to conceptualizing psychopathology. Behaviour Research and Therapy. 2002; 40(5):485–499. [PubMed: 12038642]

Krueger RF, South SC. Externalizing disorders: Cluster 5 of the proposed meta-structure for DSM-V and ICD-11. Psychological Medicine. 2009; 39(12):2061–2070. [PubMed: 19796431]

Krueger, RF.; Tackett, JL. The externalizing spectrum of personality and psychopathology: An empirical and quantitative alternative to discrete disorder approaches. In: Beauchaine, TP.; Hinshaw, SP., editors. The Oxford Handbook of Externalizing Spectrum Disorders. Oxford University Press; 2014.

Kushner MG. Seventy-five years of comorbidity research. Journal of Studies on Alcohol and Drugs. 2014; 75(Suppl 17):50–58. [PubMed: 24565311]

Kushner SC, Quilty LC, Tackett JL, Bagby RM. The hierarchical structure of the Dimensional Assessment of Personality Pathology (DAPP-BQ). Journal of Personality Disorders. 2011; 25(4): 504–516. [PubMed: 21838565]

Kushner SC, Tackett JL, Bagby RM. The structure of internalizing disorders in middle childhood and evidence for personality correlates. Journal of Psychopathology and Behavioral Assessment. 2012; 34(1):22–34.

Laceulle OM, Vollebergh WAM, Ormel J. The structure of psychopathology in adolescence: Replication of a general psychopathology factor in the TRAILS study. Clinical Psychological Science. 2015; 3(6):850–860.

Lahey BB, Applegate B, Waldman ID, Loft JD, Hankin BL, Rick J. The structure of child and adolescent psychopathology: Generating new hypotheses. Journal of Abnormal Psychology. 2004; 113(3):358–385. [PubMed: 15311983]

Lahey BB, Rathouz PJ, Van Hulle C, Urbano RC, Krueger RF, Applegate B, … Waldman ID. Testing structural models of DSM-IV symptoms of common forms of child and adolescent psychopathology. Journal of Abnormal Child Psychology. 2008; 36(2):187–206. [PubMed: 17912624]

Lahey BB, Van Hulle CA, Singh AL, Waldman ID, Rathouz PJ. Higher-order genetic and environmental structure of prevalent forms of child and adolescent psychopathology. Archives of General Psychiatry. 2011; 68(2):181–189. [PubMed: 21300945]

Lahey BB, Zald DH, Hakes JK, Krueger RF, Rathouz PJ. Patterns of heterotypic continuity associated with the cross-sectional correlational structure of prevalent mental disorders in adults. JAMA Psychiatry. 2014; 71(9):989–996. [PubMed: 24989054]

Lansford JE, Malone PS, Stevens KI, Dodge KA, Bates JE, Pettit GS. Developmental trajectories of externalizing and internalizing behaviors: Factors underlying resilience in physically abused children. Development and Psychopathology. 2006; 18(1):35–55. [PubMed: 16478551]

Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: Prevalence and predictors. JAMA. 1999; 281(6):537–544. [PubMed: 10022110]

Legrand LN, Keyes M, McGue M, Iacono WG, Krueger RF. Rural environments reduce the genetic influence on adolescent substance use and rule-breaking behavior. Psychological Medicine. 2008; 38(9):1341–1350. [PubMed: 17903338]

Leve LD, Kim HK, Pears KC. Childhood temperament and family environment as predictors of internalizing and externalizing trajectories from ages 5 to 17. Journal of Abnormal Child Psychology. 2005; 33(5):505–520. [PubMed: 16195947]

MacCallum RC, Zhang S, Preacher KJ, Rucker DD. On the practice of dichotomization of quantitative variables. Psychol Methods. 2002; 7(1):19–40. [PubMed: 11928888]

Markon KE. Modeling psychopathology structure: A symptom-level analysis of Axis I and II disorders. Psychological Medicine. 2010; 40(2):273–288. [PubMed: 19515267]

Markon KE, Krueger RF. Categorical and continuous models of liability to externalizing disorders: A direct comparison in NESARC. Archives of General Psychiatry. 2005; 62(12):1352–1359. [PubMed: 16330723]

Meyers JL, Lowe SR, Eaton NR, Krueger R, Grant BF, Hasin D. Childhood maltreatment, 9/11 exposure, and latent dimensions of psychopathology: A test of stress sensitization. Journal of Psychiatric Research. 2015; 68:337–345. [PubMed: 26037889]

Miner JL, Clarke-Stewart KA. Trajectories of externalizing behavior from age 2 to age 9: Relations with gender, temperament, ethnicity, parenting, and rater. Development and Psychopathology. 2008; 44(3):771–786.

Moffitt TE. Adolescence-limited and life-course-persistent antisocial behavior: A developmental taxonomy. Psychological Review. 1993; 100(4):674–701. [PubMed: 8255953]

Moilanen KL, Shaw DS, Maxwell KL. Developmental cascades: Externalizing, internalizing, and academic competence from middle childhood to early adolescence. Development and Psychopathology. 2010; 22(3):635–653. [PubMed: 20576184]

Newman DL, Moffitt TE, Caspi A, Silva PA. Comorbid mental disorders: Implications for treatment and sample selection. Journal of Abnormal Psychology. 1998; 107(2):305–311. [PubMed: 9604559]

Noordhof A, Krueger RF, Ormel J, Oldehinkel AJ, Hartman CA. Integrating autism-related symptoms into the dimensional internalizing and externalizing model of psychopathology. The TRAILS Study. Journal of abnormal child psychology. 2015; 43(3):577–587. [PubMed: 25099360]

Obradovic J, Bush NR, Boyce WT. The interactive effect of marital conflict and stress reactivity on externalizing and internalizing symptoms: The role of laboratory stressors. Development and Psychopathology. 2011; 23(1):101–114. [PubMed: 21262042]

Ormel J, Jeronimus BF, Kotov R, Riese H, Bos EH, Hankin BL, … Oldehinkel AJ. Neuroticism and common mental disorders: Meaning and utility of a complex relationship. Clinical Psychology Review. 2013; 33(5):686–697. DOI: 10.1016/j.cpr.2013.04.003 [PubMed: 23702592]

Patrick CJ, Hajcak G. RDoC: Translating promise into progress. Psychophysiology. 2016; 53(3):415–424. [PubMed: 26877135]

Pollak SD. Developmental psychopathology: Recent advances and future challenges. World Psychiatry. 2015; 14(3):262–269. [PubMed: 26407771]

Propper C, Willoughby M, Halpern CT, Carbone MA, Cox M. Parenting quality, DRD4, and the prediction of externalizing and internalizing behaviors in early childhood. Developmental Psychobiology. 2007; 49(6):619–632. [PubMed: 17680609]

Rodriguez-Seijas C, Eaton NR, Krueger RF. How transdiagnostic factors of personality and psychopathology can inform clinical assessment and intervention. Journal of Personality Assessment. 2015; 97(5):425–435. [PubMed: 26132431]

Rodriguez-Seijas C, Stohl M, Hasin DS, Eaton NR. Transdiagnostic factors and mediation of the relationship between perceived racial discrimination and mental disorders. JAMA Psychiatry. 2015; 72(7):706–713. [PubMed: 25901783]

Rose RJ, Dick DM, Viken RJ, Kaprio J. Gene-environment interaction in patterns of adolescent drinking: Regional residency moderates longitudinal influences on alcohol use. Alcoholism: Clinical and Experimental Research. 2001; 25(5):637–643.

Rutter M, Sroufe LA. Developmental psychopathology: Concepts and challenges. Development and Psychopathology. 2000; 12(03):265–296. [PubMed: 11014739]

Slade T, Watson D. The structure of common DSM-IV and ICD-10 mental disorders in the Australian general population. Psychological Medicine. 2006; 36(11):1593–1600. [PubMed: 16882356]

South SC, Krueger RF, Iacono WG. Understanding general and specific connections between psychopathology and marital distress: A model based approach. Journal of Abnormal Psychology. 2011; 120(4):935. [PubMed: 21942335]

Sroufe LA, Rutter M. The domain of developmental psychopathology. Child Development. 1984; 55(1):17–29. [PubMed: 6705619]

Starr LR, Conway CC, Hammen CL, Brennan PA. Transdiagnostic and disorder-specific models of intergenerational transmission of internalizing pathology. Psychological Medicine. 2014; 44(01): 161–172. [PubMed: 23663355]

Steinberg L, Albert D, Cauffman E, Banich M, Graham S, Woolard J. Age differences in sensation seeking and impulsivity as indexed by behavior and self-report: evidence for a dual systems model. Developmental Psychology. 2008; 44(6):1764–1768. [PubMed: 18999337]

Sterba SK, Prinstein MJ, Cox MJ. Trajectories of internalizing problems across childhood: Heterogeneity, external validity, and gender differences. Development and Psychopathology. 2007; 19(2):345–366. [PubMed: 17459174]

Sunderland M, Slade T. The relationship between internalizing psychopathology and suicidality, treatment seeking, and disability in the Australian population. Journal of Affective Disorders. 2015; 171:6–12. [PubMed: 25282144]

Sunderland M, Slade T, Carragher N, Batterham P, Buchan H. Age-related differences in internalizing psychopathology amongst the Australian general population. Journal of Abnormal Psychology. 2013; 122(4):1010–1020. [PubMed: 24364603]

Swanson SA, Crow SJ, Le Grange D, Swendsen J, Merikangas KR. Prevalence and correlates of eating disorders in adolescents: Results from the national comorbidity survey replication adolescent supplement. Archives of General Psychiatry. 2011; 68(7):714–723. [PubMed: 21383252]

Tackett JL. Toward an externalizing spectrum in DSM–V: Incorporating developmental concerns. Child Development Perspectives. 2010; 4(3):161–167.

Tackett JL, Krueger RF, Iacono WG, McGue M. Symptom-based subfactors of DSM-defined conduct disorder: Evidence for etiologic distinctions. Journal of Abnormal Psychology. 2005; 114(3): 483–487. [PubMed: 16117586]

Tackett JL, Krueger RF, Sawyer MG, Graetz BW. Subfactors of DSM-IV conduct disorder: Evidence and connections with syndromes from the Child Behavior Checklist. Journal of Abnormal Child Psychology. 2003; 31(6):647–654. [PubMed: 14658744]

Tackett JL, Lahey BB, van Hulle C, Waldman I, Krueger RF, Rathouz PJ. Common genetic influences on negative emotionality and a general psychopathology factor in childhood and adolescence. Journal of Abnormal Psychology. 2013; 122(4):1142–1153. [PubMed: 24364617]

Trosper SE, Whitton SW, Brown TA, Pincus DB. Understanding the latent structure of the emotional disorders in children and adolescents. Journal of Abnormal Child Psychology. 2012; 40(4):621–632. [PubMed: 22006349]

Vachon DD, Krueger RF, Rogosch FA, Cicchetti D. Assessment of the harmful psychiatric and behavioral effects of different forms of child maltreatment. JAMA Psychiatry. 2015:1135–1142. [PubMed: 26465073]

Vaidyanathan U, Patrick CJ, Iacono WG. Patterns of comorbidity among mental disorders: a person-centered approach. Compr Psychiatry. 2011; 52(5):527–535. [PubMed: 21111407]

van Lier PA, Koot HM. Developmental cascades of peer relations and symptoms of externalizing and internalizing problems from kindergarten to fourth-grade elementary school. Development and Psychopathology. 2010; 22(3):569–582. [PubMed: 20576179]

Vollebergh WAM, Iedema J, Bijl RV, de Graaf R, Smit F, Ormel J. The structure and stability of common mental disorders: The NEMESIS study. Archives of General Psychiatry. 2001; 58(6): 597–603. [PubMed: 11386990]

Vrieze SI, Hicks BM, Iacono WG, McGue M. Decline in genetic influence on the co-occurrence of alcohol, marijuana, and nicotine dependence symptoms from age 14 to 29. American Journal of Psychiatry. 2012; 169(10):1073–1081. [PubMed: 22983309]

Waszczuk MA, Zavos HM, Gregory AM, Eley TC. The phenotypic and genetic structure of depression and anxiety disorder symptoms in childhood, adolescence, and young adulthood. JAMA Psychiatry. 2014; 71(8):905–916. [PubMed: 24920372]

Watson D. Rethinking the mood and anxiety disorders: A quantitative hierarchical model for DSM-V. Journal of Abnormal Psychology. 2005; 114(4):522–536. [PubMed: 16351375]

Wiggins JL, Mitchell C, Hyde LW, Monk CS. Identifying early pathways of risk and resilience: The codevelopment of internalizing and externalizing symptoms and the role of harsh parenting. Development and Psychopathology. 2015; 27(4 Pt 1):1295–1312. [PubMed: 26439075]

Wolf AW, Schubert DSP, Patterson MB, Grande TP, Brocco KJ, Pendleton L. Associations among major psychiatric diagnoses. Journal of Consulting and Clinical Psychology. 1988; 56(2):292–294. [PubMed: 3372837]

Wright AG, Simms LJ. A metastructural model of mental disorders and pathological personality traits. Psychological Medicine. 2015; 45(11):2309–2319. [PubMed: 25903065]

Yarnell LM, Sargeant MN, Prescott CA, Tilley JL, Farver JA, Mednick SA, … Luczak SE. Measurement invariance of internalizing and externalizing behavioral syndrome factors in a non-Western sample. Assessment. 2013; 20(5):642–655. [PubMed: 23921606]

Young Mun E, Fitzgerald HE, Von Eye A, Puttler LI, Zucker RA. Temperamental characteristics as predictors of externalizing and internalizing child behavior problems in the contexts of high and low parental psychopathology. Infant Mental Health Journal. 2001; 22(3):393–415.

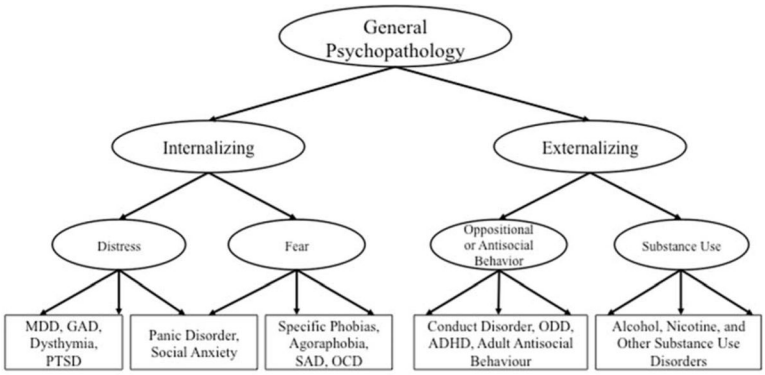

Figure 1.

A hierarchical model of our current understanding of the structure of *common* mental disorders, with child and adult disorders used as example indicators. More severe mental disorders (e.g., psychoses) are also amenable to this kind of approach, but are omitted here because our focus is on common syndromes that are generally observed across the life-course. Current research suggests that the empirically derived variables in the model offer valid constructs for future research, but disorders should not be studied in isolation. This figure oversimplifies the structure of psychopathology. For example, conduct disorder and attention deficit hyperactivity disorder have facets that are not characterised by Oppositional or Antisocial Behaviour; and extensive adult psychopathology research suggests that social anxiety is part of the Fear facet, but it has also been found to comprise part of Distress in children and adolescents (e.g., Lahey et al., 2008). However, this figure offers a broad overview of the literature. MDD = Major Depressive Disorder, GAD = Generalised Anxiety Disorder, PTSD = Posttraumatic Stress Disorder, SAD = Separation Anxiety Disorder, OCD = Obsessive-Compulsive Disorder, ODD = Oppositional Defiant Disorder, ADHD = Attention Deficit Hyperactivity Disorder.

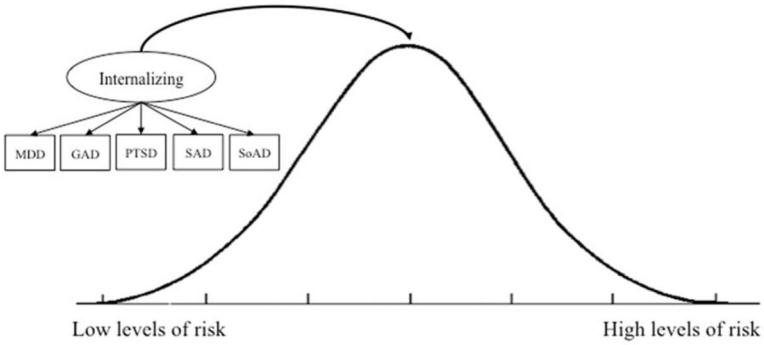

Figure 2.

The Internalizing spectrum depicted as a normally distributed continuous dimension of risk for psychopathology. In this example, Internalizing is indicated by Major Depressive Disorder (MDD), Generalized Anxiety Disorder (GAD), Posttraumatic Stress Disorder (PTSD), Separation Anxiety Disorder (SAD), and Social Anxiety Disorder (SoAD). Individually, these diagnoses would correspond to different severity levels of Internalizing, but when they are used together to indicate Internalizing, their shared variance delineates this dimension of risk. As the level of risk increases, so does the number of presenting disorders. Internalizing could also be measured using continuous symptom-level measures, or using facets from the Achenbach System of Empirically Based Assessment.

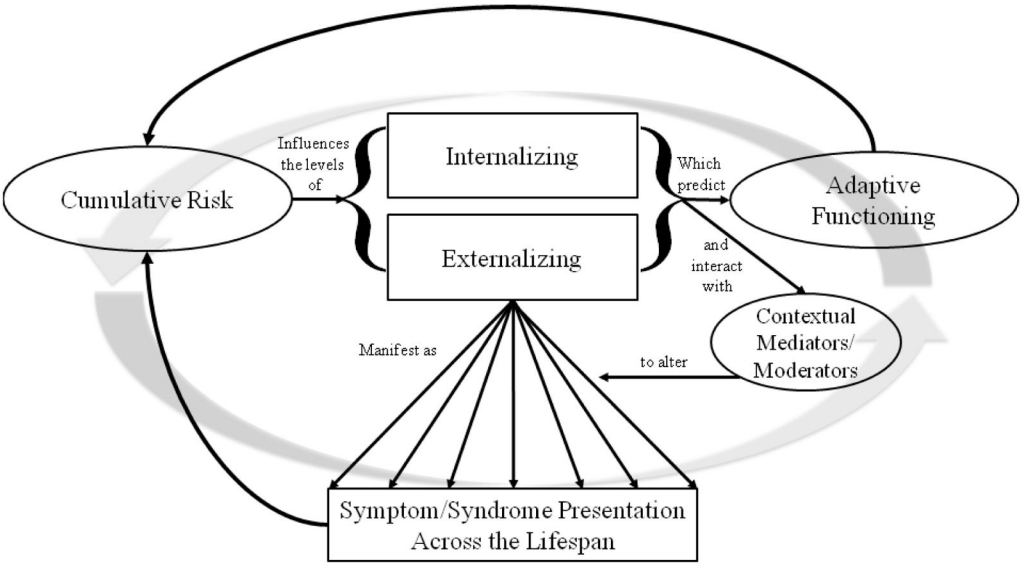

Figure 3.

A theoretical framework that depicts Internalizing and Externalizing (IE) as channels for core processes. Cumulative risk (i.e., the combined effects of genetic and environmental vulnerabilities and protective factors; cf. Busseri et al., 2006) influences the levels of IE, which predict adaptive functioning. The levels of IE also affect the overall likelihood of manifest syndromes, and the specific manifest syndromes are determined by contextual mediators and moderators interacting with IE to alter their expression. Cumulative risk factors and contextual mediators and moderators have substantial overlap, and form ongoing transactional loops with manifest syndromes and adaptive functioning. The relationships in this figure are oversimplified for illustrative purposes; in reality, all of these factors can interact with one another in complex and nuanced ways. For example, cumulative risk can impact individual syndromes directly, but this effect tends to be small and non-significant after accounting for the roles of IE (e.g., Jaffee et al., 2002; Lahey et al., 2014; Vachon et al., 2015). Similarly, manifest syndromes can affect adaptive functioning directly, but this relationship also tends to be small and non-significant after accounting for the effect of IE (e.g., Eaton, Krueger, et al., 2013; South et al., 2011). Overall, this approach represents an ontogenic process with changing inputs and outputs across the lifespan, and thus represents mechanisms of continuity, discontinuity, multifinality, and equifinality.