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EDITORIAL

Transdiagnostic heterogeneity, hierarchical dimensional models, and societal, cultural, and individual differences in the developmental understanding of psychopathology

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Neuroimaging and genetic studies have inspired hope that specific etiologies would soon be revealed for many psychiatric disorders. The power of neuroimaging and genetic technologies to generate publishable findings is everywhere evident. However, the hope that these impressive technologies would quickly reveal specific etiologies for many specific psychiatric disorders is being tempered by increasing recognition that neither the disorders nor their etiologies may be as specific as assumed.

The questionable specificity of diagnostic categories

The third through fifth editions of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-III, DSM-III-R, DSM-IV, DSM-IV-TR, and DSM-5) [1] have provided explicit criteria and decision rules for defining disorders in terms of diagnostic categories. The successive editions of the DSM have revised the categories and criteria in hope of better discriminating among what were assumed to be hundreds of discrete disorders. However, the Introduction to DSM-5 acknowledges that "the once plausible goal of identifying homogeneous populations for treatment and research resulted in narrow diagnostic categories that did not capture clinical reality, symptom heterogeneity within disorders, and significant sharing of symptoms across multiple disorders. The historical aspiration of achieving diagnostic homogeneity by progressive subtyping within disorder categories no longer is sensible; like most common human ills, mental disorders are heterogeneous at many levels, ranging from genetic risk factors to symptoms" (p. 12). The futility of defining psychopathology in terms of hundreds of narrow diagnostic categories has become evident in many ways, as exemplified in the following sections.

Comorbidity

As the DSM's explicit criteria became widely applied, it was found that many children (I use "children" to include adolescents) met criteria for multiple diagnoses. For example, studies found that 96 % of boys who met criteria for conduct disorder (CD) also met criteria for oppositional defiant disorder (ODD) [e.g., 2].

The term "comorbidity" became popular not only as a description, but also as an explanation for findings that children often met criteria for multiple diagnoses. Hundreds of publications reported comorbidity between various DSM-defined disorders, with the implication being that children meeting criteria for multiple disorders were actually suffering from each of the disorders for which they met criteria [e.g., 3].

Heterogeneity within diagnostic categories

The specificity of DSM-defined disorders is further challenged by marked differences found between children who qualify for a particular diagnosis. Marked differences are also found in responses to particular treatments for children who meet criteria for the same DSM diagnosis. And marked variations are found in the courses and outcomes of particular disorders defined according to DSM criteria [e.g., 4].

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Cross-contextual variability of symptoms

Additional challenges to diagnostic specificity are posed by variations in symptoms from one context to another. For example, teachers' reports of Attention Deficit Hyperactivity Disorder (ADHD) symptoms often contrast with parents' reports that their children concentrate intently on video games. Reports by mothers, fathers, children, mental health workers, observers, and teachers often differ with respect to many other symptoms, as well. Behavior genetic studies have shown that such discrepancies reflect genetically and environmentally influenced aspects of children's functioning, rather than mere informant biases or measurement errors [e.g., 5]. Although DSM criteria state that ADHD symptoms must be "present in two or more settings," the DSM does not specify assessment operations for determining whether symptom criteria for ADHD (or for other disorders) are met in each setting, such as home and school, nor for reconciling the frequent discrepancies in reports by different informants.

Developmental differences and changes

Those who work with children are acutely aware of the many differences between children of different ages and of the importance of developmental changes. However, by using the same diagnostic thresholds for children of diverse ages (e.g., 3 out of 15 CD symptoms for all ages; 6 out of 9 ADHD symptoms for ages <17 years), DSM diagnostic categories fail to take account of major developmental differences and changes in the prevalence and meaning of particular symptoms. As examples, the criterial symptoms of CD characterize far more adolescents than younger children, whereas the criterial symptoms of ADHD characterize far more younger children than adolescents. The lack of developmental norms for diagnostic criteria implies that disorders such as CD and ADHD exist as encapsulated entities, independent of developmental differences and changes.

The questionable specificity of etiologies

The DSM and the International Classification of Diseases (ICD*)* reflect efforts to divide phenotypic characteristics, such as symptoms, according to rules that will identify children who suffer from disorders that are thought to be traceable to specific etiologies. This model works tolerably well for infectious diseases such as measles, where a particular pathogen is necessary (although not always sufficient) for particular symptoms to occur. However, much research indicates that disorders such as ODD, CD, ADHD, autism spectrum disorders, anxiety, and depression do not have etiologies as specific as measles. The following sections briefly address some challenges to the quest for specific etiologies for psychopathological phenotypes.

Gene × environment interactions

It is widely assumed that both genetic and environmental factors and interactions between them are involved in the etiology of psychopathology. A well-publicized example of apparent candidate gene x environment interaction was reported by Caspi et al. [6], who found that New Zealanders who carried the short allele of the serotonin transporter gene 5-HTT were at higher risk for depression following childhood stressors than those who were homozygous for the long allele. Subsequent studies have yielded inconsistent results regarding the hypothesized interaction effects of 5-HTT genotypes x environmental stressors.

Kraemer [7] pointed out that the inconsistent results reflected numerous inconsistencies in testing gene x environment interactions and in operationalizing the psychopathology that such interactions were hypothesized to affect. She described efforts to determine gene x environment effects on psychopathology as facing a "perfect storm" of methodological problems. Although Kraemer acknowledged the importance of searching for gene x environment interactions, she emphasized the need to use accurate methodology for assessing and analyzing all the relevant variables, including psychopathological outcomes. Although genetic and environmental factors and their interactions are certainly apt to affect psychopathology, the multitude of relevant variables and the need for valid, generalizable assessment of both the etiological variables and the psychopathological outcomes present major challenges for efforts to discover specific etiologies.

The reality of small effect sizes

An especially comprehensive longitudinal study—the Generation R Study (R = Rotterdam)—tested the hypothesized interaction effect of 5-HTT × environmental stress on 5-year-olds' internalizing problems, as rated by both parents [8]. Significant interactions were found between 5-HTT genotypes and maternal anxiety, which was assessed at 20 weeks of pregnancy and again 3 years after the children were born. Consistent with the Caspi [6] findings, children who carried one or two 5-HTT short alleles *and* whose mothers scored high on anxiety obtained higher age 5 internalizing scores than other children. However, the effect sizes were extremely small: The interaction of 5-HTT × prenatal maternal anxiety accounted for 1 % of the variance in age 5 internalizing scores, while 5-HTT × postnatal maternal anxiety accounted for 0.2 % of the variance.

The high statistical power ($N = 2136$), plus controls for many other variables, enabled the Rotterdam team to detect what may be real, but tiny effects of the 5-HTT × environmental stress interaction. The inconsistencies among findings in other studies may reflect their lower statistical power; lack of control for other variables; the particular ages and other characteristics of their samples; and ways of operationalizing stress and psychopathology. Because the very small 5-HTT × environment effects are typical of many effects found in Generation R and other studies, they show that the quest for specific etiologies requires large samples, precise measurement of phenotypic psychopathology as well as precise measurement of hypothesized genetic and environmental etiological variables, and recognition that psychopathology involves many interacting variables, most of which have very small effects.

Transdiagnostic heterogeneity

The term "transdiagnostic" is being increasingly used in reference to aspects of psychopathology that are not limited to particular diagnostic categories. Transdiagnostic treatment and research address aspects of psychopathology that are important in their own right, whether or not they serve as criteria for particular diagnostic categories. As an example from this issue of ECAP, the Serafini et al. [9] review of research on suicidal behavior concluded that adversities, especially sexual abuse, were significantly associated with suicidal behavior. Both sexual abuse and suicidal behavior are clearly of great concern in their own right, over and above their possible associations with particular diagnostic categories. As another example from this issue of ECAP, Lereya et al. [10] found that early bullying and victimization were associated with various mental health problems at age 18. Articles by Comasco et al. and Ortuno-Sierra et al. provide additional examples of transdiagnostic approaches. Recognition of heterogeneity within diagnostic categories, plus research on phenomena that cut across diagnostic categories, are helping to advance knowledge of psychopathology beyond the confines of diagnostic categories.

Hierarchical dimensional models

As an alternative to diagnostic categories, factor analysis has been used to derive syndromes of co-occurring problems from parent, teacher, and self-ratings of thousands of children. Dimensional syndrome scores for individual children are computed by summing ratings of the problem items comprising each syndrome. These scores reflect the degree to which children manifest problems of each syndrome, as rated by parents, teachers, and/or the children themselves. Profiles display syndrome scores in relation to norms for the child's age and gender, the type of informant (parent, teacher, and self), and appropriate multicultural norms. Because each child obtains a score for each syndrome, there are many possible profile patterns of low, medium, and high scores on multiple syndromes. The profiles document individual children's patterns of syndrome scores, without requiring homogeneous categories of problems nor assumptions about whether syndromes are comorbid.

Correlations between particular subsets of syndromes, such as the correlation between rule-breaking behavior and aggressive behavior, are embodied in higher-order dimensions, such as externalizing, internalizing, and general psychopathology [Ivanova et al., in review]. Users can thus view assessment data for individual children in terms of multiple hierarchical levels, starting with ratings for specific problems at the base. At the next level of the hierarchy, the ratings of subsets of problems are summed to yield dimensional syndrome scores that are displayed on profiles in relation to norms appropriate for each child. At higher levels, scores from mutually correlated syndromes are summed to yield scores for broad-band externalizing, internalizing, and general psychopathology dimensions. Hierarchical dimensional models of this sort have been supported by confirmatory factor analyses of ratings of tens of thousands of children from dozens of societies [Ivanova et al., in review].

Societal, cultural, and individual differences

Quests for specific etiologies and effective treatments are predicated on identifying similarities between cases. However, similarities between cases are often intertwined with important differences. When working with individual children and their families, we need to view similarities between cases in relation to the multitude of characteristics that may be specific to particular children and their families. Some of these characteristics may be shaped by the societies and cultures in which children are developing. As mental health services and research must increasingly take account of societal and cultural differences, it is essential to determine the degree to which such differences affect assessment of psychopathology for both clinical and research purposes.

Analyses of parents' ratings of behavioral, social, emotional, and thought problems for over 70,000 children from 43 societies—which were grouped according to nine culture clusters (e.g., Confucian)—have revealed that societal differences accounted for 3.7–9.9 % of variance in scores for various kinds of psychopathology [Althoff et al., in preparation]. Differences between culture clusters

accounted for an additional 0.8–8.0 % of variance. Both societal and cultural differences should thus be taken into account when assessing child psychopathology. However, individual differences among children *within* societies and culture clusters accounted for an additional 86.4–95.2 % of variance in scores for various kinds of psychopathology. These findings indicate that—despite the importance of societal and cultural differences—individual differences account for much more variance in measures of child psychopathology than do societal and cultural differences. Individual differences in children's problems should thus be carefully assessed in efforts to understand and ameliorate child psychopathology.

Conclusions

Recent decades have witnessed extensive efforts to define psychopathology in terms of increasingly specific diagnostic categories. Impressive technologies have fostered expectations that specific etiologies would soon be discovered for disorders defined in terms of the diagnostic categories. However, both the phenotypic manifestations of psychopathology and underlying etiological factors exhibit great transdiagnostic heterogeneity. Increasing awareness of heterogeneity is a sign of progress in understanding the complexity of psychopathology.

Awareness of heterogeneity is especially crucial for understanding relations between development and psychopathology, because developmental changes and differences are so incompatible with static diagnostic categories. By contrast, hierarchical dimensional models can take account of heterogeneity, potentially important similarities, individual differences, and developmental changes in psychopathology. Such models are used to obtain quantitative scores from evidence-based assessment instruments that are being employed by practitioners and researchers throughout the world. The hierarchical dimensional models depict psychopathology at multiple levels, from specific problems, to narrow-band syndromes, and broad-band externalizing, internalizing, and general psychopathology dimensions. Normed dimensional scales take account of differences associated with children's age and gender, the type of informant, and variations associated with societal and cultural differences. Clinical cut points on normative distributions of dimensional scores also enable users to make categorical distinctions, if desired.

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