Chronic Non-Episodic Irritability in Childhood: Current and Future Challenges

Disruptive mood dysregulation disorder (DMDD) remains one of the most contested additions to DSM-5. The main objections to its inclusion center on 1) fears that DMDD pathologizes normal behavior (i.e., temper tantrums) and risks greater psychotropic medication use at the expense of appropriate parenting, and 2) the paucity of empirical evidence supporting either the validity of the diagnosis or its associated criteria (1). Most DSM-defined disorders have histories of substantial utility and good-to-very-good levels of diagnostic reliability as demonstrated through successive clinical studies (2). In contrast, DMDD was approved for inclusion in DSM-5 without any history of previous clinical use or published research and having achieved a level of reliability in DSM-5 field trials that was deemed "questionable" (2).

The main justification for creating the DMDD category appears to be its role in resolution of one of the most contentious recent controversies in child psychiatry, namely, the characterization of pediatric bipolar disorder. From the mid-1990s through the early 2000s, there was a dramatic rise in clinical diagnoses of bipolar disorder among youths that occurred in parallel with academic debates on the nature of juvenile mania (3). To examine the issue, some researchers proposed a differentiation of narrow and broad pediatric bipolar phenotypes (4). The narrow phenotype was defined using classic criteria for mania or hypomania, including discrete episodes of grandiosity and euphoria. The broad phenotype, later called severe mood dysregulation, was defined by chronic, non-episodic impairment that lacked hallmark mania symptoms of grandiosity and euphoria, but was typified by severe irritability and hyperarousal. Subsequent longitudinal research demonstrated that episodic irritability in childhood predicted classic adult bipolar disorder, while severe mood dysregulation and dimensional measures of chronic irritability predicted unipolar depression and anxiety (5–7). Other research demonstrated distinct patterns of brain underactivity and impaired emotional responses in youths affected by severe mood dysregulation (8, 9).

The study provides compelling evidence that DMDD is a meaningful diagnostic category with substantial long-term implications and is an important addition to published literature on the condition.

Support for including DMDD in DSM-5 was largely based on this previous research with severe mood dysregulation. The disorder was renamed to be consistent with DSM nomenclature. The severe mood dysregulation requirement for hyperarousal was removed as a result of overlap with attention deficit hyperactivity disorder (ADHD), and the age of onset was lowered from 12 to 10 years old. DMDD diagnosis requires severe tantrums or outbursts at least three times weekly that are disproportionate to the situation and the child's developmental level; a predominately angry or irritable mood between outbursts; symptom persistence for at

least 2 months; and impairment in multiple settings. DMDD cannot be diagnosed until age 6.

A small but growing body of research has examined DMDD itself. Initial research by Copeland et al. (10) diagnosed DMDD based on symptoms recorded in several extant data sets, and the authors found the disorder to be rare, more common in younger children, usually co-occurring with other conditions—particularly oppositional defiant disorder and depression—and associated with increased rates of social difficulties, behavioral problems in school, service use, and poverty. Dougherty et al. (11) studied 6-year-old children and found an 8.2% prevalence of DMDD with no differences by sex or race/ethnicity. Comorbid behavioral or emotional disorders occurred in 60.5%, and DMDD was further associated with increased ADHD, oppositional defiant disorder, peer difficulties, and parental histories of substance use disorder. In one study of severe mood dysregulation, all participants similarly met criteria for DMDD and demonstrated abnormal brain activation that associated DMDD with deficits in attentional flexibility and emotional regulation (8).

The article by Copeland et al. (12) appearing in this issue of the *Journal* examines adult outcomes of children with DMDD. Using prospectively derived data from the longitudinal Great Smoky Mountains Study, the authors assigned DMDD diagnoses and assessed outcomes in 1,420 participants who were interviewed successively in childhood, adolescence, and young adulthood. Comparisons between individuals with DMDD, individuals with other psychiatric disorders except DMDD, and individuals lacking any psychiatric disorder reveal that DMDD predicts worse long-term outcomes, with increased adult psychopathology and poverty, lower educational success, poorer overall health, and more contact with police than the other two groups. The study provides compelling evidence that DMDD is a meaningful diagnostic category with substantial long-term implications and is an important addition to published literature on the condition.

Interestingly, the patterns of increased psychopathology and poor adaptive functioning described in these children with DMDD reflect risks typically ascribed to ADHD (13, 14). Other recent research that included EEG (15) found patterns of ADHD-related abnormalities only in individuals with irritable dysregulated moods, whereas children with ADHD alone had EEG patterns similar to nonclinical comparison subjects. These findings along with results from the Copeland et al. study raise the possibility that it is the presence of chronic irritability in childhood, and not ADHD, that is the significant factor leading to poor long-term outcomes. This prospect deserves further research attention.

What relevance do studies of severe mood dysregulation and DMDD have for practicing clinicians? First, it must be acknowledged that it is no longer acceptable that every moody child with temper outbursts or aggression be given a diagnosis of bipolar disorder. As DSM-5 clarifies, a diagnosis of bipolar disorder requires episodes of irritability or elation associated with other features of mania that are distinct from usual functioning. In contrast, youths with chronic non-episodic irritability who lack discrete episodes of classic manic symptoms and meet criteria for DMDD should be diagnosed as such. Second, although DMDD criteria have not been rigorously validated and boundaries between DMDD and other disorders are not clearly delineated, it should be recognized that the syndrome identifies individuals with high risk for significant lifetime psychopathology and adaptive impairments. Appropriate identification and classification is an important prelude to initiation of responsible treatment.

There is a large step, however, from recognizing a diagnosis to the design and implementation of evidence-based interventions. Little research is currently available to guide the treatment of severe mood dysregulation and DMDD (3). Several small studies utilizing parent management training and cognitive-behavioral approaches suggest some promise from psychosocial therapies. Risperidone and other second-generation antipsychotics have Food and Drug Administration approval for the treatment of irritability in autism and are commonly used as first-line treatments in aggressive youths, but are associated with significant side effects. Some studies show benefits of stimulants on irritability and aggression, and several pilot investigations of combination stimulant and selective serotonin reuptake inhibitors are in progress. None of these interventions has sufficient evidence to support recommendations for widespread use.

Large-scale treatment research for DMDD is not likely to be immediately forthcoming. New research priorities from the National Institute of Mental Health (NIMH) will only support clinical trials of treatment interventions that target underlying mechanisms of action, such as brain circuits or psychological processes, and assess change with validated measures of neurophysiological function. The design, funding, and execution of such studies will require time and substantial creative effort. This approach, however, is consistent with NIMH's Research Domain Criteria initiative that identifies brain neural systems that underlie behavioral functions, disruptions of which likely give risk to psychopathology (16). While clarifications in DSM-5 allow us to direct children with episodic versus nonepisodic irritability into respective categories of bipolar disorder or DMDD, ultimately these syndromes, although useful, will be recognized as artificial constructs. Growing interest in the characterization of childhood irritability and its dimensions across a range of behaviors should prove essential to both the understanding of associated brain dysfunctions and the creation of treatment strategies that will effect positive long-term change.

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