

Concerns Regarding the Inclusion of Temper Dysregulation Disorder With Dysphoria in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*

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Though we understand the incredibly difficult work required in order to revise the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* and appreciate the efforts of those serving to develop it, we as a group are strongly against including temper dysregulation disorder with dysphoria (TDD) as an official diagnosis in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*. We believe that currently there is insufficient scientific support to include TDD as a unique diagnostic entity. Furthermore, we believe that the inclusion of TDD will have an adverse impact on patient care, research, and the general public's perception of child psychiatry. Our concerns are outlined below, and then we offer some alternative strategies to improve diagnostic classification of chronically irritable youths for the *DSM-5* Work Groups to consider.

Of utmost concern is the fact that the TDD diagnosis, as currently conceived, does not have symptom criteria that are specific to TDD as a syndrome. The TDD diagnosis rests on 2 primary criteria: recurrent severe temper outbursts and chronically irritable and/or sad mood. As temper outbursts are a behavioral manifestation of irritable mood, the diagnosis of TDD as it is currently proposed, can be fulfilled with the presence of a single symptom. However, the symptom of irritability is a *DSM-IV* diagnostic criterion for a range of psychiatric disorders in children and adolescents that span the mood, anxiety, and disruptive behavior disorder categories: bipolar disorder, major depressive disorder, dysthymic disorder, cyclothymic disorder, generalized anxiety disorder, posttraumatic stress disorder, acute stress disorder, and oppositional defiant disorder (ODD). In addition, irritability (with temper outbursts) is commonly present in other disorders such as attention-deficit/hyperactivity disorder (ADHD), conduct disorder, separation anxiety disorder, autism spectrum disorders, reactive attachment disorder, psychotic disorders, and substance use disorders and in children who have been maltreated or abused or those

who have suffered brain injury from trauma, developmental insults, or in utero exposure to drugs or alcohol. All of these other disorders have multiple additional criteria that provide specificity to the different syndromes. Temper dysregulation disorder with dysphoria does not have other symptoms or criteria that are unique to the TDD diagnosis. The symptoms of hyperarousal from the severe mood dysregulation (SMD) criteria of Leibenluft et al, 2003,¹ are not required in the proposed criteria. The mood criteria for TDD of chronically irritable and/or sad mood more days than not lasting for at least 1 year's duration are nearly identical to those for dysthymic disorder. The TDD criteria rely on warnings to differentiate TDD from mood and anxiety disorders, and they explicitly allow for comorbidity with disruptive behavior and substance use disorders. The requirement of persistence and chronicity in the TDD criteria is not different from many other disorders in which irritability is common, and the severity of irritability as conceptualized in TDD does not preclude diagnosing these disorders, which are known to have continua of severity. This raises the question as to whether TDD is a separate diagnostic entity that is likely to have unique pathophysiologic features or whether its creation is conflating a symptom with a psychiatric syndrome.

In fact, excerpts from the reports written by the *DSM-5* Child and Adolescent Disorders and Mood Disorders Work Groups confirm that the scientific evidence for creating TDD as a new disorder separate from ODD is currently lacking:

...[T]he work groups acknowledged that a stronger case could be made, based purely on the scientific evidence, for placing the TDD syndrome within the diagnosis of ODD, as a specifier, as opposed to adding a new, free-standing, TDD diagnosis, since virtually all youths who meet criteria for TDD will also meet criteria for ODD. Specifically, data analyses performed by the Childhood and Adolescent Disorders Work Group, using data sets from both community-based and clinic-based samples including more than 10,000 children, suggest that approximately 15% of patients with ODD would meet criteria for TDD; by definition, essentially all youths meeting criteria for TDD would also meet criteria for ODD. In that sense, it is clear that, from a pathophysiological perspective, TDD is unlikely to be categorically distinct from ODD...^{2(p7)}

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The fact that TDD is unlikely to be categorically distinct from ODD is a persuasive reason not to include it as a distinct diagnosis in the *DSM-5*. It also suggests that a substantial amount of additional research will be required until there is sufficient evidence to create a new diagnostic entity focused on irritability as a primary symptom that will have meaningful differences in phenomenology, course, and response to treatment from existing diagnoses in the *DSM-IV* such as ODD.

As noted in the *DSM-5* Task Force document "Justification for Temper Dysregulation Disorder With Dysphoria," the scientific support for the TDD diagnosis is limited, and it emerges primarily from one research group.³ This fact in itself is problematic, as replication by independent research teams is a requirement for establishing the scientific validity of research findings. Recently in psychiatry we have repeatedly seen the lack of replication of genetic and neuroimaging findings across different research groups. In addition, the studies that do have bearing on TDD do not examine it directly but instead focus on an overlapping but not identical population of youths with SMD. Although the outstanding research on SMD from the National Institute of Mental Health (NIMH) Intramural Group is groundbreaking, and it demonstrates that a subset of youths with severe, chronic irritability does not have bipolar disorder, it is not sufficient to justify inclusion of a new TDD diagnostic category. Careful comparison of the original SMD definition proposed in 2003 with the definitions used in subsequent data articles reveals several changes, and the proposed TDD definition makes additional changes, including (1) omitting the hyperarousal criteria and (2) relaxing most of the exclusion criteria, including substance use, low cognitive ability, or comorbid disruptive behavior disorders. It is crucial that both of these changes be evaluated empirically, because they are likely to have substantial impact on the rates of comorbidity and prevalence of the new diagnostic category.

The studies from the NIMH Intramural Group contrasting youths with SMD with those with a narrow phenotype of bipolar I disorder used highly distilled samples of rigorously screened subjects from families who had the motivation to travel to the NIMH campus. This strategy is entirely appropriate for pursuing the initial stages of research to identify potential pathophysiological differences between phenotypic groups. However, it is of questionable applicability to the TDD diagnostic category as it applies in more general clinical and community settings.

The contrast between the SMD subjects recruited at the NIMH Intramural Campus and subjects identified as having SMD in an epidemiologic sample highlights the problems of translating criteria developed from highly distilled samples to community samples. The SMD subjects from the Intramural studies had extremely high rates of comorbid anxiety disorders (47%–61%), ODD (83%–84%), and ADHD (80%–94%).^{4,5} In order to examine SMD in large community samples, the SMD criteria were also applied retrospectively to the sample from the Great Smoky Mountains

Study (GSMS).⁶ The subjects from the GSMS who were identified as having SMD were clearly different from the SMD subjects in the NIMH research samples. Even in the subset of SMD subjects deemed severely impaired (about 1.8% of the total GSMS sample), only about 32% met criteria for ADHD, 42% for ODD, and 21% for any anxiety disorder. In addition, there was very little longitudinal stability of the SMD diagnosis in the GSMS subjects (83% met SMD criteria at only 1 wave), despite the fact that SMD is a chronic disorder that requires a minimum duration of 1 year. We are not aware of published studies that prospectively applied SMD criteria to general clinical populations; therefore, we have no data on the phenomenology, course, or neurobiology of youths meeting the SMD criteria from the most relevant population for the *DSM-5*.

Further complicating the applicability of the published research on SMD to the TDD diagnosis is the removal of the SMD hyperarousal criteria. The rationale for this step was that, since the vast majority of SMD youths had comorbid ADHD, these symptoms when present would be indicated by the ADHD. However, one reason for the high rates of SMD-ADHD comorbidity may be the required hyperarousal criteria. Application of the proposed TDD criteria to general clinical populations might result in much lower rates of ADHD, and it would likely result in children and adolescents diagnosed with TDD who have only some features in common with the SMD subjects studied by the NIMH Intramural Group. Therefore very little research exists that has direct applicability to the TDD diagnosis, and the limited data that do have relevance to TDD have been produced by only one research group.

We suggest that the *DSM-5* Work Groups give additional consideration to the potential risks of introducing the TDD diagnosis. As noted above, the proposed TDD criteria will likely identify a broader range of patients when applied in clinical settings. Irritability and temper outbursts are among the most common presenting complaints in child and adolescent psychiatry. Since TDD has these as its primary diagnostic criteria without any other accompanying symptoms, it could readily become the default diagnosis for the vast majority of children presenting with these symptoms. It will be the responsibility of the diagnosing clinician to determine whether the exclusion criteria (no bipolar disorder; not occurring exclusively during a mood or anxiety disorder; not better accounted for by another diagnosis such as PTSD or pervasive developmental disorder) are present or not. However, it will take considerable effort to evaluate the exclusion criteria, and it is not at all clear that clinicians or research diagnosticians will be able to reliably determine whether the irritability and temper outbursts occur exclusively during a mood or anxiety disorder or whether they are better accounted for by another disorder. It will be easier to assign the TDD diagnosis, rather than to contend with the underlying depression, ADHD, anxiety, or bipolar disorder. We have already seen this play out with the SMD designation in consultations with colleagues from the United States

and other countries—children who have clear episodes of mania and/or hypomania have been given a diagnosis of SMD because of the presence of intense irritability and a reluctance to use a bipolar diagnosis in a child.

The treatment implications of a TDD diagnosis are unclear. Reports in the media have noted that the primary benefit of the TDD diagnosis will be that fewer children will be diagnosed with bipolar disorder, which would lead to fewer children exposed to antipsychotics and mood stabilizers.^{7,8} Some media commentaries have implied that youths with TDD will instead receive psychosocial treatments, which would be a more appropriate outcome.⁹ However, we know little about what kinds of psychosocial treatments would help youths diagnosed with TDD or whether psychosocial treatment would work at all. At present, there are no published studies of psychosocial treatments for TDD. In addition, to the extent that having the TDD diagnosis may encourage clinicians to inappropriately ignore diagnosis and treatment of ADHD and autism spectrum, anxiety, or mood disorders, psychiatrically ill youths will be denied medications that have been proven to treat these disorders. As these other disorders have very different pharmacologic treatments (eg, stimulants and α_2 antagonists for ADHD, serotonin selective reuptake inhibitors for anxiety disorders, second-generation antipsychotics for irritability in autism spectrum disorders) and psychosocial interventions (cognitive-behavioral therapy for anxiety disorders, intensive behavior interventions for autism spectrum disorders, and Parent Management Training for ADHD youths with oppositionality), the clinical application of TDD may result in more frequent mismatches between individual patients and evidence-based treatments.

On the other hand, the rationale that TDD will reduce the inappropriate use of medication in children and adolescents with temper outbursts also seems at odds with perceptions of how the pharmaceutical industry approaches the DSM. Official diagnostic status in DSM-5 will allow TDD to become a target for pharmaceutical companies to obtain US Food and Drug Administration (FDA) indication for the treatment of TDD. Clinical experience and prior studies indicate that youths with conduct disorder and/or explosive aggression will have short-term clinical improvement when treated with antipsychotics and mood stabilizers.^{10–14} The majority of youths who participated in these studies would have likely met the proposed TDD criteria. It is eminently possible that FDA registration studies of new antipsychotics would show an efficacy signal for TDD in short-term treatment. There may be subsets of youths who would meet rigorously assessed TDD diagnostic criteria for whom antipsychotic treatment may indeed be the treatment of choice. However, given the concerns noted above about the application of TDD in clinical settings resulting in identification of a much larger, heterogeneous group of children and adolescents who have other primary diagnoses, there will almost certainly be many youths diagnosed with TDD for whom antipsychotics would not be appropriate. Instead of reducing

the use of antipsychotics in youths, which was specified as a potential benefit of the TDD diagnosis by some media reports, it is quite possible that it will serve as justification for expanding antipsychotic use to a much broader range of children, many of whom might respond as well or better to psychosocial interventions or pharmacologic treatments targeted for ADHD, anxiety, or depression.

Adding the TDD diagnosis to DSM-5 will almost certainly have an adverse effect on the general public's perception of child psychiatry. The media is rife with charges that psychiatry pathologizes normal behavior and turns misbehavior and character flaws into medical disorders, thereby absolving individuals from responsibility for their actions. Skeptical and humorous reports have already surfaced in the media about how temper outbursts in children are now going to be classified as a disease and that the DSM-5 will have a "temper-tantrum" disorder. The DSM-5 Work Groups' acknowledgment that there is insufficient scientific basis to establish TDD as a separate diagnosis will further undermine the public's confidence that psychiatry as a discipline uses scientific evidence to support diagnosis and treatment.

The overarching reason for the creation of a separate TDD diagnosis given by the DSM-5 Child and Adolescent Disorders and Mood Disorders Work Groups was clinical necessity driven by the perceived marked overdiagnosis of bipolar disorder in youth. Although DSM-5 may be able to play some role in improving the diagnosis of bipolar disorder in youth, we believe that creation of a new, unsubstantiated diagnosis in order to prevent misapplication of a different diagnosis is misguided and a step backward for the progression of psychiatry as a rational scientific discipline. It is trying to solve one problem by creating another, potentially larger problem. Diagnosing bipolar disorder in youth can be very difficult, and misdiagnosis certainly occurs. As research clinicians who specialize in the assessment of youths with possible bipolar disorder, we have certainly seen many referrals of youths with chronic irritability who have been inappropriately assigned a diagnosis of bipolar disorder. The degree to which bipolar disorder is misdiagnosed in community treatment settings remains an empirical question. Existing research relies on diagnostic information culled from insurance claim databases, and there are multiple factors that influence why a diagnosis is placed on third-party payer claims. In addition, the most prominently cited study used the documented rate of bipolar disorder placed on claims for *individual office visits* over a 1-year period, not the rate of *individual patients diagnosed* with bipolar disorder, and the findings revealed an increase from a very low base rate of 0.025%–1% over the time period studied.¹⁵ Given that the most recent psychiatric epidemiologic study of adolescents in the United States found that the combined rate of bipolar I and II disorders was 2.3%,¹⁶ it is difficult to interpret these results as evidence of marked overdiagnosis. Additional studies will be required to answer this question.

We agree with the concern raised by the *DSM-5* Work Groups that youths with chronic irritability and explosive anger outbursts are not adequately served by the current *DSM-IV* classification system and that there are children and adolescents with this symptom presentation who are being misdiagnosed as having bipolar disorder. A major problem is that there are surprisingly few data to guide decisions regarding diagnostic classification of these youths. The complexities surrounding the conceptualization and measurement of irritability as a symptom of psychopathology in youths and the assessment and treatment of youths who have chronic explosive irritable mood should be a major focus of future research.

The diagnostic accuracy of bipolar disorder in youth can be improved through better education about rigorously applying current criteria for manic, mixed, or hypomanic episodes and ongoing research into the phenomenology, neurobiology, and longitudinal course of youths who present with symptoms of bipolar disorder that do not meet the *DSM* threshold for bipolar I or II disorders. Research into different subthreshold phenotypes that may be part of the bipolar spectrum or may be the early signs and symptoms of bipolar disorder will allow for a scientifically informed, developmentally appropriate, iterative refinement of the *DSM* criteria for bipolar disorder. Creating the TDD diagnostic category would likely lump together a very heterogeneous group of youths, including some who truly have bipolar disorder. This would not improve psychiatric diagnosis in children and adolescents.

The most conservative option available to the *DSM-5* is not to make any changes in regard to the area of irritability in youth and pediatric bipolar disorder, and this would be preferable to creating the TDD diagnosis. However, we recognize that there is a pressing clinical need to identify and better diagnose those children and adolescents with severe irritability who do not have bipolar disorder. We believe that there are viable alternative options for the *DSM-5* that could address this need and facilitate new research that are preferable to establishing TDD as a stand-alone disorder.

One option would be to establish a TDD-like (using an alternative name such as *with severe explosive anger outbursts*) course specifier for other diagnoses (such as ODD, ADHD, conduct disorder, autism spectrum disorders, mood disorders, and anxiety disorders). The course specifier has considerable appeal. A course specifier focusing exclusively on the presence of severe explosive anger outbursts across a wide range of existing *DSM* diagnoses would highlight the clinical significance of this symptom. It would also facilitate research into whether the presence of severe explosive anger outbursts is a major determinant of course and outcome.

For instance, ODD, as currently defined, is a highly heterogeneous condition that leads to a wide variety of longitudinal outcomes.^{17,18} Adding a course specifier would facilitate research into whether the presence of severe explosive anger outbursts identifies a treatment-relevant subtype of ODD that has meaningful differences in pathophysiology

and longitudinal phenomenology from other youths with ODD. Similar research questions could be addressed in regard to explosive anger outbursts in the context of mood disorders, ADHD, and anxiety disorders. Research studies could examine the prognostic and pathophysiological significance of severe explosive anger outbursts independent of the primary *DSM* diagnosis. Having a course specifier would also provide a separate diagnostic code indicative of additional symptomatology and severity that could facilitate reimbursement from third-party payers.

There are limitations to the course specifier option. It could be cumbersome to implement. There would be valid questions as to whether it should be reserved for use in children and adolescents or also used in adults. It could have impact on the usefulness of the current *DSM-IV* diagnosis of intermittent explosive disorder. However, even if TDD were included as a new disorder, it would substantially overlap with intermittent explosive disorder. There is little research supporting the implementation of the specifier across many diagnoses, although the co-occurrence of severe explosive anger outbursts with mood, anxiety, autism spectrum, and disruptive behavior disorders is widely recognized by clinicians. Moreover, the NIMH Intramural SMD research applies to ADHD, MDD, and anxiety disorders almost as much as ODD, given the presence of these comorbidities in the samples.

Another option would be to include an analog of SMD as a separate diagnosis for further study in the *DSM-5* Appendix. The diagnosis for further study could be based on the SMD criteria, including chronic irritability, anger outbursts, dysphoria, and symptom clusters hypothesized to be specific to the SMD syndrome. The SMD-like diagnosis would facilitate research into a more specific phenotype than would the *severe explosive anger outbursts* course specifier. Additional research could clarify and confirm that youths who meet diagnostic criteria for this diagnosis have pathophysiology, family history, longitudinal course, and treatment response that differs from those with existing *DSM* diagnoses.

Note that these 2 options are not mutually exclusive. The *with severe explosive anger outbursts* course specifier could address current clinical needs and certain types of research questions. The SMD-like diagnosis for further study would facilitate research into a phenotype that, with further evidence and refinement, could become a stand-alone diagnosis in the future.

We would recommend against including a TDD-like course specifier for only ODD. This would likely result in problems similar to those posed by having a stand-alone TDD diagnosis. Clinicians could lump a broad, heterogeneous group of severely irritable youths into a diagnosis of ODD + TDD, neglecting to consider the diagnosis of other disorders. Similar issues would exist regarding targeting this heterogeneous group for new pharmacologic FDA indications that might be appropriate for only a small subset who would receive the ODD + TDD diagnosis in clinical

settings. The situation might not be as problematic as one created by a stand-alone TDD diagnosis, as clinicians are used to applying comorbid diagnoses to ODD (eg, ODD and generalized anxiety disorder), but it still might create substantial problems.

The *DSM-5* should also address the issue of bipolar disorder in youth within the Mood Disorders section of the manual. The text could explicitly discuss developmental issues that permeate the assessment of irritability and the diagnosis of mood disorders as well as the difficulties faced in diagnosing bipolar disorder in children. The requirement of distinct mood episodes could be highlighted. The diagnostic criteria for manic, mixed, and hypomanic episodes could include specific warnings to exercise substantial caution in making these diagnoses when the presentation consisted of irritable mood only with nonspecific symptoms of mania such as motor hyperactivity, rapid speech, and distractibility. Additional specifications and subcategories within the bipolar disorder not otherwise specified diagnosis would facilitate ongoing research and will be clinically useful. These changes would improve diagnostic classification in adults as well. Finally, there could be specific warnings to exercise extreme caution in making a diagnosis of bipolar disorder in children under the age of 6 years. Nevertheless, we cannot expect that a substantial proportion of the diagnostic controversies and difficulties surrounding the diagnosis of bipolar disorder in youth can be solved by the *DSM-5*.

In summary, we strongly disagree with the inclusion of TDD as a new formal diagnosis in the *DSM-5*. The level of scientific evidence to support TDD is too limited to justify a new diagnostic entity. Application of the TDD criteria in clinical practice would most likely label a highly heterogeneous group of children and adolescents who will have divergent developmental trajectories of psychopathology. Temper dysregulation disorder with dysphoria is unlikely to be a treatment-relevant phenotype, and subsets of youths meeting TDD criteria might optimally respond to completely different types of pharmacologic and psychosocial interventions. In addition, including the TDD diagnosis in the *DSM-5* would likely spur the pharmaceutical industry to seek FDA approval for TDD as an indication, resulting in the substantial expansion of use of medications for youths with irritability. For some youths, this could be beneficial; however, for the potentially large subset that would respond well to psychosocial interventions, it could mean unnecessary exposure to psychotropic medication. As youths with a broad range of symptomatology are lumped together into the TDD diagnostic category, research into the pathophysiology and treatment of youths with severe irritability would be adversely affected—greater heterogeneity would reduce the signal to noise ratio. Inclusion of TDD would compromise the already precarious public perception of child and adolescent psychiatry. There are better ways to address the diagnostic difficulties associated with bipolar disorder in youth than creating a new, unsubstantiated diagnosis such as TDD.

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