Issues Pertinent to a Developmental Approach to Bipolar Disorder in DSM-5

Over the past ten years, considerable discussion has focused on the appropriate diagnostic criteria for bipolar disorder (BD) in children and adolescents. While similar discussions have occurred concerning the diagnosis in adults, in some instances, the intensity of the questions are greater for youth than adults. The questions that have arisen are both complex and numerous. After detailed consideration by the Childhood and Adolescent Disorders and the Mood Disorders Work Groups, the two work groups are jointly recommending that three actions be taken to more clearly define the boundaries of BD across the developmental spectrum. Of note, extensive discussions in both the Childhood and Adolescent Disorders and Mood Disorders Work Groups grappled with questions regarding appropriate diagnostic criteria in all age groups, and both work groups recognize the importance of developmental perspectives. Therefore, the actions articulated in the current document are designed, in general, to facilitate more precise diagnosis and more targeted treatment for BD across the lifespan. The current document reflects a consensus view of the Childhood and Adolescent Disorders and the Mood Disorders Work Groups, based on discussions within each work group as well as liaison discussions between the groups.

1. Revise the wording of the criteria for manic and hypomanic episodes in order to operationalize episodicity more clearly.

A. *Specific changes being recommended:*

1. Add “and present most of the day, nearly every day” to the A criterion
2. Add “and represent a noticeable change from usual behavior” to the stem language for the B criteria.

B. Rationale:

From its earliest descriptions and throughout all iterations of the DSM, BD has been described as an episodic illness. Indeed, in both the DSM-IV and in the proposed criteria for DSM-5, clinicians cannot make a diagnosis of BD until they have explicitly confirmed the presence of a hypomanic or manic *episode*. However, the question of what constitutes an episode has been the subject of some controversy and confusion, especially in the child psychiatry literature. In the view of the Mood Disorders Work Group, the wording of the DSM-IV criteria for mania and hypomania may have contributed to that confusion. The proposed change is therefore a clarification (level 1) whose goal would be to ensure that diagnostic practices remain consistent with both the intention of previous iterations of the DSM and across the developmental spectrum.

Consistency in diagnostic practices across the developmental spectrum is important because, while there has been debate about the existence of alternative phenotypes for pediatric BD, it is clear that the “classic” adult phenotype does present in children (Biederman et al., 2004; Birmaher et al., 2006; DelBello et al, 2007; Geller et al., 2004). That is, research on longitudinal course, family-genetics, and other aspects of validity documents strong similarities in the classic BD phenotype in youth and adults,

despite the fact that pediatric cases may tend to have a more severe clinical presentation (Birmaher et al., 2006, 2009). The classic phenotype, as been observed in both youth and adults, thus serves as an important gold standard against which the "bipolarity" of alternative phenotypes can be tested. Clearly articulated definitions of episodes across the lifespan would both reflect the literature documenting continuity between the adult and pediatric "classic" phenotype and facilitate the testing of alternative phenotypes. In addition, adopting the same definition of episodes across the lifespan reflects broader perspectives on development in the DSM. These perspectives note the importance of maintaining developmental consistency in definition, unless strong evidence supports the use of distinct criteria at different age groups. Such strong evidence is lacking for classic BD presentations.

In the view of the Mood Disorders Work Group, the wording of the DSM-IV criteria for mania and hypomania may have contributed to diagnostic confusion in two ways. Thus, two sets of changes are proposed to episode definitions, as will be applied in both youths and adults.

First, the DSM-IV "A" criterion for a manic or hypomanic episode requires "a distinct period of abnormally and persistently elevated, expansive or irritable mood." In contrast, the corresponding criterion for a major depressive episode requires depressed mood or markedly diminished interest "most of the day, nearly every day." There is a need for episode definitions in mania or hypomania that parallel those in major depressive disorder (MDD) in terms of qualifiers and precision. The absence of such qualifiers in the criteria for a (hypo)manic episode has led to questions in the child psychiatry literature as to whether changes in mood lasting as short as four hours should be considered a switch to a mood episode of the opposite pole, rather than mood variability within an episode (Tillman et al., 2003). In the consensus opinions of both the Mood and Childhood Disorders Work Groups, the "most of the day nearly every day" qualifier is a valuable component of the criterion for a major depressive episode, given the expectable variability in mood that one sees in the course of both depressive and (hypo)manic episodes. Benefits are likely to accrue by adopting parallel definitions of episodes for MDD and BD-related phenotypes. As a result, the work groups considered it important to have consistency between major depressive episodes and (hypo)manic episodes in this regard. Thus, the Work Group proposes adding "and present most of the day, nearly every day" to the A criterion of (hypo)mania.

Second, in addition to a "distinct period" of abnormal mood, an episode of (hypo)mania is characterized by the presence of a requisite number of "B" criteria "during the period of mood disturbance." In both major depressive and (hypo)manic episodes, this has been interpreted to mean that, to be "counted" toward the diagnosis of a mood episode, the non-mood symptoms had to either 1) have their onset at approximately the same time as the change in mood; or 2) if a non-mood symptom was present before the onset of the mood disturbance, the non-mood symptom must show significant worsening concurrent with the mood disturbance. Thus, for example, insomnia present prior to the onset of a depressive episode would not count toward that episode unless it worsened noticeably concurrent with the onset of the mood disturbance. Similarly, an

individual who typically had high self-esteem would not be considered to have (hypo)manic "inflated self-esteem" unless there had been a noticeable change from his/her baseline at approximately the same time as the onset of the (hypo)manic mood disturbance.

In DSM-IV, the "B" criteria for (hypo)mania communicate the need for a change from baseline inconsistently. "More talkative than usual" and "increase in goal-directed activity" clearly communicate a change from baseline, but "inflated self-esteem," "decreased need for sleep," "flight of ideas," "distractibility," and "excessive involvement in activities" are ambiguous as to whether the comparison is to that individual's baseline or to a normative standard. This has been particularly problematic in child psychiatry because of the strong overlap between the symptoms of (hypo)mania and those of attention deficit/hyperactivity disorder (ADHD). This is less of an issue for adults, since many symptoms of ADHD manifest in more subtle ways as children pass progressively through adolescence into adulthood. A child with ADHD would typically be distractible and could be seen as agitated and exhibiting excessive involvement in pleasurable activities. Furthermore, it is not uncommon for children with ADHD to have rapid speech, state that their thoughts are going fast, or need relatively little sleep to feel rested. Thus, "double-counting" symptoms toward both ADHD and (hypo)mania could result from the failure in DSM-IV to articulate with sufficient clarity the fact that the "B" symptoms must show a noticeable increase over baseline, concurrent with the "distinct period" required in the "A" criterion, in order to be viewed as a symptom of (hypo)mania. This "double-counting" could lead to inflation in the prevalence of BD in youth. Therefore, the Childhood and Adolescent Disorders and Mood Disorders Work Groups recommend adding "and represent a noticeable change from usual behavior" to the stem language for the B criteria.

2. Propose the addition of a new diagnosis: Temper Dysregulation Disorder with Dysphoria (TDD) in the Mood Disorders Section of DSM-5.

A. Specific changes being recommended:

Temper Dysregulation Disorder with Dysphoria

A. The disorder is characterized by severe recurrent *temper outbursts* in response to common stressors.
   1. The temper outbursts are manifest verbally and/or behaviorally, such as in the form of verbal rages, or physical aggression towards people or property.
   2. The reaction is grossly out of proportion in intensity or duration to the situation or provocation.
   3. The responses are inconsistent with developmental level.

B. *Frequency*: The temper outbursts occur, on average, three or more times per week.

C. *Mood between temper outbursts:*
   1. Nearly every day, the mood between temper outbursts is persistently negative (irritable, angry, and/or sad).
   2. The negative mood is observable by others (e.g., parents, teachers, peers).

D. *Duration*: Criteria A-C have been present for at least 12 months. Throughout that time, the

person has never been without the symptoms of Criteria A-C for more than 3 months at a time.

E. The temper outbursts and/or negative mood are present in at least two settings (at home, at school, or with peers) and must be severe in at least in one setting.

F. Chronological age is at least 6 years (or equivalent developmental level).

G. The onset is before age 10 years.

H. In the past year, there has never been a distinct period lasting more than one day during which abnormally elevated or expansive mood was present most of the day for most days, and the abnormally elevated or expansive mood was accompanied by the onset, or worsening, of three of the "B" criteria of mania (i.e., grandiosity or inflated self esteem, decreased need for sleep, pressured speech, flight of ideas, distractibility, increase in goal directed activity, or excessive involvement in activities with a high potential for painful consequences; see pp. XX). Abnormally elevated mood should be differentiated from developmentally appropriate mood elevation, such as occurs in the context of a highly positive event or its anticipation.

I. The behaviors do not occur exclusively during the course of a Psychotic or Mood Disorder (e.g., Major Depressive Disorder, Dysthymic Disorder, Bipolar Disorder) and are not better accounted for by another mental disorder (e.g., Pervasive Developmental Disorder, post-traumatic stress disorder, separation anxiety disorder). (Note: This diagnosis can co-exist with Oppositional Defiant Disorder, ADHD, Conduct Disorder, and Substance Use Disorders.) The symptoms are not due to the direct physiological effects of a drug of abuse, or to a general medical or neurological condition.

B. Rationale

Relatively explicit criteria have been delineated by the DSM-5 Task Force for evaluating the advantages and disadvantages of adding a new disorder to DSM-5. The consideration of TDD follows these guidelines quite closely. The rationale for the addition of this new diagnosis, following Task Force guidelines, is covered in detail in the document entitled "Justification for Temper Dysregulation Disorder with Dysphoria," posted in the Childhood and Adolescent Disorder Work Group materials. That rationale will be excerpted and summarized briefly here. Much like questions about the overlap between ADHD and BD in children, the need for this new TDD diagnosis reflects the unique features of psychopathology occurring in children relative to adults.

One issue that has received considerable attention in the child psychiatry literature is whether severe, non-episodic irritability should be considered a developmental presentation of mania. Many children present for clinical care with severely impairing forms of irritability. Because DSM-IV did not provide sufficient guidance on appropriate diagnosis for these children, classifications emerged in the literature that were not delineated precisely in DSM-IV. Specifically, it has been suggested that, while adult BD is episodic (see #1, above), BD presents in youth in a non-episodic fashion. Also, it has been suggested that mania in youth is characterized by severe irritability rather than by euphoria. Major questions on the validity of these suggestions remain, and it is impossible to draw definitive conclusions based on the extant literature. Importantly, the suggestion that mania presents in youth as severe non-episodic irritability, rather than in an episodic fashion, has had a considerable impact on diagnostic practice, despite the incomplete evidence regarding its validity.

To address these major questions regarding the nosology of severe irritability in youth, research over the past eight years has compared youth with severe non-episodic irritability to those with classic presentations of episodic DSM-IV BD. This research compared profiles in both groups of youth on the same validators used to study the adult BD phenotype. To facilitate this research, a syndrome called "severe mood dysregulation (SMD)" initially was defined; the criteria for SMD require severe, non-episodic irritability and anger outbursts, as well as hyperarousal (ADHD-like symptoms) (Leibenluft et al, 2003). Research on SMD and related presentations forms one of the more important sets of evidence supporting the suggested new diagnosis.

The term "temper dysregulation disorder with dysphoria (TDD)," rather than "SMD," is used to describe this newly proposed DSM-5 diagnosis. TDD is modeled on SMD but differs from it in two ways: i) the name and ii) in the fact that TDD does not require the hyper-arousal, ADHD-like symptoms that are a criterion for SMD. While the Childhood and Adolescent Disorders Work Group initially considered adopting SMD for addition to DSM-5, ultimately the group concluded that temper dysregulation disorder with dysphoria (TDD) is a more appropriately descriptive name than severe mood dysregulation (SMD).

With regard to the hyperarousal symptoms in SMD, concern arose regarding the overlap with ADHD. Specifically, the inclusion of hyper-arousal symptoms in the diagnostic criteria of this new syndrome would increase comorbidity with ADHD, purely due to overlapping criteria. Moreover, the inclusion of these symptoms might limit the applicability of the diagnosis, since children who present with severe temper dysregulation in the absence of ADHD would not qualify for the diagnosis. Therefore, the Childhood and Adolescent Disorders Work Group decided to propose a criteria set for TDD that does not include ADHD-like symptoms, with the understanding that such symptoms could be denoted by also assigning youth the diagnosis of ADHD, where appropriate.

The criteria for SMD, and the research studies that used them, were designed specifically to ascertain a population of youth with severe, non-episodic irritability who are as clinically impaired as those with BD. This focus on a severely ill population reflected the importance of addressing the clinical needs of youth who are as impaired as those with BD but whose diagnostic status is unclear. In addition, equating severity between the SMD and BD groups ensured that any differences detected between SMD and BD could not be attributed to differences in severity. Consistent with this strategy, research does indeed indicate that youth with SMD are as severely ill as those with episodic DSM-IV BD. However, despite this similarity in impairment, the two groups differ in outcome, gender distribution, and possibly family history. Specifically, youth with SMD, or those with related phenotypes involving chronic irritability, are at risk for later anxiety and unipolar depressive disorders. Unlike children with BD, they are not at risk for developing episodic BD (Brotman et al, 2006; Leibenluft et al, 2006; Stringaris et al, 2009). These data in SMD and chronic irritability are consistent with studies indicating that oppositional defiant disorder (ODD) is a risk factor for depression and anxiety, but not BD (e.g., Burke et al, 2005; Copeland et al., 2009). In a pilot study,

parents of youth with BD were significantly more likely to themselves have BD than were parents of youth with SMD (Brotman et al, 2007). In youth with episodic BD, as in adults with the illness, the gender ratio is approximately even, whereas SMD appears to be more common in boys than in girls (approximately 3:1) (Birmaher et al, 2009; Brotman et al, 2006). Finally, pathophysiological research indicates possible differences between SMD and BD (Dickstein et al., 2007; Rich et al, 2007; Brotman et al, 2010).

As noted above, the TDD diagnosis is based on the SMD criteria, but the two syndromes require slightly different symptoms, with TDD not requiring hyper-arousal symptoms. When considering these two similarly-defined syndromes together, the distinction between SMD/TDD, on the one hand, and BD, on the other, has important treatment implications. These emerge despite the fact that SMD/TDD and BD each are considered severe mood disorders i.e., both involve prominent mood symptoms at the time of presentation and both are associated with long-term impairment from later-manifesting mood symptoms. In DSM-IV terms, research shows that approximately 85% of SMD youth meet criteria for ADHD and ODD, demonstrating that SMD also has features of a disruptive behavior disorder. Nevertheless, the diagnoses of ADHD and ODD communicate neither the significant impairment of these youth nor the severe mood disorder from which they suffer. Indeed, concern has arisen in the field that clinicians have been assigning the diagnosis of BD to severely irritable youth in part because the BD diagnosis justifies access to the higher level of resources that these youth clearly require. While it is important for such children to have access to such resources, it also is important for diagnostic practice to reflect data on validity. Inappropriately assigning a BD diagnosis to children with non-episodic illnesses would violate this principle and might explain the rising rate of BD diagnosis in pediatric settings (Moreno et al., 2007; Blader et al., 2007). Furthermore, children with severe irritability frequently meet DSM criteria for an anxiety disorder, and many have a history of major depression; of course, the fact that these children meet criteria for other disorders (specifically, disruptive behavior disorders) further complicates their classification. Not only is the current convention, which involves categorizing them as BD, inconsistent with research on validity, but, more importantly, it limits treatment options for clinicians. Specifically, current convention renders treatment with antidepressants or stimulants relatively contraindicated without concurrent mood stabilizers or antipsychotics. This contraindication is based on research in more narrowly-defined cases of BD and thereby goes beyond the knowledge base in alternative presentations, such as TDD/SMD. Therefore, the treatment implications of differentiating the TDD/SMD subtype from BD are considerable.

It can certainly be argued that it is premature to suggest the addition of the TDD diagnosis to DSM-5, and both the Mood Disorders and the Childhood and Adolescent Disorders Work Groups considered this argument very seriously. Both work groups are concerned by the fact that the work on SMD has been done predominately by one research group in a select research setting. Moreover, many questions remain unanswered concerning this group of children. Indeed, based on these remaining questions, a subgroup of the ADHD and Disruptive Behavior Disorders and Childhood and Adolescent Disorders Work Groups expended considerable energy devising a proposal

for an SMD/TDD specifier for the Oppositional Defiant Disorder (ODD) diagnosis. The proposal for an ODD specifier, rather than a new diagnosis, reflected the Task Force guidelines stipulating that new specifiers require a lower level of evidence than do new diagnoses, as well as the acknowledged high degree of overlap between ODD and TDD. Indeed, the 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 youth 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 youth 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, which is itself a heterogeneous category with disparate longitudinal outcomes (Copeland et al., 2009).

However, the approach of adding a TDD specifier to ODD also has disadvantages. Considerable concern regarding this proposal first emerged at the March, 2009 meetings of the Childhood and Adolescent and ADHD and Disruptive Behavior Disorders Work Groups. This concern reflected issues delineated in the guidelines generated by the DSM-5 Task Force. The strong majority of individuals in these two work groups decided that an ODD specifier would not address the current clinical need posed by nosological questions about irritability and its association with mood disorders, including both MDD and BD. The potential benefit accruing from the creation of a new diagnosis was thought to be greater than that which might accrue from the creation of a specifier. DSM-5 Task Force guidelines specify that clinical need must also be considered, in tandem with scientific evidence, when evaluating the advantages and disadvantages of adding a new entity as a disorder-related specifier or a new diagnosis. Based purely on scientific evidence, inclusion of a specifier might be most easily justified. However, when both clinical need and scientific evidence are considered together, a different conclusion emerges. Specifically, for reasons outlined below, consensus emerged in both work groups that stronger support existed for adding TDD as a new disorder, in the Mood Disorder Section, as opposed as an ODD specifier, in the Disruptive Behavior Disorders Section, of DSM-5.

Evidence of a clinical need that might be better addressed by a new diagnosis, as opposed to a specifier, can be found in a few areas: current practice trends in pediatric diagnosis, the broader controversy about pediatric BD, and the need to call attention to a large group of children not currently recognized as suffering from a major, impairing form of mood disorder. Clinicians have not used the ODD diagnosis for such children; rates of pediatric BD in clinics and hospitals have increased much more than have rates of ODD. The failure to view chronically and severely irritable children as suffering from ODD might reflect the fact that ODD is not a mood disorder (while TDD, like BD and MDD, would be). Classifying severely irritable youth with a mood disorder would reflect the over-riding prominence of mood symptoms in these children. Moreover, as noted above, the persistently high level of mood symptoms of youth with TDD requires an

intense levels of services directed toward those symptoms, and such services can be difficult to justify with a diagnosis of ODD. Finally, SMD-like phenotypes, such as TDD, appear to be quite common in the community (approximately 3.2%; Brotman et al, 2006). Given the high prevalence of the TDD syndrome, and the severity of its symptomatology, it is important for these severely impaired youth to have a "home" in the DSM, so that clinicians can provide the intensive care that they require. In addition, compared to the creation of a specifier, the creation of a new diagnosis for TDD youth is also more likely to foster further research on this common and severe mood disorder. Indeed, it can be argued that one of the major "take-home" messages from the controversy about the diagnosis of pediatric BD is the fact that the research needs of a large population of children with severe irritability are not being met, particularly with respect to clinical trials.

Thus, in the opinion of the work groups, the Task Force guidelines are most appropriately followed by adding TDD as a new diagnosis, as opposed to as an ODD specifier. Specifically, the addition of a TDD diagnosis would identify a distinct group of people who need considerable clinical attention, where there is currently a lack of public awareness of this need. The Task Force guidelines recognize this as one important rationale for the addition of a new diagnosis. Moreover, placing this newly-defined TDD diagnosis in the Mood Disorder Section of DSM-5 would highlight the salience of mood symptoms in the TDD diagnosis, and would thus focus attention on the need to generate effective biological, psychological, and social treatments targeted towards mood symptoms in TDD. As delineated by the Task Force guidelines, highlighting the need to generate more effective treatments is another important rationale for the addition of a new diagnosis. Thus, when considering both the potential clinical benefit and harm of the two alternative approaches, the balance was thought to favor strongly the inclusion of TDD as a newly-defined syndrome in the Mood Disorders section. This view emerges despite the fact that the scientific evidence might provide stronger justification for placement of TDD as an ODD specifier, rather than as a unique diagnosis.

3. Address the nosological status of hypomanic episodes shorter than 4 days

A. Specific changes being recommended:

One possible way to identify and study those with short duration episodes is to include them as a specific sub-subcategory within an improved Bipolar Disorders Not Elsewhere Classified (BD-NOS) category. The Mood Disorders Work Group is considering several ways to capture subsyndromal presentations of clinical importance and frequency, and is conducting further data analyses to assess the 4-day duration criteria currently required for a diagnosis of hypomania. While the exact recommendation and format for recognizing and labeling this clinical presentation is not yet known, the Mood Disorders Work Group, in collaboration with the Childhood and Adolescent Disorders Work Group, is working on a proposal to identify this population (in both children and adults) in order to facilitate the clinical identification of this subgroup and to foster research on the treatment and nosological importance of short-duration episodes.

B. Rationale:

The question of how to classify hypomanic episodes shorter than four days is a controversial and important one in both pediatric and adult psychiatry. In DSM-IV, patients with such a presentation are classified as BD-NOS. In youth, the diagnosis of BD-NOS is commonly assigned, and it is generally used to denote one of two clinical presentations: the TDD phenotype, or short-duration (hypo)manic episodes (Axelson et al, 2006; McClellan et al., 2007). As discussed above, since the TDD phenotype can be differentiated from episodic BD by longitudinal outcome and other validators, the Childhood and Adolescent Disorders Work Group recommend that TDD be included in the mood disorder section of DSM-5, but removed from the BD category.

However, in contrast to the clinical outcome of SMD/TDD, data show that approximately 40% of youth with short (hypo)manic episodes experience full-duration episodes within, on average, 2.5 year follow-up, and family history does not differentiate those with short-duration episodes from those with long-duration episodes (Axelson et al, 2006; Birmaher, 2009). Furthermore, youth with short-duration (hypo)manic episodes are as impaired as those with BD I (Axelson et al., 2006; Birmaher et al., 2009). Thus, it is important that both adults and youth with (hypo)manic episodes shorter than 4 days receive a diagnosis within the BD category, and that this diagnosis contain as much information as possible i.e., in contrast to the non-specific designation BD-NOS. The available data in both adults and youth are being analyzed and will form the basis for a recommendation to change the overall definition of a hypomanic episode or to otherwise clarify the diagnostic status of individuals with hypomanic or manic episodes shorter than 4 days.

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