

# Differentiating Bipolar Disorder–Not Otherwise Specified and Severe Mood Dysregulation

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**Objective:** Bipolar disorder–not otherwise specified (BP-NOS) and severe mood dysregulation (SMD) are severe mood disorders that were defined to address questions about the diagnosis of bipolar disorder (BD) in youth. SMD and BP-NOS are distinct phenotypes that differ in clinical presentation and longitudinal course. The purpose of this review is to inform clinicians about the clinical features of the two phenotypes and about the research literature distinguishing them. **Method:** A literature review was performed on SMD as studied in the National Institute of Mental Health Intramural Research Program and on BP-NOS in youth. For BP-NOS, the phenotype defined in the Course of Bipolar Youth study is the focus, because this has received the most study. **Results:** SMD is characterized by impairing, chronic irritability without distinct manic episodes. Most commonly, BP-NOS is characterized by manic, mixed, or hypomanic episodes that are too short to meet the *DSM-IV-TR* duration criterion. Research provides strong, albeit suggestive, evidence that SMD is not a form of BD; the most convincing evidence are longitudinal data indicating that youth with SMD are not at high risk to develop BD as they age. The BP-NOS phenotype appears to be on a diagnostic continuum with BD types I and II. Subjects with BP-NOS and those with BD type I have similar symptom and family history profiles, and youth with BP-NOS are at high risk to develop BD as they age. Currently, little research guides treatment for either phenotype. **Conclusions:** Pressing research needs include identifying effective treatments for these phenotypes, ascertaining biomarkers that predict conversion from BP-NOS to BD, elucidating associations between SMD and other disorders, and defining the neural circuitry mediating each condition. *J. Am. Acad. Child Adolesc. Psychiatry*, 2013;52(5):466–481. **Key Words:** bipolar disorder, bipolar disorder–not otherwise specified, severe mood dysregulation, irritability

**B**ipolar disorder–not otherwise specified (BP-NOS) and severe mood dysregulation (SMD) are descriptive, heterogeneous phenotypic categories. Given the high prevalence and marked severity of these clinical presentations, clinicians are likely to encounter children with BP-NOS or SMD in their practices. However, despite cross-sectional and longitudinal differences between SMD and BP-NOS,<sup>1,2</sup> clinicians may believe that these are interchangeable terms for the same phenotype or may be unclear as to how to differentiate them. The uncertainty may also stem from a view that BP-NOS, SMD, and bipolar disorder (BD) are part of one spectrum of conditions. The purpose of this review is

to spotlight the salient clinical features of these conditions and their differences, because the diagnosis determines the treatment plan and prognosis that will be communicated to patients and parents. To offer guidance on these conditions and to promote a shared vocabulary for the field, this article reviews the clinical criteria for BD, BP-NOS, and SMD; identifies clinical features that distinguish the three conditions; and reviews literature supporting the hypothesis that BP-NOS and SMD are distinct phenotypes. The article ends by suggesting topics for future research.

An understanding of the distinction between SMD and BP-NOS begins with understanding the definition of a manic episode in the *DSM-IV-TR*. During a manic episode, the child's mood (elation and/or irritability) changes to a level that is an obvious departure from what is typical for that child. When the change in mood has a sufficient



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duration; when its onset is concurrent with the start, or worsening, of other manic symptoms (e.g., decreased need for sleep, increased goal directed activity, distractibility); and when the symptoms impair functioning and are not due to other disorders, the diagnosis of a manic episode is clear. Thus, when these symptoms are episodic, the diagnosis of BD can be straightforward.

Often, SMD and BP-NOS are considered when the clinical picture is not so straightforward. SMD and BP-NOS are more common than pediatric BD.<sup>2-6</sup> Indeed, clinical studies have reported that youth who meet the criteria for BP-NOS<sup>7</sup> or SMD<sup>1</sup> are at least as severely impaired as those with BD.

The *DSM-IV* definition of BP-NOS is very broad and nonspecific, i.e., "The Bipolar Disorder Not Otherwise Specified category includes disorders with bipolar features that do not meet criteria for any specific Bipolar Disorder."<sup>8</sup> The text offers examples such as "very rapid alternation (over days) between manic symptoms and depressive symptoms that do not meet minimal duration criteria for a Manic Episode or a Major Depressive Episode" (p. 366).<sup>8</sup> The most explicit definition of BP-NOS derives from the Course and Outcome of Bipolar Illness in Youth (COBY) study.<sup>2</sup> The authors used COBY-defined BP-NOS because it was the focus of a large, prospective, multisite study that compared BP-NOS with BD type I over an extended follow-up period. Although there are other BP-NOS definitions (Table 1 in Axelson *et al.*<sup>2</sup>), COBY-defined BP-NOS is the most thoroughly investigated BP-NOS phenotype at this time. The definition of BP-NOS in the COBY study emphasizes that it is an episodic mood disorder, similar to BD. In its most common manifestation, children with COBY-defined BP-NOS (hereafter referred to as BP-NOS) have a history of episodes that meet *DSM-IV* symptom criteria for mania or hypomania but are of shorter duration than the 4 days required by the *DSM-IV* for a hypomanic episode.<sup>7</sup> SMD, which is not in the *DSM-IV*, is a prepubertal-onset phenotype characterized by chronic, severe, *nonepisodic* irritability and hyperarousal symptoms.<sup>9</sup> Of note, the designs of the investigations underlying SMD and BP-NOS are different and thus draw on different kinds of data. SMD has been studied at a single site but through many different studies, whereas the COBY study is a single study conducted in several sites.

No study has compared youth with SMD directly with those with BP-NOS. Consequently, for researchers and clinicians alike, the distinction between SMD and BP-NOS (and between each of

these and BD) may pose diagnostic and therapeutic challenges. Indeed, the current American Academy of Child and Adolescent Psychiatry guidelines<sup>10,11</sup> define BP-NOS so broadly that it encompasses BP-NOS and SMD. This is regrettable because emerging research, reviewed below, suggests that BP-NOS and SMD differ in clinical features, longitudinal course, and family history.

At the time of this writing, the *DSM-5* is being prepared. Draft documents have proposed a new diagnosis, disruptive mood dysregulation disorder (DMDD). In addition, there is considerable discussion about how hypomanic episodes shorter than 4 days should be diagnosed in the *DSM-5*. The proposed *DSM-5* criteria for these syndromes are similar, but not identical, to the SMD and BP-NOS phenotypes discussed here. In particular, the proposal for DMDD, which arose largely from work on SMD, has generated considerable interest. Differences between the criteria for DMDD and those for SMD are detailed below, but it is important to note that the core feature of the two disorders, i.e., nonepisodic, severe, and impairing irritability, is the same. If DMDD is adopted in the *DSM-5*, it will supplant SMD in clinical and research settings. However, even if the corresponding *DSM-5* diagnoses differ somewhat from the SMD and BP-NOS phenotypes discussed here, it is nonetheless important for clinicians to understand how to differentiate these two families of disorders, i.e., those that, like BP-NOS/short-duration hypomania, are characterized by abbreviated but distinct episodes of manic symptoms versus those that, like SMD/DMDD, are characterized by severe, chronic irritability. Drawing as it does on the largest body of work currently available on this topic, a review of the existing literature regarding BP-NOS and SMD is an important avenue for educating clinicians about this differentiation, the possible treatment implications of this distinction, and important future avenues of research.

## BIPOLAR DISORDER

BD is the reference point for explaining differences among it, SMD, and BP-NOS. *DSM-IV* criteria for BD (hereafter referred to as BD type I or II) are the same for adults and children, although developmental considerations are important when evaluating *symptoms* in children. A manic episode is defined by a distinct period of elevated, expansive, or irritable mood *and* associated features that have their onset, or significantly worsen, during the period of abnormal mood.<sup>12</sup>

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