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DSM-5: Disruptive Mood Dysregulation Disorder

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Abstract

This paper will describe historical perspectives for the introduction of disruptive mood dysregulation disorder in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), criteria for the diagnosis, as well as information on epidemiology, clinical presentation and longitudinal course, pathophysiology, and treatment. The diagnosis of disruptive mood dysregulation disorder requires frequent, persistent, severe temper outbursts out of proportion to the situation and developmental context in combination with persistent, angry/irritable mood between the temper outbursts. Because of the limited available data, the inclusion of this new diagnosis in DSM-5 has been controversial. Regardless of this controversy, it is clear that youth experiencing such symptoms are highly impaired and utilize significant health services. Therefore, we need to expand our efforts to better understand the complex construct of this phenotype in order to improve the assessment, diagnosis and treatment of this condition.

Keywords

disruptive mood dysregulation disorder; children; adolescents; irritability; depressive disorder

1. Introduction

Recent publication of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; (American Psychiatric Association, 2013) has introduced a new disorder, disruptive mood dysregulation disorder (DMDD). Although DMDD is classified in the depressive disorders section (which are considered across the life span), its onset is specifically in childhood. This paper will discuss the historical perspectives for the introduction of DMDD, criteria for diagnosis, and available information on epidemiology, clinical presentation and longitudinal course, pathophysiology, and intervention strategies.

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2. Historical Perspectives

Around the mid-1990s, some clinician-scientists have asserted that mania presents differently in children and adolescents compared to adults; pediatric mania presents not as distinct euphoric or irritable episodes as defined in DSM-IV (American Psychiatric Association, 1994), but as persistent, non-episodic, severe irritability (Biederman et al., 1998; Faraone et al., 1997; Wozniak et al., 1995). Others have argued that pediatric patients with bipolar disorder manifest rapid cycling between elevated and depressive moods in a single day (Geller et al., 1998). In the United States of America (USA), in less than a decade, the rates of bipolar disorder diagnosis in children and adolescents had shown a dramatic increase (40-fold) in both inpatient and outpatient settings (Blader and Carlson, 2007; Moreno et al., 2007). The vast majority of such youth, and even some preschoolers, were primarily being treated with mood stabilizers and a new generation of antipsychotic drugs. As a result, there was a raging debate on the prevalence and presentation of pediatric bipolar disorder (Althoff, 2010; Biederman et al., 2004; Carlson and Glovinsky, 2009; Diler et al., 2009; Leibenluft, 2011; Mick et al., 2005).

Regardless of how “chronic” irritability was considered in terms of diagnosis, all agreed that the youth experiencing this type of irritability were severely impaired (Biederman et al., 2004; Carlson et al., 2009; Leibenluft, 2011). None of the DSM-IV categories captured the symptomatology of these youth, and it appears that the “bipolar disorder” label was meant to provide a “home” although it is debatable whether this is the right diagnostic home for such cases. In order to test whether non-episodic irritability is a developmental presentation of bipolar disorder, one research group in particular (Leibenluft's laboratory in the intramural program at the National Institute of Mental Health) described a syndrome called “severe mood dysregulation” (SMD). They conducted validation studies of this syndrome by comparing with the narrow-phenotype bipolar disorder (namely, episodic mania) on family history, phenomenology, pathophysiology and longitudinal course (Leibenluft, 2011). The SMD group had very high rates (≥85%) of attention-deficit hyperactivity disorder (ADHD) and oppositional-defiant disorder (ODD) over the lifetime, and a significant proportion (over 50%) also had a diagnosis of anxiety disorder (Leibenluft, 2011). On longitudinal follow-up, SMD was associated with an elevated risk for anxiety and unipolar depressive disorders, but not bipolar disorder (Brotman et al., 2006; Stringaris et al., 2010; Stringaris et al., 2009). Additionally, youth with SMD had lower familial rates of bipolar disorder than those with narrow-phenotype bipolar disorder (Brotman et al., 2007). Differences between SMD and bipolar disorder also were noted on pathophysiological markers, albeit there was overlap in some components (Brotman et al., 2010; Deveney et al., 2013; Leibenluft, 2011; Rich et al., 2011; Rich et al., 2007).

Given the explosive nature of temper outbursts and the high rates of disruptive disorder in the youth presenting with SMD syndrome, the DSM-5 Taskforce proposed the diagnosis of temper dysregulation disorder with dysphoria (TDD) (American Psychiatric Association Taskforce DV, 2010). The rationale for the introduction of TDD was partly to provide a home for these diagnostic orphans, and partly to address concerns about the potential for over-diagnosis and treatment of bipolar disorder. However, because TDD had not been systematically studied, several groups were critical of introducing this diagnosis both in the

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lay press and scientific literature (Axelson et al., 2011; Dobbs, 2012; Parens et al., 2010; Stringaris, 2011). Some have suggested that the word “temper” can mislead people into believing that this refers to temperament and that psychiatrists have given diagnostic labels to temperamental variation (Stringaris, 2011). Others have argued that simply switching from the bipolar label to the TDD label will not decrease the rate of psychopharmacologic treatment and, in fact, might actually increase medication use if the criteria are applied trivially to children with any kind of temper tantrums (Parens et al., 2010). Subsequently, TDD was changed to DMDD and included in the depressive disorders section. Probably, this was based partly on the longitudinal data suggesting high rates of depressive disorder outcomes in SMD. Moreover, some cross-sectional and longitudinal investigations of ODD revealed that the irritability or negative affect component was associated primarily with depressive and anxiety disorders rather than ADHD and conduct disorder (Burke et al., 2010; Stringaris and Goodman, 2009a, b). Similar criticisms have been raised with DMDD (Axelson, 2013; Parry, 2013; Ryan, 2013).

3. Diagnostic Criteria for DMDD

The criteria for DMDD are primarily based on those developed for SMD, with some modifications. Criteria for DMDD include the following: (1) severe, recurrent (≥3 times/week) temper outbursts (verbally and/or behaviorally) that are grossly out of proportion in intensity or duration to the situation, and inconsistent with the developmental level; (2) the mood between temper outbursts is persistently irritable or angry most of the day, nearly every day, and observable by others; (3) the symptoms must be present for 12 or more months, with no more than 3 consecutive months of symptom-free period; (4) the symptoms/behaviors must be present at least in two of three settings (i.e., at home, at school, with peers), and to a severe degree at least in one setting; (5) the diagnosis should not be made for the first time before age 6 years or after 18 years; and (6) by history or observation, the age at onset is before 10 years. Certain exclusion criteria are included: (1) the behaviors do not occur exclusively during an episode of major depressive disorder and are not better explained by another mental disorder (e.g., autism spectrum disorder, persistent depressive disorder/dysthymia, posttraumatic stress disorder, separation anxiety disorder); and (2) DMDD cannot co-exist with bipolar disorder, intermittent explosive disorder or ODD (individuals whose symptoms meet criteria for both DMDD and ODD should only be given the diagnosis of DMDD).

In addition to the temper outbursts and negative mood, SMD syndrome required the presence of at least three “hyperarousal” symptoms (namely, insomnia, agitation, distractibility, racing thoughts or flight of ideas, pressured speech, and intrusiveness) (Leibenluft, 2011). The reason for this criterion was that these symptoms are common to mania and ADHD and because such symptoms were part of the rationale for assigning the bipolar disorder diagnosis to children with severe chronic irritability (Faraone et al., 1997; Mick et al., 2005). The age of onset for SMD was before age 12 years, and the maximum allowed symptom-free period was 2 months. It is not clear why these criteria differed between SMD and DMDD.

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4. Empirical Evidence for DMDD

The development of DMDD has been controversial, in part, because there are no published data using the proposed diagnostic criteria for youth. The scientific support for DMDD comes primarily from studies of SMD which, as described above, is related but not identical to DMDD. The information presented below on prevalence, clinical presentation and longitudinal course, pathophysiology and treatment is primarily using SMD criteria.

5. Epidemiology

No epidemiological samples were recruited specifically to study SMD or DMDD. Empirical studies on SMD were from clinical samples. Leibenluft and colleagues employed SMD criteria to existing epidemiological samples. In the Great Smoky Mountains Study, a longitudinal epidemiological investigation comprising of 1,420 youth (ages 9–19 years), the lifetime prevalence of SMD was 3.3% (Brotman et al., 2006). Copeland et al. (2013) used existing data from three large epidemiological samples covering a broad age range that includes preschool (ages 2–5) and school-age (ages 9–17) cohorts (also including the Great Smoky Mountains Study described above), to examine the prevalence of DMDD. Nearly half of the school-age youth were reported to have severe temper outbursts during the 3 months prior to assessment. When the frequency criterion was applied, the prevalence dropped nearly 7-fold (6%–7%). Applying the duration criterion dropped the prevalence further (1.5%–2.8%), and finally applying the full DMDD criteria resulted in a prevalence rate of approximately 1%. The prevalence rate in the pre-school cohort (ignoring the age of onset criterion) was 3.3%. The school-age youth with the disorder had significant impairment and service use.

In a large sample of 5–18 year-olds referred for psychiatric outpatient services, SMD was diagnosed in 54.4% of children in whom both parents and teachers reported “rages” or severe temper outbursts (Carlson and Dyson, 2012). Axelson et al. (2012) assigned DMDD criteria to a clinical sample of children (ages 6–12 years) who participated in the Longitudinal Assessment of Manic Symptoms (LAMS) study, and 26% met DMDD criteria at intake. Over 50% of children (ages 5–12) in an inpatient service had been admitted because of rages (Carlson et al., 2009). Combining the information from epidemiological and clinical samples, it appears that the prevalence of DMDD is highly dependent on applying the frequency, persistence and duration criteria. If all of the criteria are applied, the DMDD diagnosis is relatively uncommon in school-age youth, but most of these youth are likely to have significant impairment requiring treatment.

Given that the diagnosis of DMDD is contingent on the frequency and persistence of symptoms, retrospective recall of this type of temporal information over extended periods can be difficult for caregivers and children (Axelson, 2013). This may, in part, account for the modest test-retest reliability (kappa = 0.25, judged to be in the “questionable” range) of DMDD in the DSM-5 field trials (Regier et al., 2013). In the LAMS study, 40% of the sample met DMDD criteria at least once during the 2-year follow-up but 52% of these participants met criteria only at one assessment, suggesting poor longitudinal stability (Axelson et al., 2012). In the Great Smoky Mountains Study, the cumulative prevalence of

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DMDD by age 16 was 4.4%% (4 times the point prevalence), again suggesting that a significant percentage of youth with DMDD met the criteria only at one assessment.

In the Smoky Mountains Study sample, the life time prevalence of SMD and DMDD were comparable (3.3% and 4.4%, respectively), given that DMDD does not include the hyperarousal symptoms required for SMD (Brotman et al., 2006; Copeland et al., 2013). However, when the overlap between SMD and DMDD was assessed, only 39% of youth with SMD also met criteria for DMDD (Copeland et al., 2013). Since the criteria for DMDD are broadly based on those for SMD, this calls into question the degree to which data from samples of youth with SMD directly apply to DMDD.

6. Clinical Presentation and Longitudinal Course

In both epidemiological and clinical samples, SMD and DMDD were frequently associated with other psychiatric disorders, most commonly anxiety/mood and disruptive disorders (Axelson et al., 2012; Brotman et al., 2006; Copeland et al., 2013; Leibenluft, 2011; Roy et al., 2013). Affected youth were severely impaired in multiple social domains. Although it is difficult to isolate the impairment associated with SMD/DMDD from that of other psychopathology, excluding the youth with comorbidity in the Great Smoky Mountain study indicated comparable degree of impairment in the SMDD group (Copeland et al., 2013).

Leibenluft and colleagues assessed rates of mood episodes in 84 youth with SMD and 93 with bipolar disorder over a median period of 28.4 months (Stringaris et al., 2010). Only one patient (1.2%) with SMD exhibited a new manic, hypomanic, or mixed episode in comparison with 58 (62.4%) of those with bipolar disorder. In a community sample of 776 youth from the greater New York region followed longitudinally in three waves, Leibenluft et al. (2006) examined the stability of episodic and chronic irritability. The longitudinal stability within irritability type was stronger than between types. Chronic irritability during adolescence (mean age 13.8 years) predicted major depressive disorder in early adulthood (mean age 22.1 years). In contrast to this, episodic irritability predicted mania. These data support the notion that episodic and chronic irritability in adolescents appear to be stable, distinct constructs. This sample was followed further, and chronic irritability during adolescence predicted depressive and generalized anxiety disorders at age 33 years (Stringaris et al., 2009). In the Great Smoky Mountains study, youth who met criteria for SMD in the first wave (mean age 10.6) were seven times more likely to be diagnosed with a depressive disorder at 18 years (Brotman et al., 2006).

The SMD/DMDD diagnosis appears to separate out youth with chronic irritability who ultimately have a low risk for developing bipolar disorder. In contrast, youth meeting criteria for bipolar disorder not otherwise specified type (i.e., those who do not meet duration criteria for bipolar disorder but have significant periods of manic or hypomanic symptoms and other bipolar disorder symptoms) do seem to be at very high risk for full bipolar disorder over time (Towbin et al., 2013). Hence, distinguishing youth with DMDD from those with unspecified bipolar disorder has important clinical implications as treatment strategies for the two are likely to be different. According to DSM-5 criteria, DMDD also should be distinguished from ODD. In the LAMS study, 58% of the participants with ODD

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met DMDD criteria, but those who met DMDD criteria did not differ significantly from their counterparts without DMDD with respect to symptom severity, comorbidity or functional impairment, making it difficult to distinguish DMDD from ODD (Axelson et al., 2012).

7. Pathophysiology

Leibenluft and colleagues conducted a series of pilot studies utilizing event-related potentials, functional magnetic resonance imaging (fMRI) or magnetoencephalography (MEG) paradigms, and compared youth with SMD, bipolar disorder and healthy controls. Behavioral data from these studies indicated that both affected groups differed from controls in face emotion labeling ability, degree of subjective distress reported while performing a frustrating task, and performance on learned response reversal paradigms (Leibenluft, 2011). In a parallel study, Roy et al. (2013) administered the Balloons Game, which assesses emotion expressivity in response to frustration, under demands of high and low regulation to children with severe temper outbursts and healthy controls. When there were no demands for self-regulation, children with severe outbursts showed reduced positive expressivity, and also showed significant deficits in controlling negative facial expressions when asked to do so.

While youth with bipolar disorder and SMD both had deficits in behavioral measures, the neural circuits mediating these pathophysiologic abnormalities appeared to differ between them. (Leibenluft, 2011). For example, a study using a rigged task to elicit frustration found that youth with bipolar disorder and SMD both reported more frustration than healthy controls. However, event-related-potential measures differentiated the two groups; youth with bipolar disorder had deficient top-down executive attention (i.e., decreased parietal P3 waves) specifically during frustration, while youth with SMD had deficits in bottom-up early attentional processes (i.e., decreased parietal, temporal and central N1 and P1 waves) during both frustrating and non-frustrating blocks (Rich et al., 2007). In an fMRI paradigm utilizing this task, youth with SMD exhibited markedly decreased activation of neural regions associated with spatial attention, reward processing, and emotional salience during frustrating trials (Deveney et al., 2013). In the face emotional processing task, youth with SMD had reduced amygdala activation compared to those with bipolar disorder and healthy controls (Brotman et al., 2010). With the MEG data, youth with SMD responded to negative feedback with significantly greater activation of the anterior cingulate cortex and medial frontal gyrus, whereas those with bipolar disorder displayed greater superior frontal gyrus activation and decreased insula activation (Rich et al., 2011).

8. Treatment

No specific treatment for DMDD or SMD exists currently (Jairam et al., 2012; Krieger and Stringaris, 2013). The only randomized, controlled trial in children with SMD found no benefit of lithium over placebo (Dickstein et al., 2009). Another controlled trial in youth with a phenotype similar to SMD (ADHD and aggressive behavior unresponsive to stimulants) found divalproex sodium combined with behavioral therapy to be more effective than stimulant plus placebo combined with behavioral therapy (Blader et al., 2009). An open-label trial using low doses of risperidone in youth with SMD showed significant

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reductions in irritability scores (Krieger et al., 2011). It is important to emphasize that there have been no pharmacological studies on DMDD, and extrapolating data from SMD may be problematic given that there is surprisingly little overlap between the two conditions.

Clinicians who conceptualize severe, non-episodic irritability as a phenotype of bipolar disorder are reluctant to treat youth with SMD/DMDD with selective serotonin reuptake inhibitors (SSRIs) or stimulants because of concerns about precipitating mania. However, if these conditions have a low risk for mania and are more similar pathophysiologically to unipolar depressive and anxiety disorders, as well as to ADHD, then antidepressant agents and stimulants would be recommended. Given the relatively high side effect burden of atypical antipsychotics (Correll et al., 2009), coupled with the risks of using SSRIs (Martin et al., 2004) or stimulants in bipolar disorder, this differentiation is important. There are no systematic data regarding the risk of stimulant-induced mania in DMDD/SMD. However, preliminary evidence suggests that youth with related phenotypes may respond as well to stimulants as those with uncomplicated ADHD (Carlson et al., 2000; Galanter et al., 2003). More research is needed to determine whether treatment with SSRIs and/or stimulants is effective and safe in treating DMDD/SMD. An important question is whether youth with DMDD/SMD who have a parent with bipolar disorder differ from their counterparts without a family history of bipolar disorder in their risk for developing mania, either spontaneously or in response to SSRIs or stimulants.

From a clinical standpoint, there has been a recent trend in treating youth who present with symptoms resembling DMDD/SMD (specifically explosive outbursts) with a combination of new generation antipsychotics and stimulants (Carlson, 2013). Although a variety of labels have been attributed to chronic irritability and explosive outbursts, a systematic review of the data on concurrent treatment with antipsychotics and stimulants for aggressive and hyperactive behavior has indicated that the combination therapy is not superior to antipsychotic or stimulant monotherapy (Linton et al., 2013). Contrary to speculation, use of a stimulant does not seem to reduce the metabolic side effects associated with antipsychotics. Therefore, concurrent antipsychotic and stimulant treatment should be considered only as a tertiary-line of treatment when monotherapy or adjunctive pharmacotherapy and behavioral intervention fail (Linton et al., 2013).

Behavioral and other psychotherapeutic interventions also should be considered in treating DMDD/SMD, particularly given their impairment in many social domains (Carlson, 2013; Copeland et al., 2013). No systematic data are available on behavioral-psychotherapeutic interventions for DMDD or SMD. In a randomized, controlled trial in children with ODD symptoms, parental intervention (based on Webster-Stratton techniques) was more beneficial in those presenting with emotional dysregulation than those manifesting headstrong characteristics (Scott and O'Connor, 2012).

9. Summary and Future Directions

DSM-5 has included the new diagnosis of DMDD in order to address concerns about the potential for the over-diagnosis and treatment of bipolar disorder in children. This provides a diagnostic home for a relatively large proportion of clinically-referred children with severe

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impairment who did not fit well into any DSM-IV category. However, the inclusion of this diagnosis has raised significant controversy because of limited empirical data. Regardless of where one stands on the issue of including this disorder in DSM-5, it is clear that the field can benefit from more research on severe anger outbursts and chronic irritability. Youth who have persistent, explosive irritability and anger are highly impaired, and outbursts of rage are a frequent precipitant of inpatient hospitalization. Hence, we need to expand our efforts to better understand the complex construct of irritability so that we can improve the assessment, diagnosis and treatment of some of our sickest patients.

It is important for clinicians to search for potential causes of severe irritability in an individual child, whether it be family conflict or other psychosocial stressors, history of maltreatment, learning or communication disorders, other Axis I psychiatric disorders, or some combination of these or other factors. This strategy will facilitate a more personalized treatment for each youth, using appropriate psychosocial interventions with active liaison with the school and all other stakeholders in addition to appropriate medications to treat the underlying psychiatric condition(s). It is important to note that although effective treatment of underlying mood, anxiety, autism spectrum, or behavioral disorders can result in substantial improvements, significant numbers of these youth do not respond adequately to existing treatments. For many of these poor responders, the severity of the anger and temper outbursts appears to be far out of proportion to any contributing psychosocial factors. So, an individually-tailored, multi-prong approach maybe the optimal solution until more empirical evidence becomes available.

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