Sam Goldstein *Editor*

Clinician Guide to Disruptive Mood Dysregulation Disorder in Children and Adolescents

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Editor
Sam Goldstein
Department of Psychiatry
University of Utah
Salt Lake City, UT, USA

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This volume is earnestly dedicated to the tireless and compassionate individuals who devote their lives to understanding and supporting children and adolescents afflicted with disruptive mood dysregulation disorder (DMDD). This complex and challenging condition demands not only patience and understanding but also a deep well of knowledge and empathy from those who care for these young individuals.

May this text serve as a beacon of guidance, illuminating the path for clinicians, educators, and caregivers alike. It is crafted with the hope that its pages will empower these dedicated professionals and loved ones with the necessary insights, strategies, and compassion to make a meaningful difference. In embracing the knowledge and perspectives shared within, we take a collective step toward a more empathetic and supportive environment for those affected by DMDD.

This text was created by a worldwide group of committed researchers and clinicians. Through our combined efforts and shared commitment, we aim to forge a world

where every child and adolescent with DMDD finds solace, hope, and the prospect of a brighter, more understanding tomorrow. In this journey, each small step we take is a leap toward a future where the challenges of DMDD are met with unwavering support and profound empathy.

A special thanks to Kathleen Gardner, after 39 years still supporting my work, and to Morgan Richards for her co-authorship on multiple chapters, invaluable tracking of our contributors and research assistance. Finally, to my wife Sherrie, our beloved children and grandchildren: this dedication celebrates your endless love and guidance. You are the heartbeats of my life, teaching me the true essence of love, strength, and joy. May our shared journey continue to be blessed with laughter and cherished moments.

Sam Goldstein

Preface

Disruptive mood dysregulation disorder (DMDD) emerged as a diagnostic entity relatively recently in the field of mental health. The history of DMDD can be traced back to the early 2000s when clinicians and researchers recognized the need for a distinct diagnostic category to describe severe and chronic irritability in children.

Prior to the formal recognition of DMDD, children displaying intense and frequent temper outbursts, often accompanied by chronic irritability, were often diagnosed with conditions such as pediatric bipolar disorder, attention deficit hyperactivity disorder, or oppositional defiant disorder. However, these diagnoses did not adequately capture the unique symptomatology and developmental trajectory observed in these individuals. Further the many proven behavioral and pharmacologic treatments for these other disorders typically fell short for youth with severe emotional dysregulation.

The initial recognition and exploration of severe mood dysregulation (SMD) as a distinct entity occurred through the efforts of several researchers and clinicians. In 2003, Leibenluft and colleagues (2003) published a seminal study describing a group of children with chronic irritability, emotional over-reactivity, and frequent temper outbursts, who did not meet the criteria for pediatric bipolar disorder. They proposed the term "severe mood dysregulation" as a potential diagnostic construct to better capture the clinical presentation of these children. They followed with a series of articles defining the parameters of this condition (Leibenluft et al., 2006; Leibenluft, 2011).

The concept of SMD gained further attention and research interest, prompting the National Institute of Mental Health (NIMH) to fund the NIMH Research Domain Criteria (RDoC) initiative in 2009. This initiative aimed to advance the understanding of mental disorders by focusing on underlying dimensions of functioning, such as emotion regulation and neural circuits. The study of SMD was a significant component of this initiative (Patrick & Hajcak, 2016).

In 2013, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) was published, and for the first time included the formal recognition of disruptive mood dysregulation disorder (DMDD) as a distinct diagnostic category. Though the reasons for its inclusion was controversial, the introduction of DMDD

in the DSM-5 aimed to address the diagnostic challenges and controversies surrounding the identification and treatment of children with severe and chronic irritability.

DMDD is characterized by persistent irritability and frequent temper outbursts that are developmentally inappropriate. The diagnosis requires the presence of these symptoms in at least two settings (e.g., home, school) and the manifestation of symptoms before the age of 10. DMDD also emphasizes the necessity of differentiating this condition from other disorders such as bipolar disorder and oppositional defiant disorder.

Since its inclusion in the DSM-5, DMDD has garnered increased attention from researchers, clinicians, and educators. Efforts have focused on elucidating the underlying neurobiological mechanisms, identifying risk factors, and refining assessment and treatment approaches.

Ongoing research has explored the neurodevelopmental aspects of DMDD, such as the role of disrupted neural circuits involved in emotion regulation. Studies have also investigated the potential overlap and comorbidity between DMDD and other psychiatric disorders, such as ADHD and anxiety disorders. Each passing year sees an increasing number of peer-reviewed studies and trade texts.

In terms of treatment, interventions for DMDD encompass a multidisciplinary approach involving pharmacotherapy, psychotherapy, and psychosocial interventions. Medications including but not limited to stimulants, SSRIs, anticonvulsants, adamantanes, and atypical antipsychotics have been utilized, alongside evidence-based psychotherapeutic interventions like cognitive-behavioral therapy (CBT) and dialectical behavior therapy (DBT).

The history of DMDD reflects the ongoing evolution and refinement of our understanding of childhood mood dysregulation. As research continues to advance, it is expected that our knowledge and treatment approaches for DMDD will further develop, ultimately improving outcomes and quality of life for affected individuals and their families. Even as this volume goes to press a quickly growing body of peer reviewed research is emerging (Lin et al., 2021; Brænden et al., 2023; Goksu et al., 2023). My thanks to the pioneering contributors to this very first clinical volume and to the families that have graciously shared their stories in many of the chapters in this volume.

Salt Lake City, UT, USA Sam Goldstein

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About the Editor

Sam Goldstein obtained his PhD in School Psychology from the University of Utah and is a licensed psychologist and certified school psychologist in the state of Utah. He is also a board certified as pediatric neuropsychologist and listed in the Council for the National Register of Health Service Providers in Psychology. He is a fellow of the American Psychological Association and the National Academy of Neuropsychology. He is an adjunct assistant professor in the Department of Psychiatry, at the University of Utah School of Medicine. He has authored, co-edited, or co-authored over fifty clinical and trade publications, three dozen textbook chapters, nearly three dozen peer-reviewed scientific articles, and ten psychological and neuropsychological tests. He is the founder and former editor in chief of the *Journal of Attention Disorders* (https://journals.sagepub.com/home/jad). Since 1980, he has served as clinical director of the Neurology, Learning and Behavior Center in Salt Lake City, Utah. The center conducts over 700 neuropsychological evaluations of children and adults yearly. www.samgoldstein.com.

Part I
Introduction

Chapter 1
DMDD at the Nexus of Internalizing and Externalizing Disorders

Sam Goldstein and Morgan Richards

1.1 Introduction

Disruptive mood dysregulation disorder (DMDD) is a new diagnosis of childhood appearing for the first time in the 2013 Diagnostic and Statistical Manual of the American Psychiatric Association Fifth Edition (DSM-5) within the Depressive Disorders section (American Psychiatric Association, 2013). It is the only depressive disorder requiring diagnosis prior to 18 years of age. The creation of the DMDD diagnosis arose as a resolution to an ongoing debate between those in the field believing that latency and younger-age children could be reliably diagnosed with bipolar disorder and those who maintained that research demonstrating many young children diagnosed with bipolar disorder were in fact not transitioning into adulthood with a continued diagnosis of DMDD. DMDD originates from the research syndrome severe mood dysregulation (SMD).

DMDD and SMD are characterized by severe, recurrent temper outburst (≥3 per week) and by persistently irritable mood (most of the day in ≥12 months) between the outbursts. Most but not all children with SMD meet DMDD criteria (Deveney et al., 2015; Freeman et al., 2016; Stoddard et al., 2015). DMDD symptoms, however, go beyond just moodiness; children with DMDD will experience severe emotional dysregulation. Symptoms typically begin before age 10, but diagnostic guidelines require that the DMDD diagnosis not be made for children under 6 years of age. The condition is characterized by irritable, angry moods most of the day, nearly every day (you rarely find this level of severity to be the case in clinical practice), severe temper outbursts that can last for long periods of time, which, at one

S. Goldstein (✉) · M. Richards
Neurology Learning and Behavior Center, Salt Lake City, UT, USA
e-mail: info@samgoldstein.com

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time was considered the hallmark of childhood bipolar disorder, and challenges and impairment in at least one if not more everyday activities (e.g., home, school, etc.). The DMDD diagnosis requires that symptoms occur consistently for at least 12 months.

Given its recent entry into the diagnostic system, it is not surprising that the current scientific research remains insufficient as this volume goes to press. Yet the combination of disruptive and nondisruptive symptoms and behaviors characterizing DMDD would seem to place this condition at the nexus of internalizing and externalizing conditions. To examine this from a different perspective, DMDD likely results from both structural and neurochemical differences in the brain. Thus, typical psychiatric medications that work very well for conditions such as attention deficit hyperactivity disorder (ADHD), depression, and anxiety may fall short of helping relieve the symptoms of DMDD.

As a new diagnosis, we know little about comorbidity, effective treatment, and outcome into adulthood. Recent studies suggest that children with DMDD are at a greater risk to experience a myriad of adult psychiatric disorders and may suffer from more adult psychiatric disorders than other childhood conditions (Ling et al., 2020). These authors suggest that DMDD has a high rate of psychiatric comorbidities such as ADHD, ASD, ODD, intermittent explosive disorder, and anxiety disorders. DMDD alone without any psychiatric comorbidity is rare, and the impairment of DMDD might be confounded by impairment due to other comorbid disorders or symptoms such as ODD or ADHD. Children with DMDD demonstrate severe functional impairment (Copeland et al., 2013; Uran & Kilic, 2020) and adverse outcomes when compared to their treatment-seeking peers without DMDD and children without psychiatric disorders (Copeland et al., 2014). ADHD is a frequent cooccurring diagnosis in DMDD (Dickstein et al., 2010; Rich et al., 2007; Stoddard et al., 2016). However, irritable mood is not a criterion nor characteristic in ADHD (American Psychiatric Association, 2013). Treatment of DMDD is based on what has been helpful for other disorders that share similar symptoms; however, children diagnosed with DMDD often end up prescribed a combination of psychiatric medications with limited or inconsistent benefit. Clinicians tend to prescribe stimulants/atomoxetine, atypical antipsychotics, and SSRIs (Topal et al., 2021). Counseling can be helpful in assisting these children to better understand their temperament and develop coping strategies. DMDD is a condition for which there is not an Individuals with Disability Education Improvement Act (IDEIA) special educational classification in the United States within the schools, creating an additional conundrum for school psychologists when children with DMDD demonstrate disruptive symptoms at school. As of the publication of this volume, there are fewer than one hundred peer-reviewed published studies specifically about DMDD, many of which are summary and/or opinion articles. There are far more studies of SMD bootstrapped to explain DMDD.

Overview: SMD, TDD and DMDD

Mania often 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). Researchers 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, in less than a decade in the 1990s, the rates of bipolar disorder diagnosis in children and adolescents demonstrated a dramatic 40-fold increase (Blader & Carlson, 2007; Moreno et al., 2007). The vast majority of such youth, and even some preschoolers, were primarily being treated with mood stabilizers and antipsychotic drugs. As a result, there was and continues to be a contentious debate about the prevalence and presentation of pediatric bipolar disorder (Althoff, 2010; Biederman et al., 2004; Carlson & Glovinsky, 2009; Leibenluft, 2011; Mick et al., 2005). Regardless of how "chronic" irritability was considered in terms of diagnosis, youth experiencing severe irritability are markedly impaired (Carlson et al., 2009). None of the DSM-IV categories correctly captured the symptom profile of these youth. Neither the bipolar disorder nor ADHD-combined labels were likely the right diagnostic classification for these children.

As noted, the original starting point for the DMDD classification is the research criteria for SMD. Multiple studies demonstrate that the SMD group presents with extremely high rates of cooccurring ADHD-combined and oppositional defiant disorder (ODD). A significant proportion also met diagnostic criteria for an anxiety disorder (Leibenluft, 2011). Longitudinal follow-up suggests that SMD is associated with an elevated risk for anxiety and unipolar depressive disorders, but not bipolar disorder (Stringaris et al., 2009, 2010). 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 are also noted on pathophysiological markers (e.g., specific areas of brain activation), although there is overlap in some of these markers (Brotman et al., 2010; Deveney et al., 2013; Rich et al., 2011).

The DSM-5 taskforce originally proposed the diagnosis of temper dysregulation disorder with dysphoria (TDD) (American Psychiatric Association Taskforce DV, 2010). In addition to filling a diagnostic need, this proposal was also able to address concerns about the reported overdiagnosis of bipolar disorder, particularly in young children. This recommendation was not without criticism due to the absence of sufficient scientific literature (Axelson et al., 2011; Dobbs, 2014). The word "temper" was criticized as misleading possibly creating confusion about temperament and pathology (Stringaris, 2011). Subsequently, TDD was changed to DMDD and included in the Depressive Disorders section. Most likely, this decision was based partly on 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 in this condition was associated primarily with depressive and anxiety disorders rather than ADHD-C and conduct disorder (CD) (Burke et al., 2010; Stringaris & Goodman, 2009a, b). Similar criticisms however have been raised with DMDD (Axelson, 2013; Parry, 2013; Ryan, 2013).

Overall, DMDD has been a controversial addition to the DSM-5 due to the lack of published validity studies, leading to questions about DMDD as a distinct disorder. Interestingly, the International Classification of Diseases-Tenth Revision-Clinical Modification (ICD-10-CM), has embraced this ideology, creating an entire diagnostic category, persistent mood (affective) disorder, unspecified. This category was implemented on October 1, 2021, and includes the American DSM 5 version of DMDD. Other international versions of ICD-10 may differ.

This ICD category also includes:

Cyclothymic disorder.
Dysthymic disorder.
Other persistent mood [affective] disorders.
Disruptive mood dysregulation disorder.
Other specified persistent mood disorders.
Persistent mood [affective] disorder, unspecified.

In this diagnostic system, DMDD differs in several ways from SMD. SMD requires recurrent temper outbursts, a persistent negative mood (which, unlike DMDD, includes depressed mood), and the presence of at least three "hyperarousal" symptoms (pressured speech, racing thoughts or flight of ideas, intrusiveness, distractibility, insomnia, and agitation). Hyperarousal criteria were included because these key symptoms in persistently irritable children often led to concern about mania. Other differences in this nomenclature include age of onset and maximum symptom-free period. For SMD, the age of onset is before 12 years old, and the maximum symptom-free period is 2 months. A similarity between the two was found in the Great Smoky Mountains Study, in which the lifetime prevalence rates of DMDD (4.4%) and SMD (3.3%) were comparable (Brotman et al., 2006).

Though there have been very few prospective studies on DMDD, studies have examined the prevalence of retrospectively diagnosed cases of DMDD or SMD in existing datasets. DMDD symptoms have been found to be relatively common in children referred for mental health challenges, but the full disorder is much less common. Rates of DMDD are also found to be substantially higher in clinical samples, especially in those with high rates of externalizing disorders and/or mood lability. However, in many cases, even in clinical samples, the temporal stability of these symptoms is low. Even those with elevated symptoms of DMDD not meeting full diagnostic criteria experience significant impairment requiring treatment. In a study by Copeland et al. (2013), school-age youth with DMDD experienced significant social impairment (relationship with parents, siblings, and teachers), school suspension, and service use (mental health and general medical), reinforcing the

findings from other studies that youth with severe non-episodic irritability are appreciably impaired, even if they do not meet the criteria for bipolar disorder.

Copeland et al. (2013) also used existing data from three large epidemiological samples including both preschool and school-age cohorts, to find that around half (46–49%) of school-age youth and around 80% of preschoolers were found to have severe temper outbursts in the last 3 months. Among school-age cohorts, the prevalence dropped to 7% when the DSM-5 frequency criterion was applied and dropped further (1.5–2.8%) adding the duration criterion. Using the full DSM-5 DMDD criteria, the prevalence rate declined to about 1%. In the preschool cohort, the prevalence rate of DMDD, utilizing the entire DSM 5 criteria except for age of onset, was 3.3%. Similar rates of the core DMDD symptoms were found in another population-based sample of 376 young children. In a large nationally representative sample of adolescents, the prevalence rate of DMDD was 0.12% using strict criteria for DMDD and increased with relaxation of the mania/hypomania exclusion criterion (0.56%), the frequency criterion (1.71%), or both (5.26%). Not unexpectedly, higher rates have been reported in clinical samples. Axelson et al. (2013) found that 26% of children participating in the Longitudinal Assessment of Manic Symptoms (LAMS) study met DMDD criteria. These children were recruited from outpatient clinics, however, and were preselected for the presence of prominent mood lability.

As the diagnosis of DMDD is contingent on the frequency and persistence of symptoms, retrospective recall of this type of information over extended periods is difficult for caregivers and children (Axelson, 2013). This likely accounts for the questionable though modest test-retest reliability (kappa = 0.25) of DMDD in the DSM-5 field trials (Regier et al., 2013). In this 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). As noted in the Great Smoky Mountains Study, the cumulative prevalence of DMDD by age 16 was 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 Juvenile Justice System, DMDD criteria were met by 3.3% of justice-involved youths in a study of nearly 10,000 youths (Mroczkowski & Havens, 2018). Results of a multinomial regression demonstrated that, after adjustment for covariates, those youth with DMDD had fewer differences compared with those with other mood disorders than did those meeting criteria for disruptive behavior disorders (DBDs) such as ODD or conduct disorder (CD). Consistent with the DSM-5 classification of DMDD as a depressive disorder, those with DMDD shared more characteristics with youths with mood disorders than with those reporting DBDs. Externalizing behaviors leading to justice involvement may overshadow internalizing symptoms of DMDD, but mood-related conditions should be identified and treated in this population.

DSM-5 Diagnostic Criteria for DMDD

In general, a clinician considering DMDD will look for severe temper outbursts and consistent irritability and anger in between the outbursts. Prior to making a diagnosis of DMDD, the clinician must rule out any other possible causes or contributing factors to the presenting DMDD symptoms. The DSM-5 diagnostic criteria a child must meet in order to receive a DMDD diagnosis are:

1. Recurrent and severe temper tantrums or outbursts.
    - The tantrums/outbursts may be expressed verbally and/or behaviorally (physical aggression toward other people or property).
    - The tantrums/outbursts are considered out of proportion (in duration and intensity) to the situation or triggering event.
    - The tantrums/outbursts are inconsistent with the child's developmental level.
    - The tantrums/outbursts occur three or more times per week, on average.
2. Persistent irritability or anger.
    - The irritable/angry mood occurs nearly every day, for most of the day.
    - The irritable/angry mood is observable by others (peers, parents, teachers, etc.).
3. The recurrent temper tantrums and persistent irritability/anger have been present for 12 months or longer.
    - Throughout the 12 months of ongoing temper tantrums and irritability/anger, the child has not had a period lasting 3 or more consecutive months without all of the diagnostic symptoms.
4. Symptoms are present in at least two of three primary settings, either home, school, or in social situations.
    - Symptoms are severe in at least one of the three primary settings.
5. DMDD diagnosis should not be assigned before age 6 or after age 18.
6. The age of onset of disruptive mood dysregulation disorder is before 10 years old.
7. The symptoms are not better explained by another mental illness, such as depression, posttraumatic stress disorder, or autism.

The Extended Phenotype of DMDD

Not unexpectedly, youth with DMDD experience higher rates of social and academic challenges; however, very few studies have utilized DMDD group criteria. Many more studies have used SMD criteria, which may or may not fully generalize the youths with DMDD. Researchers continue to raise fundamental concerns regarding the validity of DMDD as a diagnostic group (Malhi & Bell, 2019).

In one of the few DMDD studies, youth with DMDD rated themselves as having significantly more social problems than youth with other psychiatric disorders (Freeman et al., 2016). Possibly similar to the social pragmatic challenges experienced by youth with autism spectrum disorder (ASD), social processing difficulties are present in DMDD as well. By task performance (e.g., behavior), some studies find face-emotion labeling deficits in youth with DMDD, whereas others do not (Hommer et al., 2014). There is, however, an indication of a bias toward threatening or angry faces. On a neurocircuit level of analysis, hyperactivation in superior temporal gyrus when viewing angry faces is demonstrated, whereas amygdala activity findings during face-emotion processing are inconsistent, possibly due to the nature of different processing tasks (Brotman et al., 2010; Thomas et al., 2012, 2013; Kircanski et al., 2018; Stoddard et al., 2017). Taken together, in DMDD there is indication of abnormal responses to frustration by self-report, behavior paradigms, and neurocircuit activity (Rich et al., 2007, 2011). However, these results are ambiguous in terms of different results on reports of arousal in response to frustration. Further, no abnormalities in reward or punishment processing are demonstrated on the behavior level (Kircanski et al., 2018).

By self-report, one study found that youth with DMDD experience more attentional problems than youth without DMDD in psychiatric clinical assessment (Freeman et al., 2016). Two studies have examined attention without social or emotional interference on a behavioral level. Results of these studies suggest that youth with DMDD might experience impairments in selective and visual attention (Pagliaccio et al., 2017; Uran & Kilic, 2015). In social processing studies, youth with DMDD demonstrate a bias toward angry faces and experience difficulty ascertaining the correct emotional tone of a spoken sentence (Brotman et al., 2010; Thomas et al., 2012, 2013). Regarding abnormal processing in the reception of communication, a subconstruct of social processes may be responsible for this challenge. Some researchers have argued that youth with SMD also demonstrate an extended deficit in labeling emotions of others to include deficits in emotional self-monitoring (Stoddard et al., 2014). Hence, youth with DMDD might experience difficulty with theory of mind. Comparable scores on social awareness in SMD and ASD highlight this possibility (Sturm et al., 2018). However, research examining the capacity of youth with DMDD to understand the relationship between the self and mental states of others is scarce. Problems with attention and cognitive control (i.e., subconstructs of cognitive systems) is also indicated in DMDD, but again limited reproduced studies of these findings make the results equivocal.

A recent study suggests that youth with ADHD-C are more inattentive than youth with DMDD, but the DMDD group are more emotionally labile than those with ADHD-C (Uran & Kilic, 2020). These results indicate a difference in mechanisms related to attention with DMDD having a context specific and ADHD having a general deficit in attention. Notably, this also implies that emotional hyperarousal, that is, hyper-lability, is likely linked to the presence or activation of a perception bias which might represent a unique mechanism in DMDD. Thus, DMDD might be characterized by emotional hyperarousal and ADHD by cognitive hyperarousal. This study also found that children with ≥2 psychiatric comorbidities in DMDD

and ADHD-combined type had significantly higher scores on indices on "oppositional," "inattention," and "ADHD index." This implies that the inattention symptomology worsens when a general inattention deficit and emotional lability interact making inattention problems greater for both emotional and nonemotional contexts. Thus, it may be feasible to examine attention and constructs such as perception and cognitive control in conjunction with other domains as this interaction may create the specific symptomology observed in DMDD.

Literature argues that youth with DMDD exhibit low frustration tolerance, supporting the role of frustrative non-reward processes from the negative valence domain (Meyers et al., 2017). However, there is not conclusive evidence for abnormal responses to frustration in these youth. By building on previous work (Brotman et al., 2017; Meyers et al., 2017; Stringaris et al., 2018), it can be suggested that youth with youth DMDD suffer from a specific negative interpretation bias in both social processes and valence systems (i.e., "hot" cognitive abnormalities) (Ahern et al., 2019). "Cold" cognitive system abnormalities can be construed to occur primarily in conjunction with such interpretations. Inconsistent results of the association between cognitive processes with or without emotional interference (e.g., the involvement of amygdala and the ACC, face-emotion labeling deficits, and responses to frustration) might depend on the instrument's achievement in eliciting "hot" and "cold" processes (Rao, 2014).

Consistent with a developmental system perspective, youth with DMDD might suffer from an immature socioemotional system relative to their cognitive control system, that is, a significant discrepancy in the maturation and connections of their socioemotional and cognitive control brain systems (Casey et al., 2008; Steinberg, 2008). Findings of suicidal attempt as unplanned and impulsive in DMDD (Benarous et al., 2020) speak to the potential severe consequences of an immature socioemotional system on cognitive control. This speaks to the importance of studying unique mechanisms of DMDD to clarify this issue, which is challenging due to the high comorbidity rates. Dimensional approaches to psychopathology may represent a better approach to this process. Measuring irritability, the Affective Reactivity Index (Stringaris et al., 2012) has been used in recent research with this purpose. Different neural associations of irritability levels and diagnostic groups are observed (Kircanski et al., 2018; Tseng et al., 2019). Acknowledging DMDD as lying above a certain threshold on an irritability continuum (Vidal-Ribas et al., 2016), dimensional irritability measurements can both help to understand normative variation and improve our understanding of mechanisms of clinical irritability across diagnostic groups.

Building a Science of DMDD

In this initial clinical volume devoted to DMDD, effort has been made to be widely inclusive of topics and contributors from all over the world. This volume has been organized into six sections: Introduction, Foundational Issues, Assessment, Adult

Outcome, Treatment, and a Conclusion chapter. Much of our current knowledge of other conditions with overlapping symptoms is used to create a framework to understand, evaluate, and treat DMDD today.

Steve Jobs wrote: "You can't connect the dots looking forward; you can only connect them looking backwards. So, you have to trust that the dots will somehow connect in your future. You have to trust in something—your gut, destiny, life, karma, whatever. This approach has never let me down, and it has made all the difference in my life." This is the reality today for DMDD. As this volume goes to press, the first diagnostic tool devoted to the sensitive and specific assessment of youth with DMDD beyond counting DSM-5 symptoms has been published (Goldstein, 2023). As a field we take what we have learned about the broad range of child development and psychopathology, working to make sense of it all in forging a reasonable future for the clinical condition of DMDD we have created.

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Chapter 2
The Developmental Roots of DMDD

Sam Goldstein

Disruptive mood dysregulation disorder (DMDD) is a relatively new psychiatric diagnosis that primarily focuses on severe irritability, temper outbursts, and an angry mood in children and adolescents (Rao, 2014). While the exact causes of DMDD are still being studied, research suggests that the disorder has multiple developmental roots (Benarous, 2021). This chapter explores the various factors that contribute to the development of DMDD, including genetic, environmental, neurobiological influences, and temperament.

2.1 Genetic Factors

Understanding the factors that contribute to DMDD is important for effective diagnosis and treatment. Among these factors, genetics has emerged as a significant area of investigation (Moore et al., 2019). Although DMDD is a complex disorder influenced by multiple variables, including environmental factors and psychological triggers, genetic predisposition appears to be an important component (Moore et al., 2019). Evidence from family and twin studies suggests a genetic predisposition to DMDD (Moore et al., 2019). It is believed that genetic variations contribute to the vulnerability of an individual to develop the disorder. Research has identified specific genes associated with emotional regulation and impulsivity that may play a role in the development of DMDD (Moore et al., 2019). However, the interplay between genetics and other factors is complex, and further research is needed to fully understand the genetic basis of DMDD (Moore et al., 2019).

S. Goldstein (✉)
Neurology Learning and Behavior Center, Salt Lake City, UT, USA
e-mail: info@samgoldstein.com

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Family and Twin Studies

Evidence from family and twin studies has provided valuable insights into the heritability of DMDD (Moore et al., 2019). Family studies often show that individuals with DMDD are more likely to have family members who suffer from mood disorders or other psychiatric conditions, suggesting a genetic predisposition (Sparks et al., 2014). Twin studies have been particularly illuminating; they indicate that if one identical twin has DMDD, the other twin is more likely to have it as well compared to nonidentical twins (Fristad et al., 2016). This pattern suggests a genetic component in the vulnerability to DMDD.

Specific Genes and Neurotransmitters

Although the exact genes responsible for DMDD are yet to be definitively identified, research has pointed toward certain genes associated with emotional regulation and impulsivity as potential culprits (Canli et al., 2009) (Bevilacqua & Goldman, 2013). For instance, polymorphisms in serotonin-related genes have been linked with mood disorders, and given that serotonin is a neurotransmitter involved in mood regulation, it is plausible that these genetic variations could contribute to DMDD (Canli et al., 2009). In addition to serotonin, genes involved in the dopamine and norepinephrine pathways, which are also associated with mood and impulsivity, have been investigated. It is possible that abnormalities in these pathways may lead to the emotional dysregulation seen in DMDD (Blier, 2001; Diehl & Gershon, 1992).

Epigenetic Factors

Emerging research has also begun to consider the role of epigenetic factors in DMDD (Carola et al., 2021). Epigenetic changes are alterations in gene expression that do not involve changes to the underlying DNA sequence (for review, see Jaenisch & Bird, 2003). Such changes can be caused by environmental factors and may explain why some individuals with a genetic predisposition to DMDD actually develop the disorder, while others do not. Stress, for instance, can cause epigenetic changes that might activate a dormant genetic predisposition to DMDD (Carola et al., 2021).

Gene-Environment Interplay

It is important to acknowledge that genetics alone does not account for DMDD. The interplay between genetic and environmental factors adds another layer of complexity. For instance, a child may have a genetic predisposition but only develop

DMDD after experiencing significant stressors or trauma (Dick, 2011). Similarly, the absence of supportive figures and appropriate coping mechanisms could exacerbate a mild genetic predisposition, leading to the full-blown disorder (Goldstein & Brooks, 2013). As a summary, as our understanding of the genetic basis of DMDD improves, so too will our capacity for effective treatment. Pinpointing specific genes or gene clusters associated with the disorder could lead to targeted pharmacological treatments. Moreover, understanding the genetic susceptibility could also pave the way for preventative interventions for those who are at risk but have not yet developed the disorder. Furthermore, advances in genomics and bioinformatics are promising for large-scale, comprehensive studies that can map out the complex interplay between the multitude of factors involved in DMDD. Genetic screening, coupled with big data analytics, could offer unprecedented insights into this complex disorder. While there is convincing evidence from family and twin studies suggesting a genetic predisposition to DMDD, the picture is far from complete. Various genes associated with emotional regulation and impulsivity may play roles, but the intricate interplay between genetic and environmental factors cannot be overlooked. As the field of genetics continues to evolve, it brings with it the promise of more effective and individualized treatments for DMDD. However, it is crucial to continue investigating how these genetic factors interact with psychological, environmental, and epigenetic factors to contribute to this complex disorder. Only a holistic understanding will enable the development of effective diagnostic tools and treatments.

2.2 Neurobiological Factors

Neurobiological abnormalities are believed to underlie the development of DMDD (Gold et al., 2016). Neuroimaging studies have shown differences in brain structure and function in individuals with DMDD, particularly in areas involved in emotion regulation and impulse control, such as the prefrontal cortex and amygdala (Dickstein et al., 2021). These findings suggest that disruptions in neural circuits related to emotional processing and regulation contribute to the symptoms observed in DMDD. Additionally, dysregulation of neurotransmitters, such as serotonin and dopamine, may also be implicated in the development of the disorder. DMDD is not solely a behavioral issue; it is also closely tied to neurobiological factors that influence the brain's structure and function (Moore et al., 2019). Understanding the neurological underpinnings of DMDD can pave the way for more targeted and effective treatment options. Research in this area often focuses on brain imaging studies, neurotransmitter roles, and the functioning of specific neural circuits related to emotional processing and regulation (for review, see McGuire & Matsumoto, 2004).

Neuroimaging Studies

Technological advancements in neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), have opened new avenues for studying DMDD (McGuire & Matsumoto, 2004). These studies have indicated abnormalities in brain structures responsible for emotion and impulse regulation. For instance, the prefrontal cortex, a part of the brain heavily involved in decision-making, impulse control, and emotional regulation, often shows differences in activation patterns in individuals with DMDD compared to controls. The amygdala, another crucial brain structure for emotional processing, has also been studied in the context of DMDD in individuals with the disorder, especially when they are exposed to emotional stimuli (Brotman et al., 2010—more activation; Wiggins et al., 2016—less activated). This heightened activity may explain the frequent and severe temper outbursts commonly observed in DMDD.

Disruptions in Neural Circuits

The human brain operates as a network, with neural circuits connecting various regions to facilitate different functions (Tau & Peterson, 2009). In the case of DMDD, research suggests that the circuits linking the prefrontal cortex and the amygdala may be disrupted (Ryan, 2013). These neural pathways are essential for emotional regulation, and disturbances in these circuits can lead to heightened emotional responses, impulsivity, and difficulties in calming down after an emotional arousal—symptoms that are characteristic of DMDD. Understanding the intricacies of these neural circuits could provide significant insights into targeted therapeutic interventions. For instance, therapies like repetitive transcranial magnetic stimulation (rTMS) are being studied as potential treatments for mood disorders by targeting specific neural circuits. A similar approach could be considered for DMDD.

Neurotransmitter Dysregulation

Neurotransmitters like serotonin and dopamine play vital roles in mood regulation and impulse control (Seo et al., 2008). Dysregulation in the levels of these neurotransmitters has been implicated in a variety of psychiatric disorders, including DMDD. For instance, low levels of serotonin are often associated with irritability and aggression, symptoms that align with DMDD (Zubieta & Alessi, 1993). Medications like selective serotonin reuptake inhibitors (SSRIs) and dopamine agonists have been considered for treatment. However, the role of neurotransmitters in DMDD is complex and not entirely understood. Moreover, children and adolescents respond differently to these medications compared to adults, complicating the treatment landscape.

2.3 Multidisciplinary Approaches and Future Directions

Given the complex nature of DMDD, a multidisciplinary approach that considers genetic, neurobiological, and environmental factors is essential for comprehensive understanding and treatment. Ongoing research is likely to employ advanced neuroimaging technologies and genetic studies to unearth the neurobiological roots of the disorder. Such data can also be analyzed through machine learning algorithms to identify patterns that may not be immediately evident, contributing to the development of more accurate diagnostic tools and personalized treatments.

Furthermore, the study of neurobiological factors in DMDD opens the door for potential interventions that could be more effective than current treatments, including innovative psychotherapeutic methods that aim to "retrain" disrupted neural circuits. Understanding the neurobiology could also lead to the development of biomarkers for early diagnosis and intervention, which is crucial for a disorder that manifests in childhood and can have long-lasting impacts on a person's life.

In summary, the neurobiological basis of DMDD is an area of active research that has already provided valuable insights. Although much remains to be learned, existing studies point to disruptions in brain structure and function, specifically in regions and circuits related to emotional regulation and impulse control. Combined with evidence of neurotransmitter dysregulation, these findings indicate a strong neurobiological component to DMDD. As science continues to progress, it is likely that our understanding of these factors will deepen, offering hope for more effective and targeted interventions.

2.4 Environmental Factors

Environmental factors play a significant role in the development of DMDD (Vidal-Ribas et al., 2023). Adverse experiences, such as chronic stress, trauma, neglect, or inconsistent parenting, can contribute to the dysregulation of emotions and the development of irritability and mood disturbances (for review, see Leibenluft et al., 2013). Family dysfunction, including high levels of conflict, harsh discipline, and parental psychopathology, has been associated with the onset and persistence of DMDD symptoms (Dougherty et al., 2014). The quality of the child's environment, including social support, stability, and exposure to positive parenting practices, can help mitigate the risk of developing DMDD. One of the most immediate and impactful environmental factors is adverse experiences, particularly those that introduce chronic stress into a child's life (for review, see Anda et al., 2020). Experiences such as ongoing emotional, physical, or sexual abuse, neglect, or witnessing domestic violence can create a persistent state of "fight or flight" in children. This heightened state of alertness can dysregulate the normal emotional balance and lead to increased irritability and mood swings. Importantly, it is not just the "big traumas" that matter; even daily stressors like bullying, academic pressures, or familial instability can take a toll (Herts et al., 2012).