CNS Spectrums

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Editorial

Cite this article: Gupta M, and Gupta N (2022). Disruptive mood dysregulation disorder: does variance in treatment responses also add to the conundrum? The widening gap in the evidence is a signal needing attention. *CNS Spectrums* **27**(6), 659–661.
https://doi.org/10.1017/S1092852921000985

Received: 02 November 2021
Accepted: 02 November 2021

Key words:
disruptive mood dysregulation disorder; children and adolescents; bipolar disorder; attention deficit hyperactivity disorder; diagnosis

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Disruptive mood dysregulation disorder: does variance in treatment responses also add to the conundrum? The widening gap in the evidence is a signal needing attention

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Abstract

The new diagnosis of disruptive mood dysregulation disorder (DMDD) was introduced in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, to address the overdiagnosis of bipolar disorder in children and adolescents. However, there are ongoing debates about its nosology given chronic persistent irritability in children and adolescents has contextual valence. Those meeting the criteria for DMDD may, in fact, have an oppositional defiant disorder, attention deficit hyperactivity disorder, or other behavioral disorders. Similarly, in the last few years, there are many different types of treatment studies that have also yielded mixed results. These counterintuitive findings need a meticulous review for a wider debate given its clinical utility for patients, families, and practicing clinicians.

Since the introduction of disruptive mood dysregulation disorder (DMDD) in 2014 as a clinical entity, there have been many unanswered questions. There is an ongoing debate about its nosology, since the chronic persistent irritability in children and adolescents has contextual valence. In the last few years, different types of treatment studies have also yielded mixed results (Table 1). These findings further widen the debate given its clinical utility for patients, families, and practicing clinicians. The widespread criticism about the validity of DMDD predates 2014. There is no consensus on evidence-based treatment strategies for DMDD, and the aim is to examine the hypothesis if there is a high variance in treatment responses in the recent empirical research. We performed a literature search from Psych INFO, PubMed, Medline, and Google Scholar until 2021. The search strategy included the following key terms: "adolescents," "ADHD," "aggression," "bipolar disorder," "children," "disruptive behaviors," "irritability," "oppositional defiant disorder," "ODD," "rage," "temper outbursts," and "treatment" as main subject headings or text words in titles and abstracts. We identified n = 20 relevant articles among which 11 were specific about treatment, and others highlighted issues with the validity of the diagnosis.

The emerging evidence is weak. But it strengthens the chorus challenging the validity of DMDD due to its overlapping symptoms with oppositional defiant disorder, attention deficit hyperactivity disorder, and major depressive disorder. A promising diffusion tensor imaging study reported discrete alternations in white matter microstructure in DMDD as compared to altered myelination in bipolar disorder. The epigenetic mechanisms of hypermethylated DNA were also studied to link it with its possible etiology without success. The psychopharmacological treatment studies used stimulant medication, antidepressants, antipsychotics, amantadine, and naltrexone with limited generalizability. Interpersonal therapy, cognitive behavioral therapy, and parent management training have some efficacy in symptom reduction. It is also suggested to revise the age of onset in the diagnostic criterion, because it excludes children of age <6 years, and the core symptoms are present in early childhood, and subsequently, its impairments when left untreated have poor overall outcomes.

The rationale for creating DMDD as a separate category has been counterintuitive and led to diagnostic uncertainly and hesitancy among clinicians. The limited evidence suggests a more heterogeneous condition with symptoms overlapping of other disorders and responds to diverse strategies. Although chronic persistent irritability is the area of focus for new research, more clarity is needed.

Acknowledgment. None.

Funding Statement. The work received no specific grant from any funding agency, commercial, or not-for-profit sectors.

Disclosure. The authors do not have anything to disclose.

Table 1. Summary of Studies.

Author(s)	Article Type	Study Population	Concerns	Recommendations
Diagnostic Validity				
Benarous et al (2020)[1]	Research	Adolescents	Several common features between DMDD, MDD, and PDD.	Developmental trajectories and advantage of pharmacotherapy expansion to be further assessed.
Blok et al (2020)[2]	Editorial	Children	Far too many participants would be misclassified in a clinical setting.	An algorithm to estimate specific diagnoses based on underlying neurobiology could help early diagnosis and personalized treatment in future.
Wiggins et al (2018)[3]	Research	Children	Children of age <6 y should not be excluded.	Clinical identification of early-onset irritability can be improved by brief, developmentally optimized indicators.
Carola et al (2021)[4]	Research	Children	Maternal mental health affects the severity of children's symptoms, which is independent of DNA methylation levels of both mother and child.	DNA methylation does not appear to be involved in the maternal inheritance of vulnerability.
Lochman et al (2015)[5]	Perspective	Children	Misdiagnosis, outcomes, and selecting appropriate interventions	ICD-11 to include a specifier to indicate whether the presentation of ODD includes chronic irritability/anger.
Salum (2021)[6]	Editorial	Children	High levels of co-occurrence of symptoms between ADHD and DMDD; small sample size of DMDD "only cases."	Processing efficiency during distinct task demands appears to be a relevant process for both ADHD and DMDD. It could be a new target for physiological exploration.
Laporte et al (2021)[7]	Research	Preadolescents/ early adolescents	Misdiagnosis.	Recommends revision of the diagnostic criteria for DMDD. OR rule for clinical operationalization is more appropriate.
Tseng (2020)[8]	Editorial	Children	Need to address what neural mechanisms are unique to irritability compared with other co-occurring symptoms (eg, ADHD and anxiety), and are neural mechanisms similar or different across diagnostic categories.	More research targeting irritability a priori is important for developing evidence-based treatments for irritability, present alone or with other symptoms and disorders.
Treatment				
Linke et al (2019)[9]	Research	Preadolescents	Limited knowledge of efficacious treatments specifically targeting severe irritability presented in DMDD.	Exposure-based cognitive-behavioral therapy is beneficial in the context of severe irritability. More detailed assessment is required.
Carlson et al (2020)[10]	Editorial	Youth	Effects of adding CTP to MPH in the treatment.	Adjunctive CTP could be beneficial, but further work with larger samples is required. Longer-term trials required to determine stability of the response beyond 8 wk.
Towbin et al (2019)[11]	Editorial	Youth	Effects of adding CTP to MPH in the treatment.	Adjunctive CTP might be efficacious. No evidence of effect on impairment in patients.
Winters et al (2018)[12]	Research	Youth	Participants met criteria for both DMDD and ADHD.	Supports further research for using MPH as first-line treatment for DMDD. MPH treatment of youth with DMDD with and without comorbid ADHD is needed.
Tourian et al (2015)[13]	Review	Adolescents, children, and youth	Numerous treatment options: consensual treatment algorithm is lacking.	Further studies and clinical trials required to determine efficacious and safe treatment modalities.
Rice et al (2019)[14]	Case report	Adolescent	Limited studies on evidence-based treatment	Amantadine could be promising psychopharmacological intervention.
Loy et al (2017)[15]	Review	Children and youth	Limited evidence for use of atypical psychotics.	High-quality trials of longer duration evaluating antipsychotics other than risperidone.
Pan et al (2018)[16]	Research	Adolescents and children	Using MPH monotherapy for DMDD and ADHD is not well established.	Aripiprazole/MPH combination by patients with DMDD and ADHD is effective and well tolerated.
Miller et al (2018)[17]	Research	Adolescents	Feasibility, acceptability, and preliminary efficacy of IPT-MBD are unclear.	IPT-MBD could be an effective psychosocial intervention.
Parmar et al (2014)[18]	Case report	Adolescent	Need for medications that are safe in long term.	Naltrexone could improve behavioral outbursts.

Abbreviations: CTP, citalopram; DMDD, disruptive mood dysregulation disorder; IPT, interpersonal therapy; IPT-MBD, interpersonal psychotherapy for mood and behavior dysregulation; MPH, methylphenidate.

https://doi.org/10.1017/S1092852921000985 Published online by Cambridge University Press

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https://doi.org/10.1017/S1092852921000985 Published online by Cambridge University Press