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Glen Elliott, MD, PhD
Editor-in-Chief

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IN THIS ISSUE

Mood Dysregulation in Children and Adolescents

Learning Objectives

After reading these articles, you should be able to:

1. Describe how to assess and treat disruptive mood dysregulation disorder in children and adolescents. **2.** List some of the common approaches used to treat disruptive behavioral disorders in children and adolescents. **3.** Discuss some of the challenges in diagnosing bipolar disorder in children and adolescents. **4.** Summarize some of the current findings in the literature regarding psychiatric treatment for children and adolescents.

Disruptive Mood Dysregulation Disorder: A Primer

Ellen Leibenluft, MD, Melissa A. Brotman, PhD, Daniel S. Pine, MD; Researchers. Emotion and Development Branch, Intramural Research Program, National Institute of Mental Health, Bethesda, MD

Dr. Leibenluft, Dr. Brotman, and Dr. Pine have disclosed that they have no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Nine-year-old Johnny has had chronic grouchiness and severe temper outbursts since early childhood. At age 4, Johnny was asked to leave preschool because of his behavior and was diagnosed with ADHD.

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In Summary

- Persistent irritability and recurrent temper outbursts are the key features of disruptive mood dysregulation disorder (DMDD).
- DMDD is a chronic, persistent, and impairing disorder that causes problems in multiple settings.
- Best treatment options for DMDD remain unclear, with both behavioral interventions and medications under active investigation.

Q&A With the Expert

Treating Disruptive Behavior Disorders in Children
Peter Parry, MD

Child & adolescent psychiatrist; medical director, child & youth mental health services at Lady Cilento Children's Hospital, Brisbane, Australia; senior lecturer, University of Queensland, visiting senior lecturer, Flinders University

Dr. Parry has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CCPR: Dr. Parry, what sort of experience do you have working with children with disruptive behavioral disorders (DBDs)?

Dr. Parry: Beyond 20 years of general child psychiatrist clinical experience, my current role is with a preadolescent child and family inpatient unit in a large pediatric hospital in Brisbane, Australia, where we specialize in disruptive behavior disorders.

CCPR: When people talk about disruptive disorders, what does that include?

Dr. Parry: In DSM terms, attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD). But, in practice, also comorbidities with autistic spectrum disorders (ASD), learning disorders (LDs), speech and language delays, attachment problems, developmental trauma, ongoing maltreatment, and family and school dynamics abound. Puberty often exacerbates disruptive behavior—even in normal children—let alone when there are other factors. Disruptive mood dysregulation disorder (DMDD) does not seem to be used in Australia, perhaps because pediatric bipolar disorder (BD) in children was never widely used either. Also, the Australian public health system uses ICD-10 codes,

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Stimulant treatment diminished the ADHD symptoms a lot and the irritability a bit. Johnny continued to have both chronic grouchiness and outbursts when frustrated; these occurred daily at home and weekly at school. Most outbursts were verbal, but some were physical. Most recently, he has been diagnosed with disruptive mood dysregulation disorder (DMDD), a new diagnosis unveiled in 2013 in DSM-5. His therapist and his child psychiatrist have tried a number of treatments. Parent training therapy seemed to help at first, but the behaviors returned. Both SSRIs and atypical antipsychotic treatment have been somewhat effective, but the antipsychotic caused significant sedation and weight gain.

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This CME/CE activity is intended for psychiatrists, psychiatric nurses, psychologists, and other health care professionals, with an interest in the diagnosis and treatment of psychiatric disorders.

Chronic irritability: An evolving perspective

In the 1990s and early 2000s, many clinicians might have diagnosed Johnny with bipolar disorder (BD). This might have happened even though the diagnosis would not have been justifiable using DSM-IV criteria, since Johnny had never had a manic episode. At the time, many child psychiatrists thought that pediatric BD presented with chronic irritability and symptoms of ADHD, rather than with the distinct manic episodes that characterize adult BD. Research subsequently showed that chronic irritability is not how BD presents in children (Leibenluft E, *Am J Psychiatry* 2011;168(2):129–142). As it turns out, chronically irritable children are not at increased risk to develop manic episodes as they age; instead, they are at increased risk for anxiety and unipolar depression later in life. Moreover, unlike children with BD, chronically irritable children do not tend to have unusually strong family histories of BD. Rather, there are both genetic and familial links between chronic irritability and unipolar depression.

This research created a quandary. Clearly, there are many children who are chronically irritable and who tend to develop depression and not mania. They suffer just as much as children with BD, but under DSM-IV, there wasn't a distinct diagnosis for very severe, chronic irritability—a disturbance in mood—as the major problem. In an attempt to remedy this issue, the authors of DSM-5 included disruptive mood dysregulation disorder (DMDD) as a new diagnosis (Towbin K et al, *J Am Acad Child Adolesc Psychiatry* 2013;52:466–481).

Assessment and diagnosis

Irritability is among the most common reasons children are referred for psychiatric evaluation and care. In community studies, prevalence rates of severe irritability in children range from 2% to 5%. It is likely that you have and will see children with DMDD, possibly without recognizing them, so it is important to know how to make this diagnosis.

Johnny's case illustrates the two core criteria for DMDD: *temper outbursts* and a generally *irritable mood*. The temper outbursts have to occur, on average, at least three times a week. Although temper outbursts are a common feature of many psychiatric illnesses, not many children have three outbursts a week on a regular basis. Some clinicians think that the outbursts in DMDD must have a physical component, but this is not true. In fact, the most common features of temper outbursts seen in youth with DMDD include yelling, screaming, or verbally threatening someone, without any physical components. For the DMDD diagnosis, your patient's temper outbursts can be verbal (as most of Johnny's were) *and/or* physical. Seriously consider the DMDD diagnosis if your patient is verbally argumentative, snappy, and apt to engage in name calling more frequently, intensely, and persistently than typical for someone that age.

Of course, most DMDD youth have occasional physical outbursts, even if their more typical outbursts are verbal. Physical temper outbursts can include slamming a door, throwing something down, kicking furniture, physically threatening someone (eg, clenching fists, raising an arm to hit), or destroying property (eg, kicking a hole in a wall, breaking belongings). The most severe (and rarest) temper outbursts cause harm towards another person. These behaviors include intentionally throwing an object directly at someone or

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physically pushing, shoving, slapping, or kicking someone.

The second core criterion for DMDD is pervasive irritable mood. To assess this, we ask parents whether they (and others) generally see the child as grouchy and grumpy. Caregivers of youth with DMDD often say they feel like they have to "walk on eggshells" for fear of upsetting their generally angry child. Throughout the day, the child is cranky and crabby, and the people in the child's life see the child that way. When you assess a child for major depressive disorder, you have to determine whether the child is sad "most days most of the time." For DMDD, it's a very similar assessment; but, rather than focusing on sadness, you have to decide whether the child is cranky and crabby most of the time.

It's important to note that parents often avoid certain activities (like going out to a restaurant or inviting another family to visit) and avoid asking the child to do things that they ask of the child's siblings, such as homework or chores. If the parent accommodates the child by making very few requests in order to avoid an outburst and keep the child's irritability under control, this should be noted. For example, some children will exhibit two outbursts per week, below the frequency criterion for DMDD, but parents will avoid making normal demands on the child and will refrain from enforcing a request in order to avoid or terminate an outburst. In these instances, the child meets the diagnostic criterion for DMDD. This is analogous to what you would do when you are assessing avoidance in a child with a possible anxiety disorder and there is substantial parental accommodation. Even if a child does not overtly express avoidance, you would still diagnose a child with anxiety disorder if the parents make accommodations that remove any opportunity for the child to either confront or avoid a feared object. The situation with DMDD is the same.

In DMDD, irritable mood has to be present for at least a year, but usually the mood has been present for much longer than that. Again, like temper outbursts, many children with psychiatric problems present with irritability. However, only a subset of these children will have persistent irritability that is present most days for a year, as is required for DMDD.

Importantly, the temper outbursts and pervasive, persistent crankiness of children with DMDD inhibit their ability to get along at home, at school, and with their friends. Indeed, the DSM-5 criteria for DMDD require that the child's irritability be severely impairing in at least one of these three settings, and at least mildly impairing in a second setting. If parents or teachers make accommodations in an attempt to diminish the child's irritability, this would be evidence of impairment.

Treatment

We usually look to large randomized controlled trials (RCTs) to decide on best treatments. Unfortunately, no such trials exist for the treatment of DMDD. As a result, you cannot make strong recommendations to patients and families regarding any particular treatment. Instead, your recommendations can be guided only by indirect evidence on safety and efficacy. This evidence derives from RCTs on disorders related to DMDD and from small, open trials in DMDD. To treat your patient with DMDD, it is important for you to know the relevant data on psychotherapy, medications, and experimental treatments.

Psychotherapy

When selecting a treatment, you might consider psychotherapy first. This is because evidence on efficacy for problems similar to DMDD, like aggression, is as strong, or stronger, than the evidence for any other treatment, and because psychotherapy is relatively noninvasive. Moreover, open trials of psychotherapy for DMDD itself show promise.

NIMH Clinical Trials on DMDD

Dr. Leibenluft and her colleagues are conducting several research projects at the Emotion and Development Branch at NIMH that might be of interest to your patients. For further information, contact: irritablekids@mail.nih.gov or 301-496-8381. Potential subjects would be screened for DMDD criteria and might be eligible to enroll in one of several studies underway: 1. Efficacy of CBT and parent training to treat youth with DMDD; 2. SSRI effects on DMDD; and 3. Other novel treatment interventions for DMDD.

Parent training involves reinforcing pro-social behavior and using time-outs to extinguish emotional outbursts (Patterson GR. *Families: Applications of Social Learning to Family Life.* Champaign, IL: Research Press; 1975). These techniques work for various conduct problems, and early evidence suggests that they may also decrease the temper outbursts of DMDD.

Components of cognitive behavioral therapy (CBT) may also be helpful, based on research in pediatric mood, anxiety, and behavior disorders (Waxmonsky JG et al, *J Am Acad Child Adolesc Psychiatry* 2016;55(3):196–207). These techniques teach children how to regulate their emotions and how to focus their attention away from negative experiences.

Medication

Like psychotherapies, various medications have been shown to reduce temper outbursts or irritability in children being treated for disorders other than DMDD. In the absence of data from RCTs directly targeting DMDD, however, we can only use indirect evidence to guide treatment choice.

Psychostimulants

In line with Johnny's experience, data suggests that psychostimulants reduce features of DMDD in children

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which don't include DMDD. Funding is not directly tied to diagnostic labels in public or private health systems, so usually the focus is on a biopsychosocial diagnostic formulation rather than a specific diagnosis. Educational and welfare funding is tied to ASD diagnoses, and there is debate about overdiagnosis of ASD.

CCPR: How common are these disorders?

Dr. Parry: The DBDs are the most common preadolescent disorders in child psychiatry and behavioral pediatrics. In our unit, we have many pre-pubertal children with an array of oppositional, defiant, conduct, and inattention symptoms who may or may not be mildly to severely autistic. These children display highly disruptive behaviors. At the point we see them, their parents or foster caregivers cannot manage them, and their treating pediatricians, psychiatrists, and mental health services have reached some kind of impasse. They are often taking a considerable cocktail of medications. They come to us for diagnostic clarification and to review their medication regimens.

CCPR: How old are the children you're working with?

Dr. Parry: We take kids starting at around age 5 up to late puberty, including developmentally "younger" 14-year-olds. We have some capacity to admit parents along with the child to work on parenting and family aspects.

CCPR: Could you talk a little bit about your sense of how disruptive disorders evolve with different age groups like the preschoolers, school age, early teens, and then adolescents?

Dr. Parry: In terms of inpatient child and adolescent psychiatry, the preschool- and school-age groups are mostly boys and some girls with the mixture of comorbidities I mentioned. With regard to our adolescent inpatient unit, there are two main groups: one involves suicidal risks and borderline personality dynamics, usually from an environment of trauma; the second is individuals with emerging and manifest psychosis.

The DBDs [disruptive behavioral disorders] are the most common preadolescent disorders in child psychiatry and behavioral pediatrics."

Peter Parry, MD

CCPR: In the U.S., we would add to that CD kids, who certainly are in the disruptive disorder category but don't quite fit into any of those you just mentioned.

Dr. Parry: We do have them in our child unit. But, in an adolescent inpatient setting, they can quickly disrupt the therapeutic milieu, so we endeavor to discharge them as soon as a brief suicidal crisis, sometimes with substance intoxication (the most likely reason for admission), has settled. We do have a trauma-informed forensic adolescent service to refer them to, particularly in the youth detention centers if they've been sentenced, but there is a need for more forensic adolescent resources.

CCPR: How do you go about diagnosing DBD in kids?

Dr. Parry: Our model is to focus on creating a full diagnostic biopsychosocial formulation. This requires a thorough developmental history, including a trauma history if relevant. We look at school guidance testing and psychometrics testing such as the Wechsler Intelligence Scale for Children (WISC). We have a speech pathologist on our unit and often find a speech and language assessment is valuable, because many of these children don't have the language they need to understand or to express their emotions. We do ADHD scales as well and are fortunate to have a hospital school that provides further input from teachers. In community clinics, it can be too easy to make an ADHD diagnosis based on limited information from the parents and the behavior of the child in your office, which may not be typical of their overall behavior.

CCPR: How does this individualized approach help you plan treatment?

Dr. Parry: Once we have a comprehensive diagnostic formulation, the management plan becomes self-evident. You can see what proportion is medication oriented; what proportion is helping this child deal with perhaps more recent discrete loss or trauma through some psychotherapy; what proportion is child abuse and neglect, requiring us to notify child protection to assess whether the child is safe to return to his or her place of residence; what proportion warrants—and this is common—parent training or family therapy. Then we try to initiate the interventions their formulation suggests will be most helpful, while passing the diagnostic formulation on to their community-based clinicians for ongoing therapy.

CCPR: What medications do you find useful?

Dr. Parry: If we have a child who meets criteria for ADHD, we'll try the stimulants in the inpatient environment; but, if the behavior has anxiety inputs from stress and trauma and a child does not actually have the genes or early neurodevelopment adversity that would have led to a more biological ADHD, we often find that stimulants don't do much.

CCPR: What about other drugs such as antidepressants, anticonvulsants, and antipsychotics?

Dr. Parry: A lot of children these days in Australia are on SSRIs and antipsychotics, as is true also in the U.S. Very few are on anticonvulsants, unless they have epilepsy or are older adolescents with well-established manic episodes. Personally, I've only

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seen benefit using SSRIs with the DBDs if there's a significant anxiety or obsessive-compulsive component that's driving the disruptive behavior. I think SSRIs are overused particularly in milder adolescent depression. Consistent with the research, I've seen a number of adolescents develop increased suicidality, and their prescriber had oftentimes not warned them or parents of the risk. I also find the long-term risks of antipsychotics concerning.

CCPR: Can you elaborate?

Dr. Parry: Sure. Undoubtedly the antipsychotics do dampen severe disruptive behavior and may address sensory hypersensitivity as a core problem in autism. However, there is research by Nancy Andreason and colleagues on adults with schizophrenia that suggests that there is some degree of neuronal atrophy from many years of antipsychotics despite the fact they are necessary in suppressing psychotic symptoms (Ho BC et al, *Arch Gen Psychiatry* 2011;68:128–137). Unfortunately, the studies haven't been done to say what it means to the growing brain to be on risperidone for many years. Could it cause future neuronal atrophy, so that the child never reaches full cognitive potential? That's concerning to me. And that's not including the extrapyramidal side effects. One study suggests that second-generation antipsychotics (SGAs) cause fewer extrapyramidal side effects, but they still found a 6% rate of tardive dyskinesia (TD) in children and adolescents after 6 months (Wonodi et al, *Mov Dis* 2007;22(12):1777–1782). Given the scale of off-label prescribing, possible TD in children is a subject calling out for more research.

CCPR: What about metabolic syndrome?

Dr. Parry: That's a big one. We get children who have packed on so much weight that they are throwing their weight around, literally: Patients who could previously restrain them can't do so anymore, so the child ends up in an inpatient unit.

CCPR: That's understandably worrisome. Any other medications you can speak to?

Dr. Parry: We use clonidine. It's an old-fashioned, cheap drug. It suppresses the epinephrine rather than the dopaminergic neural networks, and it has a sedating effect and may reduce oppositional behavior. It's also theorized to have a stimulating effect on the prefrontal cortex that may help ADHD. Of course, it's risky in terms of overdose, and we are careful that the parents fully understand this and lock it away. It can replace an antipsychotic or at least allow for antipsychotic dose reduction. Similarly, in the inpatient setting, we use benzodiazepines, mainly lorazepam, for as-needed sedation. We very rarely see children who become paradoxically agitated on benzodiazepines. But benzodiazepines have problems of tolerance and lose effectiveness for long-term use at home, though judicious dispensing by capable parents can work in some cases.

CCRP: It sounds like, at least in your setting, that you try to use medication quite judiciously. I would assume there are kids coming in for whom others have used them less selectively. How does it work in terms of keeping kids on or taking them off prior medication?

Dr. Parry: We try to take them off as best we can. Sometimes, we don't make much headway, particularly with children with more severe ASD. But, in other cases, the combination of parent training and self-regulation strategies for the child allow for medication dose reductions.

CCPR: How do you teach self-regulation strategies?

Dr. Parry: On our child inpatient unit, we talk about basic neurophysiology with children and parents and explain things like sympathetic ("S for Stress") fight/flight/freeze responses versus parasympathetic ("P for Peace") "rest/digest/grow" nervous systems. Then we explain how diaphragmatic breath control via vagus nerve stimulation as in yawning, sighing, laughing, and yoga "ujjayi" (Sanskrit for "victory") breaths, as well as attachment security as in calm parental voice, triggers the peaceful parasympathetic system. Thus, children and parents gain an empowering understanding of their own hard-wired instinctive circuit breaker to induce relaxation and reduce anger and anxiety of fight/flight. We've also recently introduced some biofeedback computer games that work on heart rate variability to entrain engagement of the "peaceful" parasympathetic system.

CCPR: You mentioned parent training as well. What is your approach to that?

Dr. Parry: Before we introduce new skills, it's essential to be empathic with the parents, so they understand we are in no way criticizing them. One specific technique we use is the "Triple-P" parent training program.

CCPR: What does Triple-P stand for?

Dr. Parry: It stands for Positive Parenting Program, and it is a behaviorist approach that is evidence based. It was developed at the University of Queensland by Professor Matthew Sanders, and it's now used in 25 countries. There are various modules for teaching parenting skills for preadolescents, teens, children with disabilities, families in divorce situations, etc. The basic premises are creating a safe and interesting environment for your child, positive reinforcement of pro-social behavior, clear rules, distraction, planned ignoring, fair consequences, and parental self-care (for quick summaries on Triple-P and other parent training programs, see our table on page 8).

CCPR: Sounds like a solid approach. I assume there are other types of disruptive behavior patterns that are even more entrenched and challenging for families.

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Q&A With the Expert

Evolution of Childhood Bipolar Disorder in the United States

Gabrielle A. Carlson, MD

Professor of psychiatry and pediatrics, Stony Brook University School of Medicine, Stony Brook, NY

Dr. Carlson has disclosed that she has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CCPR: You have been involved in thinking about bipolar disorder (BD) as it presents in children and adolescents for a long time. Could you provide our readers with an historical perspective of how the understanding of this disorder has evolved over the past few decades? A lot of clinicians are still unclear about how bipolar disorder got to be such a common diagnosis, most specifically in the United States.

Dr. Carlson: By way of background, soon after Kraepelin published his book on manic depressive illness or manic depressive psychosis in the 1920s, child psychiatrists began looking for something similar in kids. However, they didn't find much in the way of the "classic" form of what we now call bipolar disorder—instead, they found adolescents who were mainly depressed (for a more detailed review, see Carlson GA and Glovinsky I, *Child Adolesc Psychiatr Clin N Am*. 2009;18(2):257–271). In the 1950s, an interesting series of articles in a now-defunct journal called *The Nervous Child* suggested that there might be alternate forms of manic depressive illness in kids—which in many ways remains the question even today, ie, are there alternate presentations of BD in children and adolescents compared to adults? However, early research suggested that, using strict criteria for mania and depression, manic depressive illness was extremely rare before age 12, with an increased incidence through adolescence.

CCPR: So, what changed?

Dr. Carlson: In the early 1970s, John Feighner published criteria for several psychiatric disorders (Feighner JP et al, *Arch Gen Psychiatry* 1972;26:57–63), many of which were precursors for criteria used in creating the DSM-III, which was released in 1980. Using these clinically based criteria, several researchers in the 1970s published articles asserting that a number of kids previously diagnosed as having what was then called hyperactivity might actually have mania. However, clinical studies looking at the benefits of lithium, the gold standard for treating BD, failed to show benefits with these kids, so interest waned.

CCPR: And yet, interest in BD in kids certainly picked up over the last couple of decades.

Dr. Carlson: Right. In the late 1980s, child psychiatrists became interested in emotional instability seen in some children—so-called affective storms. Children with affective storms have seemingly abrupt, intense emotional rages that are worse than uncomplicated temper tantrums. At the same time, criteria for both ADHD and BD with DSM-III had changed the face of these conditions. For instance, DMS-III focused exclusively on behaviors—hyperactivity, impulsivity, and inattention—in defining ADHD, even though those used to working with children with ADHD were well acquainted with their capacity for low frustration tolerance, terrible temper tantrums, and mood variability. In addition, mania criteria described the onset of an episode with no indication of how one would define the offset (ie, "at least a week" doesn't require an end). Thus, a child with hyperactivity and especially the so-called terrible twos, which continued to age 8, could be defined as having mania. Different interpretations of "episode," euphoria, and grandiosity gave rise to single episode durations of 3–5 years for mania rather than 3-5 months as in adults.

CCPR: So, DSM-III allowed for this expanded diagnosis of BD in kids. Did later versions of DSM change that?

Dr. Carlson: DSM-III-R, published in 1987, actually worsened the problem, because it did not even require a week of symptoms, just a "distinct period" and eliminated irritability for depression so more mood episodes seemed "mixed." At the same time, for researchers, structured interviews became the gold standard for doing research on diagnosis, which had some advantages but also led to an over-reliance on formal DSM criteria. By that, I mean that a researcher with little clinical expertise could do a "reliable" structured interview for a few examples and then be certified to diagnose complicated cases which superficially meet criteria but don't really. I suspect that accounts for a good deal of heterogeneity in investigators' findings. Other factors also contributed to the increased likelihood of diagnosing BD in kids, ranging from insurance-driven shortening of assessments to the development of a variety of medications approved for mania in adults being tested in children. The non-specific improvement of these medications for agitation in out-of-control kids regardless of diagnosis made it seem like we had a specific treatment, leading to the much increased rates of bipolar diagnoses and subsequent apparent overuse of atypical antipsychotics.

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CCPR: So, we have an explosion in the diagnosis of BD in kids. But, there were countervailing schools of thought, were there not?

Dr. Carlson: The real questions underpinning the bipolar controversy is whether there is: 1) a unique and more severe subtype in prepubertal children that is stable (ie, still looks like mania in adults) and is defined by severe, chronic irritability; 2) a developmental subtype that changes with maturity (and may, according to some data, even resolve); or 3) a disorder that is best defined the same way in prepubertal children as in adults, as we do with schizophrenia, but which is quite rare (Carlson GA and Klein DN, *Annu Rev Clin Psychol* 2014;10:529–551). In 2000, NIMH convened a consensus conference. It was at that conference that Ellen Leibenluft, who co-authored the article in this issue on disruptive mood dysregulation disorder (DMDD), proposed that chronically explosive, dysphoric kids should have their own label, distinct from kids and adolescents with more classic signs and symptoms of BD, so the two could be compared. Data would tell us whether they are alternate forms of the same condition. Fifteen or so years later, the DSM-5 team (including Dr. Leibenluft) felt they were different, so the DSM-5 defined mania more tightly and added DMDD as an alternative for children with chronic, persistent meltdowns and irritability.

CCPR: Functionally, where does that leave the average child and adolescent psychiatrist, in your opinion?

Dr. Carlson: There are two issues: Where should we be going with the phenomenology research, and what should the clinician do with a preadolescent child who presents with severe outbursts that might be mania, DMDD, or something else? I like the fact that the revised mania criteria have tried to clarify ambiguities such as what to do with comorbid symptoms, and perhaps how to separate drug activation from mania. The criteria also specify that symptoms should be most of the day, every day, which is an important distinction.

"Clinically, many of the children I see for 'severe irritability' and outbursts are what I call 'diagnostically homeless.' They have more than ADHD or ADHD/ODD … they are not 'otherwise specified'".

Gabrielle A. Carlson, MD

CCPR: What is your perspective on DMDD as a newly minted diagnosis?

Dr. Carlson: I personally believe that DMDD is not yet ready for "prime time" and certainly needs more research in terms of diagnosis and treatment (Carlson GA, *Child Adolesc Psychopharmacol* 2016;26(2):90–93). For those who espouse the NIMH Research Domain Criteria, I don't think we have an agreed-upon definition of irritability. Is it a mood (how you feel) or behavior (what you do)? If a behavior, do we define severity by frequency, pervasiveness, or what the child does during an outburst? Current diagnostic interviews do not ask about mood between outbursts. That needs better operationalizing. DMDD also almost never occurs alone. The definition says symptoms are "not better accounted for" by a variety of conditions. In my experience, if you really follow the DSM-5 criteria, DMDD is quite rare; it does not solve the problem of defining kids with severe outbursts.

CCPR: How would you characterize the state of our understanding about mood instability in children and adolescents?

Dr. Carlson: Clinically, many of the children I see for "severe irritability" and outbursts are what I call "diagnostically homeless." They have more than ADHD or ADHD and oppositional defiant disorder (ODD). They are often quirky in ways that don't fit strict definitions of autism or psychosis, or have mood problems that don't quite fit the intentions of anxiety or bipolar disorders or DMDD. They are "not otherwise specified," which so horrified the DSM-5 committees they replaced it with "unspecified" and eliminated it with autism by creating the single category of autism spectrum disorder. But many children don't fit our criteria, so clinicians have to fake it for insurance purposes but then are stuck with what to explain to parents and how to train residents and fellows. I hope, then, in our efforts to clarify mania/bipolar disorder we are not out of the frying pan and into the fire with DMDD.

CCPR: Thank you, Dr. Carlson, for a most interesting and useful walk through history.

Parent Training Programs for Disruptive Behavior Disorders			
	Triple-P (Positive Parenting Program)	**Circle of Security**	**Incredible Years**
Website	http://www.triplep.net/glo-en/home/	http://circleofsecurity.net/	http://incredibleyears.com/
Description	Approach combines social learning theory, CBT, developmental theory, planning, and problem solving	• Based on attachment theory • Starts with "Strange Situation" assessment of parent-child attachment pattern	Combines principles of Triple-P and Circle of Security
Scope	Multiple levels tailored to age, behavior severity, family mental illness, maltreatment history, disability, lifestyle (obese or chronically ill children), indigenous families	• Most useful for preschool and younger school-age children • Applicable when parenting style is dismissive, ambivalent, or disorganized	• 14 programs covering baby, toddler, preschool, school age, ASD, and language delay • Teacher as well as parent programs
Delivery	Small groups, individual one-to-one, large groups, online course. Standard is 3 x 1.5 hour weekly sessions	• Small groups, individual one-to-one, usually weekly for 20 weeks • Use of videos including "shark music" to facilitate reflection on child's inner world	• Small groups, 2x/week, 3 hours over 10 to 20 weeks • Use of videos, role-play, home activities, handouts, stickers • Weekly trainer phone support, as well peer-to-peer support

Parry Interview

Continued from page 5

Dr. Parry: Yes. A lot of the families that we see have problems that run deep—such as insecure attachment that affects the child's basic trust. In these cases, we add Circle of Security parent training, which has a smaller research base than Triple-P, though that is growing. The concepts are nicely delivered for parents, and it is becoming popular.

CCPR: What is the Circle of Security?

Dr. Parry: It's a psychoeducational model for helping parents understand the importance of secure attachment with their children while also giving their children some space. It was developed by a group of clinicians in Spokane, WA, and has its roots in John Bowlby's attachment theory and Donald Winnicott's idea of the "holding space." Circle of Security includes the concept of "shark music." Parents are shown a video of a child walking along a path towards the beach, and there's this lovely music playing. And they think, "Oh, this child is going to the beach," and this evokes a good feeling about the child having a fun day at the beach. Then the same visual is replayed, but the music changes to menacing—the *Jaws* theme, aka shark music—and now the feeling is "Oh, something dreadful is going to happen." This technique helps parents emphasize with what's going on in the child's mind. How might the shark music trigger an aggressive loss of temper in your child? Where is the shark music in the child's mind? Where is the shark music in your mind? The program also includes a "circle of repair" to help parents in healing the attachment ruptures with their children.

CCPR: That's very interesting. Thank you for your time, Dr. Parry.

Disruptive Mood Dysregulation Disorder: A Primer

Continued from page 3

with ADHD, despite earlier concerns based on anecdotal evidence to the contrary (Fernandez de la Cruz L et al, *J Am Acad Child Adolesc Psychiatry* 2015;54(1):62–70). If you do decide to try medications for your DMDD patient, stimulants' long record of safety and rapid clinical effects on core ADHD symptoms make them a reasonable first choice.

Selective serotonin reuptake inhibitors (SSRIs)

SSRIs have been shown in large RCTs to reduce many features of pediatric anxiety and depressive disorders. Since anxiety and depression are often linked with irritability, it makes intuitive sense that SSRIs would be helpful for the irritability component of DMDD. Data in adults suggests that SSRIs reduce the irritability associated with depressive disorders, but conclusive data in children is more limited—more research is ongoing at the NIMH.

You might have concerns about SSRIs causing mania in patients with DMDD. Data from open trials of SSRIs for DMDD suggests that the risk of medication-induced mania is quite low, but there's not enough data to estimate the risk level. We also know that SSRIs can cause activation or suicidal ideation in children, probably including those with DMDD, although there is a paucity of research.

Antipsychotics

Antipsychotics are usually less well tolerated than SSRIs, since they cause adverse metabolic and neurological effects, especially when used for long periods of time. This is consistent with Johnny's experience, described earlier. On the other hand, we have more data showing the effectiveness of antipsychotics on irritability in other conditions such as autism spectrum disorders and disruptive behavior disorders. As with SSRIs, you should consider antipsychotics reasonable second-line medication choices in the treatment of DMDD.

Interestingly, one small RCT found that lithium did no better than placebo in treating children with DMDD, which is consistent with longitudinal data suggesting that DMDD is not a pediatric manifestation of bipolar disorder.

Experimental treatments

Researchers at the NIMH are now testing whether computer-based training can decrease irritability in youth with DMDD. This technique trains children to not interpret ambiguous facial expressions as angry (Stoddard J et al, *J Child Adolesc Psychopharmacology* 2016;26(1):49–57). This is based on research throughout the 1990s linking "hostile attribution bias" to aggression in children (Crick NR and Dodge KA, *Child Development* 1996;67(3):993–1002). This NIMH research includes brain imaging, which might help to identify the brain circuits involved in irritability and guide the development of this and other new treatments.

Potential Causes of Disruptive Behavior in Children

Disruptive behavior is not a specific diagnosis, but rather a syndrome that often has multiple causes. Below is a list of some of the major possible factors worth considering.

Psychiatric Diagnoses and Symptoms
Attention deficit hyperactivity disorder (ADHD)
Anxiety
Autism spectrum disorder (ASD)
Bipolar disorder (BD)
Conduct disorder (CD)
Depressive disorders
Oppositional defiant disorder (ODD)
Substance misuse or abuse
Psychoses
Cognitive Difficulties
Intellectual disorders
Learning disorders
Speech and language disorders
Physical Problems
Epilepsy
Genetic syndromes
Heavy metal toxicity (eg, lead)
Psychosocial Issues
Abusive living situations
Anxious attachment due to parental mental illness
Chaotic family dynamics
Poor social modeling (eg, gangs)
Poor teacher-student compatibility
School bullying

Research Updates IN PSYCHIATRY

Bret A. Moore, Psy.D, ABPP
Dr. Moore has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

SUICIDE

Atomoxetine Does Not Increase Risk of Suicide Compared to Stimulants
(Linden S et al, *Pediatrics*, 2016;137(5) pii:e20153199)

In 2004, the FDA issued its famous and controversial black box warning regarding the possibility that antidepressants cause suicidal ideation in children and adolescents. Atomoxetine was not originally included in that rogue's gallery of medications, but since the drug was originally developed as an antidepressant, the FDA later reviewed its safety data. A post-hoc meta-analysis of placebo-controlled trials revealed an increased risk of suicidal thinking, and so atomoxetine was also slapped with a black box warning.

The big question is whether the FDA's clinical trials data is generalizable to patients we see in our offices. Furthermore, does atomoxetine actually cause suicidal events as opposed to suicidal ideation? These were the questions that recently motivated researchers to look at real-world data on atomoxetine use.

Researchers mined Medicaid data from 1999 to 2006 for 26 U.S. states to see if patients treated with atomoxetine had more suicide attempts than those treated with stimulants. Two groups were included in the analysis: first-line (initial treatment with atomoxetine or stimulant) and second-line (switched to or added atomoxetine after initial treatment with stimulant). Both groups included children and adolescents from age 5 through 18 and were substantial in size—279, 315 and 220, 215, respectively. The study's primary end point was total suicide attempts and completions.

Overall, there was no significant difference between the atomoxetine and stimulant groups regarding suicide events (completed suicide or attempt). There were 140 events in the first-line treatment group. Females attempted suicide more often, comprising 60% of the attempts, whereas a greater proportion of males completed suicide (males represented 89% of suicide completions). There were 90 suicidal events in the second-line treatment group. Similar to the first-line group, females accounted for 60% of the attempts and males comprised 73% of completed suicides. The hazard ratios (probability of a suicide event in the atomoxetine versus stimulant group) for the first- and second-line groups were 0.95 and 0.71, respectively.

CCPR's Take: Results from clinical trial data and real-world practice don't always jibe. It appears that atomoxetine is no more likely to lead to suicidal events than stimulants (which do not have any evidence of leading to suicide). Atomoxetine is typically a second-line medication for ADHD after stimulants. If you've been hesitant to try atomoxetine in children because of the black box warning, this study should allay those concerns.

AUTISM

Extended-Release Guanfacine Improves ADHD Symptoms in Autism
(Scahill S et al, *Am J Psychiatry* 2016;172:1197–1206)

Children with autism spectrum disorder (ASD) often have symptoms of ADHD. While it's not always easy to distinguish them from the core features of autism, symptoms such as impulsivity, hyperactivity, and distractibility do occur, and we often use medications to target them. Stimulants are fairly effective but tend to cause more side effects in autistic ADHD kids than in children with pure ADHD. Atomoxetine was only equivocally effective in one trial, and the immediate-release version of guanfacine was tested in a small open-label trial, resulting in improvement in about half the subjects.

Recognizing the need for more data, researchers conducted the first ever randomized placebo-controlled trial of guanfacine in ASD/ADHD, in this case using the extended-release (ER) version. Children between the ages of 5 and 14 with a diagnosis of ASD with accompanying impulsivity, hyperactivity, and distractibility were randomly assigned to either ER guanfacine (n = 30) or placebo (n = 32). During this 8-week trial, ER guanfacine was started at 1 mg once a day for all children. Depending on the child's weight and response, a maximum of 4 mg daily could be prescribed. The primary outcome measure was change from baseline on the parent version of the Aberrant Behavior Checklist (ABC) hyperactivity subscale, which was assessed at weeks 4, 6, and 8. The Clinical Global Impression-Improvement (CGI-I) scale was also used.

ER guanfacine was effective. At the end of 8 weeks, the medication group showed a 44% reduction in scores on the ABC hyperactivity subscale compared to 13% for the placebo group. For the ER guanfacine group, half were rated "much improved" or "very much improved" on the CGI-I, whereas fewer than 10% of the placebo group were so rated. Significant improvements were seen in both hyperactivity and inattention vs. placebo. The most frequently prescribed dose in both groups was 3 mg. Overall, ER guanfacine was well tolerated. The most common complaints were drowsiness, fatigue, and loss of appetite. Drops in blood pressure and heart rate from baseline were seen in the guanfacine group. Blood pressure normalized by the end of 8 weeks, but

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CME Post-Test

To earn CME or CE credit, you must read the articles and log on to www.TheCarlatChildReport.com to take the post-test. This CME test is only available to active subscribers and it must be taken by August 31, 2017. If your subscription expires before that date, you will not have access to the test until your subscription is renewed. You must answer at least four questions correctly to earn credit. As a subscriber to *CCPR*, you already have a username and password to log onto www.TheCarlatChildReport.com. To obtain your username and password, please email info@thecarlatreport.com or call 978-499-0583.

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Below are the questions for this month's CME/CE post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatChildReport.com. Note: Learning Objectives are listed on page 1.

1. According to DSM-5, one of the core criteria for diagnosing disruptive mood dysregulation disorder includes the following: (Learning Objective #1)
   - [ ] a. Temper outbursts that occur at least once a day
   - [ ] b. Temper outbursts that include a physical component
   - [ ] c. Temper outbursts that can be either verbal or physical in nature
   - [ ] d. Temper outbursts that are sporadic but include harming another person

2. Which training program for parents of children and adolescents with disruptive behavioral disorders helps address attachment issues? (LO #2)
   - [ ] a. Positive Parenting Program ("Triple-P")
   - [ ] b. Discrete Trial Learning
   - [ ] c. Multisystemic Therapy
   - [ ] d. Circle of Security

3. According to Dr. Carlson, increased rates in the diagnosis of bipolar disorder in children, especially in the U.S., is partially explained by which phenomenon? (LO #3)
   - [ ] a. ADHD criteria did not include symptoms related to emotional dysregulation
   - [ ] b. Mood instability in children increased markedly for unexplained reasons
   - [ ] c. More adults with bipolar disorder had children in the past 30 years
   - [ ] d. There was pressure from insurance companies to evaluate quickly and medicate

4. According to a recent study on atomoxetine use and suicide, what was the difference in suicide rates between the group of patients taking atomoxetine or stimulants and those switched to or added atomoxetine after initial treatment with stimulant? (LO #4)
   - [ ] a. Higher rate of suicide in patients initially taking atomoxetine and stimulant
   - [ ] b. Lower rate of suicide in patients initially taking atomoxetine and stimulant
   - [ ] c. No significant difference in suicide rates between the two groups
   - [ ] d. Inconclusive

5. An important part of the evaluation of a children with severe outbursts (not just DMDD) includes which of the following? (LO #1)
   - [ ] a. Getting children to admit they had an outburst
   - [ ] b. Clarifying when, where, and under what circumstances outbursts occur
   - [ ] c. Blaming parents or teachers for failing to adequately support their children, thus directly or indirectly producing the outbursts
   - [ ] d. Quantifying the severity (not just the frequency) of outbursts

6. Which of the following physical conditions could potentially cause disruptive behavior in children and adolescents? (LO #2)
   - [ ] a. Epilepsy
   - [ ] b. Hypothyroidism
   - [ ] c. Diabetes
   - [ ] d. Juvenile rheumatoid arthritis

7. Parental techniques that work with conduct disorders, such as time-outs, can be helpful with DMDD-related temper outbursts in children and adolescents (LO #1)
   - [ ] a. True [ ] b. False

8. In a recent study, what was the reduction in scores on the parent version of the Aberrant Behavior Checklist hyperactivity subscale for children between the ages of 5 and 14 with ASD/ADHD taking extended-release guanfacine in an 8-week trial? (LO #4)
   - [ ] a. 12% [ ] b. 24% [ ] c. 44% [ ] d. 64%

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This Issue's Focus:
Mood Dysregulation Disorders in Children and Adolescents

Next Time in *The Carlat Child Psychiatry Report:* Technology Issues With Children and Adolescents

Research Updates

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heart rate did not, remaining about 10 points below baseline. This effect was not considered clinically significant.

CCPR's Take: This was a small study of short duration, but the results were promising. When using ER guanfacine, start with 1 mg in the morning and titrate up slowly as needed. Dose it in the evening if the child becomes drowsy. By the way, ER guanfacine is now available as a cheap generic, so don't feel guilty prescribing it. On the other hand, the ER version's duration of action is only marginally longer than the IR version (about 24 hours vs. about 17 hours) so you don't gain much by choosing it.

❖ ❖ ❖