

Psychopharmacology

Experts Search for Meds to Help Youth With DMDD

Nick Zagorski

Published online: April 06, 2018

With little research being directly conducted on children with disruptive mood dysregulation disorder, clinicians look to other disorders characterized by irritability symptoms for clues on how best to treat the disorder.

Occasional bouts of temper tantrums and dramatic mood swings are to be expected during the typical development of children, but for children with disruptive mood dysregulation disorder (DMDD) irritability peppered with multiple outbursts per week are common and continual. DMDD can be hard on families and leaves children at risk for future problems such as depression, anxiety, and substance use.

DMDD is a relatively new diagnosis in *DSM-5*. Clinicians had previously believed that children with the disruptive symptoms characteristic of DMDD had pediatric bipolar disorder. (While early onset bipolar disorder typically manifests during adolescence, the typical onset for DMDD is age 10.) [Data](#) from a large clinical trial published in 2009 revealed that lithium did little to reduce the disruptive symptoms characteristic of DMDD in children.

“This was good in one respect since it showed these young kids do not have bipolar,” said Dan Matthews, M.D., a researcher at Neurobehavioral Systems in Austin, Texas, who has worked with children with behavioral disorders for over 20 years. “On the other hand, it made clinicians ask, ‘So now what do we do?’”

ADHD, Autism Medications Show Promise in Patients With DMDD



While antipsychotics may offer what Argyris Stringaris, M.D., Ph.D., calls “a short-term fix” to reduce symptoms of DMDD, he says that he worries about the long-term effects the medications might have on children.

Kings College London

Five years since DMDD first appeared in *DSM-5*, there has been little follow-up research on DMDD, and there is no consensus pharmacological option for treating this disorder. Most clinicians rely on medications that are known to reduce symptoms of irritability and temper tantrums in children with other conditions, including attention-deficit/hyperactivity disorder (ADHD) and autism.

Argyris Stringaris, M.D., Ph.D., the chief of the Mood Brain & Development Unit at the National Institute of Mental Health, noted that there appears to be a relationship between patients with ADHD and DMDD. Studies have shown that up to 85 percent of children with DMDD also have ADHD. Therefore, stimulants such as Ritalin are a commonly prescribed medication for this disorder. Children with DMDD appear to respond to stimulants, Stringaris told *Psychiatric News*, though he said this may be due to improvements in the co-occurring ADHD symptoms, which, in turn, may reduce irritability.

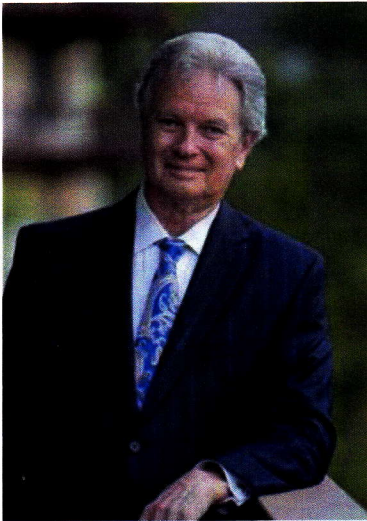
The antipsychotics risperidone and aripiprazole, which are approved by the Food and Drug Administration to treat irritability in autism, are also commonly prescribed to patients with DMDD. While antipsychotics may offer what Stringaris termed “a short-term fix” to reduce symptoms of DMDD, he said

that he worries about the long-term effects the medications might have on children. "I think a combination of stimulants plus a parenting intervention is a more benign approach."

The antidepressant citalopram might offer yet another treatment option for children with DMDD, according to Stringaris. Citalopram is the preferred treatment for premenstrual dysphoric disorder (PMDD)—another less well-understood psychiatric illness that shares similarities with DMDD, he noted. Like DMDD, PMDD is marked by extended irritability and is a known risk factor for major depression (both disorders are also categorized as depressive disorders in the *DSM-5*).

Stringaris is currently conducting a randomized clinical trial of citalopram as an add-on therapy for children with DMDD receiving stimulant medications.

Could Anticonvulsant-Dopamine Agonist Combo Reduce Explosive Outbursts?



Research by Dan Matthews, M.D., suggests a combination of the anticonvulsant oxcarbazepine and the dopamine agonist amantadine may reduce severe irritability and recurrent outbursts in children with DMDD.
Neurobehavioral Systems

Matthews said he has also found success treating patients with DMDD with a different combination of medications: anticonvulsants and the dopamine agonist amantadine. He developed this regimen when he was running an inpatient unit for children with aggression problems while he was at Duke University.

Matthews said he noticed that many patients failed to recall their outbursts shortly after they took place. "It was almost seizure-like," he said. "That led me to think an anticonvulsant like oxcarbazepine might work."

Brain scans of youth with aggression problems suggested that they had heightened activity in the amygdala (the brain's emotional center) due to a deficiency of dopamine, which resulted in a state of hypervigilance and poor impulse control. These findings may help to explain why stimulants appear to help children with DMDD (stimulants can block dopamine transporters to reduce dopamine reuptake). The findings also suggested to Matthews that a stronger dopamine activator like amantadine—which can both trigger more dopamine release and block dopamine reuptake—might be even more effective in reducing symptoms in these patients.

In some clinical studies, Matthews has shown that the oxcarbazepine–amantadine combination can dramatically lower the risk of rehospitalization in

he has tracked some children treated with this combination into their adolescence and found that in about 50 percent of cases, the children show normalized amygdala activity in addition to improved symptoms. According to Matthews, some of these children have been able to reduce or even discontinue the oxcarbazepine–amantadine combination.

While finding a good medication to treat children with DMDD is important, Matthews said he recognizes the importance of psychotherapy in rehabilitating these patients as well.

"Many of these youth have dealt with these temper problems for almost their whole lives," he said. "Once the medication restores their chemical balance, they need behavioral rehabilitation."