Disruptive Mood Dysregulation Disorder (DMDD)

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Diplomate, American Board of Preventive Medicine, Addiction Medicine
None

(We may, however, be discussing some possible off label medication uses...)
FDA Prescribing Pearls

- Chlorpromazaine (Thorazine) – FDA approved ages >6 months for schizophrenia / psychosis
- “The long term effects of ADHD medicine on young children are not known…”
- FDA – Pregnancy Category C
  - “Methylphenidate has been shown to have teratogenic effects in rabbits when given in doses of 200mg/kg/day”
Objectives

- Understand the History and Diagnosis of DMDD
- Discuss Associated Factors
- Review Treatments
- Explore the Controversy
Clinical Case

Bobby is a 10 year old male referred to a child psychiatrist for “anger issues” at home and school for the past year.
Case, cont’d

• Father’s Interview:
  – Quick temper
  – Lashes out – punching, kicking others
  – Doesn’t listen to or follow rules
  – Siblings avoid him / few friends
Case, cont’d

• Mother’s Interview:
  – Low frustration tolerance
  – “walking on eggshells”
  – “moody”
  – Daily episodes
  – Parents deny all mood/anxiety related questions
Case cont’d

• Child Interview:
  – Easy to engage
  – “mind goes blank and I see red”
  – “I can’t control myself”
  – Denies all mood/anxiety questions
Case cont’d

• History:
  – No family history of mental illness
  – No significant past medical history
  – No history of abuse
  – Developmentally appropriate milestones
  – Past treatment for ADHD by pediatrician
Diagnosis?

Disruptive Mood Dysregulation Disorder (DMDD)
DSM-5
History

• Severe Mood Dysregulation (SMD)
  – Symptoms:
    • Pervasive anger / irritability
    • Explosive Behavior
    • Hyperarousal symptoms: insomnia, agitation, distractibility, racing thoughts or flight of ideas, pressure speech, intrusiveness

• Temper Dysregulation Disorder with Dysphoria (TDD)
“In order to address concerns about the potential for the overdiagnosis of and treatment for bipolar disorder in children, a new diagnosis, disruptive mood dysregulation disorder, referring to the presentation of children with persistent irritability and frequent episodes of extreme behavioral dyscontrol, is added to the depressive disorders for children up to 12 years of age. Its placement in this chapter (Depressive Disorders) reflects the finding that children with this symptom pattern typically develop unipolar depressive disorders or anxiety disorders, rather than bipolar disorders, as they mature into adolescence and adulthood.”
“In DSM-5, the term bipolar disorder is explicitly reserved for episodic presentations of bipolar symptoms. DSM-IV did not include a diagnosis designed to capture youths whose hallmark symptoms consisted of very severe, non-episodic irritability, whereas DSM-5, with the inclusion of disruptive mood dysregulation disorder, provides a distinct category for such presentations.”
A. Severe recurrent temper outbursts manifested verbally (e.g., verbal rages) and/or behaviorally (e.g., physical aggression toward people or property) that are grossly out of proportion in intensity or duration to the situation or provocation.
B. The temper outbursts are inconsistent with developmental level.
C. The temper outbursts occur, on average, three or more times per week.
D. The mood between temper outbursts is persistently irritable or angry most of the day, nearly every day, and is observable by others (e.g., parents, teachers, peers).
E.  Criteria A–D have been present for 12 or more months. Throughout that time, the individual has not had a period lasting 3 or more consecutive months without all of the symptoms in Criteria A–D.
F. Criteria A and D are present in at least two of three settings (i.e., at home, at school, with peers) and are severe in at least one of these.
G. The diagnosis should not be made for the first time before age 6 years or after age 18 years.
H. By history or observation, the age at onset of Criteria A–E is before 10 years.
I. There has never been a distinct period lasting more than 1 day during which the full symptom criteria, except duration, for a manic or hypomanic episode have been met.

**Note:** Developmentally appropriate mood elevation, such as occurs in the context of a highly positive event or its anticipation, should not be considered as a symptom of mania or hypomania.
J. The behaviors do not occur exclusively during an episode of major depressive disorder and are not better explained by another mental disorder (e.g., autism spectrum disorder, posttraumatic stress disorder, separation anxiety disorder, persistent depressive disorder [dysthymia]).

**Note:** This diagnosis cannot coexist with oppositional defiant disorder, intermittent explosive disorder, or bipolar disorder, though it can coexist with others, including major depressive disorder, attention-deficit/hyperactivity disorder, conduct disorder, and substance use disorders. Individuals whose symptoms meet criteria for both disruptive mood dysregulation disorder and oppositional defiant disorder should only be given the diagnosis of disruptive mood dysregulation disorder. If an individual has ever experienced a manic or hypomanic episode, the diagnosis of disruptive mood dysregulation disorder should not be assigned.
K. The symptoms are not attributable to the physiological effects of a substance or another medical or neurological condition.
Diagnosis

- Integration of semi-structured and unstructured interviews
  - Children’s Interview for Psychiatric Syndromes (ChIPS)
  - Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)
  - Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS)

McTate E. & Leffler J. Diagnosing disruptive mood dysregulation disorder: Integrating semi-structured and unstructured interviews. Clinical Child Psychology and Psychiatry. 22 (2), 187-203
Figure 1. The Balloons Game. Children are instructed to pop all the green balloons to win the game and become the balloons champion. The red timer bar at the bottom of the screen indicates progression on the trial.
Money Task

- Equal number of trials on which participants could earn or lose 50 cents and trials on which there was no monetary reward or penalty
- During frustration block, participants told answers were “too slow” on 60% of correct response trials (negative feedback) and told “good job” on 40% (positive feedback)

~50% of school-age youths had severe temper outbursts

- **Frequency**
  - Dropped to 6-7%

- **Duration**
  - Dropped to 1.5-2.8%

- **All Criteria**
  - Prevalence of 1%

Prevalence

- 1-5%
- Males > Females
- School age > Adolescents
Associated Factors
Risk Factors for Development of DMDD

- Maternal mood symptoms during pregnancy
- Maternal depression within first year of life
- Low maternal level of education
- Possible inverse associations: maternal level of education, family income, smoking

Predictors of DMDD at 6 y/o

- At 3 years old: ADHD, ODD, poor peer functioning, parental lifetime substance use disorder, parental hostility

- At 6 years old: depression, ODD, functional impairments, Poor peer functioning, low parental support, low parental marital satisfaction

Common Presenting Complaints

- Aggressive behavior
- Rule-breaking
- Social difficulties
- Anxiety / depression
- Attention difficulties
- Thought problems

Parent Differences in DMDD vs. BPD

- Less likely to have bipolar diagnosis
- Higher caregiver reported irritability

Fristad M et al. Disruptive Mood Dysregulation Disorder and Bipolar Disorder NOS: Fraternal or Identical Twins? J Child Adolesc Psychopharm. 26:2, 2016
Course

- ~50% of children will meet criteria 1 year later
- Risk of Development of Unipolar Depression and Anxiety Disorders > Development of Bipolar Disorder
fMRI Findings in SMD

• Less activation on negative feedback trials: left amygdala, left and right striatum
• Less overall activation on negative feedback trials: parietal, parahippocampal, thalamic/cingulate/striatal regions
• Less striatum activation negative vs. positive

Magnetoencephalography (MEG) Findings in SMD

• Increased activation of anterior cingulate cortex and medial frontal gyrus in response to negative feedback

• Bipolar Disorder youth displayed increased superior frontal gyrus activation and decreased insula activation.

Face Emotional Processing
Task Findings in SMD

- Difficulty identifying negative emotions
- Greater fear viewing neutral faces
- Reduced positive expressivity
- Deficits in controlling negative facial expressions
- Impairments in emotional processing
  (theorized to cause elevated reactive aggression)

Common Co-morbidities

• Attention Deficit Hyperactivity Disorder
• Major Depressive Disorder
• Anxiety Disorders
• Conduct Disorder
• Oppositional Defiant Disorder*
• Intermittent Explosive Disorder*
Differential Diagnosis

- Bipolar Disorder*
- Oppositional Defiant Disorder*
- Major Depressive Disorder
- Anxiety Disorders
- Autism Spectrum Disorder
- Attention Deficit / Hyperactivity Disorder
- Intermittent Explosive Disorder*
Differential – Bipolar*

- Episodic vs. Longitudinal
- Distinct period of different behavior
- Elevated or expansive mood
- Grandiosity

Differential – ODD*

- No mood symptoms present
- Single setting
- Frequency
  - 1x / week
  - 6 months
- Lower risk of depression and anxiety disorders

Differential – IED*

• Not persistent
• Frequency of outbursts
  – 2x / week
  – 3 months
Differential – MDD, Anxiety, ASD

• Present in the context…
  – Irritability during major depressive episode
  – Irritability in GAD exacerbation, OCD
  – Irritability in specific situation (ie. change of routine)

<table>
<thead>
<tr>
<th><strong>DMDD Differentials Table</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disruptive Mood Dysregulation Disorder</strong>, which is characterized by severe recurrent temper outbursts manifested verbally and/or behaviorally that are grossly out of proportion in intensity to the provocation and that are accompanied by a persistently irritable or angry mood most of the day, nearly every day, in between the outbursts, must be differentiated from . . .</td>
</tr>
<tr>
<td>In contrast to Disruptive Mood Dysregulation Disorder . . .</td>
</tr>
<tr>
<td><strong>Depressive Disorder Due to Another Medical Condition</strong></td>
</tr>
<tr>
<td>Is characterized by dysphoric symptoms that are due to the direct physiological effects of an identified medical condition.</td>
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<tr>
<td><strong>Substance/Medication-Induced Depressive Disorder</strong></td>
</tr>
<tr>
<td>Is characterized by dysphoric symptoms that are due to the direct physiological effects of a substance or medication.</td>
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<tr>
<td><strong>Bipolar I and Bipolar II Disorders</strong></td>
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<tr>
<td>Are characterized by episodic illnesses with discrete episodes of mood perturbation that are distinguishable from the child’s baseline. In addition, the change in mood during Manic or Hypomanic Episodes is accompanied by increased energy and activity as well as associated cognitive, behavioral, and physical symptoms (e.g., distractibility, rapid speech, decreased need for sleep). In contrast, the irritability of Disruptive Mood Dysregulation Disorder is persistent and present chronically over many months.</td>
</tr>
<tr>
<td><strong>Oppositional Defiant Disorder</strong></td>
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<tr>
<td>Is characterized by a pattern of angry/irritable mood, argumentative/defiant behavior, or vindictiveness. In contrast, Disruptive Mood Dysregulation Disorder is also characterized by the presence of severe and frequently recurrent outbursts and a persistent disruption in mood between outbursts. If criteria are met for both disorders, only Disruptive Mood Dysregulation Disorder is diagnosed.</td>
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<tr>
<td><strong>Major Depressive Disorder</strong></td>
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<tr>
<td>May be characterized by irritable mood accompanying the episodes of depressed mood or diminished interest or pleasure. Children whose irritability is present only in the context of a Major Depressive Episode should receive a diagnosis of Major Depressive Disorder rather than Disruptive Mood Dysregulation Disorder. If the irritability extends outside the depressed episodes, both diagnoses may be appropriate.</td>
</tr>
<tr>
<td><strong>Anxiety Disorders</strong></td>
</tr>
<tr>
<td>May be characterized by irritable mood occurring in anxiety-provoking situations. Children whose irritability is manifest only in anxiety-provoking contexts should receive the relevant Anxiety Disorder diagnosis rather than a diagnosis of Disruptive Mood Dysregulation Disorder. If the irritability extends outside the anxiety-provoking situations, diagnoses of both Disruptive Mood Dysregulation Disorder and the Anxiety Disorder may be appropriate.</td>
</tr>
<tr>
<td><strong>Autism Spectrum Disorder</strong></td>
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<tr>
<td>May be characterized by temper outbursts, especially when routines are disturbed. If temper outbursts are better explained by Autism Spectrum Disorder, then Disruptive Mood Dysregulation Disorder is not diagnosed.</td>
</tr>
<tr>
<td><strong>Intermittent Explosive Disorder</strong></td>
</tr>
<tr>
<td>Is characterized by aggressive outbursts that can resemble the severe temper tantrums in Disruptive Mood Dysregulation Disorder; however, there is no persistent irritable or angry mood between outbursts as in Disruptive Mood Dysregulation Disorder. In addition, Intermittent Explosive Disorder requires only 3 months of active symptoms, in contrast to the 12-month requirement for Disruptive Mood Dysregulation Disorder. Intermittent Explosive Disorder is not diagnosed if criteria are met for Disruptive Mood Dysregulation Disorder.</td>
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</tbody>
</table>
Treatments

- Medication
- Therapy / Behavior Modification
- Lifestyle
Medications for SMD / Aggression

• Waxmonsky et al., 2008
  – Randomized, cross-over design
  – BMT (tx) vs. methylphenidate vs. placebo
  – Both groups improved significantly vs. placebo
• Dickstein et al., 2009
  – Only RCT in children with SMD
  – No benefit of Lithium over placebo

• Blader et al., 2009
  – ADHD and aggressive behavior unresponsive to stimulants
  – Divalproex sodium + behavior therapy more effective than stimulant + placebo + behavior therapy
Medication Trials, Cont’d

• Krieger et al., 2011
  – Open-label trial of Risperdal in youth with SMD
  – Significant reductions in irritability, AHD, depression

• Linton et al, 2013
  – Systematic review of data on treatment with antipsychotics and stimulants for aggressive and hyperactive behavior
  – Concurrent treatment not superior to monotherapy
Open Trials / Case Reports

• Successful Outcomes in Rage / Outbursts (either adults, open trials or limited number):
  – Valproate (mixed)
  – Aripiprazole
  – Quetiapine
  – Haloperidol
  – Thioridazine
  – Propranolol
  – Lithium

Risperidone in Aggression

• 10 RCTs in treatment of aggression
  – Autism, Conduct D/O, ODD, ADHD, ID
  – All demonstrated greater reduction in aggression vs. placebo

• 2 RCTs in treatment of aggression + ADHD
  – Effective treatment independent of stimulant

ADHD Medications and Aggression

• Pappadopulos et al. 2006 (Meta-analysis)
  – 18 Stimulant RCTs (methylphenidate, amphetamine mixed salts, dextroamphetamine)
    • Significant improvement in aggression
  – 4 Atomoxetine RCTs
    • Limited effect on aggression

• Connor et al. 2003 (Meta-analysis)
  – 11 Clonidine RCTs
    • Moderately significant effect of aggression

• Scahill et al. 2001
  – Guanfacine positive decreased in aggression

Failed Trials

• Non-efficacious outcomes in rage / outbursts:
  – Lamotrigine (Belsito et al. 2001)
  – Carbamazepine (Cueva et al. 1996)

• Possible improvement:
  – Bupropion (3 RCTs)
  – Fluoxetine (2 RCTs)
  – Desipramine (1 RCT)

Current Research

ClinicalTrials.gov

Search Results

Modify Search  Start Over

7 Studies found for disruptive mood dysregulation disorder

<table>
<thead>
<tr>
<th>Row</th>
<th>Status</th>
<th>Study Title</th>
<th>Conditions</th>
<th>Interventions</th>
<th>Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Active, not recruiting</td>
<td>Adapting DBT for Children With DMDD: Pilot RCT</td>
<td>• Disruptive Mood Dysregulation Disorder</td>
<td>• Behavioral: Dialectical Behavior Therapy for children&lt;br&gt;• Behavioral: Treatment as usual</td>
<td>Well Come Medical College&lt;br&gt;White Plains, New York, United States</td>
</tr>
<tr>
<td>2</td>
<td>Completed</td>
<td>Antipsychotic Added on for DMDD in Youths With ADHD</td>
<td>• Disruptive Mood Dysregulation Disorder</td>
<td>• Drug: MPH + APZ</td>
<td>CHU Amiens&lt;br&gt;Amiens, France&lt;br&gt;AP HP&lt;br&gt;Pays, France</td>
</tr>
<tr>
<td>3</td>
<td>Recruiting</td>
<td>Clinical and Actigraphic Profile of Young Patients Admitted for Attempted Suicide</td>
<td>• Suicidal Attempts</td>
<td>• Behavioral: questionnaires&lt;br&gt;• Device: actigraphic recording</td>
<td>National Institutes of Health Clinical Center, 5000&lt;br&gt;Rockville Pike&lt;br&gt;Bethesda, Maryland, United States</td>
</tr>
<tr>
<td>4</td>
<td>Recruiting</td>
<td>Psychological Treatments for Youth With Severe Irritability</td>
<td>• DMDD (Disruptive Mood Dysregulation Disorder)&lt;br&gt;A+DM (Attention Deficit Hyperactivity Disorder)&lt;br&gt;GDD (Oppositional Defiant Disorder)</td>
<td>• •</td>
<td>National Institutes of Health Clinical Center, 5000&lt;br&gt;Rockville Pike&lt;br&gt;Bethesda, Maryland, United States</td>
</tr>
<tr>
<td>5</td>
<td>Completed</td>
<td>Correlating Real and Virtual World Behavioral Fluctuations in Adolescence</td>
<td>• Attention-Deficit and Hyperactivity Disorder&lt;br&gt;• Anxiety&lt;br&gt;• Disruptive Mood Dysregulation Disorder&lt;br&gt;(and 3 more...)</td>
<td>•</td>
<td>Shalvata MH&lt;br&gt;Had Hasharon, Israel</td>
</tr>
<tr>
<td>6</td>
<td>Not yet recruiting</td>
<td>Attention Bias Modification, Attention Control and Psychoeducation for Irritability in Children and Adolescents</td>
<td>• Irritability</td>
<td>• Other: Attention bias modification training&lt;br&gt;• Other: Attention Control Training&lt;br&gt;• Other: Psychoeducation</td>
<td>Johns Hopkins University Bayview Medical Center&lt;br&gt;Baltimore, Maryland, United States</td>
</tr>
<tr>
<td>7</td>
<td>Completed</td>
<td>Interpersonal Psychotherapy for Youth With Severe Mood Dysregulation</td>
<td>• Severe Mood Dysregulation</td>
<td>• Other: IPT-MBD</td>
<td></td>
</tr>
</tbody>
</table>
• Postulated deficiencies: Vitamin C, Niacin, Thiamine, Pantothenic Acid, Vitamin B6, Magnesium, Calcium, Zinc, Iron, Tryptophan
Nutritional Supplements

• Vitamins B1 (thiamine)
  – Case reports of deficiencies in aggressive adolescents with poor diets. Behaviors improved with supplementation

• Omega-3 Fatty Acids (DHA, Fish Oil)
  – Observational improvement of behaviors with supplementation

• 5HTP (5-hydroxytryptophan), Iron supplementation (if deficient), magnesium, selenium

http://rnblog.rockwellnutrition.com/nutritional-remedies-aggressive-violent-behavior/
Dietary Options

• Feingold Diet
  – eliminates artificial coloring, flavoring and sweeteners, preservatives and foods high in salicylates from the diet

• Gluten Free / Casein-Free Diet
Therapy

- Cognitive Behavioral Therapy
- Family Therapy
- Behavior Modification
Lifestyle Modifications

• Sleep Hygiene

• Exercise

• Balanced Diet

Live.Life.Healthy
Causes of Irritability

- Psychosocial stressors
- History of maltreatment
- Family discord
- Learning disorders
- Communication disorders
- Other psychiatric disorders

DMDD Functional Outcomes

• Elevated rates of depression and anxiety

• Increased negative adult outcomes:
  – Adverse health outcomes
  – Poverty
  – Police contact
  – Low educational attainment

Controversy

Teach the Controversy
Diagnostic Utility

- Overlap with ODD and Conduct D/O
  - 96% met criteria for ODD or CD
- Overlap with ADHD and ODD/CD
  - 77% met criteria for both ADHD and ODD/CD
- “Limited diagnostic stability”
- Not associated with current or future-onset of mood or anxiety disorders
- Not associated with parental history of SPMI

Questionable reliability

- Kappa = 0.25
- Difficult retrospective recall
- Inpatient vs. Outpatient Diagnostically
Validity

• Limited published validity studies

• Support derived from SMD studies

• Frequent associations with other diagnoses

• Treatment confounders

Instability of Diagnosis

8 year review:
- 71% remission rate
- 55% new cases
- 29% had symptoms often or very often after 8 years

“If you are always trying to be normal you will never know how amazing you can be.”

Maya Angelou
Greenville, SC
Ranked 4th Best Place To Live!
Questions?