Disruptive Mood Dysregulation Disorder (DMDD) Developing Treatment Strategies

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Medication Usage Disclaimer

• The following 2 medications that will be discussed in this presentation are being used off-label:

• 1) oxcarbazzepine

• 2) amantadine HCl
1) Disruptive Mood Dysregulation Disorder (DMDD): What is it?

2) How does DMDD compare to Bipolar Disorder or to Severe Mood Dysregulation?

3) What are the criteria; how common is it? What comorbid conditions are there?

4) What is known about the neuropathology?

5) What about treatment: Any research?

6) What about crisis management?
DMDD: What is it?  
(McGough, 2014)


- **AREN’T ALL CHILDREN IRRITABLE AT TIMES?**  
  Yes but DMDD refers to:
  - Temper outbursts - at least three times a week
  - Irritable/angry moods almost daily for a year
  - Onset at least age 6 but before age 10; may continue as adult, if had childhood onset
  - With trouble functioning in multiple settings
DMDD: New DSM-5 Diagnosis
(Axelson et al., 2012)

• Designed to replace “broad spectrum” Bipolar Disorder in children and adolescence.
  – In DSM IV, mania describes discrete episodes of irritated moods (episodic irritability).
  – In DSM 5, DMDD describes non-episodic (chronic) irritability with frequent temper outbursts.
  – DMDD has very little research base, but it is very similar to the concept of Severe Mood Dysregulation (without hyper-arousal).
Epidemic of Bipolar Disorder (BD)?
(Leibenluft, 2011)

• Between 1994 and 2003 there was a 40 fold increase in the diagnosis of BD in children and adolescents. (Moreno, C. et al., 2007)
  – Psychiatrists had broadened the phenotype for pediatric bipolar, to include chronic irritability as a subtype of Bipolar Disorder.

• But, research does not support this change from narrow (episodic) to broad (chronic) phenotype.
  – Non-episodic irritability is unique; not a subtype of Bipolar Disorder (Geller et al., 2008)
The vast majority of the children being diagnosed with Bipolar Disorder were not classic, or narrow phenotype, Bipolar Disorder.

- They show non-episodic (chronic) irritability, rather than classic (episodic) irritability.

Non-episodic (or chronic) irritability appears to be a distinct condition, separate from Bipolar.

- This is the basis for Disruptive Mood Dysregulation Disorder (DMDD) in DSM-5.
DMDD versus Bipolar Disorder

- How does DMDD differ from Bipolar?
  - **Non-episodic irritability** (chronic)
    Bipolar Disorder has episodes of irritability with mania
  - **No euphoria or grandiosity**
    Bipolar Disorder may show this during mania
  - **No psychosis**
    Bipolar Disorder may show this
Abnormal Irritability
(Leibenluft, 2011)

- **Abnormal Irritability:**
  - Is an **impairing, and long-lasting mood disorder with temper outbursts:**
    - “Temper outbursts that are developmentally inappropriate, frequent, and extreme with anger or sadness between outbursts.”
  - may occur in association with mental illness:
    - Depression, Anxiety, Post-Traumatic Stress Disorder, Attention Deficit Hyperactivity Disorder, Bipolar Disorder, Autistic Spectrum
DMDD Research

- **Epidemiologic studies:**
  - Copeland et al. (2013) showed: that
  - Non-episodic (chronic) irritability with rage outbursts (meeting DMDD criteria; age 6-10) are reported in only 3% of children.
  - This population shows many co-occurring conditions, particularly depressive disorders, with higher rates of social and behavioral difficulties, poverty, use of mental health services, and school problems.
  - Dougherty et al. (2014) found an 8.2% prevalence for DMDD in 6-year-old children.
Retrospective Study of DMDD
(Copeland et al., 2013)

- Used data from existing studies of school age children with mental illness to evaluate DMDD
  - About 50% had temper outbursts, but only 6-7% of these averaged 3 or more per week.
  - 8-13% showed negative moods (sad or irritable) but only 1.5%-2.8% had chronic irritability.
  - Cumulative prevalence after 4 separate assessments was 4.4% (Close to 1 child in 20 of this sample)
  - High rates of other co-existing psychiatric disorders.
  - High rates of impairment (family, school, social)
  - High rates of mental health service utilization
Disruptive Mood Dysregulation Disorder (DMDD) DSM-5 (Zepf & Holtmann, 2012)

A. Temper Outburst
- Severe recurrent temper outbursts to common stressors
- Beyond provocation
- Not consistent with age (developmental age 6+)
- Onset before age 10
- Never elevated mood or grandiosity

B. Frequency
- Temper outbursts occur, on average, three or more times per week
- Between outbursts:
  - Mood chronically negative
  - Irritable, angry
  - Observed by others such as parents, teachers
  - For at least a year
  - In at least two settings
    - Home, school, peers
Underlying Neuropathology
DMDD versus Bipolar Disorder

• Ryan, N.D. (2013) reported:
  – DMDD exhibited markedly **decreased** activation of **paralimbic** system (cingulate gyrus, striatal, thalamic, parietal, and parahippocampal regions) after negative feedback (frustrating) trials (not in Bipolar).

• Deveney et al. (2013) reported:
  – In DMDD, the **frontal lobe** tends to show **underactivity** in comparison to Bipolar Disorder which shows over activity.
Underlying Brain Disorders

Cause of DMDD is Unknown:
Possible genetic disorder?


Premature birth with hypoxia, drugs/alcohol in pregnancy, difficult birth, malnutrition, abuse?

Biological Markers for DMDD?
(Kowatch et al. , 2009)

• BD rates do not vary by gender, but chronic irritability kids are mostly male (66-77%) (suggesting a distinct gender-based disorder).

• Parents of Bipolar kids are more likely (33%) to have BD themselves than parents of DMDD kids (2.7%), (suggesting a distinct genetic pattern).

• Gene mapping may be a way to find biological markers for DMDD.
5) TREATMENT FOR DMDD?

• No treatment strategies have been established:
  – Deveney et al. (2013)

• But, Bipolar medications may NOT be needed.

• The selection of medications for the management of maladaptive aggression in youth is a major clinical challenge in pediatric mental health
TREATMENT OPTIONS?

Most experts suggest medication, parent training and psychotherapy.


Psychosocial interventions have low risk, but it may require a combination of medication and psychosocial interventions to manage the severity.

- Aman et al. (2014)

But, what medication protocol?

Medication Protocol: (Matthews et al., 2006; Matthews et al., 2009, Matthews et al., 2013)

- A Neuropsychiatric approach to DMDD would suggest that medication strategies be based on brain issues.
- If it is true that DMDD represents a combination of top-down and bottom-up brain issues, then:
  - Medications should enhance frontal lobe function (top-down) to control irritability, and;
  - Medications should stabilize temporal-limbic (bottom-up) to stop explosive outbursts.
Angry kid
Explosive Kid

- Glassy-eyed, jaw clenched, tight muscles = RAGE
Incarceration (1-Yr Post)

% Incarcerated

- 20%
- 15%
- 10%
- 5%
- 0%

Compliant
Non-compliant

Anticonvulsant Use

19%
Re-hospitalization (1-Yr Post)

- **Compliant Anticonvulsant Use**: 6%
- **Non-compliant Anticonvulsant Use**: 48%
Impulse Control & Concentration
Emotion Generation System
[Limbic Brain]
Auditory Evoked Response

Age: 15.114
Visit: 1
Tue Apr  6 1993

Reason: cerebral dysrhythmia
Sensory Deficit: reading glasses

Protocol: xbasic
Visual Evoked Response
P-300’s
Treatment Interventions

• Medications
  1) Anticonvulsants – Limbic instability
  2) Amantadine HCl or alpha-adrenergic agonists – Frontal lobe dysfunction
  3) Stimulants – attentional deficits

• Psychosocial and Psycho-educational
  1) Psychotherapy (family and individual)
  2) Specialized academic interventions
  3) Skill-based therapies
Anticonvulsants

Name
Carbamazepine (Tegretol)
Oxcarbazepine (Trileptal)
Levetiracetam (Keppra)
Valproate sodium (Depakote)
Lamotrigine (Lamictal)
Abnormal Hippocampal Attention

- Abnormal P-300 (cognitive evoked) responses indicate inadequate Hippocampal attentional function.
- P-300 responses and attentional function are normalized at appropriate dosages of neuro-stimulant medications.
- Dextroamphetamine 0.2-0.3 mg/kg/dose 3x/day.
- Methylphenidate 0.4-0.6 mg/kg/dose 3x/day.
- Stimulants can be transitioned to a long-acting formulation after the most efficacious dosage has been determined.
Abnormal Frontal Lobe Function

Symptoms are:
Chronic irritability, impulsivity, memory problems and concentration problems.

Best addressed with amantadine HCl.
Angry kid
Explosive Kid

- Glassy-eyed, jaw clenched, tight muscles = RAGE
What is Crisis Mgt. for Defensive RAGE?

- **SEE RAGE?** Stop VERBAL de-escalation, don’t touch him/her
  - No more talk, remove others, allow rage (if safe)
- **SEE RAGE FACE:** Slowly, very slowly, back away
  - Even if he/she follows, threatens, curses, throws stuff
- **Don’t look threatening** — it is a defensive “seizure”
  - Make your face, body posture - non-threatening
- **Don’t approach or touch** — unless hold **must** occur,
  - but only for absolutely imminent danger
Crisis Management for Explosive Kid

- RAGE-like a seizure (time limited, OUT-OF-CONTROL)- just keep it safe, it will go away in a few minutes.
- Do not try to de-escalate rage (NO MORE TALK) – Do not touch or it will take an hour to stop it.
- You let it wind down on its own (like an emotional seizure). No restraint, or you will hold for an hour.
- Remove others from the room (don’t move enraged kid). Defensive rage will subside on its own.
Explosive Kid: Crisis Management

- No show of force by staff (THIS WILL TRIGGER AN ATTACK)
- Back off and watch for safety (HOLDING IS A LAST RESORT)
- Rage will run out of steam on its own (IF NO THREAT)
- Afterwards, expect fatigue, poor recall (remorse?)
- No point to punishment of out-of-control RAGE
- Use this strategy, not verbal de-escalation.
SUMMARY

• DMDD is a **new diagnosis** in DSM-5 for 2013.
• This severe mood disorder is **relatively** common (DMDD at least 3%, versus 1% for BD)
• DMDD is a **distinct condition**, with chronic (non-episodic) irritability, that does not evolve into BD.
• No **established** treatment strategies for DMDD.
• DMDD **might be managable** with combination of:

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