DSM-5 & Severe Non-Episodic Irritability in Youth

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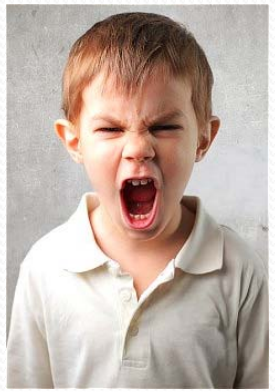
- **Severe, non-episidic irritability** is a prevalent **(3.2%)** symptom in **youth**. *(Brotman,2006)*

- It causes **severe psychiatric impairment** in them.

- Frequently meet **DSM** criteria for an *Anxiety* disorder, *ADHD, ODD, CD*, & a *history of MDD.*

- Can't be fitted into any existing **DSM** category.

- *How can the clinicians **provide** them the **intensive care** they require? (despite their unclear clinical status!)*



*In the past decade, a **school of thought** has developed amongst some **researchers** & **clinicians** that:*

1. ***Mania*** in **youth** presents by ***severe irritability*** *(rather than by euphoria).*

2. ***BD*** in ***youth*** is ***non-episodic***.

3. ***Classic BD*** is ***rare*** in youth.

- Considerable impact on diagnostic practice
- Despite **incomplete evidence** regarding its **validity!**

- Marked **upsurge** in the **rate** of the **diagnosis of BD in children** in the past decade.

  (Moreno, 2007; Blader,2007)

- A **40-fold** increase between **1994-2003** in the number of outpatient diagnosis of **BD in children.**

  (Moreno, 2007)

- A **5.6 fold** increase between **1996-2004** of US hospital **discharges** of **youth** with **BD diagnosis** (1.3/10000 to 7.3/10000).

  (Blader, 2007)

- ***Higher & more intensive level of services could be provided for them!***

  (Moreno, 2007; Blader, 2007).

- All **DSMs** are based in work on **adults.**

- DSM tries to maintain **continuity** between **adult & child** conventions *(as much as possible)*.

- The ***DSM-V work groups*** have recognized the importance of **developmental perspectives** regarding diagnostic criteria.

- Classic BD does present in youth, but is rare.

  (Biederman, 2004; Birmaher, 2006, DelBello , 2007; Geller,2004)

- Classic BD has developmental consistency.

  (Birmaher, 2006,2009)

Severe non-episodic irritability

- Broad Phenotype BD
- Severe Mood Dysregulation *(SMD)*
- Temper Dysregulation Disorder *(TDD)*
- **Disruptive Mood Dysregulation Disorder *(DMDD)***

Broad BD / SMD / TDD / DMDD:

- **Irritable mood (severe)**
- **Non-episidic (chronic)**

- A diagnostic criteria can facilitate clinical judgment & research!

(Leibenluft, 2003)

Disruptive Mood Dysregulation Disorder (DMDD)

- **Age** at **onset**: **before** age 10 years
- **Age range** for **first diagnosis:** 6-18 years
- **Severe recurrent temper outbursts** in response to ***common stressors*** *(verbal rages &/or physical aggression)*
- Intensity or duration are grossly **out of proportion** to the situation
- Inconsistent with **developmental level**
- At least **3 times per week**

(DMDD)

- **Between** temper outbursts: **Persistent irritable** or **angry mood, most** of the day, nearly **every day**, observable by others
- At least **1 year**, *(not symptom-free >3 months)*
- In **at least 2 settings: Severe** symptoms in at least **1 setting** *(at home or school, or with peers)*

- **Can co-exist** with: ***MDD, ADHD, CD, SUD***

(DMDD)

- ***Never*** *a distinct* ***manic/hypomanic*** *episode* ***> 1 day***
- ***Can not*** ***co-exist*** *with:* ***BD, ODD, IED***
- ***Not*** *exclusively during* ***MDD***
- ***Not*** *better explained by:* ***ASD, PTSD, SAD, dysthymia***
- ***Not*** *due to* ***GMC*** *or* ***substance*** *induced*

Is <u>severe, non-episodic irritability</u>

a developmental presentation of <u>BD</u>?

Robins & Guze's Criteria

*To establish the **reliability & validity** of a **psychiatric disorder***
*Clear differentiation from other clinically **similar disorders** by:*

1. Clinical **description** ***(phenomenology)***
2. ***Biological markers*** in physiologic/neuropsychologic studies
3. Prevalence in relatives ***(familial clustering)***
4. long-term **outcome**
5. ***Treatment*** response

Research over the **past 10 years** has **compared** youth with **severe, non-episodic irritability** to those with **classic DSM-IV BD.**

1. Outcome

Do DMDD youth develop classic BD over time?

- DMDD *(age 10.6)* predicts unipolar depression , in adulthood *(age 18.3)*.

  (n=1420, Great Smoky Mountain Study, Brotman, 2006).

- DMDD *(age **13.8**),* predicts **MDD, DD, & GAD** in adulthood *(age 33.2)*.

  (n=776, Children in the Community Study, Leibenluft, 2006; Stringaris, 2009)

- DMDD youth, are at risk for **unipolar depression, & anxiety disorders** in adulthood (***but not classic BD!)***.

  (Brotman, 2006; Leibenluft, 2006; Stringaris, 2009)

In a longitudinal study in a clinical sample in NIMH:

- DMDD youth *(n=84),* **do not develop BD** over time *(follow up=**28.4** months)*

- **Classic BD** youth develop **hypo/manic or mixed** episode **50** times higher.

(Stringaris, in revision)

Impairment:

Investigators of **NIMH-IRP** recruited **111** BD & **118 DMDD** *(age: BD: 12.9, SMD: 11.6)* from around the country:

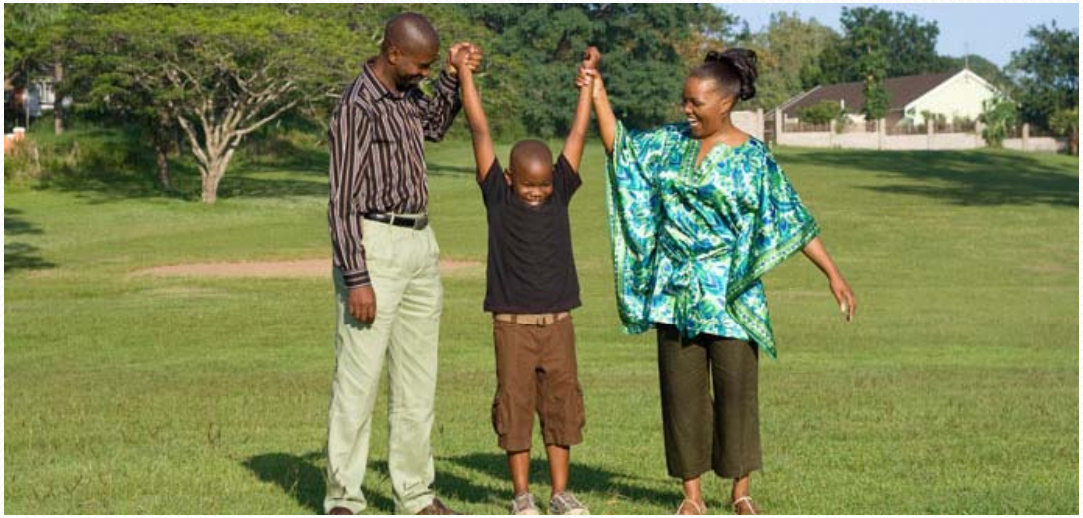
- **DMDD & BD** have **similar** levels of **severity.**
- **DMDD & BD** have **similar** levels of **impairment.**
- **DMDD & BD** have **similar number** of **medications** & **hospitalization.**
  (NIMH, IRP)

- **BD** has **higher level** of **suicide, & hospitalization** vs. **DMDD.**
  (Dickstein, 2005)

2. Familial aggregation

- **BD** were more **prevalent** *(29.4-33.3%)* in **parents of BD youth** than parents of DMDD youth *(2.7-10.1%)*.

  (Strober, 1988; Birmaher, 2006; Findling, 2005; Brotman, 2007)



3. Biological markers

Do DMDD & BD have similar biomarkers?

- There are **differences in brain function** between **DMDD** & **BD**.

- DMDD & BD youth have **deficits in face emotion labeling**, but the **neural circuitry** differ between them.
  (Brotman, b, 2010; Guyer, 2007; Rich, 2008)

- **Amygdala** activity **differs** between DMDD & BD.

  (Brotman, 2010)

- DMDD & BD youth express **more frustration** when performing a **frustrating task**, but the **neural circuitry** differ between them.

  (Rich, 2007)

- DMDD & BD youth show **deficits on response reversal & cognitive flexibility tasks**, but they are more **consistent & widespread in BD.**
  (Dickstein, 2007)

- DMDD & BD are **similar** in their ability to **decision-making task** in **rewards and punishments of different value**. *(Rau, 2008)*

- **Emotional Attention Interrupt task** results **differ** between DMDD & BD. *(Rich, 2010)*

- **Neural pathways** to **negative affect** **differ** between DMDD & BD. *(Rich, 2011)*

- Proton magnetic resonance spectroscopy measures of 3 **neurometabolites** (***myo-inositol*** *an intra-cellular second messenger linked to* ***BD, glutamate*** *the major* ***excitatory*** *neurotransmitter,* ***N-acetyl aspartate*** *a neuronal* ***energetic***), **differ** between DMDD & BD. *(Dickstein, 2008)*

- DMDD & BD have **deficit in motor inhibition**, but the **neural recruitment** differ between them. *(Deveney, 2012)*

4. Socio-demographic factors:

- Rate of **BD** in youth & adults **do not differ** by **gender**
  (Brotman, 2007; Birmaher, 2009).

- **DMDD** is more common in **boys *(2-3 fold).***
  (77.6% in epidemiological & 66.7% in clinical sample)
  (Brotman, 2006; Stringaris, in revision)

- **DMDD lower age** of **onset** vs. BD

5. Comorbidity:

- **DMDD higher comorbidity** with **ADHD** & **ODD** vs. BD.

  (Dickstein, 2005)

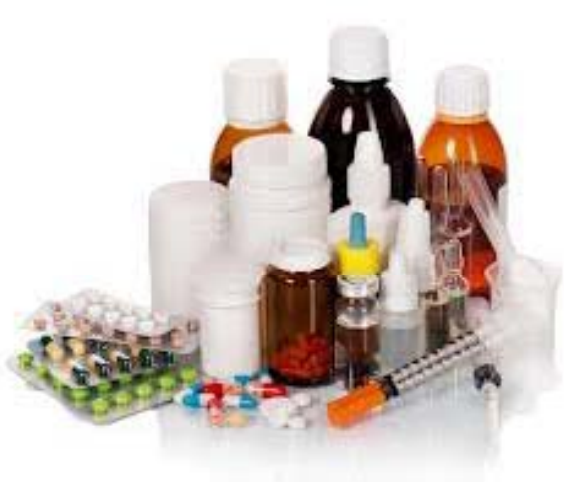
6. Treatment Response:

- Positive response to lithium in BD Children in RDB studies.
  (Carlson, 1992; Delong , 1987; Geller, 1998a; Gram, 1972; McKnew, 1981; Kafantaris, 2004)

- No response to lithium in DMDD youth.
  (n=45, ages 7–17 , RCT, lithium 0.8-1.2 meq/lit, 6 weeks)
  (Dickstein, 2009)

- Risperidone shorten the duration of rage episodes in DMDD & BD.
  (n=151, ages 5-12)
  (Carlson, 2010)

- MPH is effective in children with ADHD & DMDD.
  (68 ADHD, 33 ADHD+DMDD, ages 5–12)
  (Waxmonsky, 2008)

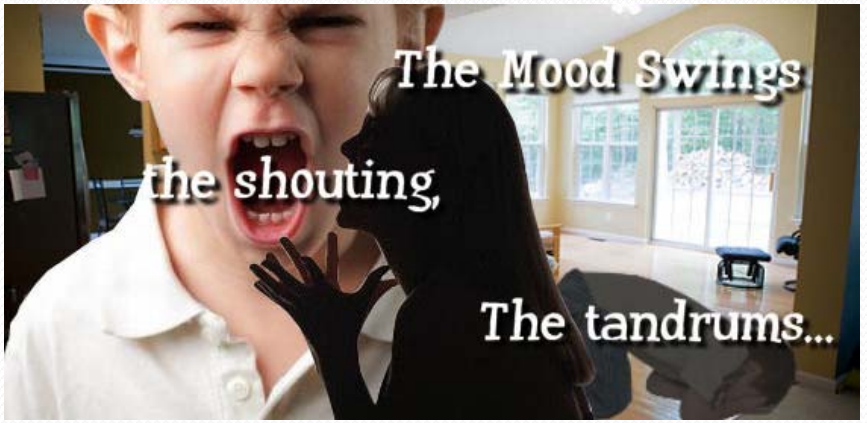


DMDD & BD are severe psychiatric disorders

- Have prominent **mood** symptoms at **presentation**
- & **long-term impairment** from later mood symptoms.

But **differ** in:

- **Age** of onset
- **Gender** distribution
- **Pathophysiology**
- **Familial** aggregation
- **Outcome**
- **Comorbidity**
- **Treatment** response



Is severe, non-episodic irritability a developmental presentation of BD?

NO!

Severe, non-episodic irritability is NOT a developmental presentation of BD.

It SHOULD NOT be in the BD category!

Is DMDD a form of BD?

or

on continuum with

Anxiety disorders, Unipolar Depression, & ADHD?

This has important treatment implications!

- If DMDD is a form of **BD**, the **1st line** treatment would be **mood stabilizers** &/or **atypical antipsychotics.**

- If DMDD is on the continuum with **anxiety disorders, unipolar depression, & ADHD**, the **1st** line treatment would be **SSRIs** & **stimulants** (which are relatively **contraindicated** in **BD**).

Potential harms associated with not adding DMDD as a diagnosis in DSM:

1. There is not any **category** for these severely impaired children.

2. **Diagnosis of BD** will be assigned to youth who do not meet BD criteria.

3. Diagnosis of BD for DMDD youth may result in **suboptimal treatment.**

Potential harm associated with adding DMDD as a diagnosis:

- DMDD will become **prematurely reified**, despite relatively **little research** on it.

Guidelines for change in DSM:

1. **Scientific** evaluation of the **evidence**
2. **Clinical** concerns

New disorders could be proposed in DSM in order to:

1. **Identify** people who need **clinical attention** *(& there is a **lack** of public **awareness** of this need)*

2. Generating **effective treatments** for a neglected, but important clinical syndrome.

(DSM-5 Task Force Guidelines)

*Weighing of both **scientific & clinical** factors*
*led to propose a **new diagnosis***
*in the **Depressive Disorders** section of **DSM-5**:*

Disruptive Mood Dysregulation Disorder (DMDD)

(Childhood & Adolescent Disorders Work Group,
& Mood Disorders Work Group)