Presentation Goals

- Irritability:
  - When is it abnormal?
  - How do we separate behavioral from environmental?
- Controversy: Understand the problem
- DSM 5: Definition & Criteria
- Research: Temper Dysregulation, Severe Mood Dysregulation, Bipolar (Pediatric), DMDD (primarily retrospective research)
- DMDD is Serious:
  - Research supporting poor outcome
  - Comorbidity (what else occurs with DMDD)
  - Etiology (Possible causes)
- Treatment

Goals of the DSM-5 task force for DMDD

- In defining Severe Mood Dysregulation, the task force had five goals:
  - To operationalize severe irritability reliably, with high threshold, far beyond that of any current DSM-IV diagnosis.
  - To identify youths who are as severely impaired as those with Bipolar Disorder so that any observed differences between severe mood Dysregulation and bipolar disorder could not be attributed to differences in severity.
  - To require symptoms common to mania and ADD, since such symptoms were part of the rationale for assigning the Bipolar Disorder diagnosis to children with severe chronic irritability.
  - To exclude preschoolers and patients whose symptoms did not begin until adolescence, because irritability may fluctuate during these developmental transitions.
  - To exclude youth with even brief episodes of mania, such as those meeting criteria for Episodic Bipolar Disorder, NOS.

History of Mood Disorder

- Mood Disorders were once not well recognized
  - Pre 1970’s
    - Depression was not generally believed to be “possible” in children.
  - Pre 1980’s
    - Bipolar was rarely diagnosed in children.
    - Around 1980, multiple studies reported that ~20% of bipolar adults had symptoms that could be traced to childhood
    - Research indicated better outcome with early intervention

The Rise of Child Bipolar Disorder

- In 1996, an ADHD clinic reported a high frequency of comorbid bipolar disorder in its study patients
  - Credited with triggering increased national interest in this diagnosis

Frequency of Childhood Bipolar

- Actual frequency is controversial
- Some experts assert child bipolar is very common:
  - “Is Your Child Bipolar” by McDonnell and Wozniak
    - states about 4% of all children are bipolar
  - “The Bipolar Child” by Papalos and Papalos
    - states present in 1/3 of all children with ADHD
    - states about 6% of all children are bipolar
Biederman’s and Wozniak’s Research

Pediatric Bipolar Epidemic?

- National studies published in 2007 showed a surge in the diagnosing of Bipolar in children:
  - 40 fold increase in office visits for child bipolar disorder from 1994 to 2003 (Moreno et al, 2007)
    - Correlated with a dramatic increase in the use of antipsychotics to treat child bipolar disorder
  - Blader and Carlson (2007) found that the rate of hospital discharges in the U.S. of youth with a primary diagnosis of BD increased from 1.3 to 7.3 per 10,000 between 1996 and 2004.

Problem: High Child Rates Don’t Match Research

- About 10 times as many kids reported to have bipolar disorder than what we should expect
- Source:
  - About 1% of adults worldwide have bipolar disorder (type I or II)
  - Approximately 40-60% of adult bipolar patients experienced a childhood onset
  - Bipolar disorder is a long term diagnosis
    - So we should expect a child bipolar rate of ~0.4 to 0.6%

Pediatric Bipolar?

- Over the last 15 years, the rates of Bipolar diagnoses in children and adolescents in the US have increased dramatically, both inpatient and outpatient.
- Increased rates occurred parallel with a rise of prescription rates of antipsychotic medication.
- Diagnostic practice seemed to be the most likely explanation for increase
  - Irritability is at the heart of the problem.

Irritability and Bipolar Disorder

- Premise that mania presented differently in youths than in adults.
  - Some researchers suggested that chronic, non-episodic irritability is a core characteristic of Bipolar in children and adolescents.
- This is inconsistent with DSM-IV criteria
  - Specifies a need for a “distinct period of abnormally and persistently elevated, expansive or irritable mood.”
  - Irritable mood is relatively less specific to Bipolar in the DSM-IV, as it required the presence of 4 additional symptoms for the diagnosis to be made
    - Compared with 3 or more for elevated or expansive mood.

The Case for Irritability

- Irritability is present the criteria for a large number of psychiatric disorders.
  - Although not formally defined, irritability refers to easy annoyance and touchiness that can manifest in anger and temper outbursts.

Childhood Development

- Many children are irritable, moody, or upset from time to time.
- Occasional temper tantrums are also a normal part of growing up.
- However, when children are unusually irritable, angry, or present with frequent temper tantrums, both intense and ongoing, it may be a sign of a mood disorder such as Disruptive Mood Dysregulation Disorder.
Chronic Irritability

- Irritable mood is a diagnostic criterion for at least 10 different disorders in DSM
  - Including GAD, PTSD, Depression
  - NOT specific to bipolar
- But, chronically irritable kids are impaired
  - Stimulates a desire to diagnose and treat something
  - Pressure to use label of “Bipolar NOS”

Criticism of Childhood Bipolar

- Massachusetts General Hospital, Psychiatric Unit
  - Accused of driving up the sharp increase in Bipolar diagnoses
  - Proponents of the DMDD challenged views held by the pediatric Bipolar Unit, led by Drs. Joseph Biederman and Janet Wozniak
    - Argued that chronic irritability in youth may be interpreted as a child’s manifestation of a manic episode.
      - Until their research was produced, Bipolar was largely an adult disorder and confined to those who showed distinct episodes of mania and depression.

“Bipolar NOS”

- Bipolar symptoms, but does not meet the full criteria of Bipolar I (mania) or Bipolar 2 (hypomania)
- Since no specific criteria, umbrella of “Bipolar” disorder enlarges

What Becomes of Chronic Irritability?

- Definite increased risk of having major depression as an adult
- Longitudinal studies: almost never found to develop an adult bipolar disorder

Disruptive Mood Dysregulation Disorder Controversy

- Controversies fall in two groups:
  - Concern that the DSM-5 might pathologize normal childhood experiences.
  - Behavior is more accurately described within the bipolar spectrum of disorders.

Criticism for DMDD

- “It is ridiculous and reckless to include an untested diagnosis in an official diagnostic manual that will profoundly affect people’s lives.”
  - Dr. Allen Frances, Duke University
  - DSM-IV chairman
- In a response to questions from the Boston Globe, Dr. Frances further stated that added the new disorder would be equivalent to a “dangerous public health experiment.”
Dysregulated Kids Might Have…
- Disorders:
  - Depression
  - Post-trauma symptoms or syndrome
  - Anxiety
  - Disruptive Behavior Disorders
  - Autism affective lability
  - Other medical (sleep, illness)
- Causative Stressors:
  - Ongoing abuse/neglect
  - Environmental instability
  - Temperament mismatch with parental expectations

Criticism for DMDD cont.
- Axelson et al. (2011)
  - Diagnosis rests on 2 primary criteria:
    - Recurrent severe temper outbursts
    - Chronically irritable and/or sad mood
  - Because temper outbursts are a behavioral manifestation or irritable mood, DMDD can be fulfilled with the presence of a single symptoms, making it unlikely to be categorically distinct form ODD
  - Scientific research is limited
    - Most of the research has emerged from a single research group.
    - Most of the research has focused on an overlapping but distinct population with Severe Mood Dysregulation.

Proponents of DMDD
- Dr. Ellen Leibenluft
  - National Institute of Mental Health
  - One of eight members of the childhood disorders panel of the APA
- Argues that a subset of children diagnosed with Bipolar whose symptoms fit the new diagnosis and should be treated different.
- Research will be discussed later in the presentation.

Missing a Diagnosis of Bipolar
- Delay in diagnosis leads to worsening due to lack of appropriate treatment.
- Study by Post et al. 2010
  - Retrospective study of 529 adults with Bipolar.
  - Delay of first treatment was found to correlate with fewer days spent well, severity and time spent depressed, and number of episodes in adulthood.
- Therefore, it is important to differentiate between Bipolar from other disorders early and to recognize any comorbidities.

Narrow vs. Broad Bipolar
- Narrow Phenotype
  - Strict Bipolar
  - Meets DSM-IV criteria
- Severe Mood Dysregulation
  - “Broad Phenotype”
  - Characterized by nonepisodic irritability and hyperarousal
  - Earlier onset than Bipolar
  - Higher comorbid rates of ADHD and ODD

Pediatric Bipolar?
- Splitting “true” pediatric bipolar from different variant:
  - A narrow definition that looks like adult BD but BD
  - A different form that includes explosive emotional outbursts that don’t look like mania (no grandiosity, delusions) and are not cyclical
    - Looks a little like ADD, but there may be more aggression.
    - Looks like disruptive behavior disorder, but more emotional lability.
  - Believed that they will not grow up with BD and should perhaps be treated with antidepressants and/or Ritalin.
  - Many will now be diagnosed with Disruptive Mood Dysregulation Disorder (under Depression in the DSM-5).
Irritability

- Leibenleft et al. (2003) conceptualized chronic irritability as a Severe Mood Dysregulation.
  - Allowed for testable comparisons to Bipolar
- SMD: “chronic and severe irritability with frequent and developmentally inappropriate temper outbursts, along with negative mood in between outbursts.”

What does the Research Show?

Bipolar vs. Severe Mood Dysregulation

- Study by Brotman et al. looked at Axis I diagnoses in parents of children with Narrow Bipolar Disorder and parents of youth with severe mood Dysregulation.
- Controversy surrounds the diagnosis of Pediatric Bipolar Disorder.
  - Specifically the nosological status of children with SMD.
- Previous research shows strong heritability for Bipolar
- No data regarding heritability for SMD.
- Study looked at to see if SMD is a phenotype of Bipolar.
  - Results would show that parents of youth with SMD should have Bipolar as often as the parents of youth with narrow phenotype Bipolar.

Bipolar vs. Severe Mood Dysregulation  Cont.

- Results
  - Parents of children with narrow phenotype bipolar disorder were significantly more likely to be diagnosed with Bipolar Disorder.

Bipolar vs. Severe Mood Dysregulation  Cont.

- Table
- Analysis
- Variables
- Results
- Comparison
- Significance
- Heritability
- Genetics
- Environment
- Interaction
- Results
Emotional Processing: SMD vs. ADD vs. Bipolar

- Research has shown that deficits in emotional processing and hyperarousal are prominent features of Bipolar, ADD, and Severe Mood Dysregulation (SMD).
- Brotman et al. compared Amygdala activation during face-emotional and nonemotional rating of neutral faces.
- For both pediatric and adult Bipolar, Amygdala dysfunction is one of the most commonly reported findings in fMRI, with Amygdala hyperactivity being reported in a variety of paradigms.
  - Pavuluri et al. (2007, 2009) found increased amygdala activation during face-emotion processing in pediatric Bipolar.
  - Children with Bipolar rate neutral faces as more hostile and fear producing than comparison groups.
- Differences are associated with Amygdala hyperactivity.

Brotman et al., 2009

Emotional Processing: SMD vs. ADD vs. Bipolar cont.

- Results
  - Nonirritable ADHD youth showed generalized Amygdala hyperactivation (not just with processing faces/emotion).
  - Children with Severe Mood Dysregulation showed Amygdala hypoactivity relative to healthy and those with Bipolar or ADD.
- Findings suggest that there may be functional differences among ADHD, SMD, and Bipolar despite overlapping behavioral deficits and clinical symptoms.

Brotman et al., 2009

Emotional Processing: SMD vs. ADD vs. Bipolar cont.

- Similarities between fMRI findings in Severe Mood Dysregulation and Major Depressive Disorder suggest that SMD is associated with subsequent depressive disorders.
  - Amygdala dysfunction in SMD predicts later Major Depressive Disorder (MDD)?

Brotman et al., 2009

Adolescent Irritability and Genetic Links with Depression

- Oppositional behavior in youth is a predictor of depression in young adults.
- Data suggests that oppositional in youth comprises at least two dimensions:
  - Irritable dimension—more strongly associated with depressive disorders vs. antisocial behaviors.
  - Headstrong/hurtful dimension—associated with antisocial behaviors vs. depressive disorders.
- Stringaris et al. (2012) tested the hypothesis that the association between irritability and depression is accounted for by genetic factors.
  - Generalist Genes: genes of general effects that underlie phenotypic overlap between disorders.

Adolescent Irritability and Genetic Links with Depression Results

- Irritability was related to subsequent depressive symptoms, whereas headstrong/hurtful dimension was associated with delinquency.
TEMPER TANTRUMS

- Normal part of childhood
- "There are children whose low frustration tolerance and behavioral dyscontrol transcend those of normal human experience; their affective Dysregulation not only is not distressing to their parents, teachers, and classmates, but also is upsetting to the affected children and threatens to derail their normal development."

John W. Barnhill, M.D., "DSM-5 Clinical Cases"

DIAGNOSTIC QUESTIONS

Diagnostic Questions - Irritability

- Irritability screening questions for children: Do you ever lose your temper, yell, or act out?
  - If yes, proceed to DMDD criteria
  - If no, seek collateral information from caregivers or proceed to another diagnostic category

Disruptive Mood Dysregulation Disorder

- Many who meet criteria for Disruptive Mood Dysregulation Disorder will also meet criteria for Oppositional Defiant Disorder
- A minority of youth with Oppositional Defiant Disorder will meet criteria for Disruptive Mood Dysregulation Disorder, because the latter is considerably more severe
- Youth who meet criteria for both Oppositional Defiant Disorder and Disruptive Mood Dysregulation Disorder should only be assigned the diagnosis of Disruptive Mood Dysregulation Disorder
**PREVALENCE**

**Increased Mood Recognition**
- About 20% of children will experience an episode of major depression before the age of 18.
  - At any one point in time, up to 2% of pre-pubescent and up to 8% of post pubescent children have depression.
- Frequency of bipolar disorder is controversial.
  - Reports range from 0.6% to 6%.

**Hilt, MD, 2012**

**Depression in School Age Children**
- Typically presents with:
  - Behavior problems and social withdrawal
  - Irritable or angry mood
    - More common than sad mood
  - Re-appearance of tantrums
  - Body complaints like stomachaches, headaches, and fatigue.
- Usually do not see excessive sleep/fatigue like with adults.

**Hilt, MD, 2012**

**Prevalence, Comorbidity, and Correlates of DMDD**
- Copeland et al. (2013) reviewed three community studies to estimate prevalence, comorbidity, and correlates of DMDD in community populations.
  - Studies:
    - The Duke Preschool Anxiety Study
    - The Great Smokey Mountains Study
    - Caring for Children in the Community
  - Prevalence rates were estimated from studies involving 7881 observations of 3258 participants from 2 to 17 years old.

**Hilt, MD, 2012**

**Study Demographics**

<table>
<thead>
<tr>
<th>Character</th>
<th>Duke Preschool Anxiety Study</th>
<th>Great Smoky Mountains Study</th>
<th>Caring for Children in the Community</th>
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<tr>
<td>subjects</td>
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<td>sex</td>
<td>51.6%</td>
<td>49.2%</td>
<td>50.0%</td>
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<td>mean</td>
<td>42.1%</td>
<td>41.3%</td>
<td>41.3%</td>
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<td>SD</td>
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<td>Preschool Age Psychiatric Assessment</td>
<td>Child and Adolescent Psychiatric Assessment</td>
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**Prevalence Rates**

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<th>Study</th>
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<th>Depression</th>
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<th>Total</th>
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<tr>
<td>Rate</td>
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<td>57.6%</td>
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<td>7881</td>
<td>7881</td>
<td>7881</td>
<td>7881</td>
</tr>
<tr>
<td>n%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Studies are weighted and F-values are unweighted. The criteria that a child must be at least 5 years old to be diagnosed with attention-deficit/hyperactivity disorder was not applied. The exclusion criteria were not applied, and rates with applying exclusion criteria are provided in Table 2.
Co-Occurrence Rates of DMDD

- DMDD Only
- DMDD+INT: DMDD plus emotional disorders - Anxiety, depression
- DMDD+EXT: DMDD plus behavioral disorders - Conduct disorder, Oppositional defiant disorder, or ADHD
- DMDD+Both: DMDD plus both emotional and behavioral disorders

Comorbidity

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<thead>
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<th>Comorbidity</th>
<th>No Diagnosis</th>
<th>Any Diagnosis</th>
<th>MDD</th>
<th>Anxiety</th>
<th>ODD</th>
<th>Conduct Disorder</th>
<th>ADHD</th>
<th>Sex</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Problems Anxiety Study</td>
<td>29.0</td>
<td>39.4</td>
<td>1.4</td>
<td>9.0</td>
<td>4.1</td>
<td>23.7</td>
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<tr>
<td>Anxiety</td>
<td>72</td>
<td>126</td>
<td>9.9</td>
<td>6.1</td>
<td>19.9</td>
<td>9.9</td>
<td>8.0</td>
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<td>ODD</td>
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<td>177</td>
<td>11.7</td>
<td>7.0</td>
<td>3.6</td>
<td>3.5</td>
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<td>16.1</td>
<td>7.3</td>
<td>3.6</td>
<td>3.5</td>
<td>1.1</td>
<td>0.004</td>
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<tr>
<td>ADHD</td>
<td>7.7</td>
<td>16.1</td>
<td>7.3</td>
<td>3.6</td>
<td>3.5</td>
<td>1.1</td>
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<td>9.9</td>
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<td>9.9</td>
<td>9.9</td>
<td>9.9</td>
<td>0.003</td>
<td></td>
</tr>
</tbody>
</table>

Results

- DMDD occurred at relatively low rates in the community.
  - Most often occurred with other psychiatric disorders.
- Propensity toward comorbidity extended to all common psychiatric disorders, but was strongest for ODD and depressive disorders.
- DMDD was comorbid with psychiatric disorders and was associated with high levels of social impairment, school suspension, all types of service use, and family poverty.
Disruptive Mood Dysregulation Disorder

• Many who meet criteria for Disruptive Mood Dysregulation Disorder will also meet criteria for Oppositional Defiant Disorder
• A minority of youth with Oppositional Defiant Disorder will meet criteria for Disruptive Mood Dysregulation Disorder, because the latter is considerably more severe
• Youth who meet criteria for both Oppositional Defiant Disorder and Disruptive Mood Dysregulation Disorder should only be assigned the diagnosis of Disruptive Mood Dysregulation Disorder

DIFFERENTIAL DIAGNOSIS & ETIOLOGY

NIMH

• Studying SSRI & Stimulant treatment for DMDD
• However, remember they are really using criteria for SMD:
  – Basically DMDD with Activation (ADD SYMPTOMS)

Possible etiology

• “True” bipolar-lifelong
• Other medical: head trauma, Lyme disease...
  – Sleep
  – ASD
  – Severe ADHD
• Anxiety/High Beta
  – Trauma
• Mood/Depression
• ODD/Behavioral
• Cortical Dysrhythmia
• Ring of Fire

DMDD THRU Three lenses

BRAIN SYSTEMS
• Amen subtypes:

NEUROTRANSMITTERS
• Horachek subtypes

BRAIN ACTIVITY
• Raw EEG
• Quantitative EEG

“TRUE BIPOLAR”
Bipolar I and Bipolar II Disorders

- Characterized by episodic illnesses with discrete episodes of mood perturbation that are distinguishable from the child’s baseline.
- The change in mood during a Manic or Hypomanic Episode is accompanied by increased energy and activity as well as associated cognitive, behavioral, and physical symptoms
  - Distractibility, rapid speech, decreased need for sleep
- In contrast, the irritability of DMDD is persistent and present chronically over many months.

What about “True” Bipolar?

- Defined by the Overall Pattern
  - Hypomania/mania involves discrete episodes of mood change of 4+ days
  - Episodes are a clear departure from baseline functioning
  - “Hallmark” symptoms (per B. Geller/E. Leibenluft)
    - Elation
    - Grandiosity
    - Increased energy/goal directed activity
    - Hypersexuality
    - Decreased need for sleep

Hilt, MD, 2012

Power of Bipolar Family History

- Increases chance of a child developing bipolar, but not dramatically
  - first degree relative bipolar disorder, increases likelihood by 5x
  - second degree relative bipolar, increase likelihood by 2.5x
  - Even given a generous prevalence of 2% bipolar in the population, most children of a bipolar parents (~90%) will not have bipolar disorder

Youngstrom E & Dunn L, JAACAP 44:7, 2005
Hilt, MD, 2012

Course Of True Bipolar Disorder

- Substance Abuse in up to 60%
- Anxiety disorders in up to 50%
- Psychotic features in up to 50%
- Relationship Disruptions
- Work Disruptions
- Hospitalizations
- Suicidality
  - Reported up to 15% eventually complete suicide

Stern TA and Herman JB, 2004
Hilt, MD, 2012

Bipolar Treatments

- Atypical antipsychotics
- Mood Stabilizers
- Combination therapy
- Antidepressants, if used cautiously
- Family therapy (support/education/adherence)
- Sleep hygiene
- Psychotherapy for:
  - depression treatment
  - coping skills
  - supporting medication treatment adherence

Hilt, MD, 2012

Differential DX and Comorbidity

- Juvenile Bipolar is rarely independent
- Improper dx can result in children who are not Bipolar being given medications (ex: lithium) which are ineffective at treating symptoms of other conditions such as ADD or TDDD-like syndrome.
  - Potential for adverse side effects

Hilt, MD, 2012
Bipolar and ADHD

• Share 5 overlapping symptoms:
  – Over talkativeness
  – Distractibility
  – Physical restlessness
  – Lack of inhibition
  – Inappropriate responses to social situations

• Comorbidity
  – 62% comorbidity rate
  – Geller et al. (1998)
    • Compared youth with Bipolar and ADD vs. control
    • Found that social anxiety, excessive sleep, racing thoughts, and all other mania items, except for excessive energy and distractibility, were significantly more frequent among children with Bipolar than ADD.
    – Elston: 86.7% BP vs. 3% ADHD

Bipolar Comorbidities

• Birmaher et al (2006)
  – ADD is more common in prepubertal Bipolar
  – Panic, conduct, and substance abuse disorders were more common in adolescent onset Bipolar.

• Axelson et al. (2006)
  – Anxiety
  – Comorbidity is seen approximately 39% of youth with Bipolar
  – More common in Bipolar II (60%)

• Youth with Bipolar have higher rates of substance use disorders than youth with other psychiatric illnesses.
  – ~16% (B.I. Goldstein et al. 2008)

Substance/Medication-Induced Depressive Disorder

• Characterized by the dysphoric symptoms that are due to the direct physiological effects of a substance or medication

Depressive Disorder Due to Another Medical Condition

• Characterized by dysphoric symptoms that are due to the direct physiological effects of an identified medical condition.

Temper Tantrums: Case Study

- Zack is an 8 year old boy brought to a specialty child psychiatric clinic due to increasing tantrums and somatic complaints without apparent cause.
- Zack's mother reported that the symptoms appeared related to the nights that he spent with his aunt.
- Started spending every Friday night with her when his mother took on a night shift at work.
- 2 months prior to the consultation, Zack reported nausea and headaches on Fridays and complained that his aunt's house was "creepy."
- In recent weeks, Zack screamed and hid when it came time to go to his aunt's home.
- Zack had no objections to seeing his aunt/cousin anywhere else.
- Zack had never previously had particularly significant separation, behavioral, or emotional issues.
- Zack has yet to achieve consistent overnight continence, however, and did wet the bed approximately twice weekly.
- Family history was negative for all psychiatric illness on this mother's side.

David H. Rubin, M.D., "DSM-5 Clinical Cases"
Temper Tantrums: Case Study

- Diagnosis:
  - Enuresis, nocturnal only

Case Study: Brendan

- Brendan is a 10 year old male who came to the clinic for a cognitive assessment due to concerns about:
  - Reading/writing
  - ADHD

- Medical history
  - Brendan had a head injury at 4 years of age.
    - Running and fell, hitting his head on the floor boards
    - Required 4-5 staples to mend the wound
Case Study: Brendan’s QEEG

- Intermittent slowing in frontal region—predominantly left.
- Neurologist recommendation:
  - Positive TBI is consistent with previous history of head injury and abnormalities in raw EEG should be further investigated with sleep deprived EEG and activating procedures to rule out any seizure activity.

SLEEP

Different than adults, children when tired often become:

Hyperactive & Irritable

As many as 1 out of nine students lack restorative sleep

- Impeded sleep can present as problems with inattention, inability to focus, and distractibility
- Many children present with learning difficulties, aggression, cognitive deficits
- Excessive daytime sleepiness can be perceived as ‘teenage laziness’ results in reduced academic function and extracurricular performance

Danny

- 11 Year old boy
- Fifth Grade
- Diagnosed ADHD 2nd grade
- Treated with Concerta
  - More alert, better able to attend
  - Irritability especially in late afternoon
  - Parents report better academics, but
  - “He is not himself when taking medication”
**Too much activity between sites**

**Causes:**
- Delta: Sleep Disorder/Chronic Poor Sleep
- T&A, 6 months later—symptoms resolved

**MISDIAGNOSIS**

- 25% of children ages 5-7 with ADHD symptoms of
  - Inattention
  - Impulsivity or
  - Over activity
- Were found to have a sleep disturbance (light sleeper or heavy snorer)
- They were simply **OVERTIRED**

*Pediatrics Journal, March 2003*

**Autism Spectrum Disorder**

- May be characterized by temper outbursts, especially when routines are disturbed.
- If the temper outbursts are better explained by Autism Spectrum Disorder, then DMDD is not diagnosed.
- Remember that a new change to DSM 5
  - A child can now be diagnosed with both ADHD & ASD
  - Recognizes significant research in last decade

**Bipolar Comorbidities**

- **ASD**
  - 2-11% in children with Bipolar
  - Children with Bipolar and ASD have shown to have worse clinical and neuropsychological functioning and outcome than children with only Bipolar.
SEVERE ADHD

PFC Problems
- Short Attention Span
- distractibility
- Impulsivity
- Procrastination
- Disorganization
- Poor Judgment
- Poor Planning
- Conflict Seeking

ADHD: Off and on Adderall

DOPAMINE

Dopamine Low
- INATTENTIVE
- DISTRACTABLE
- DISORGANIZED
- NOVELTY BIAS
- EASILY BORED
- LATE
- CREATIVE
- DIGRESSIVE

Electroencephalography (EEG)
- Dr. Hans Berger (1873-1941)
- Brain shows continuous electrical activity

First EEG recording
**EEG**

**Diagnostic Concerns**

**BILLY**

- 8 Years old
- Poor response to stimulant trial—increased tantrums
- Easily frustrated, especially when communicating
- Many serious behavior problems at school and home
- Reading issues

**Meta-Analysis of Quantitative EEG Power Associated with ADHD**

- Relative Theta Power / Relative Beta Power
  - Pooled Effect Size is 3.08 versus normal controls
  - 95% Confidence Interval
  - “Large” Effect Size
  - 9 Studies total N=1498

  - Sensitivity – 86 – 90%
  - Specificity – 94 – 98%


**DIAGNOSTIC CONCERNS**

- Rating Scale vs. QEEG Accuracy
  - False Positive
  - False Negative
  - Accuracy

**BILLY**

- 8 Years old
- Poor response to stimulant trial—increased tantrums
- Easily frustrated, especially when communicating
- Many serious behavior problems at school and home
- Reading issues
Diagnostic Overlap Example: ADHD and Bipolar

- Mania symptoms, during period of abnormal mood:
  - Distractible
  - Flight of ideas/racing thoughts
  - Activity (goal directed) increase
  - Talkative (pressured speech)
  - Indiscretions/risk taking
  - Sleep need decreased
  - Grandiosity

- All but the last two are ADHD symptoms easily re-interpreted as “bipolar”

Hilt, MD, 2012

• Expressive Language Disorder
• ADHD

ANXIETY

Anxiety Disorders

- Children’s whose irritability is manifest only in anxiety-provoking contexts should receive the relevant Anxiety Disorder diagnosis rather than a diagnosis of DMDD.
- If the irritability extends outside of the anxiety-provoking situations, diagnoses for both DMDD and the Anxiety Disorder may be appropriate.
**Basal Ganglia Problems**

- Anxiety, panic
- Conflict avoidant
- Predicts worst
- Tics, Tourette’s
- Fine motor problem
- Motivation issues

**Noradrenaline High**

- Over aroused
- Sensitive
- Fearful
- Intense emotions
- Indignant
- Angry
- Hyper motoric
- Impatient
- Insomnia
- Slender
- Sensitive stomach

---

**Arousal Spectrum of Cognitive Dysfunction in ADHD with Deficient Arousal**

- Deficient arousal
- Excessive arousal
- Cognitive dysfunction
- Halucinations/psychosis
- Insomnia
- Slender stomach

**Treating ADHD by Desensitizing Arousal in Prefrontal Cortex**

- Deficient arousal
- Excessive arousal
- NE/DA firing
- Phasic and tonic firing
- Substance abuse
- Anxiety
- Atomoxetine
- Guanfacine ER

---

**PHARMACOLOGICAL TREATMENT OF ADHD**

- Alpha 2A adrenergic (NE) agonists have been used in ADD since the 1980s (Hunt 1985, 1987)
- Operate predominantly in prefrontal area
- A number of studies have shown clonidine & guanfacine helpful, especially for calming motor over-activity, impulsiveness & temper in ADD & PDD/ASD
- Both medications are approved for reducing hypertension in those over 12 years of age
- Guanfacine (Tenex) has been marketed since 1986

**PHARMACOLOGICAL TREATMENT OF ADHD**

- Research studies are consistently showing efficacy with ADD (p<.006) across dosage groups and throughout day
- Working memory and executive functioning show improvements along with behavioral improvements
- Use with comorbid anxiety, tics, aggressive behavior supported
- A variety of research indicate potential benefit for excessive D1 stimulation brought on by chronic stress. (see Sallee, F. Medscape Review, 2009).
Proposed: A New ADHD Subtype
Over Aroused

- Hypersensitivity to amygdala firing
- Flight, fight, freeze
- Over-aroused vs. under aroused state
- Too fast & too much activity
- Comorbid with physiological anxiety
- Headaches/stomachaches
- Comorbid with temper & aggression
- Often comorbid with tics

Case Study: Katelyn

- Katelyn is a 9 year old female who came to the clinic for an assessment due to behavior problems at home and school.
- Katelyn’s mother was concerned about her anger and low frustration tolerance.
- Previously diagnosed with:
  - ADHD, Combined Type
  - R/O Reactive Attachment Disorder
- On symptoms inventory, based on DSM criteria, parents reported the following:
  - 4 of 9 symptoms of inattention
  - 1 of 6 symptoms of hyperactivity
  - Symptoms of anger:
    - Loses temper, argues with adults, defies or refuses what you tell her to do, does things deliberately to annoy others, blames others for mistakes or misbehaviors, is touchy or easily annoyed by others, is angry and resentful, takes anger out on others or tries to get even.

Case Study: Katelyn's QEEG

- Anterior regions demonstrate some faster frequencies
- Occasional slowing in the frontal regions and phase reversal in the frontal regions
- QEEG demonstrates a negative ADD but presence of high beta will mimic symptoms. Use of stimulants can exacerbate the problem

Increased stress . . .

- Increases cortisol levels in the brain
- Makes learning even more difficult
- Increases activity in the brain involved in vigilance and arousal (the "flight or fight" responses)
- The brain interprets others’ actions as threatening and in need of an aggressive response

THE MOST RECENT RESEARCH

- Indicates that our children’s reactivity to stress is becoming more disrupted
- It is essential that they learn methods to modify the toxic effects of cortisol
- Relaxation Response is ESSENTIAL
  - For Self Control of Anxiety & Anger
  - Mediate Depression
  - Maintain Learning & Memory
  - Long Term Brain Health
MOOD
DEPRESSION

Major Depressive Disorder

- Children whose irritability is present only in the context of a Major Depressive Episode should receive a diagnosis of Major Depressive Disorder rather than DMDD.
- If the irritability extends outside the depressed episodes, both diagnoses may be appropriate.

Very Young Children

- Depression in Preschool age children is still being investigated.
  - Reported to occur in up to 1% of preschoolers
  - Situational triggers are common:
    - Neglect
    - Abuse
  - Preschoolers with depression look different:
    - Much less likely to have an internal sense of feeling “depressed”
    - Most predictive symptom:
      - Losing interest in previously enjoyed activities
    - For 98%, presenting symptom is Irritability or Sadness

Serotonin

- Moody
- Disinhibited
- Obsessive
- Worried
- Migraines
- Insecure
- Needy

Limbic System Problems

- Sad, moody
- Irritable
- Negative thoughts
- Low motivation
- Sleep/appetite
- Social isolation
- Loss of libido

Hilt, MD, 2012
Serotonin Low

- Stuck on thoughts
- Stuck on behaviors
- Perfectionistic
- Distracted more by thoughts than stimuli
- Fragile, vulnerable
- Pessimistic - glass half full
- Intense longing to have someone or something help feel less insecure, lonely, & empty
- Once starts arguing, hard to stop

Susan

- 9 Year old girl in 3rd grade
- Two previous assessments
- Diagnosed with ADHD both times
- Initial positive response to stimulants
- After 8-12 weeks became more moody & irritable
  - "I'm no good" "I just want to die"
- Ritalin, Concerta, Adderall, Methadate
- Therapy (play and family) for 1+ years
- Neurolex ADHD Indicator POSITIVE

NeuroLex

Order Number: 13244  Code: Blend

Eyes Closed Raw Data Analysis

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Causes:
- Mood Component
- May respond to SSRI

UCLA Department of Neuroscience QEEG Unit

Studying QEEG as predictive of Med Response

Outcome

- Mood improved
- No negative/suicidal thoughts

At six month follow-up:
  - Attention & mood significantly improved

Odd: Oppositional
Oppositional Defiant Disorder
- Characterized by a pattern of angry/irritable mood, argumentative/defiant behavior, or vindictiveness.
- If criteria are met for both disorders, only DMDD is diagnosed.

Serotonin Low-Noradrenaline High
- High Energy
- Impulsive
- Agitated depression

SL-NH
- Keyed Up-angry
- Argumentative
- Extreme mood swings
- Oppositional
- Critical of others
- Defensive
- High Energy moves & talks a lot
- Headaches & stomachaches
- “Just sticking up for what is right”
- Apprehensive-vigilant

Cingulate Problems
- Worrying
- Holds grudges
- Stuck on thoughts
- Stuck on behaviors
- Addictive behaviors
- Oppositional/argumentative

ODD

Case Study: Virginia
- Virginia is a 10-year-old female who was referred by her audiologist for a cognitive assessment.
- Virginia’s parents reported that she struggled with her academics and were concerned about bad temper, approach to academics (lack of detail to complete tasks), and her reaction in school on a daily basis.
- On symptoms inventory, based on DSM criteria, Virginia’s parents reported the following:
  - 6 of 9 symptoms of inattention
  - 5 of 8 symptoms of defiance:
    - Loses temper, argues with adults, blames others for own misbehaviors or mistakes, is easily annoyed by others, is angry and resentful, takes anger out on others
  - 2 of 6 symptoms of a phobia
    - Virginia had difficulty controlling her anger.
    - Her temper tantrums were described as “impressive”
    - Stomps feet, yells, slams doors/cupboards, and occasionally breaks things
    - When things do not go her way, she is described as “explosive” and “waiting to ignite”
  - Virginia has had numerous developmental evaluations including:
    - Auditory processing
    - Speech/language pathology
    - Unintegrated reflexes
Case Study: Virginia cont.

- Social skills:
  - Feels uncomfortable around people she does not know well.
  - Feelings are often or easily hurt.

- Sensory integration:
  - Particularly sensitive to certain clothing or tags on clothing.

Diagnosis
- Adjustment Disorder with Mixed Disturbance of Emotions and Conduct
- Sensory Processing Disorder
- Anxiety, NOS
- R/O ADHD

Case Study: Virginia's QEEG

- Falls outside normal limits at 7.53

CORTICAL DYSRHYTHMIA

Temporal Lobe Functions

- Non-dominant
  - Rhythm, music
  - Read faces, social cues
  - Recognize problems

Temporal Lobe Problems-1

- Emotional instability
- Memory problems
- Feeling of panic
- Spaciness, confusion
- Illusions/shadows
Temporal Lobe Problems-2

- Headaches
- Abdominal pain
- Mild paranoia
- External aggression
- Internal aggression
- Learning struggles

Case Study: Andrew

- Andrew is a 10 year old male who was referred by his psychologist for an ADHD evaluation.
- Andrew’s parents reported that he struggles with: attentiveness, organization, memory, and shy behaviors.
- Andrew’s parents reported that he often defies them and throws tantrums which include: pounding on walls, slamming doors, and yelling.
  - With physical contact,
- On symptoms inventory, based on DSM criteria, Andrew’s parents reported the following:
  - 9 of 9 symptoms of inattention
  - 3 of 6 symptoms of hyperactivity
  - Symptoms of opposition:
    - Loses temper, argues with adults, defies or refuses what he is told to do, does things to deliberately annoy others, blames others for own mistakes or misbehaviors, is touchy or easily annoyed by others, is angry or resentful, takes anger out on others or tries to get even.

Case Study: Andrew’s QEEG

- Irregularities in the frontal temporal regions
- Recommended sleep deprived EEG with photic stimulation and hyperventilation
- Learning disorder and somewhat EEG are the only significant findings.

RING OF FIRE

Normal Brain Internal Scan

Bipolar Brain Internal Scan
Ring of Fire

Serotonin Low & Dopamine Low
Noradrenaline High

- Over Aroused
- Disinhibited
- Impulsive
- Moody
- Tics
- Cognitive
  - Inattentive
  - Distractible
  - Disorganized

Case Study: Alexis

- Alexis is a 7 year old female who presented to the clinic due to concerns about: ADHD, defiant behaviors, and inability to learn from consequences.
- On symptoms inventory, based on DSM criteria, Alexis’ parents reported the following:
  - 7 of the 9 symptoms of inattention
  - 4 of the 6 symptoms of hyperactivity
  - 3 of the 3 symptoms of impulsivity
- Conduct Disorders (ODD):
  - Loses temper, argues with others, blames others for own misbehaviors or mistakes, is touchy or easily annoyed by others, is angry and resentful, takes anger out on others or tries to get even, lies to get things or to avoid punishment.
- Anxiety:
  - Excessive worry, is on edge most of the day, difficulty staying asleep, excessive fear.
- Other symptoms:
  - Laughs or cries at inappropriate times
- Adderall XR helped with some of her symptoms of inattention and impulsivity, but has serious side effects including:
  - Extreme difficulty falling asleep at night
  - Permanent suppression
- Alexis’ school social worker reported that Alexis performs well academically, but struggles with behavioral regulation.
  - Tends to be “off-task and defiant, but manageable.”

Case Study: Alexis

- Diagnosis:
  - Disruptive Mood Dysregulation Disorder
- Vigilance was increased with medication, but maybe associated with management of fatigue.
- Alexis and her parents that she experiences great difficulty in sleeping and the fatigue that results from this may be countered by stimulant medication.
- Sleep interventions may be considered as these might ultimately be more effective.
- Alexis’ parents were strongly recommended to focus on stabilizing and regulating Alex’s behavior, sleep, and nutrition.
- Recommendations for behavior:
  - Stabilizing consequences and working on behavior modification
  - Parent training to implement appropriate and effective interventions
  - Nutrition: “Little Sugars Addict’s Complete Recovery Program” by Kathleen DesMaisons
  - Develop skills for coping with negative thoughts.
  - “Stamp out ANTS” Model

Case Study: Alexis’s QEEG

- Within normal limits with Theta/Beta ratio=2.00

Intermittent Explosive Disorder

- Characterized by aggressive outbursts that can resemble the severe temper tantrums in DMDD; however, there is no persistent irritable or angry mood between outbursts as in DMDD.
- Intermittent Explosive Disorder requires only 3 months of active symptoms, in contrast to the 12-month requirement for DMDD.
- Intermittent Explosive Disorder is not diagnosed if the criteria are met for DMDD.
Medications will not resolve:

• Family stress/conflict
• Poor parenting strategies
• School stress/conflict
• Strong willed temperament
• Intellectual deficits
• Developmental impairments

THANK YOU!

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