Pediatric Bipolar Disorder and ADHD

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September 4, 2007

Bipolar Illness Soars as a Diagnosis for the Young

By BENEDICT CAREY

The number of American children and adolescents treated for bipolar disorder increased 40-fold from 1994 to 2003, researchers report today in the most comprehensive study of the controversial diagnosis.

Experts say the number has almost certainly risen further since 2003.

Many experts theorize that the jump reflects that doctors are more aggressively applying the diagnosis to children, and not that the incidence of the disorder has increased.

But the magnitude of the increase surprises many psychiatrists. They say it is likely to intensify the debate over the validity of the diagnosis, which has shaken child psychiatry.
Mood Disorders affect 14.3% of Adolescents
Bipolar Disorder affects 2.9% of Adolescents
TABLE 2 Lifetime Prevalence of DSM-IV Disorders by Sex and Age Group and Severe Impairment in the National Comorbidity Survey–Adolescent Supplement (NCS-A)

<table>
<thead>
<tr>
<th>DSM-IV Disorder</th>
<th>Sex</th>
<th></th>
<th></th>
<th>Age</th>
<th></th>
<th></th>
<th>Adolescents with Severe Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>%</td>
<td>SE</td>
<td>Male</td>
<td>%</td>
<td>SE</td>
<td>13-14 y</td>
</tr>
<tr>
<td>Mood disorders</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Major depressive disorder or dysthymia</td>
<td>15.9</td>
<td>1.3</td>
<td>7.7</td>
<td>0.8</td>
<td>8.4</td>
<td>1.3</td>
<td>12.6</td>
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<td>Bipolar I or II</td>
<td>3.3</td>
<td>0.4</td>
<td>2.6</td>
<td>0.3</td>
<td>1.9</td>
<td>0.3</td>
<td>3.1</td>
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<tr>
<td>Any mood disorder</td>
<td>18.3</td>
<td>1.4</td>
<td>10.5</td>
<td>1.1</td>
<td>10.5</td>
<td>1.3</td>
<td>15.5</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Agoraphobia</td>
<td>3.4</td>
<td>0.4</td>
<td>1.4</td>
<td>0.3</td>
<td>2.5</td>
<td>0.4</td>
<td>2.5</td>
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<td>Generalized anxiety disorder</td>
<td>3.0</td>
<td>0.6</td>
<td>1.5</td>
<td>0.3</td>
<td>1.0</td>
<td>0.3</td>
<td>2.8</td>
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<tr>
<td>Social phobia</td>
<td>11.2</td>
<td>0.7</td>
<td>7.0</td>
<td>0.5</td>
<td>7.7</td>
<td>0.6</td>
<td>9.7</td>
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<td>Specific phobia</td>
<td>22.1</td>
<td>1.1</td>
<td>16.7</td>
<td>0.9</td>
<td>21.6</td>
<td>1.6</td>
<td>18.3</td>
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<td>Panic disorder</td>
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<td>0.3</td>
<td>2.0</td>
<td>0.3</td>
<td>1.8</td>
<td>0.4</td>
<td>2.3</td>
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<tr>
<td>Posttraumatic stress disorder</td>
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<td>0.7</td>
<td>2.3</td>
<td>0.4</td>
<td>3.7</td>
<td>0.5</td>
<td>5.1</td>
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<td>Separation anxiety disorder</td>
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<td>0.6</td>
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<td>0.5</td>
<td>7.8</td>
<td>0.6</td>
<td>8.0</td>
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<td>Any anxiety disorder</td>
<td>38.0</td>
<td>1.4</td>
<td>26.1</td>
<td>0.8</td>
<td>31.4</td>
<td>1.9</td>
<td>32.1</td>
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<tr>
<td>Behavior disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Attention deficit hyperactivity disorder</td>
<td>4.2</td>
<td>0.5</td>
<td>13.0</td>
<td>1.0</td>
<td>8.8</td>
<td>0.9</td>
<td>8.6</td>
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<tr>
<td>Oppositional defiant disorder</td>
<td>11.3</td>
<td>0.9</td>
<td>13.9</td>
<td>1.2</td>
<td>12.0</td>
<td>1.2</td>
<td>12.6</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>5.8</td>
<td>1.1</td>
<td>7.9</td>
<td>1.2</td>
<td>4.4</td>
<td>1.2</td>
<td>7.5</td>
</tr>
<tr>
<td>Any behavior disorder</td>
<td>15.5</td>
<td>1.2</td>
<td>23.5</td>
<td>1.6</td>
<td>18.2</td>
<td>1.5</td>
<td>19.5</td>
</tr>
</tbody>
</table>
Pediatric-Onset Bipolar Disorder: Why is it Underdiagnosed?

The symptoms of ADHD and mania overlap and are difficult to disentangle

Talkativeness, hyperactivity (physical agitation/energy), distractibility are symptoms of ADHD and mania

ADHD is a common disorder of childhood (5-10%) and often includes emotional dysregulation
Changes to the Bipolar Diagnosis in DSM-5

A change to **criterion A for Mania** and Hypomania to require in addition to changes in mood

*changes in energy and activity*

ie “a distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy”
Changes to the Bipolar Diagnosis in DSM-5

Removal of the old 'mixed episode' entirely and replacing it with a 'mixed specifier' involving the presence of 3 non-overlapping symptoms from the opposite pole that can be applied to episodes of mania, hypomania or depression...and even to depressions experienced by those with a lifetime dx of unipolar disorder.

FOR example: 2-3 manic or hypomanic symptoms occurring for at least 2-3 days simultaneously with a fully syndromal episode of depression

Used to be ‘mixed’ meant simultaneous presence of fully manic and fully depressive syndrome nearly every day for at least one week.
How to use the mixed specifier:

• Full criteria for a manic or hypomanic episode with at least **3 depressive symptoms** nearly every day:
  – Subjective depression
  – Worry
  – Self reproach/guilt
  – Negative evaluation of self
  – Hopelessness
  – Suicidal ideation or behavior
  – Anhedonia
  – Fatigue
  – Psychomotor retardation
How to use the mixed specifier:

- Full criteria for a major depressive episode with at least 3 **concurrent hypomanic** symptoms:
  - Elevated mood
  - Decreased need for sleep
  - Goal directed activity
  - Increased energy and visible hyperactivity
  - Grandiosity
  - Accelerated speech
  - Racing thoughts
Bipolar NOS

• Will include 3 categories:
  – Subsyndromal
  – Other specified
  – Unspecified due to insufficient information
The New Temper Tantrum Disorder
Will the new diagnostic manual for psychiatrists go too far in labeling kids dysfunctional?
By David Dobbs | Posted Friday, Dec. 7, 2012, at 1:12 PM ET
Disruptive Mood Dysregulation Disorder

DMDD Criteria

A. The disorder is characterized by severe recurrent temper outbursts that are grossly out of proportion in intensity or duration to the situation.
   1. The temper outbursts are manifest verbally and/or behaviorally, such as in the form of verbal rages or physical aggression towards people or property.
   2. The temper outbursts are inconsistent with developmental level.

B. Frequency: The temper outbursts occur, on average, three or more times per week.

C. Mood between temper outbursts:
   1. Nearly every day, most of the day, the mood between temper outbursts is persistently irritable or angry.
   2. The irritable or angry mood is observable by others (e.g., parents, teachers, peers).

D. Duration: Criteria A-C have been present for 12 or more months. Throughout that time, the person has not had 3 or more consecutive months when they were without the symptoms of Criteria A-C.

E. Criterion A or C is present in at least two settings (at home, at school, or with peers) and must be severe in at least in one setting.

F. The diagnosis should not be made for the first time before age 6 or after age 18.

G. The onset of Criteria A through E is before age 10 years.
DMDD Exclusionary Criteria

H. There has never been a distinct period lasting more than one day during which abnormally elevated or expansive mood was present most of the day, and the abnormally elevated or expansive mood was accompanied by the onset, or worsening, of three of the “B” criteria of mania (i.e., grandiosity or inflated self-esteem, decreased need for sleep, pressured speech, flight of ideas, distractibility, increase in goal directed activity, or excessive involvement in activities with a high potential for painful consequences; see pp. XX). Abnormally elevated mood should be differentiated from developmentally appropriate mood elevation, such as occurs in the context of a highly positive event or its anticipation.

I. The behaviors do not occur exclusively during an episode of Major Depressive Disorder and are not better accounted for by another mental disorder (e.g., Autism Spectrum Disorder, Posttraumatic Stress Disorder, Separation Anxiety Disorder, Dysthymic Disorder). (Note: This diagnosis cannot co-exist with Oppositional Defiant Disorder or Bipolar Disorder, though it can co-exist with Attention Deficit/Hyperactivity Disorder, Conduct Disorder, and Substance Use Disorders. Individuals meeting 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.) The symptoms are not due to the effects of a drug or to a general medical or neurological condition.
• Since 2001, the rate of bipolar-disorder diagnosis among children and teens has jumped more than 4,000 percent (times 40).

• Bipolar disorder often gets treated with combinations of antipsychotic and mood-stabilizing drugs (lithium and Risperdal, for instance) that have strong side effects.

• Carries a “huge” stigma and attendant effect on self-image.

• The new diagnosis could theoretically also lead to a reduction in the number of kids getting "medicated" for bipolar disorder unnecessarily and an increase in kids getting more “appropriate” interventions.
Examining the Proposed Disruptive Mood Dysregulation Disorder Diagnosis in Children in the Longitudinal Assessment of Manic Symptoms Study

David Axelsson, MD; Robert L. Findling, MD, MBA; Mary A. Fristad, PhD, ABPP; Robert A. Kowatch, MD, PhD; Eric A. Youngstrom, PhD; Sarah McCue Horwitz, PhD; L. Eugene Arnold, MD; Thomas W. Frazier, PhD; Neal Ryan, MD; Christine Demeter, MA; Mary Kay Gill, MSN; Jessica C. Hauser-Harrington, PhD; Judith Depew; Shawn M. Kennedy, MA; Brittany A. Gron, BS; Brieana M. Rowles, MA; and Boris Birmaher, MD

Conclusions: In this clinical sample, DMDD could not be delimited from oppositional defiant disorder and conduct disorder, had limited diagnostic stability, and was not associated with current, future-onset, or parental history of mood or anxiety disorders. These findings raise concerns about the diagnostic utility of DMDD in clinical populations.

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Conclusions: In grown-up subjects with child BP-I, the 44.4% frequency of manic episodes was 13 to 44 times higher than population prevalences, strongly supporting continuity.
Persistence of Pediatric Bipolar Disorder

Four-Year Longitudinal Course of Children and Adolescents With Bipolar Spectrum Disorders: The Course and Outcome of Bipolar Youth (COBY) Study


N=214 Bipolar I and N=169 Bipolar II and NOS, followed for 4 years with the Longitudinal Interview Follow Up Evaluation

Recurrences common
Symptomatic on average for 60% of the follow-up period.
40% had symptoms during 75% of the followup period.
25% of BPD II and 38% of BPD NOS converted to BPI
Persistence of Pediatric Bipolar Disorder

HIGH LEVEL OF PERSISTENCE OF PEDIATRIC BIPOLAR-I DISORDER FROM CHILDHOOD ONTO ADOLESCENT YEARS: A FOUR YEAR PROSPECTIVE LONGITUDINAL FOLLOW-UP STUDY

Wozniak, Petty, Schreck, Moses, Faraone, Biederman

78 of 105 youth with Bipolar I disorder followed up after 3.6 years

• Baseline age 10.5 years, 76% male
• Age of onset bipolar disorder 4.9 years
• Duration of BPD at baseline 7.6 years
Persistence of DSM-IV BP-I in youth at 4-year Follow-up (N=78/105)

- Full BP-I disorder: 73.1%
- Subthreshold BP-I disorder: 6.4%
- Full or subthreshold MDD: 5.1%
- Euthymic: 6.4%
- Treated: 9.0%

Only 5 were euthymic without treatment
Pediatric-Onset Bipolar Disorder

• ADHD plus BPD has been neglected at both ends of the life cycle due to skepticism regarding pediatric onset bipolar disorder and continuity of ADHD into adulthood

• Clinical and research skepticism leads to a reluctance to diagnose and study the condition
Differential Diagnosis with ADHD

- Overlapping symptoms include:
  a) Distractibility
  b) Physical hyperactivity
  c) Talkativeness
The first scientific article to systematically document the comorbidity between ADHD and Bipolar Disorder

Attention-Deficit Hyperactivity Disorder and Juvenile Mania: An Overlooked Comorbidity?


ABSTRACT

**Objective:** To evaluate the psychiatric, cognitive, and functional correlates of attention-deficit hyperactivity disorder (ADHD) children with and without comorbid bipolar disorder (BPD). **Method:** DSM-III-R structured diagnostic interviews and blind raters were used to examine psychiatric diagnoses at baseline and 4-year follow-up in ADHD and control children. In addition, subjects were evaluated for cognitive, academic, social, school, and family functioning. **Results:** BPD was diagnosed in 11% of ADHD children at baseline and in an additional 12% at 4-year follow-up. These rates were significantly higher than those of controls at each assessment. ADHD children with comorbid BPD at either baseline or follow-up assessment had significantly higher rates of additional psychopathology, psychiatric hospitalization, and severely impaired psychosocial functioning than other ADHD children. The clinical picture of bipolarity was mostly irritable and mixed. ADHD children with comorbid BPD also had a very severe symptomatic picture of ADHD as well as prototypical correlates of the disorder. Comorbidity between ADHD and BPD was not due to symptom overlap. ADHD children who developed BPD at the 4-year follow-up had higher initial rates of comorbidity, more symptoms of ADHD, worse scores on the CBCL, and a greater family history of mood disorder compared with non-BPD, ADHD children. **Conclusions:** The results extend previous results documenting that children with ADHD are at increased risk of developing BPD with its associated severe morbidity, dysfunction, and incapacitation. J. Am. Acad. Child Adolesc. Psychiatry, 1996, 35(8):997–1008. **Key Words:** bipolar disorder, attention-deficit hyperactivity disorder, comorbidity.
Bipolar Disorder in Girls and Boys with and without ADHD

Biederman et al. J Affect Disord. 1997; 44:177-188
Mania-Like Symptoms Suggestive of Childhood-Onset Bipolar Disorder in Clinically Referred Children

JANET WOZNIAK, M.D., JOSEPH BIEDERMAN, M.D., KATHLEEN KIELY, B.A., J. STUART ABLON, B.A., STEPHEN V. FARAONE, PH.D., ELIZABETH MUNDY, B.A., AND DOUGLAS MENNIN, B.A.

ABSTRACT

Objective: To examine the prevalence, characteristics, and correlates of mania among referred children aged 12 or younger. Many case reports challenge the widely accepted belief that childhood-onset mania is rare. Sources of diagnostic confusion include the variable developmental expression of mania and its symptomatic overlap with attention-deficit hyperactivity disorder (ADHD). Method: The authors compared 43 children aged 12 years or younger who satisfied criteria for mania, 164 ADHD children without mania, and 84 non-ADHD control children. Results: The clinical picture was fully compatible with the DSM-III-R diagnosis of mania in 16% (n = 43) of referred children. All but one of the children meeting criteria for mania also met criteria for ADHD. Compared with ADHD children without mania, manic children had significantly higher rates of major depression, psychosis, multiple anxiety disorders, conduct disorder, and oppositional defiant disorder as well as evidence of significantly more impaired psychosocial functioning. In addition, 21% (n = 9) of manic children had had at least one previous psychiatric hospitalization. Conclusions: Mania may be relatively common among psychiatrically referred children. The clinical picture of childhood-onset mania is very severe and frequently comorbid with ADHD and other psychiatric disorders. Because of the high comorbidity with ADHD, more work is needed to clarify whether these children have ADHD, bipolar disorder, or both. J. Am. Acad. Child Adolesc. Psychiatry, 1995, 34, 7:867–876. Key Words: bipolar disorder, attention-deficit hyperactivity disorder, comorbidity, children.
• Subjects
  – Prepubertal Mania (N=43)
  – 16% of 262 referrals < 12 year
  – mean age 7.9 years
Prepubertal Bipolar Disorder

Wozniak & Biederman, et al., 1995

Subjects
Prepubertal Mania (N=43)
16% of 262 referrals
mean age 7.9 years
Diagnostic Overlap of BPD and ADHD [Second Cohort]

N=406

N=101

N=14

Biederman, JAD 2004
Is Comorbidity with ADHD A Marker for Juvenile Onset Mania?

Faraone, Biederman & Wozniak, et al, 1996

Rates of ADHD

- Manic Children: N=68
- Manic Adolescents (Childhood Onset): N=25, p≤0.05 vs Controls & Manic Adols (Adol Onset)
- Manic Adolescents (Adolescent Onset): N=17, p≤0.05 vs Manic Adols (Adol Onset)
- Manic Adults
Most bipolar adults in STEP-BD (N=983) reported onset in childhood or adolescence

- About 65% of adults with onset < 18
- Almost a third with onset < 13

Perlis, Miyahara, Marangell, Wisniewski, Ostacher, DelBello, Bowden, Sachs, Nierenberg, Biol Psych 2004;55:875-881
Because both BPD and ADHD disorders are known to be familial, one useful approach to understand their relationship is the use of family aggregation data

(Pauls, 1999)

Using family genetic data, we investigated the relationship between ADHD and bipolar disorder in children and adolescents in a familial risk analysis study
## Meta-Analysis of Controlled Family Studies of Pediatric Bipolar Disorder: Familiality in BP-I Probands vs Controls

<table>
<thead>
<tr>
<th>Study</th>
<th>BP-I probands (N)</th>
<th>BP-I</th>
<th>CONTROLS</th>
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<tbody>
<tr>
<td>Kutcher 1991</td>
<td>N=23</td>
<td>15%</td>
<td>1%</td>
</tr>
<tr>
<td>Wozniak 1995</td>
<td>N=16</td>
<td>13%</td>
<td>3%</td>
</tr>
<tr>
<td>Faraone 1997</td>
<td>N=15</td>
<td>16%</td>
<td>3%</td>
</tr>
<tr>
<td>Geller 2006</td>
<td>N=95</td>
<td>28%</td>
<td>4%</td>
</tr>
<tr>
<td>Wozniak 2010</td>
<td>N=157</td>
<td>18%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Wozniak J Clin Psych, 2012
Morbid Risk of Bipolar Disorder in First Degree Relatives of Youth with Bipolar Disorder, Bipolar+ADHD, ADHD, and Controls

Overall Association: $\chi^2=113.8$, $p<0.0001$

- a: $p<0.05$ vs. controls
- b: $p<0.05$ vs. ADHD

*No significant difference in risk between relatives of those in the BPD alone group vs. those in the BPD+ADHD group
Morbid Risk of ADHD in First Degree Relatives of Youth with Bipolar Disorder, Bipolar+ADHD, ADHD, and Controls

Overall Association: $\chi^2 = 2383.9, p < 0.0001$

a: $p < 0.05$ vs. controls; b: $p < 0.05$ vs. ADHD; c: $p < 0.05$ vs. BPD+ADHD
• Cosegregation

- Among relatives of the BPD+ADHD probands
  - 46% (n=33) of the 71 relatives with BPD, also had ADHD
  - 20% (n=111) of the 555 relatives without BPD, had ADHD
  - $\chi^2=24.92$, $p<0.001$

- Among relatives of the BPD only probands
  - 0 of the 7 relatives with BPD also had ADHD
  - 6% (n=3) of the 54 relatives without BPD, had ADHD
  - $\chi^2=0.41$, $p=0.69$
Percent of First Degree Relatives with Bipolar Disorder in Youth with Bipolar Disorder, Bipolar+ADHD, ADHD, and Controls (Familiality)

Percent of Relatives with Bipolar Disorder

<table>
<thead>
<tr>
<th>Group</th>
<th>Probands</th>
<th>Relatives</th>
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</thead>
<tbody>
<tr>
<td>BPD</td>
<td>n=19</td>
<td>n=61</td>
</tr>
<tr>
<td>BPD+ADHD</td>
<td>n=220</td>
<td>n=626</td>
</tr>
<tr>
<td>ADHD</td>
<td>n=162</td>
<td>n=511</td>
</tr>
<tr>
<td>CONTROL</td>
<td>n=136</td>
<td>n=411</td>
</tr>
</tbody>
</table>

BPD+ADHD

J Psychiatr Res. Jan 2013
Percent of First Degree Relatives with ADHD in Youth with Bipolar Disorder, Bipolar+ADHD, ADHD, and Controls with ADHD (Familiality)

J Psychiatr Res. Jan 2013
Meta-Analysis of the Relative Risk of ADHD Among Relatives of Bipolar I Probands

For each comparison, the dot is the relative risk and the horizontal line is the 95% confidence interval (95% CI). The center of the diamond at the bottom is the weighted relative risk across all studies, and the width of the diamond is its 95% CI. MGH=reanalysis of child and adult proband studies from Massachusetts General Hospital Pediatric Psychopharmacology Program (see Method section).

From: Examining the Comorbidity Between Attention Deficit Hyperactivity Disorder and Bipolar I Disorder: A Meta-Analysis of Family Genetic Studies

Meta-Analysis of the Relative Risk of Bipolar I Disorder Among Relatives of ADHD Probands

<table>
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<tr>
<th>Author (Reference)</th>
<th>Type of Relative</th>
<th>Diagnostic System</th>
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<td>Bhatia et al. (61)</td>
<td>Mixed</td>
<td>DSM-III</td>
</tr>
<tr>
<td>Cantwell (62)</td>
<td>Parent</td>
<td>DSM-II</td>
</tr>
<tr>
<td>Geller et al. (48)</td>
<td>Parent</td>
<td>DSM-IV</td>
</tr>
<tr>
<td>Geller et al. (48)</td>
<td>Sibling</td>
<td>DSM-IV</td>
</tr>
<tr>
<td>MGH adult (63)</td>
<td>Offspring</td>
<td>DSM-IV</td>
</tr>
<tr>
<td>MGH adult (63)</td>
<td>Sibling</td>
<td>DSM-IV</td>
</tr>
<tr>
<td>MGH adult (63)</td>
<td>Parent</td>
<td>DSM-IV</td>
</tr>
<tr>
<td>MGH child (64, 65)</td>
<td>Parent</td>
<td>DSM-III-R</td>
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<tr>
<td>MGH child (64, 65)</td>
<td>Sibling</td>
<td>DSM-III-R</td>
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<tr>
<td>Nigg and Hinshaw (66)</td>
<td>Parent</td>
<td>DSM-III-R</td>
</tr>
<tr>
<td>Stewart and Morrison (67)</td>
<td>Mixed</td>
<td>DSM-II</td>
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Figure Legend:

Meta-Analysis of the Relative Risk of Bipolar I Disorder Among Relatives of ADHD Probands. For each comparison, the dot is the relative risk and the horizontal line is the 95% confidence interval (95% CI). The center of the diamond at the bottom is the weighted relative risk across all studies, and the width of the diamond is its 95% CI. MGH = reanalysis of child and adult proband studies from Massachusetts General Hospital Pediatric Psychopharmacology Program (see Method section).

CONCLUSIONS

Family history can be an external validator in cases of complicated comorbidity.

BPD+ADHD follow a pattern consistent with genetic cosegregation, suggesting a genetic subtype.
Why is appropriate diagnosis important? Because it leads to the best evidence based treatment.

Treatment Risk versus Benefit includes the risk of not treating with attendant:

- Suicide attempts and completed suicide
- Substance Abuse and Addiction
- Reckless Behavior with Arrest
- Other consequences of hypersexuality and dangerous impulsivity
Bipolar adults with childhood and adolescent onset had more lifetime suicide attempts and violence

Perlis, Miyahara, Marangell, Wisniewski, Ostacher, DelBello, Bowden, Sachs, Nierenberg, Biol Psych 2004;55:875-881
Number of Subjects Participating in Pediatric Anti-Manic Trials

- Atypical Antipsychotics: n=1474
- Traditional Mood Stabilizers: n=915
- Other Anticonvulsants: n=244
- Naturopathic Treatments: n=71

Liu, JAACAP 2011
Mean Change in YMRS from Baseline by Medication Class

- Traditional Mood Stabilizers: -10.99
- Other Anticonvulsants Atypical Antipsychotics: -11.03
- Naturopathic Treatments: -16.8

Liu, JAACAP 2011
FDA Approved Treatments for Pediatric Bipolar Disorder

• All medications, described in this presentation constitute off-label use in the USA with the exception of the following FDA approved medications:

  – Lithium: manic or mixed states, patients aged 13-17 years
  – 2007 Risperidone: manic or mixed states, patients aged 10-17 years
  – 2008 Aripiprazole: manic or mixed states, patients aged 10-17 years
  – 2009 Olanzapine: manic or mixed states, patients aged 13-17 years
  – 2009 Quetiapine: monotherapy or adjunct to lithium or divalproex sodium, manic states, patients aged 10-17 years
  – 2009 Ziprasidone was approved by FDA Advisory Panel as second line therapy
Euthymic youths with bipolar disorder and ADHD may benefit from short-term concomitant treatment with methylphenidate.

A 4-week double-blind, placebo-controlled trial in youths ages 5 to 17 years with bipolar disorder and ADHD, were currently receiving a stable dose of at least one thymoleptic, and while euthymic continued to have clinically significant symptoms of ADHD.

Patients received 1 week each of placebo, methylphenidate 5 mg twice daily, methylphenidate 10 mg twice daily, and methylphenidate 15 mg twice daily using a crossover design. Subjects were randomly assigned to receive one of six possible dosing orders. The primary outcome measure was the total score on the parent-completed ADHD Rating Scale-IV.

RESULTS

Lower scores during best dose treatment compared to the week of placebo treatment were found on the ADHD Rating Scale-IV (p < .05), suggesting a therapeutic benefit. A large effect size (Cohen's d = 0.90) was found for methylphenidate. Treatment was generally well tolerated. Rating Scale-IV.