Update On Juvenile Bipolar Disorder: Implications for Clinical Work

ASAP Annual Meeting
New York, NY
March 14, 2009

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Note: the presenter has no personal or financial relationships with any products or services presented in this CME activity. Off-label uses of medications are discussed.

Goals of Talk

- Identify 3 main approaches to JBD diagnosis in the research literature.
- Review data on prevalence of JBD and continuity, or not, with adult BD.
- Using case examples, illustrate how to use diagnostic refinements to guide treatment decisions.

Outline of Talk

- Two cases from my private practice that will be used throughout presentation
- Review recent data on increase in JBD diagnoses
- Review 3 distinct approaches to diagnosis in literature
- Review longitudinal data on JBD
- Brief review of evidence base for medications
- Case conclusions
- Summary and final thoughts

A Controversial Diagnosis

The Carlat Psychiatry Report

AN UNBIASED MONTHLY COVERING ALL THINGS PSYCHIATRIC

VOLUME 4, NUMBER 8 WWW.THECARLATREPORT.COM AUGUST 2006

Bipolar Disorder in Children: Is the Diagnosis Valid?

We've all noticed the trend: children are increasingly being diagnosed with bipolar disorder. According to the *Wall Street Journal*, the number of children diagnosed with bipolar increased by 26% from 2002 to 2004 (May 25, 2005).

This issue is controversial, because psychiatrists are already accused of overmedicating children. Over the last several years, we have been criticized for prescribing children antidepressants that may cause suicidal ideation; for overusing stimulants, which may exacerbate pediatric cardiac problems and, most recently, for a fivefold rise in the use of antipsychotics in children from 1993 to 2002 (*Arch Gen Psychiatry* 2006;63:679-685).

Now, with a surge of research interest in establishing bipolar disorder as a bona fide diagnosis in children, we may be setting ourselves up for another public relations fiasco.

The key questions are: 1. Does bipolar disorder exist in children? 2. If it does exist, is it the same creature as bipolar disorder in adults? 3. Do medications help pediatric bipolar disorder?

Recently, two intriguing articles were published to help us answer these questions. The first was a 10-year update on pediatric bipolar disorder published in the "orange journal" (*J Am Acad Child Adolesc Psychiatry* 2005;44(9):872-887), and the second was an editorial by child

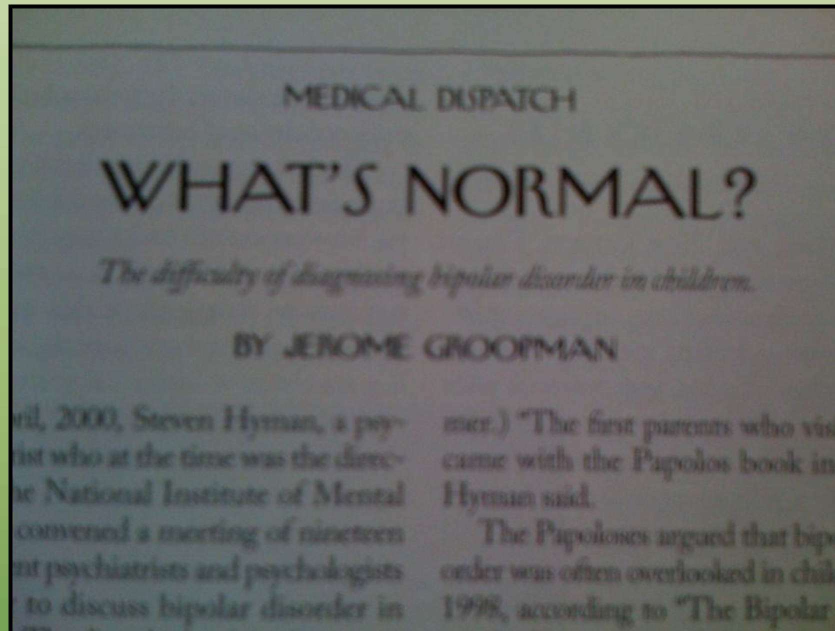
IN THIS ISSUE:

Focus of the Month:
Topics in Bipolar Disorder

- Bipolar Disorder in Children: Is the Diagnosis Valid?
- The STEP-BD Study: An Introduction
- Do Antidepressants Cause Switching?
- Bipolar II Disorder: A Useful Concept?
- Expert Q & A:

Disagreements within the field

A Controversial Diagnosis



MEDICAL DISPATCH

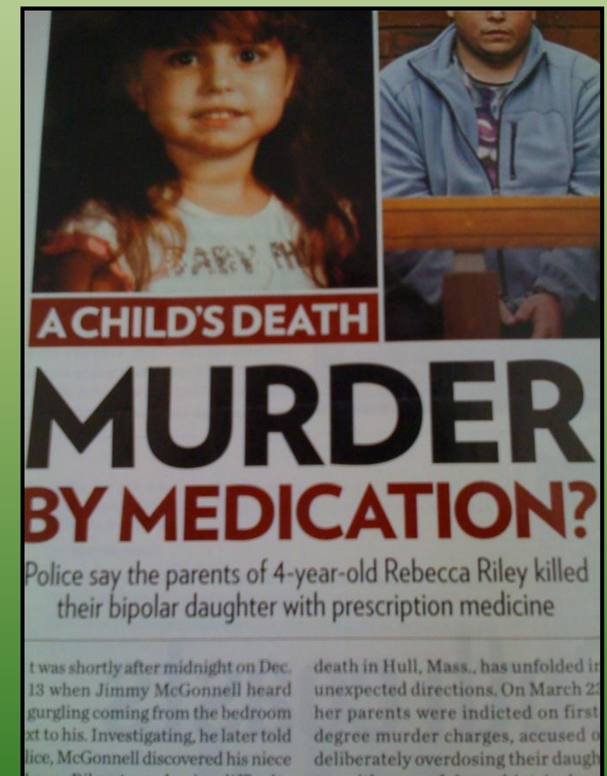
WHAT'S NORMAL?

The difficulty of diagnosing bipolar disorder in children.

BY JEROME GROOPMAN

ril, 2000, Steven Hyman, a psy-
rist who at the time was the direc-
he National Institute of Mental
convened a meeting of nineteen
nt psychiatrists and psychologists
to discuss bipolar disorder in

mer.) "The first parents who visi
came with the Papolos book in
Hyman said.
The Papoloses argued that bipo
order was often overlooked in child
1998, according to "The Bipolar



A CHILD'S DEATH

MURDER BY MEDICATION?

Police say the parents of 4-year-old Rebecca Riley killed their bipolar daughter with prescription medicine

t was shortly after midnight on Dec. 13 when Jimmy McGonnell heard gurgling coming from the bedroom xt to his. Investigating, he later told lice, McGonnell discovered his niece

death in Hull, Mass., has unfolded i unexpected directions. On March 2 her parents were indicted on first degree murder charges, accused o deliberately overdosing their daugh

Publicity outside the field

A Controversial Diagnosis

Patients
with
real
challenges

A Controversial Diagnosis

How should we approach these cases?

Case One: Ian

- *13 yr old boy, custody about to change*
- *Dx'd w/ JBD age 5, on multiple high doses of meds (ziprasadone 80 tid, methylphenidate 20 bid, trileptal 300 tid, citalopram 40 bid, clonidine 0.2 qhs)*
- *Multiple medical work-ups and multidisciplinary assessments including mri showing global atrophy, and NP testing showing low IQ*

Note: details of cases have been changed to protect the identity of the patients

Ian Cont'd.

- *Symptoms mostly around poor, at times out of control behavior.*
- *In special, separate classroom for most of his education.*
- *Mom receiving SSDI and other payments because of Ian's disability.*

Ian Cont'd.

- *Recent hospitalization for SI.*
- *Eight year custody battle, Dad about to win.*
- *Dad limited and contentious contact with treaters in past.*
- *Dad believed all problems caused by meds and Ian's mother's poor parenting, and that in fact nothing was wrong with his son.*
- *Dad wants me to take over care and take Ian off all meds.*

Case Two: Melissa

- *13 yr old girl BIB parents b/c "nothing has helped."*
- *Dx'd w/ JBD two years ago. Prior to that, dx'd with an eating disorder and depression. Early childhood unremarkable.*
- *Current meds aripiprazole and paroxetine, on lithium and depakote in past.*
- *Had gained 75 lbs and developed PCOS on depakote.*
- *Also recent abnl glucose and pre-diabetes.*

Melissa Cont’d.

- *Parents’ concerns mostly around social contacts and behavior.*
- *Very poor social judgment, dressed and acted sexually provocatively, didn’t respond well to limit setting.*
- *Struggling at school, spending hours on internet pursuing boys, erratic and unpredictable sleep patterns.*

Melissa Cont'd.

- *Mom had h/o post-partum psychosis and bipolar disorder. Well managed on depakote for years.*
- *Parents not convinced Melissa has same illness, worried about SE of meds, especially recent weight gain.*

Increased Diagnosis of JBD

- Moreno et al, 2007- 40x increase in number of outpt. visits for JBD from 25 to 1003 visits per 100,000 population (from 1994 to 2003).
- Case et al, 2007- 5x increase in number of JBD dx on inpt. units in community hospitals
- Olfson 2006- 6x increase in number of office visits by youth that included a prescription for an anti-psychotic.

What are People Diagnosing?

- Anecdotally, clinicians clearly disagree on whom to diagnose with JBD.
- Researchers themselves disagree, and while many say they use DSM IV criteria, each group means something different by that.
- Three main approaches in literature.

DSM IV Criteria for Mania

Category A Symptoms

- "*Distinct* period of abnormally and **persistently** *elevated, expansive or irritable* mood" lasting *at least 7 days* for mania or four days for hypomania

Category B Symptoms

- Three B sx if euphoric, 4 if irritable
- Sx include grandiosity, decr. sleep, pressured speech, racing thoughts, distractibility, incr GDA, pleasure seeking/risky behavior.
- Mania- sx 'severely impairing'
- Hypomania- sx 'noticeable to others'

3 Main Research Approaches

- Narrow phenotype, or strict adult criteria (Leibenluft *et al* 2003)- NIMH COBY study.
- Cardinal symptoms and brief frequent cycles (Geller & colleagues, Wash. U.).
- Persistent, impairing irritability approach (Biederman et al, MGH).

Narrow Phenotype

- Apply adult criteria strictly -- *distinct* manic episodes of long duration.
- Don’t require euphoria or grandiosity (irritability alone sufficient).
- Mood sx must occur only during a distinct time frame -- not chronic and unremitting.
- AACAP Practice parameter, and NIMH-COBY research group.

Cardinal Side Effects & Brief, Frequent Cycles

- Find very rapid mood changes and complicated cycling patterns.
- “ultradian” cycling- mean 3.5 cycles/day.
- More stringent criteria for quality of mood sx- must be grandiosity or euphoria (irritability alone not enough).
- Geller’s group out of Washington University.

Severe, Persistent Irritability

- Does not require cardinal sx of grandiosity or euphoria.
- Does not focus on distinct episodes.
- Severe, persistent, impairing irritability is considered sufficient for criteria of mania to be met, even if not a change from pt's baseline.
- Beiderman & colleagues at MGH

Consensus Developing?

- Narrow phenotype group should be called BP I (or II depending on length).
- Cardinal sx/brief frequent cycles called BP NOS (slightly more controversial).
- What to call persistent irritability group? Should they be considered BP NOS or something else entirely?

Something Else: SMD?

- Severe Mood Dysregulation is term NIMH group uses to refer to these kids.
- Several differences between narrow phenotype and SMD group appearing in literature.
  - Parents of narrow phenotype kids more likely to have dx of BD themselves (Brotman 2007)
  - Differences in affective response to frustration between kids with narrow phenotype and SMD (Rich et al 2007)

Ian's Case Cont'd.

- *On MSE Ian loud, disruptive, very immature, hard to manage in office, likes Candyland. Thick glasses, marked strabismus, clearly different appearing from his peers.*
- *Dad very focused on teaching him to behave and "act his age." Lots of consequences for bad behavior (losing tv, writing sentences) which Dad feels is making a difference already.*
- *Mom mostly focused on how disturbed Ian is, that Dad is wrong, and impressing upon me all the things she's done for him over the years. Very convinced Ian will fall apart quickly if I stop or change meds.*
- *Start working with Ian weekly and Dad monthly and see many improvements. Agree to trial med taper and then holiday.*

Case Two Cont'd.

- *Melissa on MSE likeable, happy, overweight, dressed in provocative and tight clothing in style typical for her age. Wearing heavy make-up, inexpertly applied, giving her slight resemblence to manic pt on inpt unit. Has a lot to say, but speech not obviously pressured, nor TP tangential. Is hard to follow at times, but talking a lot about peers I don't know.*
- *Keep Melissa on current meds and work with her weekly, parents monthly. Erratic sleep, problems with school, and poor judgment (esp. w/boys) continue without change*
- *Get NP testing to r/o NLD, and find profound Exec Fxn defecits, no other pattern*

More Melissa

- *Six months of individual tx and taper down paroxetine- no significant change (sometimes better, sometimes worse).*
- *Lab testing now shows elevated lipids and abnl glucose testing.*
- *Begin to discuss trial taper of aripiprazole.*

Longitudinal Data on JBD

- Do kids with JBD go on to become adults with classic/true bipolar disorder?
- Increase in dx of adults with bipolar disorder (at least on inpt units- Blader and Carlson 2007). Some loosening in strictness of adherence to DSM IV criteria for adults.
  - Advocated by researchers who believe in more "spectrum" approach to BD
  - Implications for interpreting family hx of BD

Retrospective, Longitudinal Data on JBD

- Recent review of data from STEP-BD trial and Bipolar Collaborative Network showed 15-28% of adults w/ BD report onset of illness prior to age 13 (Post and Kowatch 2006).
- DMDA survey of bipolar members showed 31% thought sx started before age 15 (Lish 1994).
- If 1-2% of adult population has BD, and 15-30% had onset prior to age 15, then 0.15-0.6% of kids should have JBD.

Prospective Longitudinal Data

- Community (non-clinical) sample 150 14-16 yr olds, 13% endorsed four or more manic sx (Carlson 1988).
- Community sample of 1500 adolescents followed to age 24 found 1% adolescent prevalence and 2% prevalence in young adulthood of BD (Lewinsohn 2000).
- Same study found 5% prevalence of subsyndromal BD in adolescence -- no incr rate of BD by age 24 (did have impaired fxn and greater use of MH services).
- 203 9-13 yr old boys- 124 w/ dx ADHD. 25 (20%) met criteria for mania initially , six years later only one did (4%).

Longitudinal Data Cont’d.

- 4500 youths (GSM study) age 9-13 no cases of mania and 0.10 rate of hypomania (Costello 1996).
- 1,037 indiv assessed for mental illness age 11, 13, 15, 18, 21 and 26 yrs. Of the 26 yr olds who had a dx of mania 93% had a previous psychiatric dx -- most common. conduct d/o, ODD and depression, not mania. (Kim Cohen et al 2003).
- Geller group follow-up (Geller 2008)
  - 115 bipolar kids (dx’d with cardinal sx/brief frequent episodes approach) followed for eight years. Half now 18 yrs old. 88% recovery and 73% relapse. Vast majority reporting daily/ultradian cycling (81% in second episode, 68% in third episode).
  - Continuity with previous sx, but not classic adult BP I or II

JBD Psychopharm Evidence

- Gold Standard: randomized double blind placebo controlled trial
  - NONE showing benefit for any medication in JBD (no matter what dx criteria used)
  - Only one single med study done (Wagner et al 2006), used oxcarbazepine, no difference from placebo

Psychopharm Evidence Cont'd.

- One other RCT, double blind, placebo controlled (Del Bello et al 2002) compared valproate plus quetiapine to valproate plus placebo. Some benefit.
- Three other PCTs
  - Discontinuation study of lithium (Kefantaris 2004)- no benefit Li vs. placebo
  - Two stimulant studies with ADHD and JBD kids, (Scheffer et al 2005 and Findling et al 2007) both showed stimulant could be added without flipping to mania, some benefit.

Psychopharm Evidence Cont'd.

- Two double blind randomized trials, no placebo arm
  - Li vs DVPX as maintenance for youths already stable on Li/DVPX combo tx. Found no difference (Findling 2005)
  - Quetiapine vs. DVPX for adol mania, no statistical difference between groups

Ian Conclusion

- *Ian is tapered off all medications.*
- *Two wks later Dad calls, worried about behavioral escalation, discuss starting risperidone*
- *Ian's behavior stabilizes w/o meds, starts special program for kids with developmental delays.*
- *Weekly tx and monthly parent guidance continue.*
- *Over next 3yrs, beh. improves markedly, maintained on no meds.*
- *Academics don't improve, never learns to master reading or do more than basic arithmetic. Dad continues to believe meds caused all his problems, and Ian would otherwise be a normal kid.*

Melissa Conclusion

- *Melissa's aripiprazole decreased. Has a terrible weekend (not sleeping, agitated, behaviorally OOC w/ parents) so we immediately raise the dose again.*
- *Less than a month later, Melissa comes in and insists on stopping all meds. Soon decompensates and ends up hospitalized, eventually in a residential school.*
- *On follow-up three years later, she's enrolled in college, doing well, stabilized on aripiprazole alone. Mom feels she started to get better once paroxetine completely stopped.*

Summary & Final Thoughts

- Diagnose JBD judiciously, using narrow phenotype criteria if possible -- in particular look for distinct episodes.
- Be aware evidence base for continuity with adult BP disorder is limited, as is evidence for psychopharm interventions.
- Look for what dx criteria being used when read the research on JBD. Expect many advances and clarifications coming soon, using these clearer diagnostic categories.
- If have a case that doesn't meet narrow phenotype criteria, feel less convinced this should be treated as you would treat an adult with classic BP.

Summary and Final Thoughts

Re: Ian

- Probably would have fallen into SMD category. No clear episodes, chronic irritability, clear and dramatic environmental stressors, no “cardinal symptoms.”
- I think treating the environmental stressors, improving Dad’s caretaking abilities, meeting both parents, providing emotional outlet, helping with school placement all helped more than any meds did .

Final Thoughts Cont'd.

Re: Melissa

- More classic BPI, "narrow phenotype" picture: clearly defined onset, hypersexuality, impulsivity and decreased sleep. Still not sure if grandiosity or euphoria, but looked like classic manic pt visually and intuitively.
- Also, Mom had clear hx classic BPI, including post-partum psychosis.

Melissa, continued

– In retrospect, I should have worked harder to get her off paroxetine. I also should probably not been so willing to experiment with decreasing aripiprazole. Even though trial decrease went poorly, I think parents and patient both were aware of my ambivalence, and this may have contributed to pt. discontinuing meds a month later.

Conversation Starters

- Why has use of JBD diagnosis increased so rapidly, even though such limited agreement around diagnosis?
- As fewer psychiatrists do therapy (Moitabai and Olfson 2008), does this make them more likely to "buy into" dx that emphasize meds over therapy? (If do more tx, prescribe less, per study above)

More conversation starters

- As hospital stays have gotten shorter (Case 2007) does this lead to emphasis on meds over assessment?
- Have financial pressures played a role?
  - Public concern over apparent conflicts of interest by JBD researchers.
  - Clinicians face financial pressures to ‘upcode’ dx to get more coverage for both inpt and putpt work.
  - Many mental health parity laws only apply to ‘biologically based’ mental illnesses- JBD qualifies, PTSD or Adj d/o does not.

Acknowledgements

I would like to thank Lois Flaherty M.D., Peter Chubinsky M.D., Timothy Dugan M.D., Nancy Rappaport, and Georgia Ede M.D. for their help and encouragement.

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