Bipolar Disorder and its New Step Sibling, DMDD

Robert Hilt, MD
PAL Conference
Bellingham WA
October 2015

PARTNERSHIP ACCESS LINE
Mental Health Consultation Outreach for children

UW Medicine

Seattle Children's
HOSPITAL · RESEARCH · FOUNDATION

Disclosures

- My DSM-5 companion book will be published in December by American Psychiatric Association Publishing
- I have no other financial interests to disclose
- I will be discussing non-FDA approved use of medications in this presentation, which will be so designated on these slides.

A Patient

- 6 year old boy new to your practice
- ADHD diagnosed at age 4
- On and off stimulants for 2 years
  - methylphenidate and amphetamine
  - works for a while, then no help
  - has always been "moody" and "irritable"
- Struggling at school socially, but "really smart"
- Mom has been told he might be bipolar

A Patient, continued

- Mom says she can't control him at home
  - Behaves a little better for mom's boyfriend
- Mom just got diagnosed as bipolar, and medications have helped her
- She asks you to prescribe "something" to treat his bipolar mood swings……

What To Do Now?

- What roles would you assume as the primary care provider with this question?
  - Diagnosis?
  - Psychoeducation?
  - Referral?
  - Treatment?

Frequency of Childhood Bipolar

- Controversial
- Some well established clinicians assert there is a very high incidence
  - "The Bipolar Child" by Papolos and Papolos
    - States about 6% of all children are bipolar
  - "Is Your Child Bipolar" by McDonnell and Wozniak
    - Based on their estimates, incidence is 4%.

Child vs Adult Rates

- Adult Lifetime prevalence rates of bipolar disorder are 1 to 2%
- Bipolar disorder is essentially a lifelong diagnosis
- So kids with bad mood swings cannot all have "true" bipolar disorder

- UCLA Child Bipolar Clinic found only 18% referred with a "bipolar" diagnosis actually had a bipolar disorder (Weintraub et al 2014)

Why is Bipolar diagnosis so challenging?

- Symptom overlap
- High rates of co-morbidities
- Developmental issues
- Environmental influences
- “Expert” opinions differ
- Influence of popular media/drug industry
- Non-specific medication impacts
- Extensive history needed to understand patterns

What is Mania?

- >1 week episode of irritable or expansive mood
- At least 3 of the following (4 if *only* irritable mood)
  - **D**istractible
  - **I**ndiscretions
  - **G**randiose
  - **F**light of ideas
  - increased goal directed **A**ctivities
  - little need for **S**leep
  - **T**alkative

What DSM-5 changed about Mania

- Increased the required level of increased energy/activity symptoms
  - Now says this must be present "most of the day, nearly every day"

- Duration criteria are unchanged:
  - Manic symptoms ≥ 1 week is Bipolar I

  - Manic symptoms ≥ 4 days is Bipolar II
    - No hospitalization or psychosis

The Other DSM-5 Bipolars

- "Other Specified Bipolar" (F31.89) means too few mania symptoms to meet Bipolar II criteria, and the clinician states why

- "Unspecified Bipolar Disorder" (F31.9) is the current term for Bipolar NOS

Some Bipolar child controversies

- Can children with extreme irritability and ADHD-like symptoms be considered bipolar?
- Can children with chronic (rather than episodic) mood symptoms be considered bipolar?
  - Adults with bipolar disorder have EPISODES of mania and depression
- Can children with irritability without elation be considered bipolar?

ADHD vs. Bipolar

- Three bipolar symptoms ≈ ADHD symptoms
  - distractibility
  - activity increase
  - talkativeness
    - Just have to add in “expansive mood” and voila, you have a “bipolar” child
  - This interpretation was one trigger for the bipolar diagnosis explosion

Manic symptoms versus ADHD
(Kowatch et al, 2005)

Symptom	ADHD	PBD*
Irritability	72%	98%
Accelerated Speech	82%	97%
Distractibility	96%	94%
Unusual Energy	95%	100%

* Pediatric Bipolar Disorder

Cyclothymic Disorder

- Recurrent episodes of hypomanic symptoms
- Never meet enough criteria to diagnose either hypomania or depression
- Problems persist at least 12 months in children (24 months in adults)
  - Up to ½ with this problem are diagnosed with bipolar disorder as adults

Intermittent Explosive Disorder

- Unplanned aggressive impulse dyscontrol
- Now only diagnosable above 6 years of age
- Greater definition of what is required to meet threshold, with alternatives:
  - ODD: Aggression from argument/temper tantrum
  - CD: Some aggression is proactive/predatory
  - DMDD has the persistently negative mood state, should not be diagnosed along with IED
- Best treatment: still poorly defined

"Rapid Cycling" Bipolar Controversy

- 4 or more distinct, full criteria manic, hypomanic, or depressive episodes in < 1 year
  - Rapid cycling pattern is rare in adults
- Kids are naturally more mood reactive, thus may hear a story of "rapid cycling"
  - Rarely fits the actual definition above
- Consider "rapid cycling bipolar" in kids if:
  - Mood episodes are sustained (not labile)
  - No triggers identifiable for mood changes

Our Overlapping Terms Don't Help

- Mood Instability
- Mood Swings
- Emotion Dysregulation
- Affective Dysregulation
- Mood Dysregulation
- Emotion Regulation
- Affective Lability
- Irritability
  - Components of many different disorders

Experts Debate Irritability and Mania

- Geller: Irritability has high sensitivity but poor specificity
- Wozniak: irritability may be primary mood symptom; episodicity not relevant
- Hunt/Birmaher: episodic irritability alone can represent mania; “irritable-only” mania exists but is rare
- Leibenluft: episodic irritability more suggestive of bipolar than chronic irritability

A few of the “irritable” disorders

- Bipolar disorder
- Rapid cycling bipolar
- Cyclothymic disorder
- Disruptive mood dysregulation disorder
- Severe mood dysregulation
- ADHD
- Depression
- ODD
- Conduct disorder

Chronic versus Episodic Irritability

- Community sample of 776 children and adolescents interviewed at 3 points in time
- Irritability rating scales used to tease out chronic versus episodic irritability.
- Chronic irritability
  - 2yr later associated with ADHD
  - 7 yr later associated with depression
- Episodic Irritability
  - 2yr later associated with simple phobia
  - 7 yr later associated with mania/bipolar

(Liebenluft et al, 2006)

Chronic vs Episodic Irritability

- Kids with episodes of irritability (rather than chronic) have a greater chance of:
  - elation and/or grandiosity
  - symptoms of mania
  - psychotic symptoms
  - depressive episodes
  - suicidality
  - A parent with Bipolar Disorder

Chronic irritability in youth predicting Major Depressive Disorder

- Chronic irritability at age 14 predicts MDD at age 22
  - OR= 2.29 (1.22-4.31) (Leibenluft et al, 2006)
- Oppositional defiant disorder at age 7 predicts MDD at age 18
  - OR=1.06 (1.01-1.10) (Burke et al, 2005)
- Familial association between MDD and disruptive behavior disorders (Weissman et al, 2005)

Defining that controversial group: "Severe mood dysregulation"

- A research construct from last decade
- Chronic: persistent sx's; no distinct mania
- Irritable: reactivity to negative emotional stimuli
  - > 3x/wk, baseline anger/sadness
- 3 or more ADHD-like "Hyperarousal"symptoms:
  - insomnia, agitation, distractibility, rapid thoughts, pressured speech, and intrusiveness.
- Very impairing

Did SMD lead to Bipolar Disorder?

- Brief answer: no.
  - Follow-up studies of SMD from age 10 to 18 generally show subsequent incidence of MDD at age 18 far more than Bipolar
  - Parental history for Bipolar far greater in Bipolar group (33%) than SMD group (2.7%)
  - Another study showed that after 2.4 years, only 1.2% of SMD patients experienced a manic episode, vs. 62.4% of patients with Bipolar

SMD children in the Great Smoky Mountain Study

- Longitudinal epidemiologic data set (Costello et al)
- N= 1,420, 4 waves, ages 9-18

- Questions
  - What is the prevalence of SMD?
    - Answer: 3.2%
  - What is the diagnostic outcome of children with SMD at the last wave (mean age 18.3 + 2.1 y)?
    - Answer: only major depression was a significantly more likely diagnosis in this group

Severe Mood Dysregulation (SMD)

- "Chronically irritable children whose diagnosis is in doubt."
- Clinical syndrome, not a diagnosis
- A real problem, confers risk of psychopathology, but NOT for bipolar disorder
- SMD increases risk of depressive disorder and GAD at 20 year follow-up.

Stringaris et al, 2010

Disruptive Mood Dysregulation Disorder (DMDD) (296.99, F34.8)

- The evolution of the SMD label
  - Just removed "hyperarousal" symptom
- Chronic, severe, persistent irritability
  - Temper outbursts
    - grossly out of proportion to the situation
    - developmentally inappropriate
  - Persistently irritable or angry mood in between temper outbursts, present most of the day, nearly every day, and noticed by others

Disruptive Mood Dysregulation Disorder

- Severe temper outbursts
  - > 3 episodes per week
  - Outbursts occur in multiple settings
- Persistently negative mood between outbursts
- Duration > 12 months
  - No remissions of >3 months
- Child is > 6 years old
  - Onset before age 10
- No manic episodes (defined as >1 day) within the year

DMDD is a *mood* diagnosis

- ODD/Conduct are disruptive behavior diagnoses
  - May help to differentiate
  - If symptoms fit both DMDD and ODD, only diagnose DMDD
- *Clinical course and treatments are not known*
  - Uncommonly persists beyond 2 years
  - Controversies still exist around DMDD
    - *Is this just ODD plus depression?*

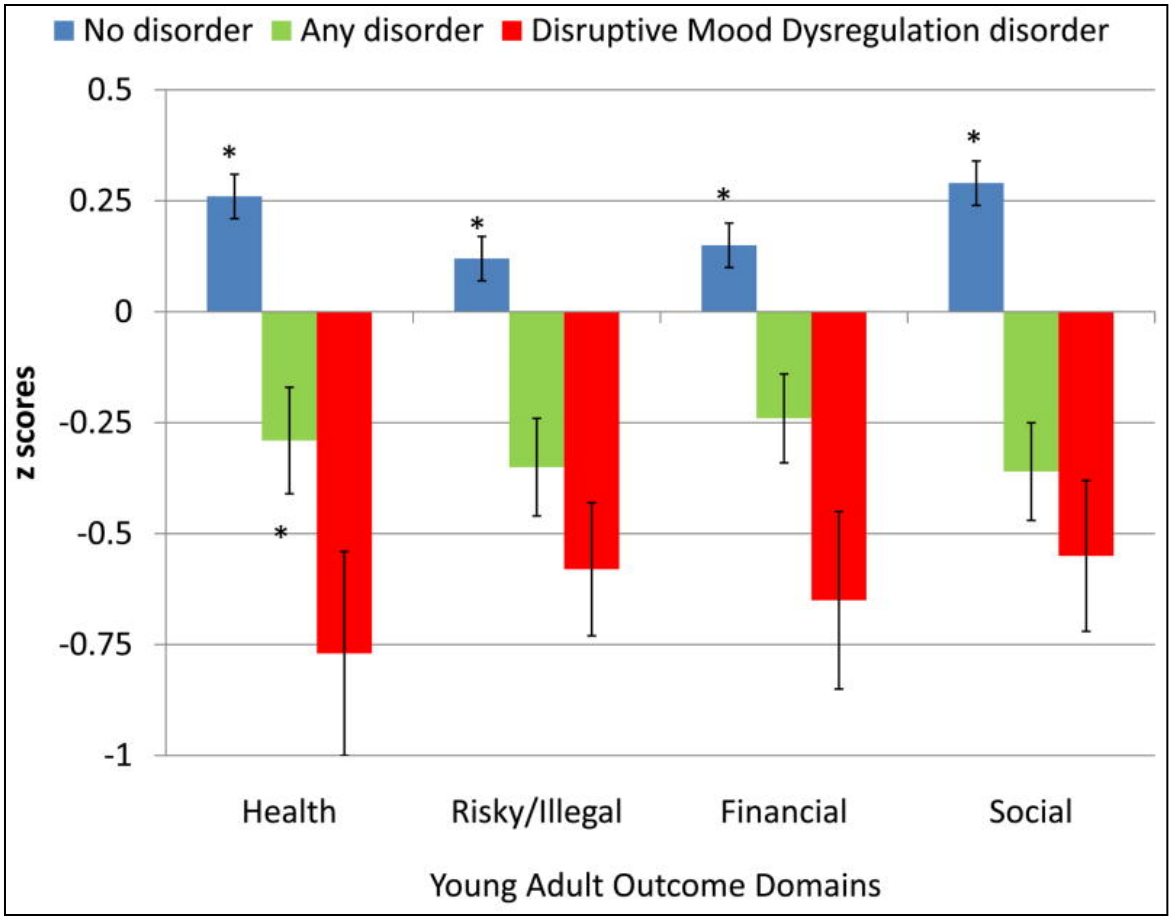
DMDD has comorbidities

- 74-81% have comorbid ADHD
- 31-49% had comorbid anxiety
- 17-42% had comorbid depression
- 3-32% had comorbid autism spectrum disorder

- ODD comorbidity rates approached 100%, but recall that DMDD diagnosis trumps ODD

Margulies et al., 2012; Axelson et al., 2012; Roy et al., 2014; Carlson and Dyson, 2013

Poor Outcomes if Have DMDD



Copeland WE et al, 2014 (from the Great Smoky Mountains Dataset)

How Do You Treat DMDD?

- Honestly, no one knows for sure

- Principles we think you should address:
  - Behavior management supports
  - Mood treatments (therapy yes/ meds maybe)

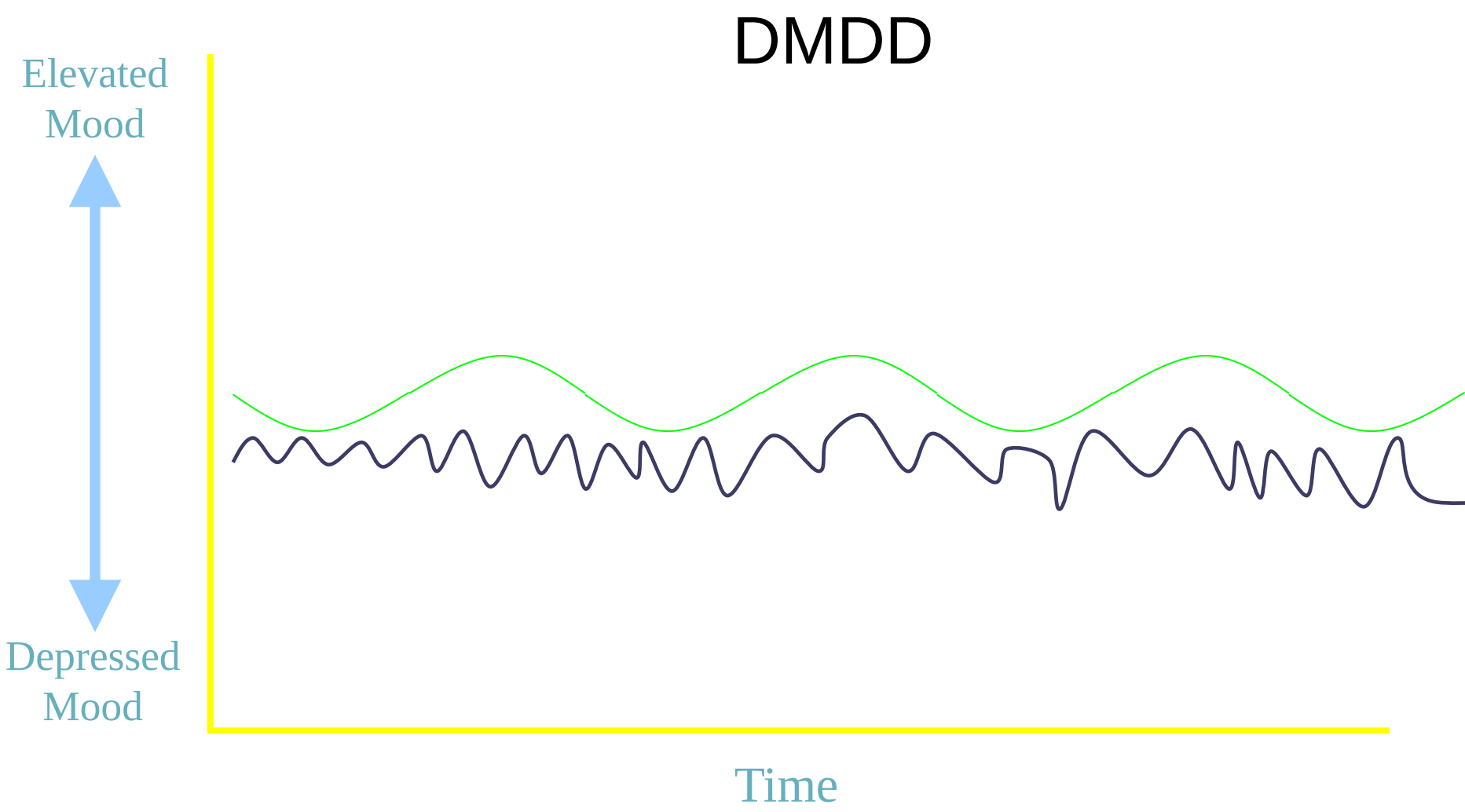
Differential Diagnoses With Mood Dysregulation & Irritability

- Bipolar Disorder
- Depression (esp. kids)
- PTSD
- Anxiety/OCD
- DBD, ODD
- ASD rigidity
- Conduct Disorder
- Substance Use
- Parent-Child Relational Problem
- Attachment Disorder, Borderline Traits

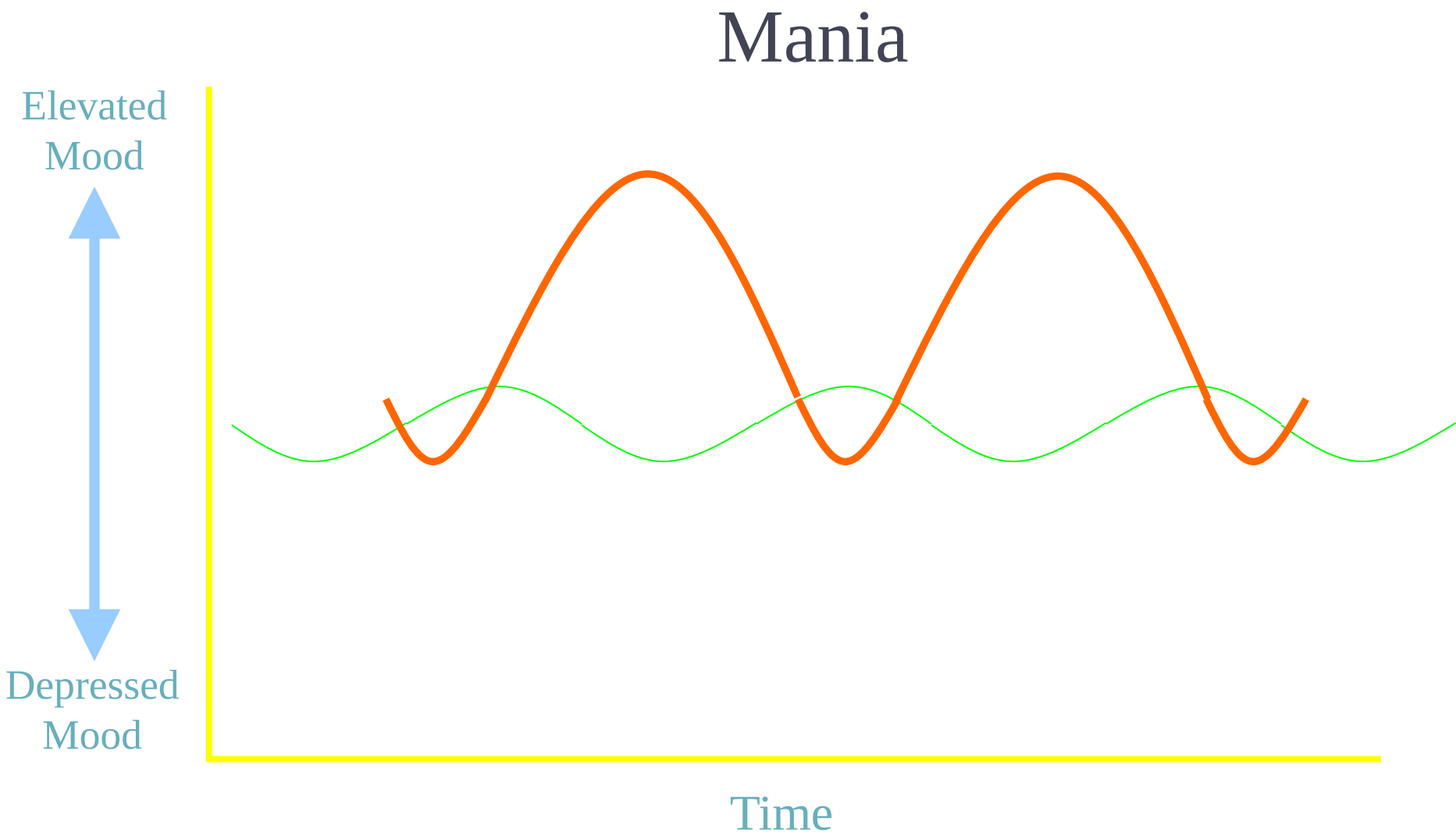
Our Bipolar NOS Problem

- Now “Bipolar Disorder Unspecified”
- Used as broad catch-all
- Sounds better than “I don’t know”
- Used to justify medication treatment

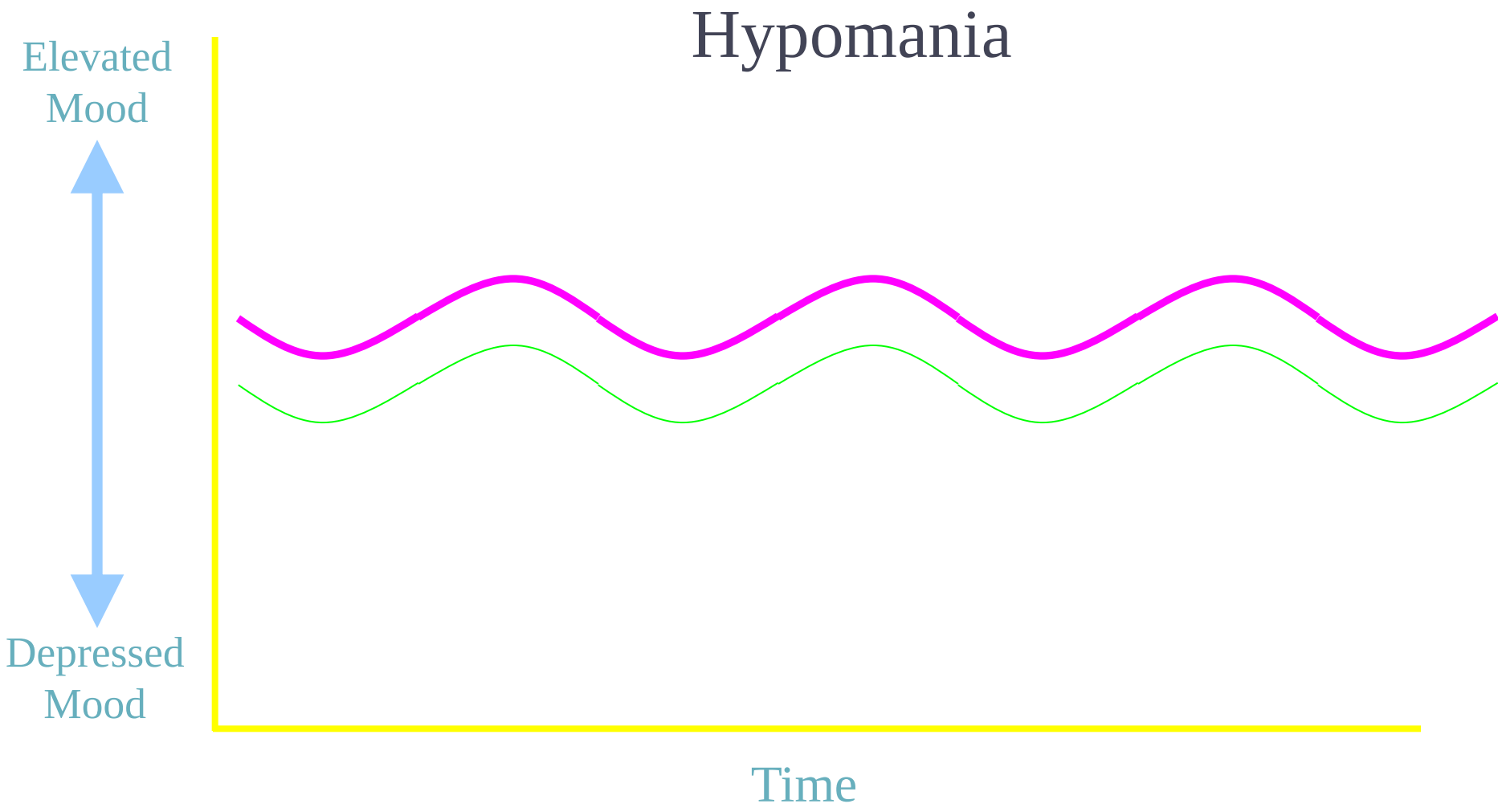
Mood Spectrum:



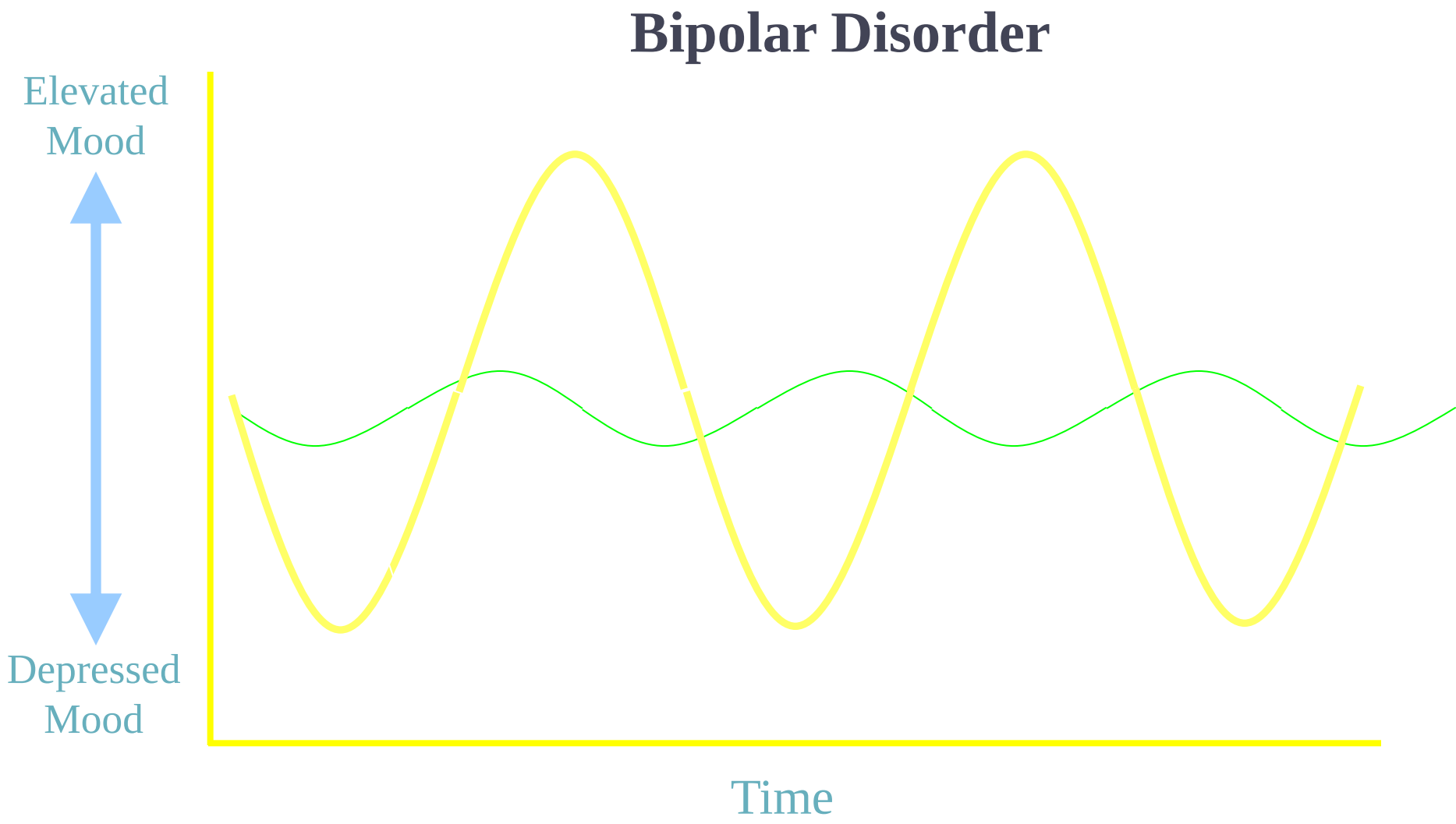
Mood Spectrum:



Mood Spectrum:



Mood Spectrum:



Bipolar "Hallmark" Symptoms

- Increase our diagnostic specificity
- More likely bipolar disorder if…
  - Elation
  - Hyperactivity
  - Grandiosity
  - Hypersexuality
  - Decreased need for sleep

Mania Diagnostic Perspective

- Compare child to the prototypic "manic" patient
  - Pressured speech -- not just talkative
  - Clearly grandiose ideas with impaired reality testing/lack of insight
  - Thought process is fast and jumping around
  - Episodes last days (not minutes or hours)
  - Little need for sleep (versus poor sleep.)

Return to the Case
(6 yr old irritible and moody boy)

1) Decide if he just has under-treated ADHD
2) Look for depression, anxiety, ODD
3) Ask for more details beyond his being "moody" and "irritable"
   - How is his mood most of the day?
   - What causes (if anything) his mood to change?
   - When not upset, what does he look like?
   - Can he "pull out of it"
   - Does he "listen" when he is asked to do something he wants to do?

Parent's Answers in this case

- Mom says he "never listens to me" especially when asked to do chore/homework/go to bed.
- Goes into rages when doesn't get his way
- Throws things at mom, hits her. Says "I hate you."
- Tried "everything," even spanking, taking away the X-box.
- With dad or other adults he behaves better. Some talking back, but manageable. Knows he needs to cool it or he going to get in trouble.

Symptoms At School

- In 2nd grade, teacher said he was not listening well in beginning of year, is better now
- In kindergarten he didn't follow rules well
- Performing at grade level
- Not having rages at school
- Generally more of a problem at home more than at school

Social History and Development

- Mom is primary caregiver.
- 1 younger brother, mom thinks she might be pregnant.
- No contact with dad. Left before he was born.
- Mom has few supports.
- Developmental milestones were OK
- Read early. Very verbal. Reads “anything about history” and “remembers everything.”
- No in utero drug exposure identified.

How to answer Mom's Question if this is Bipolar Disorder?

- Probably not
- Pattern doesn't fit
- Lack of hallmark symptoms
  - Difficult diagnosis (no "tests")
- Bipolar diagnosis best made "over time"
  - Down side of labeling too early

Bipolar Rating Scales?

- Rating Scales
  - Young Mania Rating Scale
    - Useful for monitoring symptoms over time
    - Not a diagnostic tool (very low specificity)
  - DISC or KSADS
    - Used in research, have flaws
    - Impractical for your office practice
- Rating scales are too misleading to recommend for diagnostic use
  - intentionally excluded from the PAL guide.

What about Family History?

- Avoid overcalling a positive family history
  - many adults who call themselves bipolar may not have that illness
  - first degree bipolar relative increases OR by 5
  - second degree bipolar relative, increase OR by 2.5
  - given a generous prevalence of 2% bipolar in the population, most children of a bipolar parent (~90%) will not have bipolar disorder

Youngstrom E & Duax J, JAACAP 44:7, 2005

Looking back from adult bipolar….

- Bipolar adults look back and note symptoms became bipolar-like in their teen years (50-66%)
- Many bipolar adults had major depression episodes as children
- The younger the child's first major depression, the more likely bipolar disorder is in the future

What if a "Bipolar" Child Really is Bipolar?

What if a “Bipolar” Child Really is Bipolar?

- Though rare in a PCP practice, becomes more likely the older the child.
- Assemble a team. Real deal bipolar disorder is a big problem and requires multi-modal treatment

Course Of True Bipolar Disorder

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

Stern TA and Herman JB, 2004

Bipolar Treatment

- If clear manic episodes, strongly recommend referral to child psychiatrist
- Management difficult because:
  - High rate of substance abuse
  - High rate of medication non-compliance
  - Even with medication, recurrences happen
  - High rates of family disruption from the illness
  - Suicidal behavior is common

Brent et al, 1988, 1993

If No Child Psychiatrist Can Assume Care, Then What?

- Get collateral information to help establish correct diagnosis
  - This may require separate/designated appointment(s) with caregivers and/or patient to get sufficient history
- Seek consultant advice (PAL)
- Advocate for multimodal care
  - Specialist for medication management
  - Parent/caregiver involvement
  - School support (IEP if attendance/performance impacted)
  - Individual support

Bipolar Treatments (for when you are left holding the bag)

- Medication management
- Safety monitoring and crisis planning
- Individual Support (symptom management, coping skills, adherence monitoring, psychoeducation)
- Family support (psycho-education, risk assessment/response, adherence/relapse prevention)
- Lifestyle coaching and support (sleep hygeine, stress mitigation, drug/alcohol risks, exercise, social rhythm therapy)

Bipolar Medications

Classes of Bipolar Medication

- "Mood Stabilizers"
  - Antipsychotic Medications
  - Anti convulsants (AEDs)
- Depression Medications (SSRIs, SNRI)
  - Avoid unless already on a "mood stabilizer"
- Sleep Aides

Antipsychotics

Antipsychotics

- Ideal world
  - mental health specialists handle all prescribing
- Real world
  - primary care pressured to originate or continue these meds

Antipsychotics- What do we really know with kids?

- Treat psychosis, but also benefits in:
  - Mania/bipolar disorder
  - Tic and Tourette's disorder
  - Irritability associated with autism
  - Impulsive aggression of conduct disorder/ODD
  - Explosive affect & impulsive aggression

Atypical Antipsychotics (2nd gen.)

- Aripiprazole (Abilify)
- Olanzapine (Zyprexa)
- Quetiapine (Seroquel)
- Risperidone (Risperdal, Invega)
- Ziprasidone (Geodon)

  - Asenapine (Saphris)
  - Clozapine (Clozaril, FazaClo)
  - Lurasidone (Latuda)
  - Iloperidone (Fanapt)

Atypical Antipsychotics

- 99% of antipsychotic prescriptions for children are atypicals
- Big business for big pharma
- Atypical hallmark is serotonin receptor antagonism in addition to D2 activity
  - lower extra pyramidal symptoms
  - lower tardive dyskinesia risks

Time of Onset of Effects

- All atypical antipsychotics studied have shown benefit over baseline in bipolar
- Adolescent schizophrenia time to onset of effect
  - risperidone took 8 days vs placebo (PANSS)
  - olanzapine took 2 weeks vs placebo (BPRS-C)
  - aripiprazole took 4 weeks vs placebo (PANSS)
- The few trials comparing two antipsychotics found no difference (except clozapine)

Antipsychotics for Pediatric Bipolar Disorder

- Studies of the following all showed benefit
  - olanzapine
  - risperidone
  - quetiapine
  - aripiprazole
  - asenapine
- Roughly similar effect sizes

- So choose one based on onset time, side effects

Risperidone (Risperdal)

- ½ life 20 hours
- available liquid, dissolving tab, tabs, depot
- doses over 6mg per day behave like 1st generation antipsychotic in adults
- for mood or aggression treatment, usually don't need doses greater than 2mg
- TD incidence reported less than 0.5%

- The usual 1st line choice antipsychotic
  - Relatively predictable benefits
  - Lots of research in kids for different indications

Quetiapine (Seroquel)

- ½ life 6 hours
- some prescribe just as sleep aide
  - Risking permanent TD from a childhood sleep aide is not reasonable
  - However sleep aide AND bipolar treatment is worthwhile
- lower potency, may be experienced as “milder”
- Need generous doses for the anti-mania effect (i.e. 400mg a day)

Pathak S 2013

Aripiprazole (Abilify)

- ½ life 75 hours
- Pills, IM form available
- Novel: mixed agonist/antagonist
  - Often takes much longer to see benefits
  - some get agitation because of the med
- Reputation as weight neutral—not true in kids

- If need to help right away, not my preferred choice
  - More hit-or-miss than the other antipsychotics

Lurasidone

- *NO data in kids yet*
- ½ life 18 hours
- low antihistaminic activity
- minimal weight gain/metabolic problems in adults
  - I would not count on that for kids
- some akathisia and EPS making it more like risperidone or typicals
- seems to have a relatively rapid onset of clinical activity
- For adults, shown to have benefit for bipolar depression

Antipsychotic just for Irritibility/Aggression?

- Maladaptive aggression
  - inappropriate intensity/frequency/duration
  - associated with PDD, conduct d/o, adhd
  - atypical antipsychotics often prescribed
- risperidone if conduct d/o, low IQ
  - (ES 0.9, combined n=875)
- methylphenidate if comorbid ADHD
  - (ES 0.9, combined n=844)

E Pappadopulos et al 2006

FDA Antipsychotic Approvals

- Acute Mania (ages 10 years and older)
  - Risperidone, Aripiprazole, Quetiapine, Olanzapine, Ziprasidone, Asenapine
- Schizophrenia
  - Risperidone, Aripiprazole, Quetiapine, Olanzapine
    - (age 13 and older)
  - Paliperidone (age 12 and older)
  - Molindone and Haloperidol (age 12 and older)
- Irritability associated with autism
  - Risperidone (5 - 16 years)
  - Aripiprazole (6 - 17 years)

Atypical Antipsychotics

	Dosage Form	Usual Starting Dose	Sedation	Weight Gain	EPS (stiff muscles)	Bipolar (+) child RCT evidence?	FDA bipolar approved?	Editorial Comments
Risperidone (Risperdal)	0.25,0.5, 1,2,3,4mg 1mg/ml	0.25mg QHS	+	+	+	Yes	Yes (Age >10)	Generic forms. More dystonia risk than rest
Aripiprazole (Abilify)	2,5,10,15, 25,30mg 1mg/ml	2mg QD	+	+	+/-	Yes	Yes (Age >10)	Long ½ life, can take weeks to build effect
Quetiapine (Seroquel)	25,50,100, 200,300, 400mg	25mg BID	++	+	+/-	Yes	Yes (Age >10)	Pills larger, could be hard for kids to swallow.
Ziprasidone (Geodon)	20,40,60, 80mg	20mg BID	+	+	+/-	No	No	Greater risk of QT lengthen, EKG check
Olanzapine (Zyprexa)	2.5, 5,7.5, 10,15, 20mg	2.5 mg QHS	++	++	+/-	Yes	Yes (Age >13)	Greatest risk of weight gain, ↑cholesterol

Table + and – from Fedorowicz VJ. Fombonne E. (2005), Lublin, H; et al (2005), and Correll CU et al (2009)

Monitoring for all atypical antipsychotics: AIMS exam at baseline and Q6months due to risk of tardive dyskinesia. Warn of dystonia risk. Weight checks, fasting glucose/lipid panel Q6months at minimum.

Atypical Antipsychotic Risks

Common Side Effects (>10%)	Less Common Side Effects	Notable Rare Reactions (≤2%)
Weight gain (olanzapine >others)	Tremors	Tardive Dyskinesia
Muscle rigidity	Nausea or abdominal pain	Neuroleptic Malignant Syndrome
Parkinsonism	Akathisia (restlessness)	Lowered blood cell counts
Constipation	Headache	Elevated liver enzymes
Dry mouth	Agitation	Prolonged QT interval (ziprasidone > others)
Dizziness	Orthostasis	Tachycardia
Somnolence/fatigue	Elevated glucose	
	Elevated cholesterol/triglycerides	

From Hilt R, 2012

Atypical Antipsychotic Monitoring

Monitoring recommendation	Frequency Suggestion
Height and weight	At baseline and at each follow-up (at least every 6 months)
Fasting blood sugar, TG, Cholesterol	At least every 6 months
Screen for stiffness, movement disorder or tardive dyskinesia (like AIMS exam)	At least every 6 months
CBC with Diff	Once to catch if any suppression, a few months after initiation
BP/Pulse	at least once after starting medication
Cardiac history	At baseline, get EKG if in doubt about risk from a mild QT increase

From Hilt R, 2012

Lithium

- Rapid absorption
  - peaks in 0.5 to 2 hours
- Half life ~24 hours
  - longer if poor renal function (renal excretion)
- Narrow therapeutic index
- Drug levels 0.6 to 1.2 mEq/L
- Don’t go past 1.4 mEq/L
- Don’t combine with NSAIDS

Lithium

PROS

- FDA approved for mania >12 years
- Some evidence helps refractory depression
- Anti-suicide properties
- Some EB dosing guidelines (adjust for age/GFR)

CONS

- Narrow therapeutic index (close monitoring for toxicity w/ illness/dehydration; no NSAIDs)
- Usually best in combination, so committing to polypharmacy if you start here (best w/ atypical or VPA)
- SE in therapeutic range similar to early toxicity (tremor, diarrhea)
- SE often limit use (weight gain, acne, GI); HS dosing can minimize
- Hard to predict who will respond
- No evidence for maintenance treatment /slow anti-manic effects

Lithium Monitoring

- Baseline
  - renal screen (BUN/creatinine)
  - thyroid function
  - cbc with diff
  - calcium/phosporous
  - pregnancy test ? (epstein anomoly)
  - EKG
  - lithium level 5 days after start
- Q3 months
  - lithium level
- Q6 months
  - TSH, renal function

  - Warn about NSAID use, dehydration from sports

Depakote

- Possible use with aggression, bipolar
- Baseline
  - CBC, Diff with platelets
  - LFT
  - amylase?
  - Pregnancy test?
- Monitoring
  - hepatotoxicity risk highest if young, and in first 6 months
  - CBC/LFT every 6-12 months thereafter
  - Weight
  - Adult mania: levels 50-125 mcg/mL

Valproic Acid (Depakote)

PROS

- Single daily dosing can be effective (Depakote ER)
- Can be useful for maladaptive/non-specific aggression
- Studies suggest more helpful in combination

CONS

- Requires blood draws (levels, LFTs, CBC)
- Risk of hepatotoxicity (highest in first 6 months)
- High side-effect burden (weight gain, GI, tremor, sedation, rash)
- Less ideal for females (risk of birth defects (NTD), PCOS)

Valproic Acid

- How well does it work?
  - Fair, usually works best in adolescents in combination with an antipsychotic (better than either one alone)
  - Some RCT's have suggested that it works better than lithium on acute manic symptoms
  - Broad effects: also used for externalizing behavior disorders, conduct disorder
  - Lost in head-to-head trial with quetiapine
  - Similar long-term stabilizing effect to Lithium after stabilization with both divalproex and lithium

DelBello MP et al, 2002, 2006, Bowden C et al, 2004, Rana M et al, 2005, Findling, R et al 2005

Carbamazepine (Tegretol)

PROS

- Some empirical supports for aggression
- Similar response rates as Li and VPA (38%) (Kowatch et al, 2005)

CONS

- Drug/drug interactions (OCPs, Lithium)
- Blood draws to check levels (auto-induced metabolism)
- Weak evidence of benefit in bipolar (McClellan and Werry, 1997)
- Risk of aplasia and liver failure

Oxcarbazepine (Trileptal)

- FDA approved for adults with bipolar
- less medical risks than Carbamazepine
  - less liver/blood toxicity
- weight neutral
- levels don't correlate with efficacy or toxicity
- Only blinded adolescent bipolar mania trial (n=116) was negative in 2006
  - Not a great treatment choice for pediatric bipolar

Lamotrigine (Lamictal)

PROS

- Less sedation and lower side effect profile in general
- Some studies report bipolar depression help

CONS

- Not helpful for manic phase
- Requires monitoring of CBC and liver function
- Significant rash risk
- Slow titration (age >12)

Sleep Aides

- (Lifestyle)- limit caffeine, exercise, no drugs/alcohol
- (Sleep hygiene)
- Melatonin (mild sleep aide, can help regulate sleep cycle)
- Anti-histamines
- Trazodone
- Benzodiazepines
- Newer sleep aides

Reminder: Medications will not resolve…

- Family stress/conflict
- Abuse/neglect
- Poor parenting strategies
- School stress/conflict
- Strong willed temperament
- Intellectual deficits
- Developmental impairments

Questions?