Youth At Risk for Bipolar Disorder: The Importance of Recognizing Early Symptoms

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Objectives

Have a better understanding of:

I. The risk of developing psychiatric disorders, especially mood disorders, among first-degree relatives of patients with bipolar disorder.

II. The early manifestations of mood disorders among individuals at increased familial risk for bipolar disorder.

III. Treatment options for early symptoms of mood disorders in individuals at increased familial risk for bipolar disorder.
What is bipolar disorder

Psychiatric disorder with fundamental changes in mood and energy
Group of symptoms in bipolar disorder

**Mania**
- Euphoria or Irritability
- Increased energy or motivation
- Decreased need for sleep
- Psychomotor acceleration
- Increased sex drive

**Depression**
- Sadness
- Decreased energy or anhedonia
- Insomnia or hypersomnia
- Psychomotor retardation
- Decreased sex drive
Longitudinal course of bipolar disorder
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Definition of at-risk

Individuals who are first-degree relatives of patients with bipolar disorder (usually their siblings or children).

Family history of bipolar disorder is the most strong predictor of development of bipolar disorder.
“Bipolar disorder runs in families”

Risk in relatives (%)

- BD families: 8.7
- MDD families: 17.9
- HC families: 5.2

Smoller & Finn, 2003
Bipolar disorder is highly heritable

Risk of developing bipolar disorder

Goodwin & Jamison, 2007
Rates of psychiatric disorders in at-risk children

Pre-school (2-5 y.o.)

- Any psychiatric disorder: 26.4%
- No psychiatric disorder: 74.6%

School-aged (7-17 y.o)

- Any psychiatric disorder: 47.9%
- No psychiatric disorder: 52.1%

Birmaher et al., 2009; Birmaher et al., 2010
Psychiatric disorders in preschool children of parents with bipolar disorder

Birmaher et al., 2010

- ADHD
- Disruptive behavior disorders
- Any anxiety disorder
- Elimination disorders
- Pervasive developmental disorders
- Any mood disorder
- Bipolar NOS
- Depression NOS

Birmaher et al., 2010
Psychiatric disorders in school-aged children of parents with bipolar disorder

Birmaher et al., 2009
ADHD in at-risk youth

- Childhood ADHD does not appear to be part of the typical developmental illness trajectory of bipolar disorder.
- Problems with attention and distractibility may be part of early clinical presentation of bipolar disorder.
Anxiety disorders in at-risk youth

- Longitudinal study of 141 at-risk youth
- At 17 years old, 23.4% had a mood disorder
- Childhood diagnosis of anxiety disorder was associated with increased risk of later onset of major mood disorders in at-risk youth

Nurnenberger et al., 2011
Substance use disorders in at-risk youth

- Lifetime SUD was diagnosed in 24% of at-risk youth.
- Cannabis use being most common SUD.
- Peak hazard of SUD is between 14 and 20 years of age.
- Male sex, a prior mood disorder, and parental history of SUD increase risk of SUD in at-risk youth.
- SUD increases risk for psychosis in at-risk youth.
- The estimated hazard of a major mood disorder in those offspring with compared to those without a prior SUD was almost 3-fold.

Duffy et al, 2012
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Longitudinal studies show that, in at-risk youth:

- Mood disorders most often start during adolescence
- Sub-syndromal mania, major depressive episodes, and disruptive behavior disorders are associated with subsequent mania

Axelson et al., 2015
Anxiety, depression, and mania predict onset of bipolar in at-risk

Combination of:
- anxiety or depressive symptoms
- affective lability
- sub-clinical manic symptoms
- age at onset of bipolar disorder in parent

increase probability of bipolar spectrum diagnosis in at-risk

Hafeman et al., 2016
Can the risk of developing bipolar spectrum disorders in at-risk be calculated?

A theoretical model in which an individual with 6 factors below will have an increased chance of developing bipolar disorder within 5 years:

- Higher anxiety
- Higher depressive symptoms
- Higher manic symptoms
- Higher mood lability
- Poor psychosocial functioning
- Younger age of bipolar onset in parent

Hafeman et al., 2017
Possible trajectory of mood disorders in at-risk youth

Duffy et al., 2016
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Antidepressants and psychostimulants in at-risk youth

- Concern that antidepressants and stimulant treatment may induce mania in at-risk individuals
- However, treatment delay may lead to poorer outcomes

- Few case reports of stimulant-induced mania
- Risk is still unknown for stimulants
- More case reports of antidepressant-induced mania
- 21% of cases with family history of bipolar disorder
- 36% of at-risk youth with depression and treated with antidepressants had antidepressant-induced manic symptoms

- Careful with patients with prior history of antidepressant-induced mania, psychosis, younger age of depressive symptoms, family history of bipolar disorder
- **Red flags**: changes in sleep, irritability, and psychosis

Goldsmith et al., 2011
Increased risk for adverse events in at-risk youth: antidepressants

- Antidepressant medications may be poorly tolerated in at-risk youth
- About 60% had adverse reaction to antidepressant that led to antidepressant discontinuation
- Most common adverse event: increase in irritability
- Risk of adverse events of antidepressant therapy is higher in younger individuals
- Need for safer pharmacological interventions

Strawn et al., 2014
Symptoms severe enough for medications?
Depressive, manic, ADHD and/or anxiety symptoms severe enough to interfere with functioning or participation in treatment.

Yes

Adjust medication as necessary

On existing medication?

No

Start Medication. Wait 2 weeks after achieving stable dose on all meds before randomizing. Goal is to reduce symptoms to the point a patient can participate in therapy.

Unipolar Depression
No Hx AIM
1st line: CIT, BUP, SERT or ESC
2nd line: VFX, DUL, LTG

Hx AIM
1st line: LTG
2nd line: LIT or QUE

Unipolar Depression
ADHD, Not on ATD
1st line: BUP

ADHD and on ATD
1st line: MPH or MAS
2nd line: ATX

Unipolar Depression
Anxiety (No hx AIM)
1st line: CIT, SERT, ESC, FLUV
2nd line: CNZP, GBP

Anxiety (hx AIM)
1st line: CNZP, GBP

Bipolar Disorder NOS
Manic/Mixed Sxs
1st line: ARIP*, QUE†, RIS, LIT**
2nd line: LIT, DVX, LTG
3rd line: OLZ, ZIP, CBZ, OXC, ASN, LUR, PAL

Bipolar Disorder NOS
Depressive sxs
1st line: LG, LIT* or QUE
2nd line: ASN

ADHD
1st line: MPH or MAS
2nd line: Guanfacine
3rd line: ATX

Schneck et al., 2017
Non-pharmacological approaches: Family-focused therapy
Family therapy for at-risk youth

- Youth in family therapy had more rapid recovery from their initial mood symptoms (hazard ratio = 2.69, p = .047), more weeks in remission, and a more favorable trajectory of manic symptoms over 1 year than youth in EC.

- Family therapy may hasten and help sustain recovery from mood symptoms among youth at high risk for BD.

Miklowitz et al., 2013
Non-pharmacological approaches: mindfulness

- Being completely aware of what’s happening in the present
- Experience life without judgment or preconceived notions
- Aware of what is going on inside and all that’s happening around you
- It means not living life on “autopilot.”
Mindfulness for at-risk youth

- Small clinical trial for at-risk youth with anxiety disorders
- 10 adolescents, mean age=13 years old, 80% girls
- 12 weeks of mindfulness-based cognitive therapy
- Reduction in anxiety symptoms after therapy, either rated by clinic or by the youth
- Emotion regulation improved after therapy
- High levels of feasibility, acceptability and usefulness of the intervention by parents and youth.

Cotton et al., 2016
Conclusions

- At-risk youth are at increased risk to develop psychiatric disorders, particularly mood disorders.

- The most consistent predictors of onset of bipolar spectrum disorders among at-risk youth are anxiety, depression, sub-syndromal mania, emotional lability, and poor psychosocial functioning.

- No specific treatment exist for psychiatric disorders in at-risk youth; risk of inducing mania has to be considered when prescribing antidepressants to at-risk
Thank you