MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

Juvenile Depression

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Disclosures

Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.

Agenda

- Phenomenology of Depression in Youth
- Differential Diagnosis
  - Bipolar Disorder
  - Disruptive Mood Dysregulation Disorder
- Treatment

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DSM 5 Diagnosis

- Criteria for mood disorders the same as for adults except dysthymia only requires one year instead of two

Developmental Differences

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Children

- somatic complaints, anxiety, withdrawn and sad appearance, poor self-esteem, mood-congruent auditory hallucinations
- behavioral problems, psychomotor agitation
- may have irritable mood instead of depressed mood

Adolescents

- anhedonia, psychomotor retardation, delusions, hopelessness
- negativistic, restlessness, aggression, social isolation, school difficulties, substance abuse
- melancholia, suicide attempts (and lethality), impairment of functioning increase with age

Phenomenology

- Reality testing intact or improved
- Depressive episodes are remembered
- Mistook for “tumult of adolescence”
- Not necessarily a life long illness with one episode
- Melancholic – decreased sleep, decreased appetite, diurnal variation
- Atypical–increased sleep, increased appetite, carbohydrate cravings, sensitivity to criticism

Epidemiology

Prevalence increases with increasing age

Children: point prevalence 1-2%

- Females=males

Adolescents: cumulative prevalence 14-25%

- Rate in females twice that in males

Etiology

Genetics

- 50% of the variance in the transmission of mood disorders is genetic
- Possible evidence for MAOI-A gene and serotonin transporter gene

Biologic

- MRI scans show low frontal lobe volume and high ventricular volume

Environment

- Having one depressed parent doubles the risk for child (both parents depressed quadruples the risk)
- Family conflict or divorce, abuse or neglect, more rejection and less expression of affect, less support, communication problems, family SES, recent stressor or loss

Comorbidity

- 40% to 70% have comorbid disorders
- Most common comorbid disorders are:
    - Dysthymic Disorder and Anxiety Disorders (30%–80%)
    - Disruptive Disorders (10%–80%)
    - Substance Abuse (20%–30%)
- Psychosis occurs in 25% of depressed youth
    - usually a single, critical voice

Sequelae

Increased risks for later adolescence and adulthood:

- Bipolar disorder
- Suicidal behavior
- Homicidal behavior
- Tobacco use
- Alcohol and drug use
- Impaired interpersonal relationships
- School problems
- Increased physical problems
- Early pregnancy
- Impairment in global functioning

Course

- Recurrence of Major Depression is common:
    - 40% by 2 years, and 70% by 5 years
- Development of Bipolar I and II is also common:
    - 20% to 40% of adolescents with Major Depression develop Bipolar I within 5 years of onset of depression

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Diagnostic Considerations

- Predictors of manic switching:
  - family history
  - psychomotor retardation
  - psychosis
  - rapid onset of depression
  - earlier onset of depression
  - atypicality
  - affective storms- tantrum quality
- Rates of manic switching peak ages 10–14.
- No antidepressant uniquely “safe.”
- Disagreement about diagnostic implication of manic switching only in context of antidepressants

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Controversy

- Was added to DSM-5 by committee concerned with the increase in diagnosis of bipolar disorder
- Was designed to capture children with chronic, nonepisodic irritability and temper tantrums but without mania
- Built around the idea that these children have not been shown to transition to mania in longitudinal studies

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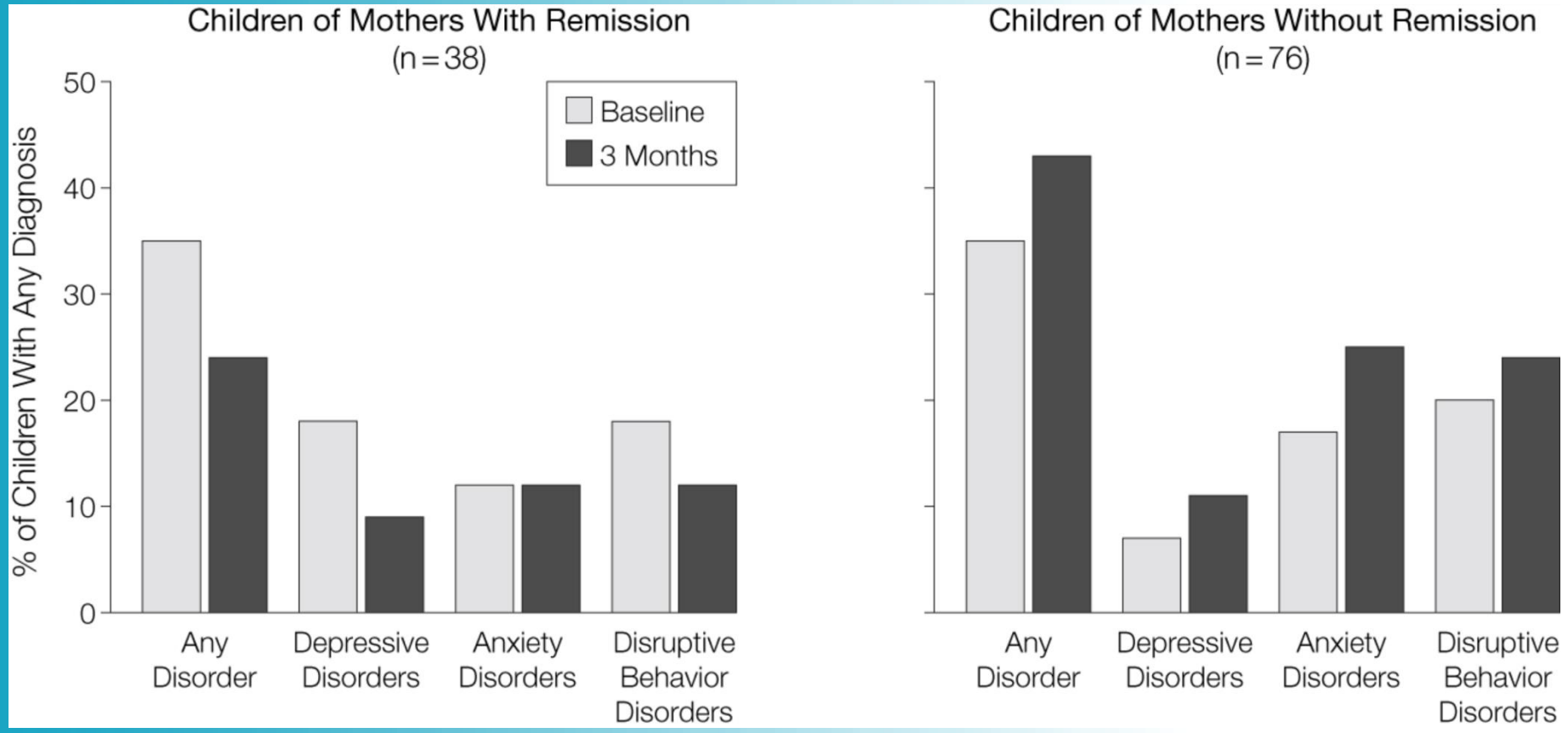
Treatment

- Treat the parents
- Treat co-morbidity
- Psychopharmacology
- CBT: 5 positive and 1 negative trial to date in children and 6 positive and 1 negative in adolescents
- Encourage increased physical activity (Psychosomatic Medicine, 2004)

Treating Mothers



Weissman et al. *JAMA.* 2006;295(12):1389-1398.

Psychopharmacology

- ***TCAs*** generally avoided due to potential lethality and side effect burden only clomipramine has empiric support
- ***MAOIs*** 80% of adolescents do not comply with dietary restrictions
- ***SSRIs, SNRIs, Atypical Antidepressants*** favored in practice due to relative safety in overdose and lower side effect burden

Psychopharmacology

- Those most likely to benefit:
  - substantial impairment in multiple domains
  - psychotic depression
  - diurnal variation
  - melancholia
  - (bipolar depression)
  - severe or recurrent episodes
  - children that refuse therapy

Medications for Pediatric Depression

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Starting doses:

- Fluoxetine*@ (Prozac) @ 5-10 mg QD
- Sertraline*(Zoloft) 12.5-25 mg QD
- Citalopram (Celexa) 5-10 mg QD
- Paroxetine** (Paxil) 5-10 mg QD or 12.5 mg CR
- Fluvoxamine* (Luvox) 12.5-25 mg QD
- Venlafaxine (Effexor) 12.5-25 mg IR or 18.75-37.5 XR
- Bupropion (Wellbutrin) 37.5 mg IR or 100 mg SR
- Mirtazapine (Remeron) 3.75-7.5 mg QHS
- Escitalopram@ (Lexapro) 2.5-5 mg QD
- Duloxetane (Cymbalta) 20 mg QD
- Desvenlafaxine (Pristiq) 25 mg QD
- Vilazodone (Viibryd) 10 mg QD
- Vortioxetine (Trintellix) 5 mg QD
- Cariprazine (Vraylar) 1.5 mg QD

*=FDA approved to treat Pediatric OCD
@=FDA approved to treat Pediatric Depression
**=currently FDA recommends NOT using to treat Pediatric Depression

Evidence: Antidepressants

- **Fluoxetine and Escitalopram** are the only FDA approved agents.

- Controlled data, published and unpublished readily available.

TADS

Treatment of Adolescent Depression Study

- NIMH sponsored multi-center controlled clinical trial
  - 13 sites
- 12-17 year olds with MDD
  - N=439
- Aim to compare efficacy of fluoxetine, CBT, combination, & placebo over 36 weeks with 1 year follow-up.
  - Fluoxetine 10-40 mg/day

March et al. *JAMA*. 2004;292(7):807-820.

TADS

- TADS study looked at fluoxetine alone, fluoxetine + CBT, and CBT alone. Rates of improvement:
  - 71% for combo
  - 61% for fluoxetine alone
  - 43% for CBT alone
  - 35% for placebo

TORDIA

Treatment of SSRI-Resistant Depression in Adolescents

- Adolescents (12–18) who failed 8 weeks of SSRI
  - N=334 patients; 6 centers
- Randomized to 12 weeks of switch to
  - Another SSRI
    - Paroxetine, citalopram or fluoxetine (20–40 mg)
  - Another SSRI + CBT
  - Venlafaxine (150–225 mg)
  - Venlafaxine + CBT
- CBT 9 times in 12 weeks

Brent et al. *JAMA*. 2008.

TORDIA

- Higher response rate to switch to
  - New Medication + CBT (54.8%) vs.
  - New Medication alone (40.5%)
- No difference in response rate to switch to
  - Venlafaxine (48.2%) vs.
  - Second SSRI (47%)
    - No difference between the SSRIs
- No difference between treatments in
  - Adverse events
  - Self harm or suicidal adverse events
  - 17 subjects attempted suicide; no completers

Brent et al. *JAMA*. 2008.

Treatment

Mild to moderate: Therapy

Moderate to severe:

- Antidepressants plus therapy
- Antidepressants
- Therapy

Therapies:

- Cognitive-behavioral Therapy
- Family Therapy
- Psychodynamic Psychotherapy

Treatment

- Monotherapy
    - Consider SE profile
    - First degree relative response
    - Comorbidities
    - Risk of Bipolar Disorder
- Increase dose, consider rapid titration
    - Full response 8 weeks
- Incomplete response
    - Cross titration v augmentation
- Combination therapy
- ECT with antidepressant vs. ECT maintenance

Treatment

- Continue antidepressants 1 calendar year after remission "for no reason"
- Slow wean
- One recurrence, repeat, though likely will relapse after a second wean so could consider indefinite maintenance treatment

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Thank you!