Treating Adolescent Depression

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Disclosures
• None

Objectives
• Is the depression caused by a general medical condition or medication?
• Is the depression related to drug or alcohol abuse?
• Is this depression related to a stressful life event?
• Is this a chronic, mild depression?

Objectives
• Is this another type of depressive disorder?
• Is this Major Depression?
• Is there a coexisting mental disorder?
• Is this a dangerous disorder?

Black Box Warning
• 2004 FDA warning
  Antidepressants may cause suicidal thinking and behavior
  • 372 studies with 100,000+ patients
  • Antidepressants 4% (none fatal)
  • Placebo 2%
  • Only applies to children and adolescents <18 yo
  • No increased risk after 24 yo
  • 65 and older has clear protection
Unintended Consequences

Primary care prescribing dropped 4.61%
Diagnosing dropped
- Children – 44%
- Adolescents – 37%
- Adults – 29%
Observational – not necessarily causational
- I.e. Insurance Company reimbursement changes
- How medications are covered

Significant increase in Psychotropic drug poisonings
- Two years after warning
- 10 to 17 yo increased 21.7%
- 18 to 29 yo increased 33.1%
- Suicide rate gradually increased 1999 to 2010
- No increase after warning (also no decrease)
Need to harm
- 111 to 143
- Treat and Monitor

Suicide Still a Symptom

- Suicide
- 17% of students seriously consider suicide in previous 12 months (9-12 grade 2013) - 22.4% F, 11.6% M
- 11% made a plan – 16.9% F, 10.3% M
- 8% attempted suicide -10.6%, F, 5.4% M
- 2.7% suicide attempt required medical attention – 3.6%, F, 1.8% M
- Suicide is the 3rd leading cause of adolescent death in the US (Accidents 48%, Homicide 13%, Suicide 11%, Cancer 6%)

Unintended Consequences

US Mental Health Research Network
Claims Cohort study
2 Years after warning

Scope of the Problem

- Children: 1 year prevalence rate of 2%
- Adolescents: 1 year prevalence rate of 4% to 8%
- National Comorbidity Survey: 6.1%, 15-24 years
- Lifetime prevalence (up to age 18) 15%-20%
- 65% of adolescents report some depressive symptoms
- 5% to 10% of youth with subsyndromal symptoms have considerable psychosocial impairment, high family loading for depression, and an increased risk for suicide and developing MDD (Fergusson et al., 2005)

Spectrum of Depression:

- Major Depressive Disorder, Single Episode
- Major Depressive Disorder, Recurrent
- Dysthymic Disorder
- Adjustment Disorder with Depressed Mood
- Adjustment Disorder with Mixed Anxiety and Depressed Mood
- Bipolar Disorder
- Seasonal Affective Disorder
- Substance-Induced Mood Disorder
Scope of the Problem

Development of overall rates of clinical depression (1-year point prevalence combining new cases and recurrences by age and gender) (Hankin, et al., 1998)

- Mean length of episodes: 7 to 9 months
- 6% to 10% become protracted
- Recurrence: 30-50%
- Approximately 20% develop bipolar disorder
- Associated with significant:
  - comorbidity
  - functional impairment
  - risk for suicide
  - substance use

Scope of the Problem

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Etiology

- Genetics
- Prenatal factors
- Parental depression*
- Cognitive style in adolescence
- Stressful life events
- Hormonal fluctuations
- Lack of parental care

Medical Causes

- Various medical causes
  - Hypothyroidism
  - Anemia
  - Autoimmune disorder
  - Chronic fatigue syndrome
  - Sleep disorder
  - Etc.
- Shared Symptoms
  - Fatigue
  - Low energy
  - Sleep disturbance
  - Appetite disturbance

Co-occurring Substance Use Disorders

- 43% of adolescents receiving mental health services had been diagnosed with a co-occurring SUD.
- CMHS (2001) national health services study
- 33% of adolescents with significant emotional and behavior problems reported alcohol and drug dependence.
- SAMHSA 1994-96 National Household Survey
- 62% of adolescent males and 82% of adolescent females entering SUD treatment had a significant co-occurring emotional/psychiatric disorder.
- SAMHSA/CSAT 1997-2002 study
- 75-80% of adolescents receiving inpatient substance abuse treatment have a co-existing mental disorder

Stressful Life Event

- Acute family problems—parental mental health concerns, abuse/neglect, cultural/generational conflicts, unresolved grief
- School issues—learning disability, attendance problems, harassment, isolation
- Peer/partner issues—pregnancy, sexual pressure, break-ups, sexual orientation issues, loss of friends
- Adjustment Disorder
### Types of Depression

#### Subtypes of Depression

**Unipolar Depression**
- Non-Psychotic
- Psychotic

**Bipolar Disorder**
- Manic (Type I)
- Hypomanic (Type II)

#### Symptoms

1. Feeling tired or having little energy
2. Little interest or pleasure in doing things
3. Trouble falling, staying asleep or waking up early
4. Poor appetite, weight loss or overeating
5. Feeling sad or having little energy

#### Categories

- Mild
- Moderate
- Severe

### Pittsburgh Bipolar Offspring Study

- 248 children of parents with bipolar disorder and matched controls
- Followed for an average of 8 years
- Three strongest predictors
  - Anxiety or depression at the start of the study
  - Affective lability at baseline and shortly before the diagnosis of bipolar
  - Low level manic symptoms shortly before diagnosis

### Patient Health Questionnaire 9 Symptom Checklist Modified for Adolescents (PHQ-9 A)

- 9 items (0) – none, several, more than half, nearly every day
- Days with symptoms over last 2 weeks
- Similar to adult version with more questions about suicide
- Parents often provide best source of information – describe affect

#### Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Affect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Down, depressed, irritable or hopeless?</td>
<td>Irritable or cranky mood</td>
</tr>
<tr>
<td>2. Little interest or pleasure in doing things?</td>
<td>Boredom, loss of interests in sports, video games, giving up favorite activities</td>
</tr>
<tr>
<td>3. Trouble falling, staying asleep or waking up too much?</td>
<td>Changes in sleep pattern, delays in going to or falling asleep, need for or decrease in night sleeping</td>
</tr>
<tr>
<td>4. Poor appetite, weight loss or overeating?</td>
<td>Failure to gain weight as Normally expected, overweight and weight gain</td>
</tr>
<tr>
<td>5. Feeling tired or having little energy?</td>
<td>Persistently feels tired, feels lazy</td>
</tr>
</tbody>
</table>

#### PHQ-9 A

- Self-critical; blaming oneself for things beyond one’s control; “No one likes me. Everyone hates me”; feels stupid |
- Declines to perform in school due to decreased motivation and ability to concentrate |
- Difficulty sitting still, pacing or very slowed down with little spontaneous movement |
- Frequent thinking and talking about death, wishing about death, giving away favorite toys or belongings |
PHQ-9 A

In the past year have you felt depressed or sad most days even though you felt ok sometimes? Yes No

If you are experiencing any problems on this form, how difficult have these problems made it for you to do your work, take care of things at home or get along with other people? Not Somewhat Very Extremely

Has there been a time in the past month when you have had serious thoughts about ending your life? Yes No

Have you EVER in your WHOLE LIFE tried to kill yourself or made a suicide attempt? Yes No

PHQ-9 Score Provisional Diagnosis Treatment Recommendation Patient Preference should be considered

5-9 Minimal Symptoms* Support, educate to call if worse, return in one month

10-14 Minor depression Dysthymia* Major Depression, mild Support, watchful waiting Antidepressant or psychotherapy Antidepressant or psychotherapy

15-19 Major Depression, moderately severe Antidepressant or psychotherapy Antidepressant or psychotherapy

>20 Major Depression, severe Antidepressant and psychotherapy (especially if not improves on monotherapy)

* If sx last >2 years consider Dysthymic disorder

Diagnostic Dilemmas: Comorbidity

- Depression
  - 40% to 90% have co-morbid dx; 50% 2+
    - Dysthymia and anxiety – 30% to 80%
    - Disruptive Disorders – 10% to 80%
    - Substance Abuse – 20% to 30%
  - Community-based study—43% of depressed youth had at least one other concurrent diagnosis, most commonly anxiety (18%). (Rhode, et al., 1994)
  - Odds Ratios—Anx 8.2; Conduct and ODD 6.6; ADHD 5.5 times more common in depressed youth

Treatment Options

Depending on severity:
- Watchful waiting
- Supportive management
- Psychosocial interventions
- Cognitive Behavioral Therapy (CBT)
- Interpersonal Therapy
- Medication

Treatment of Adolescent Depression Study (TADS)

- NIMH, multicenter, long term study of Adolescent depression
- Four arms
  - Fluoxetine monotherapy (10-40 mg)
  - Cognitive Behavioral Therapy monotherapy (CBT)
  - Combination of Fluoxetine with CBT
  - Placebo
- 12 week study

Treatment of Adolescent Depression Study (TADS) - Response

Suicidal thinking improved across all treatment with greatest for AD+CBT
Treatment of Adolescent Depression Study (TADS) – Remission

<table>
<thead>
<tr>
<th>Percent in Remission</th>
<th>Fluoxetine only</th>
<th>CBT only</th>
<th>Placebo</th>
<th>Fluoxetine + CBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>22%</td>
<td>16%</td>
<td>17%</td>
<td>0%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Patients with Response only had persistent vegetative sx – low energy, sleep problems (Kennard et al. 2006)

Treatment of [SSRI]-Treatment Resistant Depression in Adolescents study (TORDIA)

- Follow up study of patients with persistent symptoms
- Adolescents 12-18
- Switch study – 4 groups
  - Different SSRI (paroxetine, citalopram, fluoxetine)
  - Different SSRI + CBT
  - Switch to venlafaxine
  - Switch to venlafaxine + CBT

Management of Depressive Episode: Duration of Treatment

- CBT + medication Switch – marked increase in response
- No difference with switch to venlafaxine
- 72 week remission rate 60%
- No difference between choices
- Switch to another SSRI maybe more rapid and fewer suicidal ideations than switch to venlafaxine

Sequential Treatment of Pediatric MDD to Increase Remission and Prevent Relapse study

- 144 patients – average age 13.8 +/- 2.6 years
- Randomized to medications or medications + CBT
- No difference in time to remission – most reached remission in 3 months
- Risk of relapse 2X lower in CBT + medication vs. medication alone
  - 36% vs 62%
  - Time of relapse was longer by 3 months

Medications approved for use in pediatric patients

<table>
<thead>
<tr>
<th>Class</th>
<th>Medication</th>
<th>FDA indication</th>
<th>Age range</th>
<th>Target dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI</td>
<td>Fluoxetine</td>
<td>Major Depressive Disorder</td>
<td>6-17</td>
<td>40mg/day</td>
</tr>
<tr>
<td></td>
<td>Fluvoxamine</td>
<td>Obsessive Compulsive Disorder</td>
<td>7-17</td>
<td>150mg/day</td>
</tr>
<tr>
<td></td>
<td>Sertraline</td>
<td>Obsessive Compulsive Disorder</td>
<td>6-17</td>
<td>150mg/day</td>
</tr>
<tr>
<td></td>
<td>Escitalopram</td>
<td>Major Depressive Disorder</td>
<td>12-17</td>
<td>&gt;75mg/day</td>
</tr>
<tr>
<td>SNRI</td>
<td>Duloxetine</td>
<td>Generalized Anxiety Disorder</td>
<td>7-17</td>
<td>50-100mg/day</td>
</tr>
</tbody>
</table>
### Adverse Side Effects of SSRIs
- Suicidality*
- Manic switch
- Akathisia
- Agitation
- Irritability
- Disinhibition
- Nightmares/sleep disturbances
- Gastrointestinal
- Weight gain
- Sexual dysfunction
- Bleeding
- Possible congenital abnormalities
- Withdrawal syndrome
- Serotonin Syndrome

### Medications Issues
- 3 to 8 fold increase in the use of antidepressants in children and adolescents from approx. 1990-2000 ([Zito, et al., 2002; Rushton, et al. 2001](#))
- Resistance/Adherence: Adolescent Attitudes ([Gray, 2003](#))
  - 69% stopped taking meds by end of 4 weeks
  - 58-61% report bias against meds
  - “Medicine might... change my personality, control my thoughts, not let me be myself”
- Issues around belief in efficacy of meds and stigma about MI

### Which Antidepressant?
- Two considerations: effectiveness and safety
  - SSRIs are safest
  - Fluoxetine is most effective
- Begin fluoxetine
  - Start with 10mg of fluoxetine
  - Increase to 20mg after one week
  - 20mg for pre-pubertal children
  - 30 or 40mg for adolescents
  - If not fluoxetine try another SSRI (e.g., sertraline or escitalopram)
- Continue treatment 6 months after recovery

### Who gets better?
- Younger (<15) better than older is responding to medications
- Longer term treatment (>9 mos)
  - Girls more likely to relapse (61.1 vs 31.3)
  - More severe more likely to have persistent symptoms
  - Suicidality poorer response
  - Anxiety or OCD more likely to have persistent symptoms
  - Early response good long term predictor

### Other Treatments
- Electroconvulsive therapy (ECT): good evidence of effectiveness in severe cases
- Transcranial Magnetic Stimulation (TMS)
- Light Therapy (in seasonal mood disorder)
- Adjunctive treatment
  - Buspirone
  - Methylfolate
  - Omega 3 Fatty Acids
  - Vitamin D
  - 5-Adenosyl Methionine (SAMe)
  - Exercise

### Characteristics of Cognitive-Behavioral Therapies:
1. Thoughts cause Feelings and Behaviors.
2. Brief and Time-Limited.
   - Average # of sessions = 16 VS psychoanalysis = several years
3. Emphasis placed on current behavior.
4. CBT is a collaborative effort between the therapist and the client.
   - **Client role** - define goals, express concerns, learn & implement learning
   - **Therapist role** - help client define goals, listen, teach, encourage.

5. Teaches the benefit of remaining calm or at least neutral when faced with difficult situations. (If you are upset by your problems, you now have 2 problems: 1) the problem, and 2) your upsetness.


7. CBT is structured and directive. Based on notion that maladaptive behaviors are the result of skill deficits.

8. Based on assumption that most emotional and behavioral reactions are learned. Therefore, the goal of therapy is to help clients unlearn their unwanted reactions and to learn a new way of reacting.

9. Homework is a central feature of CBT.

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**Interpersonal Therapy-Adolescent**

- Principle of IPT-A is that interpersonal problems may cause or exacerbate depression and that depression, in turn, may exacerbate interpersonal problems. Treatment will target patient’s interpersonal problems to improve both interpersonal functioning and his/her mood.
- Essential elements of interpersonal therapy include identifying an interpersonal problem area, improving interpersonal problem-solving skills, and modifying communication patterns.

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**Summary**

- Is the depression caused by a general medical condition or medication?
- Is the depression related to drug or alcohol abuse?
- Secondary to or complicated by?
- Is this depression related to a stressful life event?
- Adjustment Disorder
- Is this a chronic, mild depression?
- Dysthymic Disorder

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**Summary**

- Is this another type of depressive disorder?
- Bipolar Disorder, Seasonal Affective Disorder?
- Is this Major Depression?
- Assess for severity
- Is there a coexisting mental disorder?
- Anxiety disorder, ADHD, Oppositional Defiant Disorder, Substance use disorder
- Is this a dangerous disorder?
- Safety Plan, Hospitalization