Recognizing and Treating Depression in Children and Adolescents.

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How common is depression?

- Functionally impairing depression occur in 2-10% of children and adolescents
- 0.3% in preschoolers
- 2% of elementary school children
- 5.10% adolescents
- Prepubertal depression Boys=Girls
- After puberty F/M ratio is 2:1
Epidemiology

• 10-20% of adolescents have had at least one major depressive episode by age 18y.o.

• Untreated episode can last 7-9 mo and about 50% of patients will relapse within 5 years of their first episode

• Substance abuse and anxiety increase the risk of depression by two- to threefold
Epidemiology

• One study of 9863 students age 10-16y.o. found that
• 29% of American Indian
• 22% Hispanic
• 18% Caucasian
• 17% Asian-American
• 15% African-American exhibited symptoms of depression.
Age specific clinical symptoms:

• > 19y.o. Depressed mood or anhedonia and at least four of the nine following symptoms that last at least 2 wk with functional impairment: (1) sleep and appetite changes, (2) psychomotor changes (slowing or agitation), (3) hopelessness, (4) worthlessness, (5) diminished energy, (6) poor concentration, (7) tearfulness, (8) suicidal thoughts, and (9) suicide plan
Age specific clinical symptoms

- 12-18y.o. Same as adult criteria except more impulsivity, irritability, and behavioral changes; more reckless behavior; poor school performance; more sleep and appetite disturbances than displayed by younger children; suicidal thoughts and attempts similar to those in adults; genetic link to depression stronger; chronic course more likely.
Age specific clinical symptoms

- 9-12y.o. Same as adult criteria except more complaints of boredom, low self-esteem, guilt, hopelessness, wanting to run away from home, and fear of death. Compared to adolescents, children of this age group are less likely to suffer from delusions or make serious attempts to commit suicide.
Age specific clinical symptoms

- 6-8y.o. Same as adult criteria except for difficulty verbalizing feelings; more somatic complaints (e.g., "my tummy hurts, " "I don't feel good"); outbursts of crying, shouting; unexplained irritability; perceptual abnormalities, anhedonia observed by others.
Age specific clinical symptoms

- 3-5 y.o. Same as 6–8 yr olds, except symptoms not necessarily present over an entire 2-wk period; markedly diminished interest in play; feelings of worthlessness or suicidal, self-destructive themes persistently evident in play or caregivers may notice that healthy child is not interested in play.
Neurobiological changes in depression

- Depression is thought to be secondary to changes in cerebral blood flow and metabolism of brain regions participating in neuroanatomic circus involved in mood disorders
- Functional and structural brain abnormalities
- Serotonergic, cathecholaminergic, HPA, CRH system dysfunctions
Neurobiological changes in depression

• Recent studies suggest HPA axis hyperactivity in adults with depression and anxiety
• Hyperactivity of CRH primary through CRH1 receptor is well established in depression and PTSD
• Variation in the gene encoding the Serotonin 2A receptor associated with outcome of antidepressant treatment.
Neurobiological changes in depression

• Decreased blood flow in pre-frontal cortex and metabolism was found to correlate with severity of depression

• Decreased blood flow and metabolism in Basal ganglia and possibly temporal lobe

• Cognitive impairment may correlate with decreased metabolism in frontal and cerebellar areas
Neurobiological changes in depression in Youth

- Smaller hippocampal volume and amygdala
- Blunted growth hormone secretion
- Significantly lower concentration of Glutamate in the brain (anterior cingulate cortex)
Differential diagnosis

- Bipolar mood disorder
- Anxiety disorders
- Psychotic illness
- PTSD
- Other co-morbidities: ADHD, ODD, OCD, GID.
Suicide and risk factors

• Suicidality is the main concern as it is common in youth with or without the depression

• 19% of 15-19 y.o. thinking about suicide with 9% attempting suicide each year

• 35-50% depressed pt will attempt suicide and 2-8% will complete it over decade.
Suicide and risk factors

• Rate of completed suicide in youth is rare 0.008% in youth ages 15-19 y.o. over 12 month

• Suicide completion rates in youth decreased from 1995-2005 with reasons cited for this reduction include limited access to firearms and treating depression
Suicide risk factors:

- Prior attempts
- Family history of suicide
- Childhood sexual abuse
- Personality traits
- Substance use
- Untreated mental illness
- Environmental
Treatment

- Therapy: CBT, Interpersonal therapy
- Pharmacological
- Psychosocial interventions especially in children 8y.o. and younger, including family counseling and environmental modifications.
- Effectiveness of CBT vs. psychopharmacology has not been adequately assessed in children and adolescents.
Treatment

• One study compared placebo with Fluoxetine and CBT, Fluoxetine alone, and CBT alone in depressed adolescents

• Combination of CBT and Fluoxetine produced best therapeutic outcome, and all treatments were more effective than placebo.
Treatment of depression

- CBT considered first line of treatment with efficacy rate of 60-70%.
- Choice of treatment will depend on severity of presenting symptoms, developmental stage, available resources, etc.
Psychopharmacology

• In October of 2004 FDA issued black box warning on all of the antidepressants regarding an increased risk for suicidal behaviors/ideations

• This was based on the results of 24 placebo-controlled trials of 4400 children and adolescents, which found that antidepressant use was associated with an approximate 4% frequency of new onset suicidal behavior compare to 2% with placebo. None of the children in clinical studies completed suicide.
Psychopharmacology

• Fluoxetine is FDA approved for treatment of depression in children 8y.o. or older, bulimia and OCD in adolescents 18y.o. and older.
• Doses 10-40 mg/day
• No withdrawals due to long half-life of 4-5 weeks
• Drug-drug interactions (elevated plasma levels of TCA, Carbamazepine, other SSRI’s)
Psychopharmacology

- Sertraline is FDA approved for OCD in children 6-12y.o. and depression, PTSD, OCD in adolescents 18y.o. and older
- Half life of 5-7 days, possible withdrawals
- Doses 25-100mg/day
- Drug-drug interactions, 2 weeks wash out with MAOI’s
Psychopharmacology

• Fluvoxamine is FDA approved for OCD in children 8y.o. and older
• Doses 25-200mg/day, increased in increments of 4-7 days by 25mg.
• Other existing drugs has no FDA approvals in children and adolescents.
• Strattera an ADHD medication received FDA warning on suicidality because of mechanism of action through the catecholamine pathway.
Psychopharmacology

• No published controlled clinical trials have established the efficacy of Bupropion, Venlafaxine or Cymbalta.

• Controlled clinical trials have shown no significant difference between TCA’s and placebo in the treatment of depression in youth
## Published trials of SSRI’s vs. placebo in youth

<table>
<thead>
<tr>
<th>Drug</th>
<th>Length of Tx.</th>
<th>Age</th>
<th>No. of Pts.</th>
<th>% improved Drug vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>8wk</td>
<td>8-18</td>
<td>48/48</td>
<td>16.2 vs 6.7 (p=0.002)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>56 vs. 33 (p=0.02)</td>
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<tr>
<td>Fluoxetine</td>
<td>9wk</td>
<td>8-17</td>
<td>209/210</td>
<td>65 vs. 53 ns</td>
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<td></td>
<td></td>
<td>52 vs 37 (p=0.03)</td>
</tr>
<tr>
<td>Sertraline</td>
<td>10wk</td>
<td>6-11</td>
<td>86/91</td>
<td>24 vs. 22 ns</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-17</td>
<td>103/96</td>
<td>21.5 vs 18.2</td>
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<tr>
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<td></td>
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<td></td>
<td>Non significant</td>
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Published trials of SSRI’s vs. placebo in youth

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<tbody>
<tr>
<td>Paroxetine</td>
<td>8wk</td>
<td>12-18</td>
<td>93/87</td>
<td>69 vs. 59 on HAMD</td>
<td>65 vs. 48</td>
</tr>
<tr>
<td>Imipramine</td>
<td>8wk</td>
<td>12-18</td>
<td>95/87</td>
<td>Non significant</td>
<td>52 vs. 48</td>
</tr>
<tr>
<td>Citalopram</td>
<td>8wk</td>
<td>7-17</td>
<td>89/85</td>
<td>36 vs. 24 (p&lt;0.05)</td>
<td>47 vs. 45</td>
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Antidepressants with well established efficacy for the tx of depression in Youth

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Line</th>
<th>Dosing Information</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Fluoxetine</td>
<td>First line</td>
<td>≤11 yr, 5 mg/day; ≥12 yr, 10 mg/day (10–40 mg/day)</td>
<td>Well studied in OCD and bulimia</td>
</tr>
<tr>
<td>Sertraline</td>
<td>First line</td>
<td>≤11 yr, 12.5 mg/day; ≥12 yr, 25 mg/day (25–200 mg/day)</td>
<td>Effective for OCD and other anxiety disorders</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Second line</td>
<td>≤11 yr, 10 mg/day; ≥12 yr, 20 mg/day (20–60 mg/day)</td>
<td>Lower risk of drug interactions</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Second lined</td>
<td>≤11 yr, 37.5 mg IR b.i.d.; ≥12 yr, 100 mg ER/day (100–400 mg/day)</td>
<td>Can increase levels of atomoxetine, amphetamine</td>
</tr>
</tbody>
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Recommendations

• Multimodal treatment
• Fluoxetine should be considered as a first line antidepressant
• In youth the risk of suicide is highest in first weeks to months of treatment or when doses are changed
• Monitor for risk of switching to mania/hypomania
• Refer to a child psychiatrist.
For More Information

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