Medicating Children and Adolescents

Is This an Evidence-Based Practice?
Short-term Benefits of Stimulants for ADHD

Stimulants are highly effective in “dramatically reducing a range of core ADHD symptoms such as task-irrelevant activity (e.g., finger tapping, fidgetiness, fine motor movement, off-task during direct observation) and classroom disturbance.”

--NIMH investigators in 1995
Assessment of Long-term Effects of Stimulants, Early 1990s

“Stimulants do not produce lasting improvements in aggressivity, conduct disorder, criminality, education achievement, job functioning, marital relationships, or long-term adjustment.”

-- APA’s *Textbook of Psychiatry*, 1994
Long-Term Results from NIMH’s MTA Study

- At end of 14 months, “carefully crafted medication management” had proven to be superior to behavioral treatment in terms of reducing core ADHD symptoms. There was a hint that medicated children also did better on reading tests.

- At the end of 36 months, “medication use was a significant marker not of beneficial outcome, but of deterioration. That is, participants using medication in the 24-to-36 month period actually showed increased symptomatology during that interval relative to those not taking medication.” Medicated children were also slightly smaller, and had higher delinquency scores.

- At end of six years, medication use was “associated with worse hyperactivity-impulsivity and oppositional defiant disorder symptoms,” and with greater “overall functional impairment.”

“We had thought that children medicated longer would have better outcomes. That didn’t happen to be the case. There were no beneficial effects, none. In the short term, [medication] will help the child behave better, in the long run it won’t. And that information should be made very clear to parents.”

--MTA Investigator William Pelham, University at Buffalo

A Meta-Analysis of the Literature, 2005

In a review of 2,287 studies:

There is “no good quality evidence on the use of drugs to affect outcomes relating to global academic performance, consequences of risky behaviors, social achievements, etc.”

-- Drug Effectiveness Review Project
Oregon Health and Science University, 2005

Medicated ADHD children were ten times more likely than unmedicated ADHD children to be identified by teachers as performing below age level.

A small effect size showed worse ADHD symptoms in the medicated group.

Medicated children had elevated diastolic blood pressure.

Conclusion: Medication does not translate into long-term benefits to the child’s social and emotional outcomes, school-based performance, or symptom improvement.

Adverse Effects From ADHD Medications

- **Physical**: Drowsiness, appetite loss, lethargy, insomnia, headaches, abdominal pain, motor abnormalities, tics, jaw clenching, skin problems, liver disorders, weight loss, growth suppression, hypertension, and sudden cardiac death.

- **Emotional**: Depression, apathy, a general dullness, mood swings, crying jags, irritability, anxiety, and a sense of hostility from the world.

- **Psychiatric**: Obsessive-compulsive symptoms, mania, paranoia, psychotic episodes, and hallucinations.
Long-Term Risks With Stimulants

- Desensitized brain-reward system?
- Increased risk of addiction?
- Conversion to bipolar diagnosis: 10% to 25% now convert

Castner, “Long-lasting psychotomimetic consequences of repeated low-dose amphetamine exposure in rhesus monkeys,”
Antidepressants and Children Prior to Prozac Era

- Studies of tricyclics: “There is no escaping the fact that research studies certainly have not supported the efficacy of tricyclic antidepressants in treated depressed adolescents.” -- *Journal of Child and Adolescent Psychology*, 1992

- Usage: In 1988, one in 250 children under 19 years of age taking an antidepressant
The Corruption of the Scientific Literature in Pediatric Antidepressant Trials

Pediatric trials of antidepressants:

--Biased by design
--Published results didn’t square with actual data
--Adverse events were downplayed or omitted
--Negative studies went unpublished or were spun into positive ones

“The story of research into selective serotonin reuptake inhibitor use in childhood depression is one of confusion, manipulation and institutional failure.”

--Lancet, 2004

FDA’s Report on SSRI Pediatric Trials

- 12 of 15 pediatric trials of SSRIs failed to show efficacy for the drug
- The FDA rejected the applications of six manufacturers seeking pediatric labeling for SSRIs
- Although the FDA approved Prozac for pediatric uses, the trials were highly biased by design.

The British View of SSRIs in Children

• In 2003, the Medicines and Health Regulatory Agency essentially banned the use of SSRIs, except for fluoxetine (Prozac), in patients under 18 years old.

• *Lancet* editorial, 2004: These drugs are “both ineffective and harmful in children.”

• *British Medical Journal*, 2004: “Recommending [any antidepressant, including Prozac] as a treatment option, let alone as first line treatment, would be inappropriate.”

Adverse Effects of SSRIs in Children

- **Physical:** Insomnia, sexual dysfunction, headaches, gastrointestinal problems, dizziness, tremors, nervousness, muscle cramps, muscle weakness, seizures, and akathisia (associated with increased risk of suicide).

- **Emotional/Psychiatric:** Psychosis, mania, behavioral toxicity, panic attacks, anxiety, apathy, an emotional dulling.
Long-Term Risks With SSRIs in Children

- Apathy Syndrome
- Cognitive Impairment
- Conversion to bipolar diagnosis; 25% to 50% of long-term users convert.

Pediatric Bipolar in the Literature Prior to the Use of Stimulants and Antidepressants

• 1945, Charles Bradley: Pediatric mania is so rare that “it is best to avoid the diagnosis of manic-depression.” --Journal of Pediatrics

• 1950, Louis Lurie: “Observers have concluded that mania does not occur in children.”--Journal of Pediatrics

• 1952, Barton Hall: “Manic-depressive states are illnesses of the maturing or matured personality.”--Nervous Child

• 1960, James Anthony: “Occurrence of manic depression in early childhood has yet to be demonstrated.”--Journal of Child Psychology and Psychiatry
The Discovery of Juvenile Bipolar Illness -- The First Case Studies

• 1976, Washington University: At least three of five children diagnosed with mania had been treated with a tricyclic or Ritalin prior to becoming manic. -- *American Journal of Diseases of Childhood.*

• 1980, Massachusetts General Hospital: At least seven of nine children diagnosed with manic-depressive illness had been previously treated with amphetamines, methylphenidate, or other medications to affect behavior. -- *Journal of Pediatrics*

• 1982, UCLA: Twelve of 60 adolescents treated with antidepressants turned “bipolar” within three years; this is seen as evidence that antidepressants can “unmask” the disease. -- *Archives of General Psychiatry*
The Stimulant-to-Bipolar Pathway, Part One

Stimulants can induce mania and psychosis

- In a Canadian study, six percent of ADHD children treated with stimulants for an average of 21 months developed psychotic symptoms.
- In a study of 195 bipolar children, Demitri Papolos found that 65% had “hypomanic, manic and aggressive reactions to stimulant medications.”
- University of Cincinnati reported that 21 of 34 adolescent patients hospitalized for mania had been on stimulants “prior to the onset of an affective episode.”

Stimulants can induce mood swings used to diagnose bipolar

<table>
<thead>
<tr>
<th>Stimulant-induced symptoms</th>
<th>Bipolar Symptoms</th>
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<tbody>
<tr>
<td><strong>Arousal</strong></td>
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<tr>
<td>Increased energy</td>
<td>Increased energy</td>
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<tr>
<td>Intensified focus</td>
<td>Intensified goal-directed activity</td>
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<tr>
<td>Hyperalertness</td>
<td>Agitation</td>
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<tr>
<td>Euphoria</td>
<td>Severe mood change</td>
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<tr>
<td>Agitation, anxiety</td>
<td>Decreased need for sleep</td>
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<tr>
<td>Insomnia</td>
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<td>Irritability</td>
<td>Destructive outbursts</td>
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<td>Hostility</td>
<td>Increased talking</td>
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<tr>
<td>Hypomania</td>
<td>Distractibility</td>
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<td>Mania</td>
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<td>Psychosis</td>
<td>Mania</td>
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<td><strong>Dysphoric</strong></td>
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<td>Somnolence</td>
<td>Sad mood</td>
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<tr>
<td>Fatigue, lethargy</td>
<td>Loss of energy</td>
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<td>Social withdrawal</td>
<td>Loss of interest in activities</td>
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<tr>
<td>Decreased spontaneity</td>
<td>Social isolation</td>
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<td>Reduced curiosity</td>
<td>Poor communication</td>
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<tr>
<td>Constriction of affect</td>
<td>Feelings of worthlessness</td>
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<tr>
<td>Depression</td>
<td>Unexplained crying</td>
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<tr>
<td>Emotional lability</td>
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</tbody>
</table>
The SSRI-to-Bipolar Pathway

- In first pediatric trial of Prozac, 6% of treated children suffered a manic episode; none in placebo group.

- In study of antidepressant-induced mania for all ages, Yale University investigators found the risk highest in those under 13 years of age.

- Harvard University researchers find that 25% of children treated for depression convert to bipolar within four years.

- Washington University researchers report that within 10 years, 50% of prepubertal children treated for depression convert to bipolar illness.

Confirming the Iatrogenic Pathways to Juvenile Bipolar Illness

Surveys of Juvenile Bipolar Patients

- University of Louisville researchers report that 49 of 79 juvenile bipolar patients (62%) had been treated with an antidepressant prior to their becoming manic.

- Demitri Papolos reported that 83% of 195 bipolar children had been initially diagnosed and treated for another psychiatric disorder; two-thirds had been exposed to an antidepressant.

- At the Luci Bini Mood Disorders Clinic in New York City, 84% of the bipolar children treated between 1998 and 2000 had been exposed to other psychiatric drugs before bipolar diagnosis. “Strikingly, in fewer than 10% [of the cases] was diagnosis of bipolar disorder considered initially,” the investigators wrote.

Long-Term Outcomes for Medicated Juvenile Bipolar Patients are Poor

- Washington University: Juvenile bipolar patients exhibit symptoms “similar to the clinical picture reported for severely ill, treatment-resistant adults.”

- Demitri Papolos reported that 87% of his 195 juvenile bipolar patients suffered from “ultra, ultra rapid cycling.”

- At Luci Bini clinic in NYC, 66% of juvenile patients were “ultra, ultra rapid cyclers,” and another 19% from rapid cycling only a little bit less extreme.

- University of Pittsburgh: Early onset bipolar patients are symptomatic 60% of time, and shift polarity on average 16 times per year.

Reviews of Medications for Juvenile Bipolar Disorder

- Washington University: At end of two years, mood stabilizers, lithium, stimulants, and antidepressants all failed to help bipolar youth fare better. Those treated with an antipsychotic “were significantly less likely to recover than those who did not receive a neuroleptic.”

- Hayes, a medical consulting firm, in 2008: “Our findings indicate that at this time, anticonvulsants [mood stabilizers] and atypical antipsychotics cannot be recommended for children diagnosed with bipolar disorders.”

The Epidemic in Children

Children on SSI Disability Due to Mental Illness

Prior to 1992, the government’s SSI reports did not break down recipients into subgroups by age. Source: Social Security Administration reports, 1988-2007.
Atypicals in Youth 6 to 17 Years Old

• 4.2% of Medicaid youth prescribed an antipsychotic in 2004
• .9% of privately insured prescribed an antipsychotic in 2006
• Only 3.3% of prescriptions for schizophrenia or schizoaffective disorder

Source: Crystal, S. “Broadened Use of Atypical Antipsychotics,” Health Affairs, 2009
Adverse Effects With Atypicals

- University of Maryland: Nine percent of children treated with antipsychotics for median time of 484 days developed tardive dyskinesia.

- Side effects include metabolic dysfunction, obesity, type-II diabetes, hormonal abnormalities, movement disorders, cardiovascular problems, emotional blunting, sedation, and cognitive problems. Adverse events worse in children and adolescents than in adults.

- Possible brain shrinkage and likely cognitive decline long-term.

- Early death

Nancy Andreasen, former editor of the *American Journal of Psychiatry*, on antipsychotics:

“What exactly do these drugs do? They block basal ganglia activity. The prefrontal cortex doesn’t get the input it needs and is being shut down by drugs. That reduces psychotic symptoms. It also causes the prefrontal cortex to slowly atrophy.”

The Evidence for Long-Term Use Of Psychotropics in Children

American Academy of Child and Adolescent Psychiatry, 2009

- Three long-term studies cited
  - The MTA results for ADHD at 24 months, which showed that those withdrawn from drugs saw their ADHD symptoms spike. The paper doesn’t cite the 3-year and 6-year MTA results.
  - Zoloft for obsessive-compulsive disorder. Study was for one year, and was not placebo-controlled.
  - Zoloft for major depression. Study was for 24 weeks and was not placebo-controlled.

Summing up the Evidence

1. Stimulants for ADHD
   a) short-term efficacy
   b) no long-term efficacy
   c) risk of long-term harm

2. Antidepressants for Depression
   a) except for Prozac, no short-term efficacy
   b) risk of long-term harm

3. The bipolar boom
   a) iatrogenic pathways to diagnosis
   b) poor long-term outcomes
Long-term Worries With Psychotropics

- Increased risk of disability (bipolar pathway)
- Physical ailments
- Emotional lethargy
- Cognitive decline
- Early death