THE USE OF PSYCHOTROPICS WITH TROUBLED YOUTH
OVERVIEW OF THE EVIDENCE

Robert Foltz, Psy.D.

INTRODUCTIONS

- Started working in Psychiatric Inpatient (1988)
- Started working in Residential Treatment (1993) – clinician & administrator
- Private practice (1998)…
- Started teaching (2009) – evidence based treatments for youth, child / adol psychopathology, pediatric psychopharm
- Adolescent Subjective Experience of Treatment (ASET) study

To learn more visit: https://vitalchild-solutions.com/
CHALLENGING OUR CURRENT SCIENCE

- Largest / Best studies
- Looking at Outcomes
- Considering Risk
- Questions, Discussion, More Questions

IT'S ABOUT YOUNG PEOPLE

- At least 20% of America's youth have a diagnosable mental illness (approx 14.7 million)
- 50% of all diagnoses are applied by 14 years old
- 75% of all diagnoses are applied by 24
- Symptom onset is usually 2 years before a diagnosis
ASSessment leads to diagnosis
Diagnosis leads to treatment
Treatment leads to outcomes

INCREASING USE

- The use of psychotropic medications by adults in the U.S. increased 22% from 2001 to 2010
- One in five adults currently takes at least one psychotropic medication
- More than 8 million kids take one or more psychotropic medication - a rate higher than any other country in the world
- In 2010, sales included:
  - $16 billion on antipsychotics
  - $11 billion on antidepressants
  - $7 billion on ADHD meds

$1,100 per second!
FDA APPROVAL…
“THE EFFICACY WAS ESTABLISHED…”

- From the Physician’s Desk Reference
- Concerta 3 & 4 week studies
- Adderall XR 3 weeks
- Focalin 4 weeks
- Strattera 6, 8, 9 weeks
- Abilify 4 and 6 weeks (with Sz)
- Geodon 4, 6 and 52 weeks (with Sz)
- Zyprexa 6 weeks (with Sz)
- Seroquel 6 weeks (with Sz)
- Zoloft 6 and 8 weeks

CAN WE ASSUME THAT GOOD SCIENCE IS ACCURATELY GUIDING GOOD PRACTICE?
LET’S START WITH TRAUMA…
FROM THE DSM

Individuals with PTSD may demonstrate:
- Quick tempered & even engage in verbal or physical aggression with little or no provocation
- Reckless or self-destructive (dangerous driving, excessive alcohol / drug use, self-injurious / suicidal)
- Heightened sensitivity to perceived threats
- Very reactive to unexpected stimuli
- Concentration difficulties, problems focusing, forgetful
- Problems with sleep
- Dissociative symptoms
- Developmental regression
- Auditory “pseudo hallucinations”
- Paranoid ideation
- Difficulty regulating emotions
- Difficulty maintaining interpersonal relationships

NCTSN - 2012

![Graph showing the relationship between number of traumas and percent of youth with different types of problems.

- Attachment Problems
- Behavior Problems
- Academic Problems
- Criminal Activity]
FIRST LINE ADHD TREATMENT
HOW THEY WORK

- From the Concerta information:
- “Methylphenidate HCl is a central nervous system (CNS) stimulant. The mode of therapeutic action in Attention Deficit Hyperactivity Disorder (ADHD) is not known. Methylphenidate is thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.”

- Ritalin and Concerta are both methylphenidate…Concerta is long acting.

### Table: FDA APPROVAL STIMULANTS

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Generic</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Adderall XR</td>
<td>Dextroamphetamine Sulfate Sulfate</td>
<td>1. N=584 3 weeks</td>
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<tr>
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<td>2. N=327 4 weeks</td>
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<tr>
<td>Adderall III</td>
<td>Methylphenidate HCl</td>
<td>1. N=397 2 weeks; ( n \approx \ 3 )</td>
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<td>2. N=210 1 week, then 11 week open-label</td>
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<tr>
<td>Concerta</td>
<td>Methylphenidate HCl</td>
<td>1. ( n \approx \ 2 ) ( n \approx \ 1 )</td>
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<tr>
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<td>2. N=416 3 weeks</td>
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<td>3. ( n \approx \ 4 ) ( n \approx \ 4 )</td>
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<td>4. N=127 4 weeks (adolescents)</td>
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<tr>
<td>Daytrana</td>
<td>Methylphenidate</td>
<td>1. N=25 5 week open, 2 week DBB blind</td>
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<tr>
<td>Transdermal</td>
<td></td>
<td>2. N=16 5 week, 2 week maintenance</td>
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<tr>
<td>patch</td>
<td></td>
<td>3. N=2 5 week, 2 week maintenance</td>
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<tr>
<td>Everxin</td>
<td>Amphetline Sulfate</td>
<td>1. N=305 8 week open,</td>
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<td>2. N=97 2 week crossover</td>
</tr>
<tr>
<td>Focalin XR</td>
<td>Dexmethylphenidate HCl</td>
<td>1. N=303 5 week open optimization, 2 week crossover</td>
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<tr>
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<td>2. Two additional studies – minimal details</td>
</tr>
<tr>
<td>Ritalin LA</td>
<td>Methylphenidate HCl</td>
<td>1. N=134 2 weeks</td>
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<tr>
<td>Quillivant XR</td>
<td>Methylphenidate HCl</td>
<td>1. N=45 4 to 6 week open optimization, 2 week crossover</td>
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<tr>
<td>Vivanse</td>
<td>Lisdexamfetamine Dimesylate</td>
<td>1. N=290 4 weeks</td>
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<td>2. N=52 3 week open optimization, 2 week crossover</td>
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<tr>
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<td>3. N=129 4 week open optimization, 2 week crossover</td>
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</tbody>
</table>

Adapted from [https://www.webmd.com/add-adhd/guide/adhd-medication-chart#1](https://www.webmd.com/add-adhd/guide/adhd-medication-chart#1)
EXTRAORDINARY

- The United States uses over 75% of the world’s Ritalin supply…and over 60% of the amphetamine supply.

- There are no neurological measures to reliably identify ADHD. Specifically, one of the most prominent child psychiatrists notes “neuroimaging techniques are not valid tools for ADHD diagnosis; imaging measures are not sensitive or specific enough to be used for diagnostic purposes” (Biederman, 2011).

MTA Study: Objective and Design

Objective: To compare the long-term efficacy of pharmacotherapy, behavioral therapy, and combination therapy in the treatment of ADHD.

- 578 Children ADHD, Combined type
- Age Range: 7-9.9 years
- Randomly assigned
- 14-month study

- Medication management (primarily methylphenidate)
- Behavioral treatment
- Combination treatment: medication and behavioral therapy
- Routine Community Care

The MTA Study
### MTA VARIABLES

<table>
<thead>
<tr>
<th>19 Measures</th>
<th>Medication &gt; Behavior Tx</th>
</tr>
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<tbody>
<tr>
<td>Inattention – Teacher</td>
<td>Inattention – Teacher</td>
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<tr>
<td>Inattention – Parent</td>
<td>Inattention – Parent</td>
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<tr>
<td>Hyper/Impulse – teacher</td>
<td>Hyper/Impulse – Teacher</td>
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<tr>
<td>Hyper/Impulse – parent</td>
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<tr>
<td>Hyper/Impulse – observer</td>
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<tr>
<td>Aggression – teacher</td>
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<tr>
<td>Aggression – parent</td>
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<td>Aggression – observer</td>
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<tr>
<td>Social Skills – teacher*</td>
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<tr>
<td>Social Skills – parent*</td>
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<tr>
<td>Anxiety scale – child</td>
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<td>Sociometrics – peers</td>
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<tr>
<td>Power Assertion – parent</td>
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<td>Personal Closeness – parent</td>
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<tr>
<td>Reading</td>
<td></td>
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<tr>
<td>Mathematics</td>
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<tr>
<td>Spelling</td>
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</tbody>
</table>

Parents & Teachers were NOT “blind” to Tx

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![Graphs showing ADHD and ODD symptoms and Columbia Impairment Scale](image)
MTA LONGER TERM

- At 8-year follow-up:
  - The MTA group as a whole was functioning significantly less well that the non-ADHD classmate sample recruited at 24 months.
  - “Our results suggest that the initial clinical presentation in childhood, including severity of ADHD symptoms, conduct problems, intellect, and social advantage, and strength of ADHD symptom response to any treatment, are better predictors of later adolescent functioning than the type of treatment received in childhood for 14 months.”

POOR OUTCOMES

- “Type or intensity of 14 months of treatment for ADHD in childhood (at age 7.0-9.9 years) does not predict functioning 6 to 8 years later.”

- “We found poorer performance for the MTA children as a group versus LNCG children for 91% of the variables.”
**MTA CONCLUSION**

- “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, *Daily Telegraph*, Nov. 2007 (cited in MadInAmeric.com)

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**LATEST MTA FINDINGS**

**JANUARY 2017**

- Following subjects for 15+ years now,
  - “significant persistence of the disorder due to higher levels of symptom severity into adulthood”
  - “the comparisons of ADHD-treated and ADHD-untreated groups suggest that in the long-term, symptom-related benefit of treatment with medication may dissipate and not remain significant but growth-related cost may remain statistically significant in adulthood”
  - “comparisons of groups with continuous and interrupted use of medication from childhood through adolescence suggest greater treatment may not result in greater symptom-related benefit but may result in greater growth-related cost” *(doi:10.1111/jcpp.12684 Young adult outcomes in the MTA p. 671)*
Most ADHD youth are engaged in treatment to improve their academic performance. It is important to note that “stimulants have no effect on academic achievement in the short-term. No long-term effects have been reliably reported on any outcome measure”

(APA Working Group, 2006, p. 43).
TREATMENT OF ADOLESCENT DEPRESSION STUDY
TADS

- TADS is randomized, controlled trial designed to evaluate the effectiveness of three active treatments:
  - Fluoxetine (N = 109)
  - CBT (N = 111)
  - COMB (N = 107)
  - Placebo (N = 112)
THE MEDICATION GROUP

- Treatment is conducted in Stages up to a total of 9 months, depending on how well the teen is doing. The first Stage lasts up to 12 weeks and at the end of it, teens assigned to Prozac and teens assigned to Placebo will be told what they have been getting. Teens who had been getting Placebo may, if they want to, choose to receive any of the other three treatments for the next 12 weeks. All others who are doing well will continue to receive their same treatment for another 6 months.

THE CBT GROUP

- The CBT group received 15 sessions of specific CBT interventions
Adolescent clients prescribed Cymbalta?
- It functions as an SNRI
- Does it work?
A Double-Blind Efficacy and Safety Study of Duloxetine Fixed Doses in Children and Adolescents with Major Depressive Disorder, May 2014

- 463 children & adolescents
- 36 weeks (10 weeks of treatment)
  - 2 doses of Cymbalta (60mg & 30mg)...224 youth
  - 20mg of Prozac...117 youth, considered active controls
  - Placebo...122 youth

Outcome Measures: Childrens Depression Rating Scale, Adverse Events, Columbia Suicide Severity Rating Scale

Authors note that the results are “inconclusive” because neither the drug (Cymbalta), nor the active control (Prozac), “separated from placebo” at study endpoint.
"only 50 percent of patients respond to these drugs and effective remission occurs less than 30 percent of the time."
ANTIPSYCHOTICS

- Typical
- Atypical
- Third Generation

OFF LABEL USE

- While many drugs are not FDA approved for use in youth, doctors can use them
- This trend has increased…and includes many antipsychotics
**“HALDOL IS CLEARLY NEUROTOXIC. SHOULD IT BE BANNED?”**

This summary is based on 28 published studies highlighting the neurotoxic effects of typical antipsychotics.

<table>
<thead>
<tr>
<th>Receptor Blockade</th>
<th>Clozapine</th>
<th>Risperidone</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Ziprasidone</th>
<th>Aripiprazole</th>
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The molecular mechanisms of neurotoxicity of older-generation antipsychotics, including haloperidol, fall into several major categories:

- apoptosis
- necrosis
- decreased cell viability
- inhibition of cell growth
- increased caspase activity (the “death spiral”)
- impaired glutamate transport
- mitochondrial damage.
CONCERNS WITH RISPERDAL

- 2017 - “Our results indicate that there was a significant decrease in the thickness of fetal hippocampus with the disturbed cytoarchitectural pattern, and volume of striatum and choroid plexus was also reduced. Furthermore, RIS treated young rat offspring displayed memory impairment on different mazes of learning and memory. The current study concludes that maternal exposure to clinically relevant doses of RIS may induce neurostructural changes in developing hippocampus and striatum, and cognitive sequelae in young offspring, respectively.”

- 2016 - Prenatal exposure to RIS induced significant stunting of fetal body and brain weight, substantial reduction in the thickness of neocortical layers and apoptotic neurodegeneration in fetal brains, and delayed postnatal development and growth of the offspring; as well as long-lasting impact on anxiety like impaired behavioral responses on explorative mazes.

ABILIFY -2008

- Multicenter, 257 adolescents
- 6 weeks
- Double-blind
- Randomized
- Placebo controlled
- 13 – 17 year old, diagnosed with Schizophrenia
- PANSS score of 70 or more, measured weekly
- Placebo vs. Abilify 10mg or Abilify 30mg

Conclusion: Both 10- and 30-mg/day doses of aripiprazole were superior to placebo in the acute treatment of adolescents with schizophrenia. Aripiprazole was generally well tolerated.
OVERALL EFFECTIVENESS?
WHAT ARE YOUR IMPRESSIONS?

WORTH THE RISKS?
HOW DO WE BALANCE THE COSTS & BENEFITS OF THIS APPROACH?

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