Psychopharmacology of Autism

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Disclosure of Financial Interests

- Nothing to disclose
Off-Label Use Of Medication

In this presentation, all discussion of use of medication refers to “off-label” use other than risperidone and aripiprazole for irritability in children and adolescents with autistic disorder.
Potential Targets of Pharmacotherapy

1. Motor hyperactivity, inattention
2. Interfering repetitive behavior
3. Irritability (aggression, self-injury, severe tantrums)
4. Impaired social relatedness
5. Sleep disturbance
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Stimulants in Autism

- Historical data and beliefs negative
- Small studies support use of MPH in autism\textsuperscript{1,2}
- Anecdotal reports of a high frequency of adverse drug effects including stereotypies and social withdrawal

MPH = methylphenidate.

RUPP Autism Network Study of MPH in Children With PDD + Hyperactivity

- 72 Children (age, 5–14 y) with autism, Asperger’s Disorder, or PDD NOS and significant “ADHD” symptoms

- Study design
  - 7-day test-dose period
  - 4-week double-blind trial of 3 dose levels (0.125, 0.25, 0.50 mg/kg/dose) of MPH TID and placebo in random order

PDDNOS = pervasive developmental disorder not otherwise specified.
ADHD = attention deficit/hyperactivity disorder.
MPH Summary

- 35/72 subjects (49%) responded to MPH
- 13/72 (18%) exposed to MPH dropped out due to adverse events
Treating Hyperactivity: Other Medications

- Clonidine efficacious in 2 small placebo-controlled trials\(^1,2\)
- Open-label guanfacine in RUPP MPH nonresponders is positive, suggesting that guanfacine may be an alternative\(^3\)
- Encouraging open-label and controlled crossover design data with atomoxetine

\(^3\) Scahill L et al. *J Child Adolesc Psychopharmacol*. 2006;16(5):589-598
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Serotonin Reuptake Inhibitors (SRIs)

- Rationale for studying SRIs in autism
  - Similarities to obsessive-compulsive disorder
  - Serotonin abnormalities in autism
Citalopram in PDDs

- 149 children (9.4 ± 3.1 years) with PDDs and significant repetitive behavior
- 12-week, double-blind, placebo-controlled, parallel groups design
- Citalopram started at 2.5 mg/day; max dose = 20 mg/day; (mean dose = 16.5 ± 6.5 mg/day)
- No drug-placebo difference in response on CGI-I or in score reduction on CY-BOCS-PDD
- Significantly more adverse events with citalopram than placebo: increased energy level, impulsiveness, decreased concentration, hyperactivity, stereotypy, diarrhea, insomnia, and dry skin or pruritus

ACTN Study of Fluoxetine in Autism: SOFIA

- 14-week, double-blind, placebo-controlled
- Largest trial of SSRI in autism to date
- 158 subjects, ages 5-17 y
- Fluoxetine not effective for repetitive behaviors in youth with autism vs. placebo

ACTN = Autism Clinical Trials Network
Autism Speaks, press release 2009
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Acute Risperidone Trial: RUPP in Children and Adolescents

- 101 subjects (82 boys, 19 girls)
- Diagnosis: autistic disorder
- Significant irritability (ABC Irritability ≥18)
- 8 weeks, double-blind, placebo-controlled, parallel groups
- Mean age = 8.8 ± 2.7 y; range = 5–17 y
- Risperidone 1.8 mg/d; range = 0.5–3.5 mg/d

Acute Risperidone Trial: RUPP

Response criteria: ≥25% improvement in the ABC-I score, and a rating of “much improved” or “very much improved” on the CGI-I.

ABC-I = Aberrant Behavior Checklist–Irritability.
CGI-I = Clinical Global Impressions–Improvement.
Aripiprazole in Autism – 52-Week, Open-Label Study

- 52-week, open-label, flexible dose (2-15 mg/day), long-term study
- Subjects enrolled from two 8-week RCTs or as de novo subjects
- 303 subjects (de novo n=86, prior aripiprazole n=174, prior placebo n=70) received treatment. 199 subjects (60.3%) completed 52 weeks of treatment
- Mean dose of aripiprazole = 9.6 mg/day
- The majority of subjects maintained response (CGI-I = 1 or 2) throughout the 52-week study
- 6.1% of subjects discontinued due to lack of efficacy; 10.6% of subjects discontinued due to adverse effects (aggression and weight increase)

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D-Cycloserine in Children with Autism

- 80 children (6.5 ± 2.8 years; range 3-12 years) with autistic disorder and significant social withdrawal
- 8-week, double-blind, placebo-controlled, parallel groups design
- D-cycloserine 1.7 mg/kg/day divided twice daily or placebo
- No drug-placebo difference on the CGI-I, ABC Social Withdrawal subscale, or Social Responsiveness Scale
- D-cycloserine generally well-tolerated
- Majority of responders maintained response during 16-week open-label extension

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Medications for Sleep Disturbance

- Melatonin
- Clonidine
- Trazodone
- Mirtazapine
- Hydroxyzine
- Doxepin
- Diphenhydramine and Benzodiazepines (paradoxical reaction, disinhibition)
Lurie Center for Autism

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