Psychopharmacology of Autism

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Question 1

- A 3 year old girl presents with impaired receptive and expressive language. She has stereotyped hand movements although her parents say that up to the age of 18 months she seemed to have purposeful hand skills. Her height and weight are age appropriate but her head growth has decelerated since she passed her second birthday. The most appropriate diagnosis is:
  - A Autistic disorder
  - B Rett's disorder
  - C Asperger's disorder
  - D Childhood disintegrative disorder
  - E Pervasive developmental disorder NOS

Question 2

- The RUPP Network study on the treatment of irritability in Autism presents evidence on the use of which atypical antipsychotic for this presentation?
  - A Haloperidol
  - B Quetiapine
  - C Olanzapine
  - D Risperidone
  - E Aripiprazole

Question 3

- Which of the following is a semi-structured interactive assessment that can be conducted during an evaluation for an autism spectrum disorder in children?
  - A. Autism Diagnostic Observation Schedule (ADOS)
  - B. Autism Diagnostic Interview Revised (ADI-R)
  - C. Childhood Autism Rating Schedule (CARS)
  - D. Pervasive Developmental Disorders Screening Test (PDDST)
  - E. Checklist for Autism in Toddlers (CHAT)

Teaching Points

- PDDs are characterized by deficits in social relatedness and communication and the presence of repetitive behaviors
- Autism is much more commonly associated with mental retardation as compared to Asperger's disorder
- Rett's disorder has been associated with mutations in the MECP2 gene
- Risperidone and Aripiprazole are FDA approved for treatment of irritability in autism

Pervasive Developmental Disorders

- Autistic Disorder
- Asperger's Disorder
- Rett's Disorder
- Childhood Disintegrative Disorder
- Pervasive Developmental Disorder Not Otherwise Specified

Leo Kanner

Autistic Disorder

CORE SYMPTOM DOMAINS

1) **Impairment in Social Interaction**
2) **Impairment in Communication**
3) **Restricted repetitive patterns of behavior, interests, and activities**

Autistic Disorder

- Symptom criteria met before the age of 3 y
- Boys:Girls = 4:1
- 75% have comorbid mental retardation
- Nearly 50% never develop functional verbal communication
- 33% eventually develop seizure disorder

Hans Asperger

Asperger's Disorder

- Impairment in Social Interaction
- Restricted repetitive patterns of behavior, interests, and activities
- No clinically significant delay in language
- No clinically significant delay in cognitive development
- "All-encompassing" preoccupation

Andreas Rett

Rett's Disorder

- Females
- Deceleration of head growth
- Stereotyped hand movements
- Loss of purposeful hand skills
- Loss of social engagement
- Severe language disorder
- Severe to profound mental retardation

Childhood Disintegrative Disorder

- Normal Development for ≥ 2 years
- Significant loss of previously acquired skills (before age 10 years)
- Abnormalities in 2 of 3 areas:
  - Social
  - Communication
  - Repetitive behavior

PDD NOS

- Presentations that do not meet the criteria for Autistic Disorder because of late age of onset, atypical symptomatology, or subthreshold symptomatology, or all of these.

PDDs: Assessment I

- Medical work-up
  - Audiological
  - Neurological (seizures in ~1/3)
  - Genetic screening
    - Fragile X Syndrome in ~1%: CGG repeats in Xq27.3
    - Rett: X-linked, rare boys, mutations in the MECP2 (Methyl-CpG-binding protein) gene
    - Amino/organic acid metabolism
    - Other genetic diseases associated with autism include: Angelman syndrome, duplication of 15q11-q13, Tuberous Sclerois, Down syndrome, San Filippo syndrome, phenylketonuria, Smith–Magenis syndrome, 22q13 deletion, adenylosuccinate lyase deficiency, Cohen syndrome, and Smith–Lemli–Opitz syndrome) see Cohen, D et al, Journal of Autism and Developmental Disorders, Vol. 35, No. 1, February 2005
  - Physical examination with close attention to skin and dysmorphology

Assessment II

- Family history
- Developmental milestones
- Syndromal vs non syndromal autism
- Genetic testing for rare syndromes should be based on clinical findings
- For isolated autism with moderate mental retardation consider:
  - Karyotyping,
  - Check for Fragile X mutation,
  - FISH for 15q11-q13 duplication and 22 q13 deletion (VCFS)
  - Bratton-Marschall test (adenylosuccinate lyase deficiency)
  - Check for mucopolysaccharides in urine (San Fillipo syndrome)

PDDs: Assessment III-Diagnostic Assessment

Screening instruments:

- Checklist for Autism in Toddlers (CHAT)
- Childhood Autism Rating Scale (CARS) observational assessment-15 items-score of 30-36=mild-mod Autism
- Pervasive Developmental Disorders Screening Test (PDDST)
- Autism Behavior Checklist (57 item checklist)

PDDs: Assessment III- Diagnostic Assessment

Structured Evaluation- 'gold standard'

- ADI-R (Autism Diagnostic Interview - Revised) a comprehensive parent interview
- ADOS (Autism Diagnostic Observation Schedule) a semi structured interactive assessment conducted with the child

PDDs: Assessment III

- Neuropsychological & Language
  - Developmentally Appropriate Instruments: WISC-IV, Leiter International Test of Intelligence-revised, Mullen Scale of Early Development, Bayley
- Rating Scales
  - Aberrant Behavior Checklist (Aman et al, 1985)

  58 items: Subscales:
    - Irritability/Lethargy/Stereotypy/Hyperactivity/Speech
    - Normative data, reliable, valid, sensitive to change (Scahill 2005)
  - Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS, version for PDD (Scahill et al, 2006)
    - Repetitive behaviors

Potential Targets of Pharmacotherapy

1. Motor hyperactivity, inattention
2. Repetitive behavior
3. Aggression, self-injury, severe tantrums
4. Impaired social relatedness
5. Sleep disturbance

Potential Targets of Pharmacotherapy

1. **Motor hyperactivity, inattention**
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Stimulants in Autism

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

MPH = methylphenidate.

[1]Quintana H et al. *J Autism Dev Disord*. 1995;25:283-294.
[2]Handen BL et al. *J Autism Dev Disord*. 2000;30:245-255.

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.
RUPP Autism Network. *Arch Gen Psychiatry* 2005; 62:1266-1274.

Test-Dose Phase

- 6 out of 72 subjects were unable to tolerate ≥2 dose levels of MPH and were dropped from the study
- 16 out of the remaining 66 subjects had intolerable adverse effects at the highest dose of MPH; entered modified crossover phase
- Irritability was the most common reason for intolerability

RUPP Autism Network. *Arch Gen Psychiatry* 2005; 62:1266-1274.

Crossover Phase

- 58/66 subjects completed the crossover phase
- 7 subjects dropped out due to intolerable adverse effects
- There was a statistically significant main effect of dose of MPH on the ABC Hyperactivity subscale score as rated by both teacher (Primary Outcome Measure; P =.009) and parent (P <.001)

ABC = Aberrant Behavior Checklist.

RUPP Autism Network. *Arch Gen Psychiatry* 2005; 62:1266-1274.

Crossover Phase: Other ABC Subscales

- Statistically significant worsening of parent-rated Social Withdrawal at high-dose MPH ($P<0.0001$)
- No statistically significant changes in other subscales (Irritability, Stereotypy, Inappropriate Speech)

ABC = Aberrant Behavior Checklist.

RUPP Autism Network. *Arch Gen Psychiatry* 2005; 62:1266-1274

Categorical Response

- 44 subjects were rated as responders to at least 1 week of treatment (MPH or placebo) – MPH (n = 35) – Placebo (n=9)
- Subject age, IQ, *diagnosis (trend, P =.07), and weight did not moderate treatment response
- *Subjects diagnosed with Asperger's disorder and PDD NOS were more likely to be classified as responders to both placebo and MPH than those with autism

RUPP Autism Network. *Arch Gen Psychiatry* 2005; 62:1266-1274.

Categorical Response

	Placebo	Low	Medium	High
Asperger's disorder/ PDD NOS (n=19)	6 (32%)	7 (37%)	7 (37%)	6 (32%)
Autism (n=47)	6 (13%)	13 (28%)	15 (32%)	12 (26%)

Response to each dose of MPH was superior to placebo for autism subgroup (P <.001), but not for the Asperger's disorder/PDD NOS subgroup (P >.05)

RUPP Autism Network. *Arch Gen Psychiatry* 2005; 62:1266-1274.

MPH Summary

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

RUPP Autism Network. *Arch Gen Psychiatry* 2005; 62:1266-1274.

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]

[1]Jaselskis CA et al. *J Clin Psychopharmacol*. 1992;12:322-327.
[2]Fankhauser MP et al. *J Clin Psychiatry*. 1992;53:77-82.
[3]Scahill L et al. *J Child Adolesc Psychopharmacol*. 2006;16(5):589-598.

Atomoxetine in Higher-Functioning PDD

- Prospective open-label study in 16 drug-free children (age, 6–14 y) with PDDs and nonverbal IQ of ≥70
- Significant ADHD symptoms
- Atomoxetine dosing: 0.5 mg/kg/d x 1 wk, then 0.8 mg/kg/d x 1 wk, then 1.2 mg/kg/d. Dose increased to 1.4 mg/kg/d at Week 4 for nonresponders
- Mean dose: 1.2 ± 0.3 mg/kg/d

Posey DJ et al. *J Child Adolesc Psychopharmacol,* 2006; 16(5):599-610.

Atomoxetine in PDD With ADHD Symptoms

- 12/16 (75%) *much* or *very much improved* on the CGI scale
- 2/16 (13%) *much worse* due to irritability
- Conclusions
  - Encouraging results
  - Possible alternative to stimulants and α_2-adrenergic agonists
  - Placebo-controlled studies needed

CGI = Clinical Global Impressions.

Posey DJ et al. *J Child Adolesc Psychopharmacol*, 2006; 16(5):599-610.

Potential Targets of Pharmacotherapy

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3. Aggression, self-injury, severe tantrums
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Serotonin Reuptake Inhibitors (SRIs)

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

SRIs in Autism

- Clomipramine better than placebo and desipramine in children and young adults with autism[1]
- Fluvoxamine better than placebo in **ADULTS** with autism[2]
- Fluvoxamine no better than placebo and poorly tolerated in **CHILDREN** with PDDs[3]
- Fluoxetine better than placebo and well tolerated in children with PDDs[4]

[1]Gordon CT et al. *Arch Gen Psychiatry.* 1993;50:441-447.
[2]McDougle CJ et al. *Arch Gen Psychiatry*. 1996;53:1001-1008.
[3]McDougle CJ. Unpublished data.
[4]Hollander E et al. *Neuropsychopharmacology*. 2005; 30:582-589.

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

King BH et al. *Arch Gen Psychiatry*. 2009; 66(6):583-590.

Potential Targets of Pharmacotherapy

1. Motor hyperactivity, inattention
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3. **Aggression, self-injury, Severe tantrums**
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5. Sleep disturbance

Typical Antipsychotics

- Several RCTs of haloperidol associated with improvement in a variety of symptoms including aggression and irritability
- Adverse effects: dystonia, dyskinesias

RCT = randomized clinical trial.

Anderson LT et al. *Am J Psychiatry.* 1984;141:1195-1202.
Campbell M et al. *J Am Acad Child Adolesc Psychiatry.* 1997;36:835-843.

Atypical Antipsychotics

- Serotonin antagonism in addition to dopamine antagonism
- Lower risk of dyskinesias
- Individual drugs include
  - Clozapine
  - Risperidone
  - Olanzapine
  - Quetiapine
  - Ziprasidone
  - Aripiprazole
  - Paliperidone

Clozapine

- Case reports only
- Can lower the seizure threshold
- Risk of agranulocytosis
  - Frequent blood draws necessary

Risperidone in Children With Autism and Serious Behavioral Problems

RUPP Autism Network

Indiana University (Christopher J. McDougle, MD)

Kennedy-Kreiger, Johns Hopkins (Elaine Tierney, MD)

Ohio State University (Michael G. Aman, PhD)

Yale Child Study Center (Larry Scahill, MSN, PhD)

UCLA (James T. McCracken, MD)

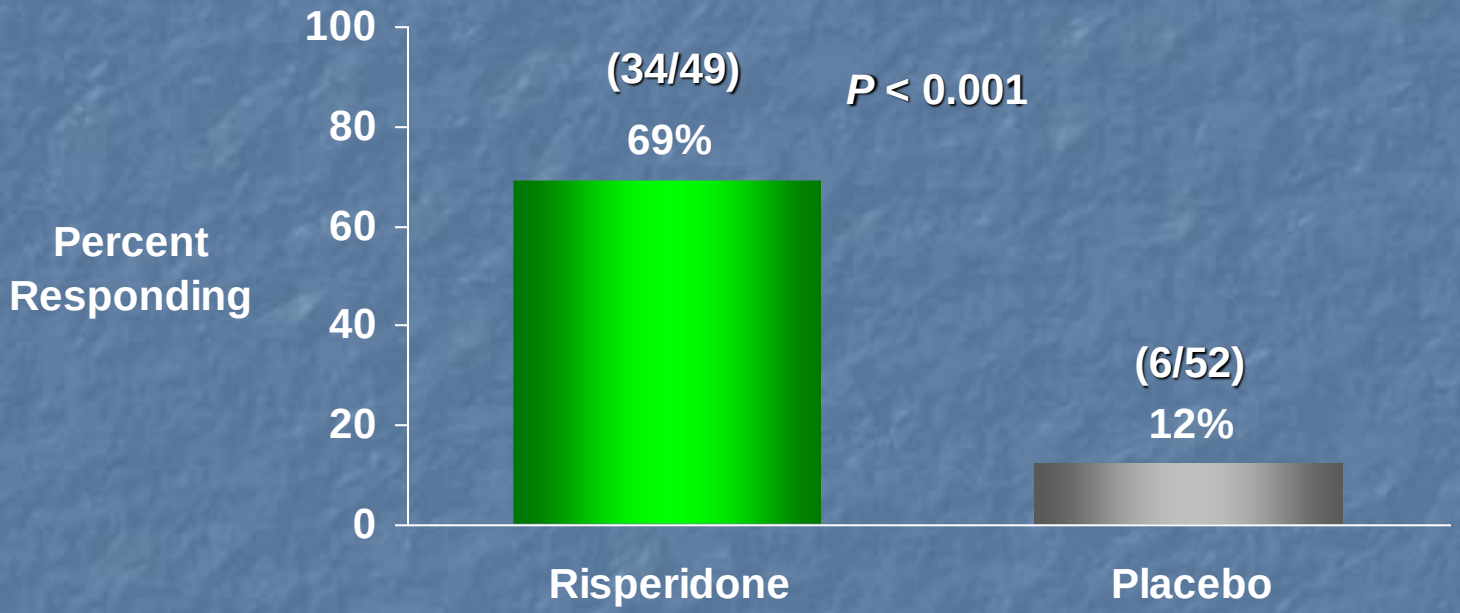
NIMH (Benedetto Vitiello, MD)

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

RUPP Autism Network. *N Engl J Med.* 2002;347:314-321.

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.
RUPP Autism Network. *N Engl J Med.* 2002;347:314-321.

Acute Risperidone Trial: RUPP

- Adverse effects
- Mean increase in weight
  - Risperidone, 2.7 ± 2.9 kg
  - Placebo, 0.8 ± 2.2 kg; $P < 0.001$
- Increased appetite, fatigue, drowsiness, dizziness, and drooling were more common in the risperidone group; all $P < 0.05$
- AIMS and Simpson-Angus: no EPS

AIMS = Abnormal Involuntary Movement Scale.
EPS = extrapyramidal symptoms.
RUPP Autism Network. *N Engl J Med.* 2002;347:314-321.

Baseline and Endpoint ABC Scores by Group

	Risperidone		Placebo	
ABC	**Baseline**	**Endpoint**	**Baseline**	**Endpoint**
Irritability $P < 0.001$	26.2 (7.9)	11.3 (7.4)	25.5 (6.6)	21.9 (9.5)
Social Withdrawal $P = 0.03$/NS	16.4 (8.2)	8.9 (6.4)	16.1 (8.7)	12.0 (8.3)
Stereotypy $P < 0.001$	10.6 (4.9)	5.8 (4.6)	9.0 (4.4)	7.3 (4.8)
Hyperactivity $P < 0.001$	31.8 (9.6)	17.0 (9.7)	32.3 (8.5)	27.6 (10.6)
Inappropriate Speech $P = 0.03$/NS	4.8 (4.1)	3.0 (3.1)	6.5 (3.6)	5.9 (3.8)

RUPP Autism Network. *N Engl J Med.* 2002;347:314-321.

RUPP Risperidone – Parent Management Training Trial

- 124 children (4 to 13 years) with PDDs and significant irritability
- 24-week, three-site, randomized, parallel groups trial
- Children randomized 3:2 to COMB (n=75) or MED (n=49)
- Parents in COMB received a mean of 10.9 PMT sessions

RUPP Autism Network. J Am Acad Child Adolesc Psychiatry. 2009.,48(12): 1143-1154

RUPP Risperidone – Parent Management Training Trial

- Primary Outcome Measure (Home Situations Questionnaire [HSQ]); COMB > MED (P=.006)
- COMB > MED on ABC Irritability (P=.01), Stereotypic Behavior (P=.04), and Hyperactivity/Noncompliance (P=.04)
- Final Risperidone dose for MED (2.26 mg/day) vs. COMB (1.98 mg/day) (P=.04)

ABC = Aberrant Behavior Checklist.

RUPP Autism Network. *J Am Acad Child Adolesc Psychiatry*. 2009,48(12): 1143-1154

Olanzapine vs. Haloperidol

- 12 children with autism (7.8 ± 2.1 y)
- 6-week open-label, parallel groups
- Olanzapine 7.9 ± 2.5 mg/d

  Haloperidol 1.4 ± 0.7 mg/d
- Response: Olanzapine 5/6 Haloperidol 3/6
- Weight Gain:

  Olanzapine 9.0 ± 3.5 lbs; range 5.9 – 15.8 lbs

  Haloperidol 3.2 ± 4.9 lbs; range - 5.5 – 8.8 lbs

Malone RP et al. *J Am Acad Child Adolesc Psychiatry*. 2001;40:887-894.

Olanzapine – Double-Blind, Placebo Controlled Study

- 11 children with pervasive developmental disorders (9 y)
- 8-week, double-blind, placebo-controlled
- Olanzapine 10 ± 2.04 mg/d
- Response: Olanzapine 3/6 Placebo 1/5
- Weight Gain: Olanzapine 7.5 ± 4.8 lbs
  Placebo 1.5 ± 1.5 lbs

Hollander E et al. *J Child Adolesc Psychopharmacol*. 2006;16(5):541-548.

Quetiapine

- **Four open-label studies:**

1. Age range 6-15 y, Dosage range 100-350 mg/d, Response 2/6 (Martin et al. 1999)
2. Age range 10-17 y, Dosage range 100-450 mg/d, Response 2/9 (Findling et al. 2004)
3. Age range 5-28 y, Dosage range 25-600 mg/d, Response 8/20 (Corson et al. 2004)
4. Age range 7-17 y, Dosage range 265-689 mg/d, Response 6/10 (Hardan & Handen 2005)

Ziprasidone

- Retrospective case series, 14.15 ± 8.29 wk
- 12 subjects
- Mean age = 11.62 ± 4.38 y; range = 8 to 20 y
- Mean dose = 59.23 ± 34.76 mg/d; range = 20-120 mg/d
- Response: 6/12 (50%) on CGI-I
- No significant weight gain

McDougle CJ et al. *J Am Acad Child Adolesc Psychiatry*. 2002;41:921-927.

Ziprasidone

- 6-week prospective, open-label study
- 12 subjects
- Mean age = 14.5 ± 1.8 y; range = 12 to 18 y
- Mean dose = 98.3 ± 40.4 mg/d; range = 20 to 160 mg/d
- Response: 9/12 (75%) on Clinician CGI-I
- No significant weight gain
- QT_c increased a mean of 14.7 msec; none > 448 msec

Malone et al. *J Child Adolesc Psychopharmacol*. 2007;17:779-790.

Aripiprazole in Asperger's Disorder and PDD NOS

- 14-week prospective, open-label study
- 25 subjects (6 female, 19 male; age = 8.6 y, range = 5-17 y)
- IQ = 82, range = 50-132
- Target Symptoms = Irritability, aggression, self-injury (ABC Irritability subscale score ≥ 18)
- Dose 7.8 mg/d, range 2.5 – 15 mg/d

Stigler et al. *J Child Adolesc Psychopharmacol*. 2009; 19(3):265-274.

Aripiprazole in Asperger's Disorder and PDD NOS

Response: CGI-I = "Much Improved" or "Very Much Improved" and a ≥ 25% improvement in ABC Irritability subscale score 21/25 (84%)

ABC Irritability Subscale Score:

Baseline = 28, Endpoint = 8.8

Adverse Effects:

Mild tiredness = 16, Moderate tiredness = 1

Mild EPS = 6

Weight gain = 19, Mean = 2.3 lbs, range = -3.3 – 7.7 lbs

Stigler et al. *J Child Adolesc Psychopharmacol*. 2009; 19(3):265-274.

Aripiprazole in Autism – Flexible Dose Study

- 98 children and adolescents with autism (age 6-17 years) with significant irritability
- 8-week, double-blind, placebo-controlled, parallel groups, flexibly-dosed (2-15 mg/day) trial
- Aripiprazole (8.5 mg/day) more efficacious than placebo on Aberrant Behavior Checklist Irritability subscale (P<.001)
- Discontinuation rates: PLA=5.9% Aripiprazole=10.6%
- Most common AEs with aripiprazole were fatigue and somnolence
- Weight gain PLA=1.0 kg Aripiprazlole=2.1 kg

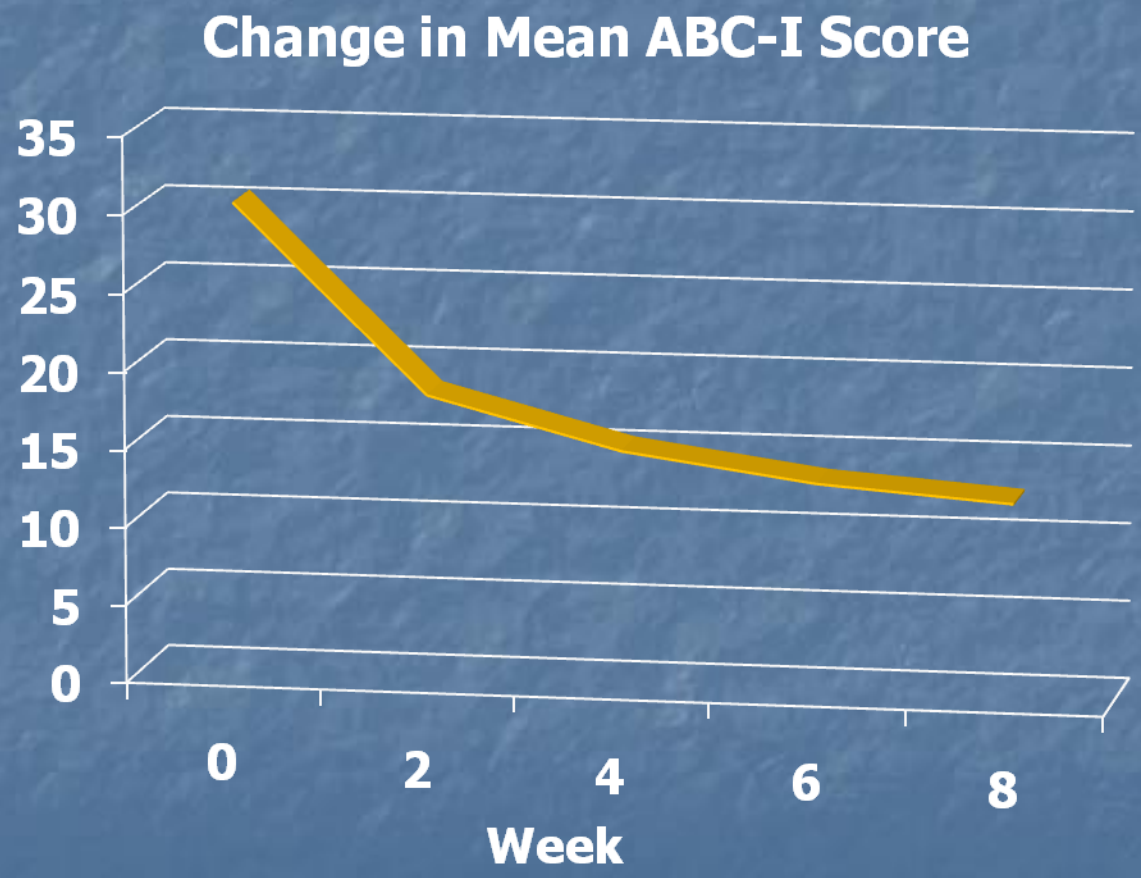
Owen et al. *Pediatrics. 2009.,124: 1533-1540*.

Aripiprazole in Autism – Fixed Dose Study

- 218 children and adolescents with autism (age 6-17 years) with significant irritability
- 8-week, double-blind, placebo-controlled, parallel groups, fixed-dose (5 mg, 10 mg, 15 mg) trial
- Aripiprazole (5 mg, 10 mg, 15 mg) more efficacious than placebo on Aberrant Behavior Checklist Irritability subscale (P<.05 for all)
- Discontinuation rates: PLA=7.7%, 5 mg=9.4%, 10 mg=13.6%, 15 mg=7.4 %
- Common AEs leading to discontinuation: sedation, drooling, tremor, akathisia, EPS
- Weight gain PLA=0.3 kg, 5+10 mg=1.3 kg, 15 mg=1.4 kg

Marcus et al. *J Am Acad Child Adolesc Psychiatry. 2009,48(11): 1110 – 1119.*

Paliperidone for Irritability in Adolescents and Young Adults with Autism: Preliminary Results



Stigler et al. Preliminary data from poster presentation at 2010 APA.

Paliperidone for Irritability in Adolescents and Young Adults with Autism: Preliminary Results

- 8-week, prospective, open-label study
- 25 subjects enrolled; mean age=15.2 y (12-21 y); IQ = 50
- Concomitant meds allowed; stable for 2 mos prior to study
- Mean dose, 6.9 mg/d; range, 3-9 mg/d
- 83% (20/24) responded based on CGI-I and ABC-I
- Two exited early [nonresponse (1); moderate sedation (1)]
- Mean weight gain 2.3 kg (-3.6 to +7.9 kg); Mean change in age- and sex-normed BMI: 23.1 (BL) to 23.8 (Endpoint)

Stigler et al. Preliminary data from poster presentation at 2010 APA.

Potential Targets of Pharmacotherapy

1. Motor hyperactivity, inattention
2. Repetitive behavior
3. Aggression, self-injury, severe tantrums
4. **Impaired social relatedness**
5. Sleep disturbance

Medications Studied for Social Impairment in Autism

- Not effective
  - Fenfluramine
  - Naltrexone
  - Lamotrigine
  - Amantadine
  - Risperidone
  - Fluoxetine
  - Citalopram

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

Posey DJ et al. *AACAP Poster 3.53,* 2008.

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Medications for Sleep Disturbance

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

Complementary and Alternative Medicine (CAM)

- Secretin
- Gluten-free and Casein-free diet
- Oral Immunoglobulin
- Omega-3 fatty acids
- Vitamin B_6/Magnesium

Prognosis For Autistic Disorder

- Three consistent outcome factors:
  - IQ
  - The presence or absence of speech
  - The severity of the disorder
- Up to 28% of children with no neurologic disorder in early childhood develop seizures in adolescence or later. Peak age of onset is 11-14 years old
- A small number of children with autism show intellectual and language decline in adolescence
- While a significant number of children with autism may have coexisting psychiatric disorders there is no increased risk for schizophrenia

Future Directions

- **Motor Hyperactivity/Inattention**
  - Double-blind, placebo-controlled trial of atomoxetine
  - Double-blind, placebo-controlled trial of guanfacine
- **Repetitive Behavior**
  - Pilot studies of riluzole
- **Aggression, Self-Injury, Severe tantrums**
  - Pilot studies of paliperidone
- **Impaired social Relatedness**
  - Controlled trial of D-cycloserine + Social Skills Training
  - Double-blind, placebo-controlled trial of memantine
  - Pilot studies of intranasal oxytocin

Lurie Center for Autism

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http://www.massgeneral.org/children/services/treatmentprograms

(781)-860-1700

Question 1

- A 3 year old girl presents with impaired receptive and expressive language. She has stereotyped hand movements although her parents say that up to the age of 18 months she seemed to have purposeful hand skills. Her height and weight are age appropriate but her head growth has decelerated since she passed her second birthday. The most appropriate diagnosis is:
  - A Autistic disorder
  - B Rett's disorder
  - C Asperger's disorder
  - D Childhood disintegrative disorder
  - E Pervasive developmental disorder NOS

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  - B. Autism Diagnostic Interview Revised (ADI-R)
  - C. Childhood Autism Rating Schedule (CARS)
  - D. Pervasive Developmental Disorders Screening Test (PDDST)
  - E. Checklist for Autism in Toddlers (CHAT)

Answers

- 1) B
- 2) D
- 3) A