

# Where We Will Go

In using  
medication in children  
with ASD

## 1. Approaching the idea

### All About Approach

- Concepts to challenge
- Some evidence

2. Using medication  
to target comorbid  
psychiatric  
conditions

3. Using medication  
to target behaviors,  
not syndromes

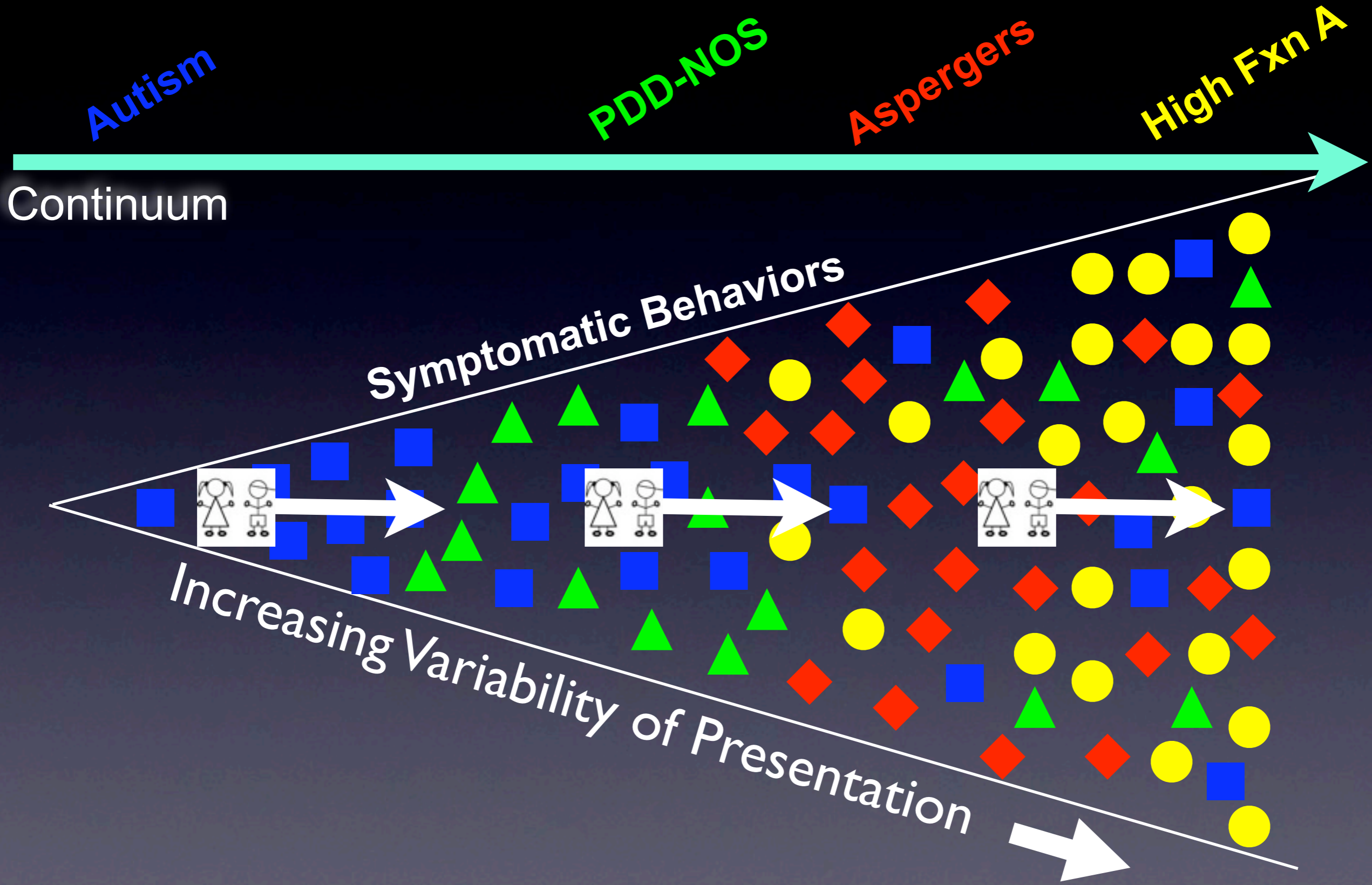
**Autism Spectrum Disorders Seminar**

**March 20, 2009**

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Division of Child Psychiatry



# • Most Children with ASD Become Adults with ASD



Adapted From Rosenn, D. (1997). "Rosenn Wedge". From Aspergers: What we have learned

# Challenges in Rx of Autism

## Neurodevelopmental Disability Primary Goals of Treatment

### Minimize

- Core Features
- Associated Deficits
- Family Distress

### Maximize

- Functional Independence
- Quality of Life

### Facilitate

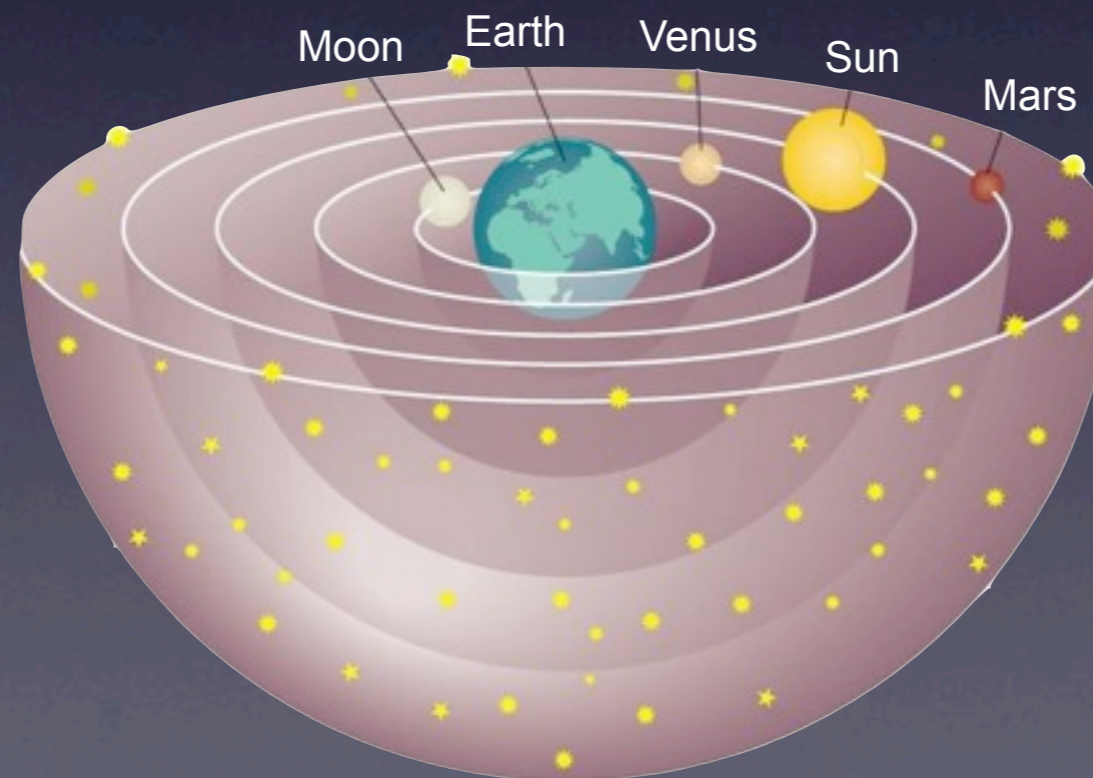
- Development
- Learning
- Socialization

# Challenges in Rx of Autism

## Pharmacology vs Behavioral Therapy

### Alternative Perspective

- a. How can we best use medication in children with ASD
- b. Can we recognize serious mental illness?
- c. Can we treat serious mental illness?
- d. Are we restrained by perspectives formed before understanding the neurobiology of mood/anxiety/attention?**



# Challenges in Rx of Autism

Difficult Yes

Impossible No

## Severity of Disorder

**Autism**

++++

+++

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**Asperger's**

+

	++++	+++	++	+
<b>Social Interaction</b>	Aloof	Physical Need Only	Passive Acceptance	Bizarre One-Sided
<b>Social Communication</b>	None	Needs Only	Replies if Approached	Spontaneous But Repetitive, One-sided
<b>Social Imagination</b>	None	Imitates Others	Imitates Occasional Theme	Acts Out One Theme Repetitively
<b>Repetitive Activities</b>	Simple, Body Directed	Simple, Object Directed	Complex Routines	Abstract & Verbal
<b>Language</b>	None	Echolalic	Idiosyncratic	Grammatical But Long Winded & Repetitive
<b>Sensory Response</b>	Very Marked	Marked	Occasional	Minimal
<b>Stereotypies</b>	Very Marked	Marked	Occasional	Minimal
<b>Special Skills</b>	None	One Below Chronologic age	One at Chronologic Age	One Above Chronologic Age

Adapted from Wing

## Challenges in Rx of Autism

# Goals of Biologic Therapy

**Relief of Pain**

**Restoration**

**Function**

**Development**

**Augmentation**

**Parenting**

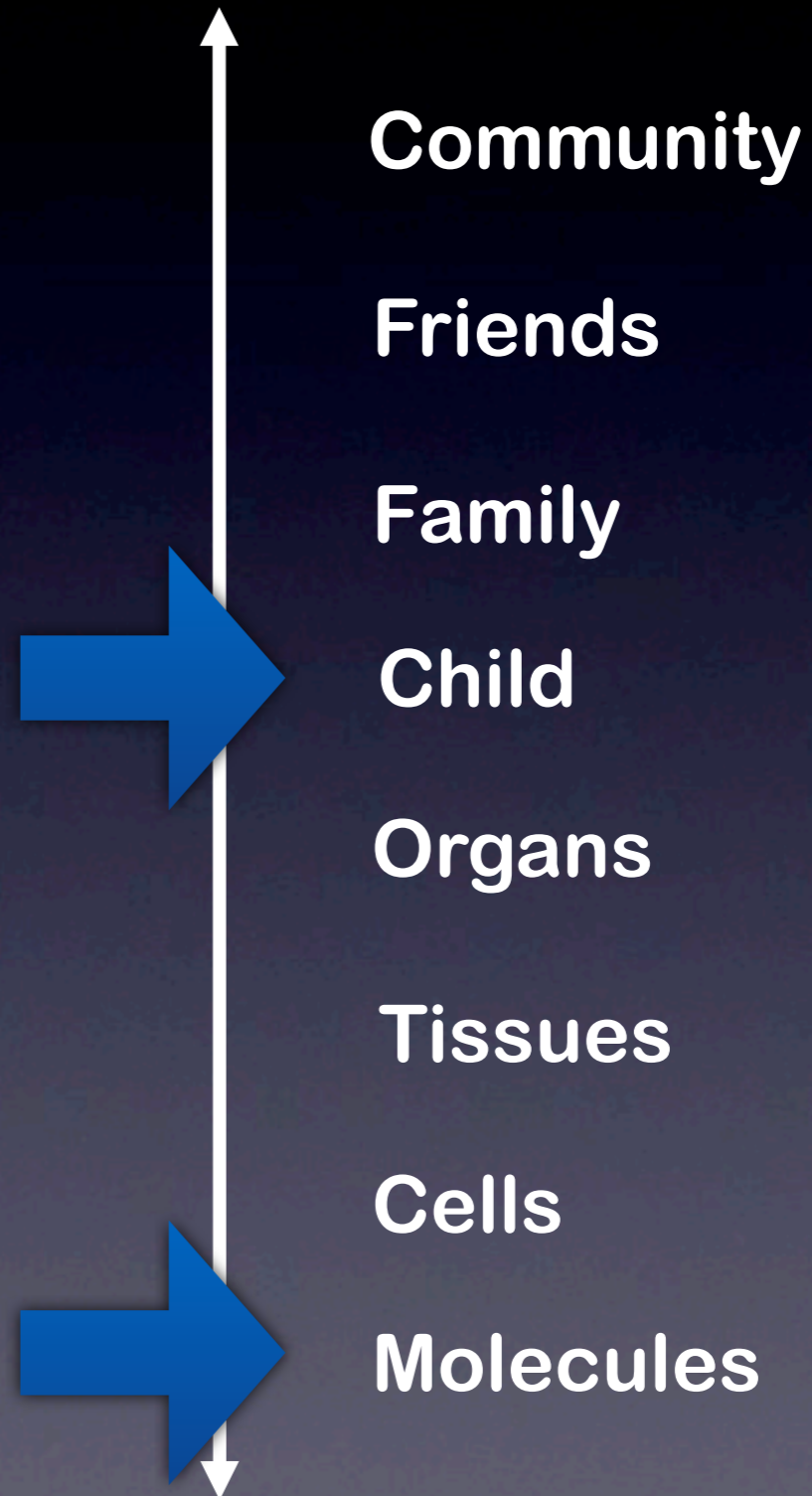
**Therapy**

**School Based Help**

# Medications: Purpose of Treatment

**ASDs** Impact Children  
at All Levels

**Rx** Impacts Children  
at All Levels



## Experiment

**Set of Observations**

**Reports: Parents, Teachers & Child**

**Performed to Solve a Problem**

**Child Demoralized or Impaired**

**To Test a Hypothesis**

**With Determination & Persistence,**

**We Can Help this Child**

**With Informed Partnership**

**Parents & Child & Pediatrician**

## Identify & Assess Target Behaviors

### • Parent Interview @ Behavior

- Intensity
- Duration
- Exacerbating Factors/Triggers
- Ameliorating Factors
- Time Trends
- Degree of Interference with Function
- Input from School

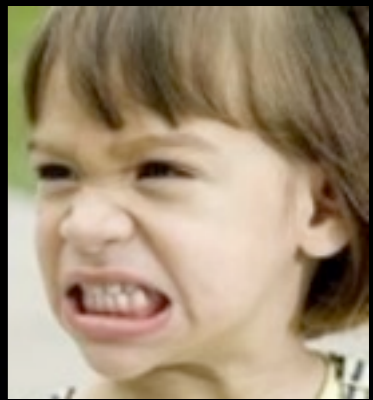
### • Assess Existing & Available Supportive Services

### • Assess Possible Contributing Medical Factors

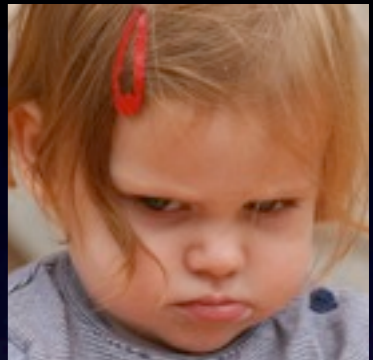
### • Consider & Choose Medication

### • Establish Plan for Monitoring Effects

### • Consider Careful Withdrawal after 6-12 mos



Rage is Relative



# Treating Comorbidity in Autism

## ASD & ADHD: Evidence

Medication	Study Year	Design	Age Range	Daily Dose	Outcome
Methylphenidate	RUPP 2005	Double Blind Placebo Control	5 - 14	7.5mg - 50mg	50% but < than Non ASD kids
Amphetamine	1972				No Change
Atomoxetine	Arnold 2006	Placebo Controlled Crossover	5 - 15	44mg +/- 22mg	Better than Placebo
Imipramine	1971				Minimal Speech Improvement
Nortriptylene	1966				Maybe Dec Hyperactivity
Clonidine	1992				Dec Hyperarousal Better Social
Guanfacine	2006	Open Label	5 - 14	1 - 3 mg	Dec Hyperactivity

Adapted from: Pharmacological Treatment Options for Autism Spectrum Disorders in Children & Adolescents, Leskovec Thomas, Harv Rev Psychiatry 2008;16:97-112

# Treating Behavior in Autism

## Aggression, Irritability, SIB: Evidence

Medication	Study Year	Design	Age	N	Daily Dose	Improvement			
						Agg	Irr	SIB	Other
<b>Haloperidol</b>	1982 Campbell	Double Blind Placebo Control	2 - 7	33	0.5 - 3 mg	Significant Reduction in Maladaptive Behavior			
<b>Pimozide</b>	1992 Ernst	Open Label	4 - 8	8	3 - 6 mg	Global Improvement			
<b>Risperidone</b>	2002 McCracken 2005 McDougale	Double Blind Placebo Control	5 - 17	101	1.8 mg	+		+	Improved Self Stim
<b>Risperidone</b>	2005 Troost	Open Label	5 - 17	36	1.45 mg	+		+	Improved Repetitive
<b>Risperidone</b>	2004 Shea	Double Blind Placebo Control	5 - 12	79	0.06 mg/ kg	+	+		
<b>Risperidone</b>	2006 Luby	Double Blind Placebo Control	2.5 - 6	24	0.5 mg/kg	Improved Autism Rating			

Adapted from: Pharmacological Treatment Options for Autism Spectrum Disorders in Children & Adolescents, Leskovec Thomas, Harv Rev Psychiatry 2008;16:97-112

# Treating Behavior in Autism

## Aggression, Irritability, SIB: Evidence (Cont)

Medication	Study Year	Design	Age	N	Daily Dose	Improvement			
						Agg	Irr	SIB	Other
<b>Olanzapine</b>	1982 Holl&er	Double Blind Placebo Control	6 - 14	11	8 - 10 mg	Improve CGI Sxs			
<b>Quetiapine</b>	1999 Martin 1999 Findling	Open Label	10 - 17	9	292 mg	"Therapeutic Effects Suboptimal"			
<b>Ziprasidone</b>	2002 McDougle	Open Label	8 - 20	12	25 - 95 mg	+	+		Improve Agitation
<b>Valproic Acid</b>	2006 Holl&er	Double Blind Placebo Control	5 - 17	13	500 - 1150 mg	Improve Repetitive			
<b>Buspirone</b>	1998 Buitelaar	Open Label	6 - 17	22	15 - 45		+		Improve Anxiety
<b>Apipirazole Topamax Beta Blockers</b>	No Studies								

Adapted from: Pharmacological Treatment Options for Autism Spectrum Disorders in Children & Adolescents, Leskovec Thomas, Harv Rev Psychiatry 2008;16:97-112

**Treating Behavior in Autism: Targeting Clusters**

**Cook Book?**

# Intervention for Autistic Spectrum Disorders

Journal of the American Society for Experimental  
NeuroTherapeutics  
Vol 3 (April 2006) 207-216

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# Treating Behavior in Autism: Targeting Clusters

## **Anxiety / Compulsive Cluster**

**Rigidity, Obsessive, Compulsive, Rituals, Transitional Issues,  
Difficulty Shifting Attention, Overattention to Small Things**

## **Hyperactivity Cluster**

**Hyperactivity, Impulsivity, Reactivity, Aggression, Agitation, Irritability**

## **Attention Deficit Cluster**

**Poor Attention, Auditory Processing Deficits, Aloofness, In Own  
World, Not Connected, Daydreams, Distracted, Not Completing Tasks**

## **Social Cluster**

**Aloofness, Expressive Language Deficit, Pragmatic Language Deficit,  
Cognitive Distortion, Low Social Motivation**

## Anxiety / Compulsive Cluster

Rigidity, Obsessive, Compulsive, Rituals, Transitional Issues, Difficulty Shifting Attention, Overattention to Small Things

First Line

SSRIs		
Fluoxetine	4	mg/day
Escitalopram	2.5	mg/day
Citalopram*	5	mg/day

Second Line

Atypical AP		
Risperidone	0.25	mg/hs
Aripiprazole	2.5-5	mg/day
Quetiapine*	12.5-25	mg/hs

# Treating Behavior in Autism: Targeting Clusters

## Hyperactivity Cluster

Hyperactivity, Impulsivity, Reactivity, Aggression, Agitation, Irritability

First Line

### Stimulants

Methylphenidate	2.5	mg/day
Dextroamphetamine	1.25*	mg/day

Second Line

### Alpha Agonists

Guanfacine	0.5	mg/hs
Clonidine	0.05	mg/hs

Third Line

### Atypical AP

Risperidone	0.25	mg/hs
Aripiprazole	2.5-5	mg/day
Quetiapine*	12.5-25	mg/hs

### SNRI

Atomoxetine <10kg	10	mg/day
Atomoxetine >10kg	18	mg/day

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## Attention Deficit Cluster

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