

A Rational Approach to Behavior Management & Psychopharmacology in Children with ASD

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Disclosures

- Dr. Coplan is author of *Making Sense of Autistic Spectrum Disorders: Create the brightest future for your child with the best treatment options* (Bantam-Dell, 2010), and receives royalties on its sale



- This presentation will include a discussion of off-label drug use

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“Behavior”

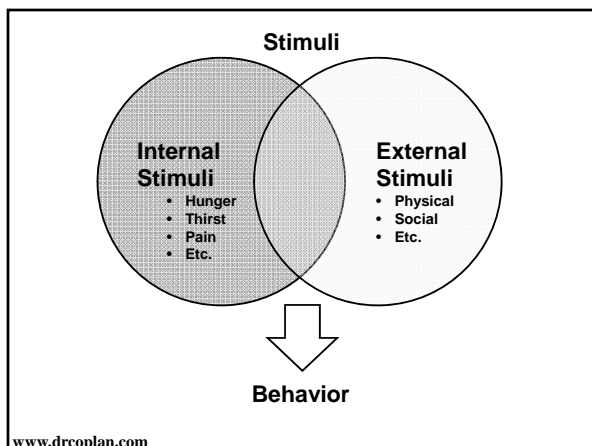
- “The manner of conducting one’s self”
- “Anything than an organism does involving action and response to stimulation”
- “The actions or reactions of a person or animal in response to internal or external stimuli”

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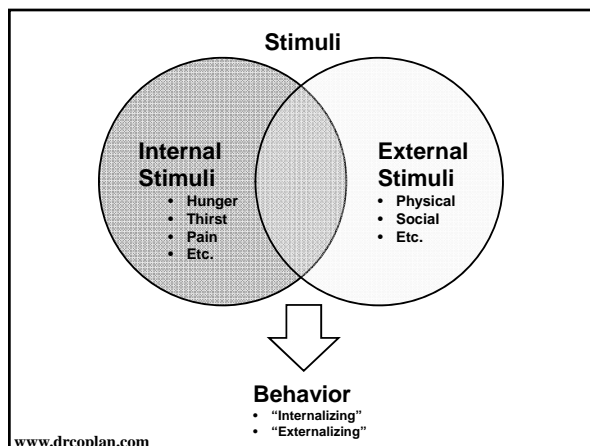
Stimuli

- Internal stimuli
 - Hunger
 - Thirst
 - Pain
 - Other...
- External Stimuli
 - Physical
 - Light, sound, touch, etc.
 - Social
 - Reinforcers (Positive & Negative)
 - Aversives

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“Internalizing” Behavior

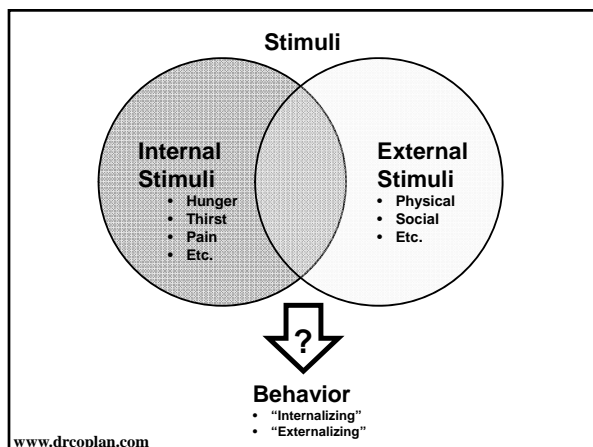
- Anxiety
- Perfectionism
- Obsessiveness / Rigidity
- Depression

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“Externalizing” Behavior

- Tantrums
- Property Destruction
- Aggression towards others
- Self-injurious behavior (SIB)

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Behaviors

- Acute change or chronic?
- General health?
 - Vital signs, I&O, Level of consciousness
- Anything new in child's life?
 - Recent change of meds?
 - Change of caregivers?

Behaviors

- What is the child's developmental level?
- Is the behavior normal for the child's developmental level?
 - Tantrums / Noncompliance
 - “Impulsivity” / “Inattention”

Behaviors

- What is the child's ability to communicate?
 - Does “disruptive” behavior serve a communicative function?
 - Is this child in pain, or frustrated and unable to tell us why?

The ABC's of Behavior Analysis

- What is the Antecedent?
- What is the Behavior?
- What is the Consequence?
 - Reinforcers
 - Positive
 - Negative
 - Aversives

Antecedents

- Imposition of a task
- Change in routine
- Denial of access to object or activity
- Other....
- Or: No apparent antecedent

Consequences 1: Reinforcers

- Reinforcers lead to an increase in frequency of the antecedent behavior
 - Positive Reinforcement (adds something)
 - Negative Reinforcement (removes something)
 - Negative reinforcement does not = "punishment"

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Positive Reinforcement

- Attention (in neurotypical children)
- Access to desired object or activity
 - Token Economy

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Negative Reinforcement

- Escape (from a task, e.g.)
- Removal of an undesirable object (non-preferred food, e.g.)
 - Negative reinforcement does not = "punishment"

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Food Selectivity

Positive and Negative Reinforcement of unwanted behavior

- Parent removes non-preferred food (negative reinforcement)
- Parent provides child with his/her preferred food (positive reinforcement)
- Alternatives
 - *FirstThen*
 - Put refusal on extinction
 - The kitchen is *closed* between meals
 - Desensitization (non-preferred food is on table, on plate, touch, lick, mouth, eat)

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Consequences 2: Aversives

- Aversives lead to a *decrease* in the antecedent behavior
- Logical Consequences
 - If child refuses to use toilet, child must carry backpack with own spare clothes, when family is in public
- Over-correction
 - If the child spills milk on purpose: child must mop the entire kitchen floor

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Token Economy

- Concretely specified behaviors
- Earn and Lose Points (Tokens)
- Points ➔ Access to specified reward
 - Reward determined by child's interests
 - Preferred toys
 - Computer time
 - Etc.
 - NO access to reward at other times
 - "Extra" treats not as effective

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Token Economy

Camp David
Trading Post Rules

Rewards		Fees	
Good Day	+30	Bad Day	0
Doing Chore - Each	+10	Cursing - Each Time	-20
Doing a Good Deed	+10	Disrespect Parents	-10
Compliment About You	+10	Lies - Each	-20
Do Morning Work (NO Whining)	+10	Don't Do Morning Work (Whining)	-10
Do Pre-Bedtime Checklist	+5	Don't Do Pre-Bedtime Checklist	-5
		Ask More Than Once	-5
		Touch Another Kid or Being Mean	-10

Red = 5 White = 10 Blue = 50

Disruptive Behavior: Function & Best Response

- Attention
 - 1-2-3 ➔ "Time Out"
- Access
 - Never grant access to desired object in response to disruptive behavior
- Escape
 - Never permit the child to terminate a task with disruptive behavior. Walk child through task first, *then* ➔ Time Out.

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But.....

Children with ASD have atypical responses to internal and external stimuli

What good is Time Out if the child has no eye contact?

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Behavioral Symptoms in ASD

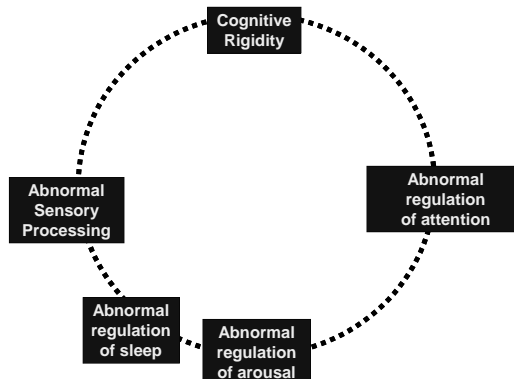
Core Deficits
Cognitive Rigidity
Abnormal regulation of attention
Abnormal regulation of arousal
Abnormal regulation of sleep
Abnormal sensory processing



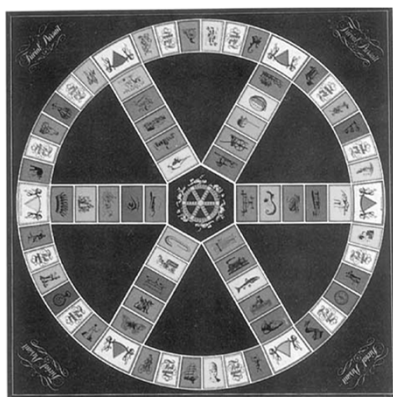
Symptoms
Routines, Stereotypes
Perseveration / Inattention
Agitation / Lethargy
Insomnia
Sensory seeking / avoidance

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Neuropsychological Deficits in Persons with ASD

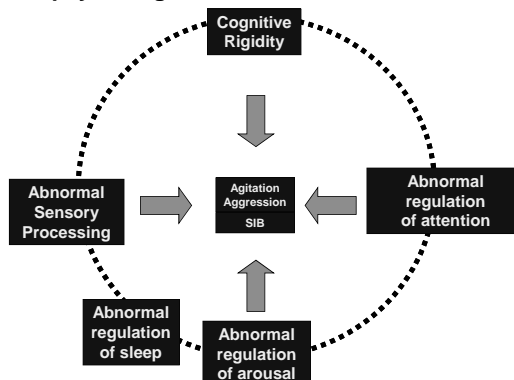


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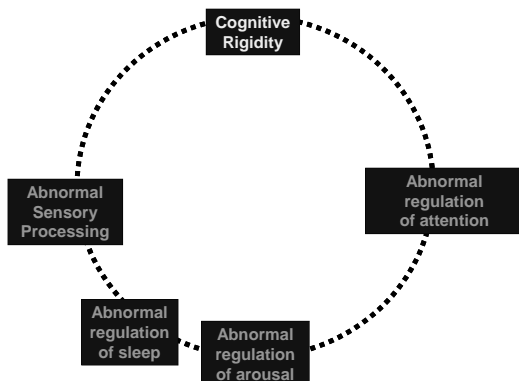
Neuropsychological Deficits in Persons with ASD



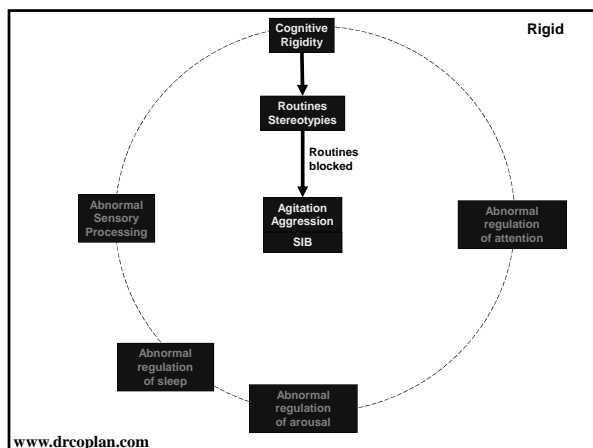
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Cognitive Rigidity

- *Insistently* repetitious behavior
- Problems with changes in routine, transitions, unmet expectations
- Perfectionism
- (Anxiety)
- (Depression)

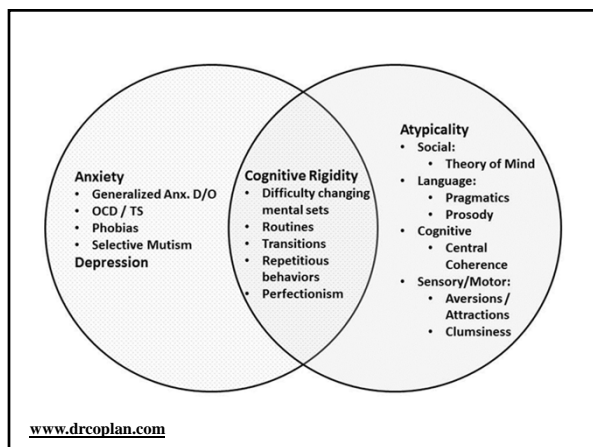


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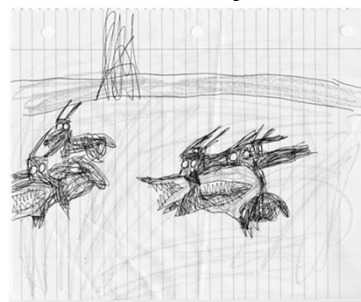


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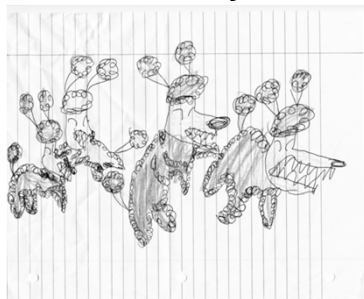


Anxiety



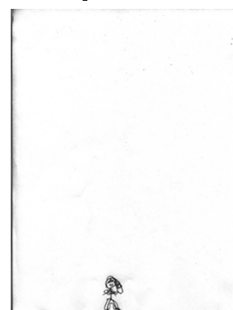
RD. 7 y.o. F, nl IQ, PDD-NOS and Anxiety. Fam Hx: GAD
www.drcoplan.com

Anxiety



RD. 7 y.o. F, nl IQ, PDD-NOS and Anxiety. Fam Hx: GAD
www.drcoplan.com

Depression



www.drcoplan.com KO: 10 yr old female, PDD-NOS, normal IQ

Cognitive Rigidity

- **Interventions**
 - **Visual Schedules**
 - What am I supposed to be doing *do now*?
 - What am I supposed to do *next*?
 - CBT, Relaxation Techniques
 - SSRIs?

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When My Worries Get Too Big!

A Relaxation Book for Children Who Live with Anxiety

Written and Illustrated
by Kari Dunn Buron

Foreword by Brenda Smith Myles

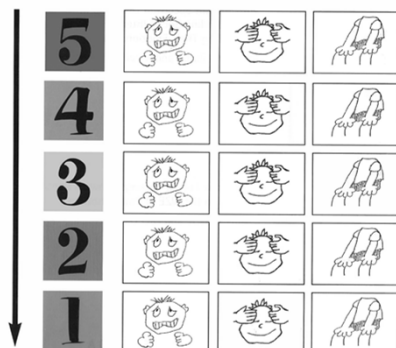


APC

Autism Asperger Publishing Company
P.O. Box 22173 • Shawnee Mission, Kansas 66203-0173
www.asperger.net

My Calming Sequence

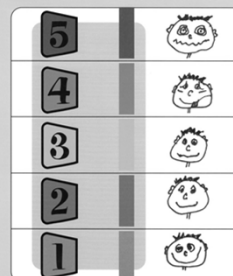
Sometimes my worries are way too big! I can stop, squeeze my hands and take a deep breath. I can also rub my head and rub my legs. This can help me to stay calm.



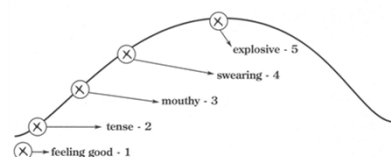
The Incredible 5-Point Scale

Assisting students with autism spectrum disorders
in understanding social interactions
and controlling their emotional responses

Kari Dunn Buron and Mitzi Curtis



Emily's Anxiety Curve



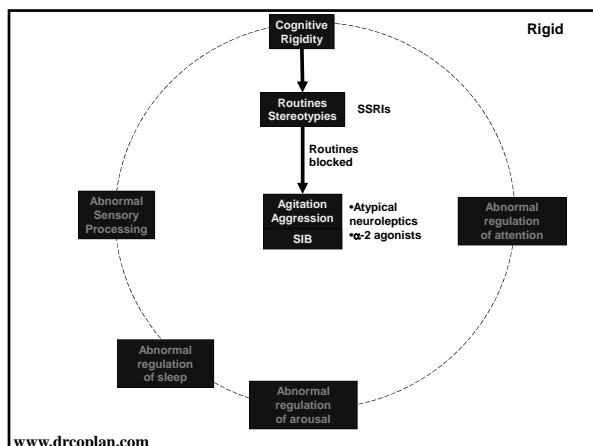
Emily thinks	Mrs. Olson thinks
5 hitting	hitting
4 running out of the room	swearing
3 swearing	mouthy
2 mad/tense	challenging
1 ok	working

The Incredible 5-Point Scale. Kari Dunn Buron and Mitzi Curtis. Autism Asperger Publishing Company

SSRIs in ASDs

- **Primary targets**
 - Cognitive Rigidity
 - Anxiety
 - Depression
- **“Downstream” benefit:**
 - Disruptive Behavior

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Dimensional predictors of response to SRI pharmacotherapy in obsessive-compulsive disorder

Landeros-Weisenberger et al. J. Affective Disord. v121, Issues 1-2, 2/2010, 175-179

OCD Subtypes:

- “Aggressive” Obsessions & Checking Behavior (AGG)
- Sexual / Religious (SR)
- Contamination & Washing (CW)
- Symmetry & Exactness (SYM)
- Hoarding (HRD)

Dimensional predictors of response to SRI pharmacotherapy in obsessive-compulsive disorder

Landeros-Weisenberger et al. J. Affective Disord. v121, Issues 1-2, 2/2010, 175-179

Baseline demographical and clinical characteristics				
	Total	Clomipramine	Fluvoxamine	Fluoxetine
Number	165	62	79	24
Age	35.9 ± 11.0	35.1 ± 10.8	37.2 ± 11.7	34.0 ± 8.9
Gender	69 M	27 M	32 M	10 M

Dimensional predictors of response to SRI pharmacotherapy in obsessive-compulsive disorder

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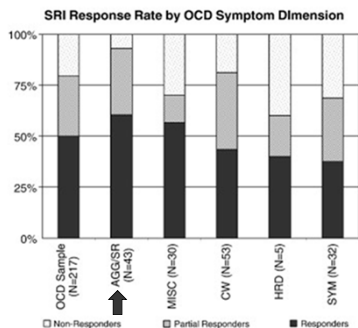
Result:

- Subjects with “aggressive obsessions” and checking behavior (and/or Sexual Religious obsessions) showed the best response to SRIs

Analog of “Insistence on Sameness” / Meltdowns in ASD?

Dimensional predictors of response to SRI pharmacotherapy in obsessive-compulsive disorder

Landeros-Weisenberger et al. J. Affective Disord. v121, Issues 1-2, 2/2010, 175-179



Pharmacotherapy for anxiety disorders in children and adolescents

Ipser JC, Stein DJ, Hawkrig S, Hoppe L. Cochrane Database of Systematic Reviews 2009, Issue 3.

- Studies reviewed: 22 RCTs/ 2,519 participants
 - Short-term (average 11 wks)
 - Mean age 12 yrs
 - Drugs studied (versus placebo)
 - SSRIs :15 (fluoxetine 6, fluvoxamine 2, paroxetine 3, sertraline 4)
 - SNRIs: 5, (clomipramine 3), venlafaxine 2)
 - Benzodiazepines: 2: (alprazolam 1, clonazepam 1)
 - Tricyclic antidepressants: 1 (desipramine)
- Meta-analysis
 - Response rate: Medication 59%; Placebo 31%
 - 7.3% of subjects treated with SSRIs withdrew because of side effects
 - “The overwhelming majority of evidence of efficacy was for the SSRIs, with the most evidence in paediatric OCD”

A Placebo Controlled Crossover Trial of Liquid Fluoxetine on Repetitive Behaviors in Childhood and Adolescent Autism

Hollander, E, et al. Neuropsychopharmacology (2005) 30, 582-589

Subjects

- 45 subjects → 39 completers: 30 (77%) male, 9 (23%) female
- Age 5 - 16 years (mean 8 yr.)
- Mean IQ 64; range 30-132; MR: 23 (59%)

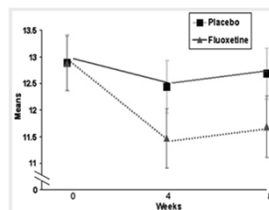
Protocol

- Fluox. or Placebo x 8 wk / 4 week "washout" / Fluox. or Placebo x 8 wk
- Mean dose 9.9 mg / d (+/- 4.4 mg)
- Children's Yale-Brown Obsessive-Compulsion Scale (CY-BOCS)
- Clinical Global Improvement Scale-Autistic Disorder (CGI-AD)
- Fluoxetine Side Effects Checklist (FSEC)

A Placebo Controlled Crossover Trial of Liquid Fluoxetine on Repetitive Behaviors in Childhood and Adolescent Autism

Hollander, E, et al. Neuropsychopharmacology (2005) 30, 582-589

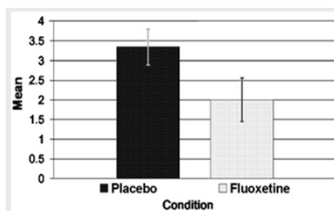
Fluoxetine was superior to placebo in the treatment of repetitive behaviors by CY-BOCS (linear trend x treatment interaction $z=-2.075$, $SE=0.407$, $p=0.038$)



A Placebo Controlled Crossover Trial of Liquid Fluoxetine on Repetitive Behaviors in Childhood and Adolescent Autism

Hollander, E, et al. Neuropsychopharmacology (2005) 30, 582-589

Fluoxetine was marginally superior to placebo on the improvement of the CGI change scores ($z=-1.907$, $SE=0.703$, $p=0.056$)



A Placebo Controlled Crossover Trial of Liquid Fluoxetine on Repetitive Behaviors in Childhood and Adolescent Autism

Hollander, E, et al. Neuropsychopharmacology (2005) 30, 582-589

Fluoxetine did not significantly differ from placebo on treatment emergent side effects

Symptom	Fluoxetine	Placebo
Anxiety/nervousness	15.9% (6/39)	33.3% (12/36)
Insomnia	35.9% (14/39)	47.2% (17/36)
Drowsiness/fatigue/sedation	17.9% (7/39)	11.1% (4/36)
Agitation	46.2% (18/39)	44.4% (16/36)
Diarrhea	5.1% (2/39)	19.4% (7/36)
Anorexia	15.4% (6/39)	11.1% (4/36)
URI	10.3% (4/39)	19.4% (7/36)
Weight gain	0% (0/39)	2.8% (1/36)

A Placebo Controlled Crossover Trial of Liquid Fluoxetine on Repetitive Behaviors in Childhood and Adolescent Autism

Hollander, E, et al. Neuropsychopharmacology (2005) 30, 582-589

Conclusion

"Our results demonstrate that liquid fluoxetine reduced repetitive behaviors in children and adolescents with autism. We found a statistically significant reduction in repetitive behaviors, with a moderate to large effect size (0.76)."

Selective serotonin reuptake inhibitors (SSRIs) for autism spectrum disorder (ASD).

Williams, K., et al., Cochrane Database Syst Rev, 2010. 8: p. CD004677

- Studies reviewed: 7 randomized controlled trials / 271 participants
 - Fluoxetine (2), fluvoxamine (2), fenfluramine (2), citalopram (1)
 - Subjects: Children (5); Adults (2)
 - Varying inclusion criteria for Dx of ASD and IQ
 - 17 different outcome measures
- "Data were unsuitable for meta-analysis"

Selective serotonin reuptake inhibitors (SSRIs) for autism spectrum disorder (ASD).

Williams, K., et al., Cochrane Database Syst Rev, 2010. 8: p. CD004677

- **Treatment-emergent symptoms**
 - Citalopram: 1 child with new onset seizures (continued to have seizures after citalopram was stopped)
 - Fenfluramine: Increased stereotypies; withdrawal, sadness; decreased appetite ("With monitoring, dose adjustment and time, all but one of these adverse effects were resolved")
 - Fluoxetine (Hollander 2005): 6 of 37 children had their dosage reduced due to agitation
 - 2 children in the placebo group had their "dosage" reduced.
 - Difference between groups: Not significant
 - Reviewers disregard the fact that by the end of the trial, "anxiety and nervousness" was lower in the fluoxetine group compared to placebo: 15.9% vs. 33%.
 - Fluvoxamine: No significant difference in side effects between SSRI and placebo

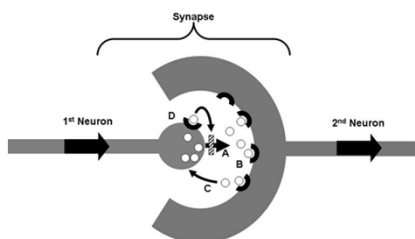
Selective serotonin reuptake inhibitors (SSRIs) for autism spectrum disorder (ASD).

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Authors' conclusion:

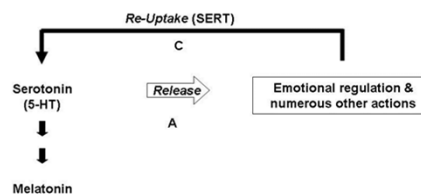
"There is no evidence that SSRIs are effective as a treatment for children with autism. In fact, there is emerging evidence that they are not effective and can cause harm. As such SSRIs cannot be recommended as a treatment for children with autism at this time."

Neurotransmitters



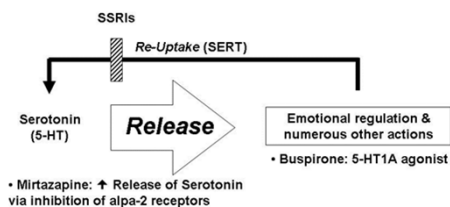
- A: Release of transmitter by 1st neuron
- B: Transmitter acts at receptor sites on 2nd neuron
- C: Transmitter is taken up, and re-stored in 1st neuron
- D: Autoreceptor on 1st neuron: detects release of transmitter

Serotonin: The master neurotransmitter



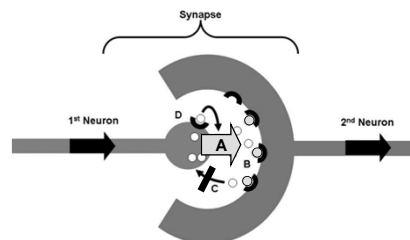
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Serotonin-promoting (serotonergic) drugs

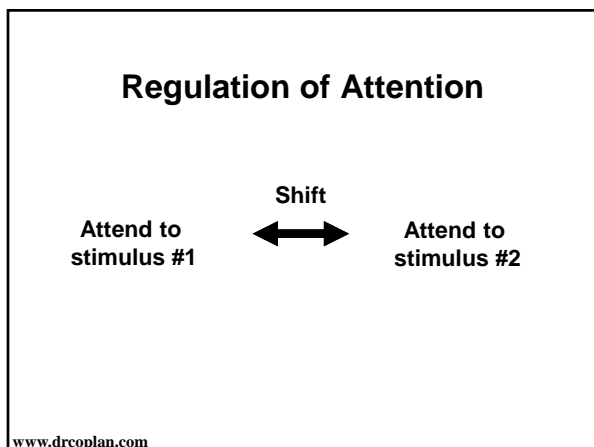
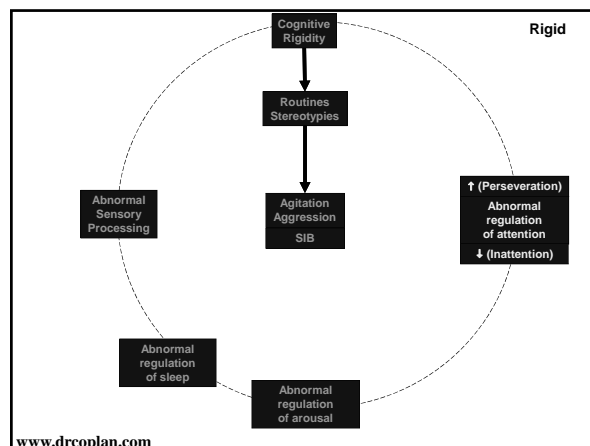


Selective Serotonin Reuptake Inhibitors block the re-uptake of Serotonin

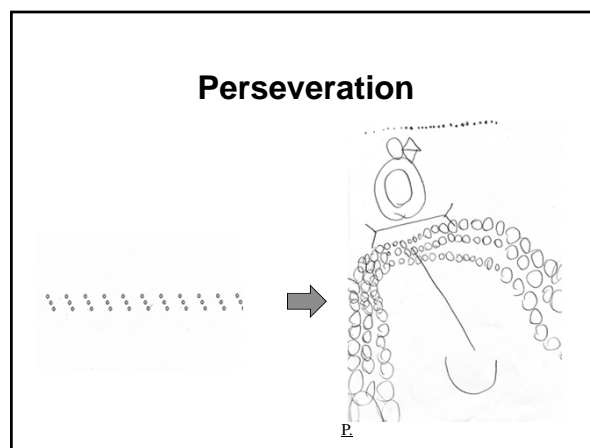
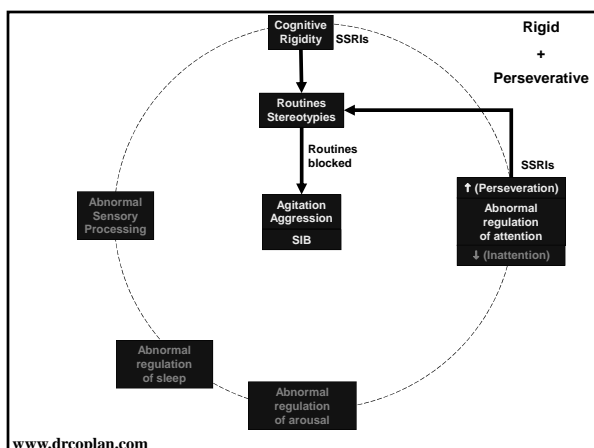
Serotonin promoting (serotonergic) drugs

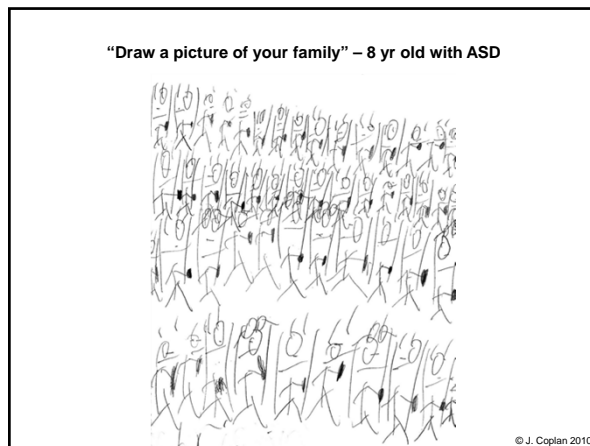
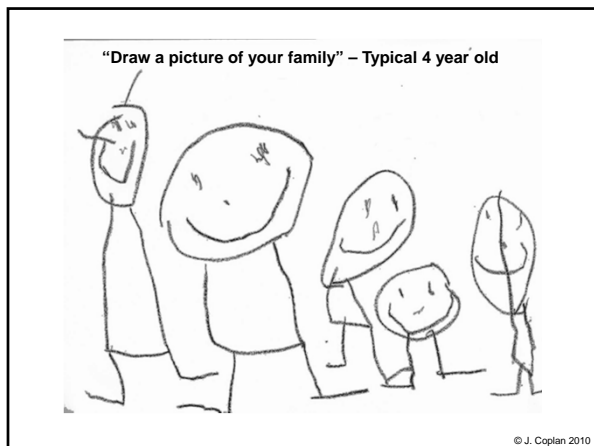


- A. Promote release of serotonin (Mirtazapine)
- B. Mimic the action of serotonin at the 2nd neuron (Buspirone)
- C. Block re-uptake of serotonin (SSRIs)



- ### Abnormal Regulation of Attention - 1
- **Perseveration**
 - Inability to “Let go and shift”
 - Gets “stuck”
 - “*Overattention Deficit Disorder*”
 - **Compounds the effects of cognitive rigidity**
- www.drcoplan.com





Abnormal Regulation of Attention (Perseveration)

- **Interventions**

- Verbal preparation for transitions
- Visual Schedules
- SSRIs?

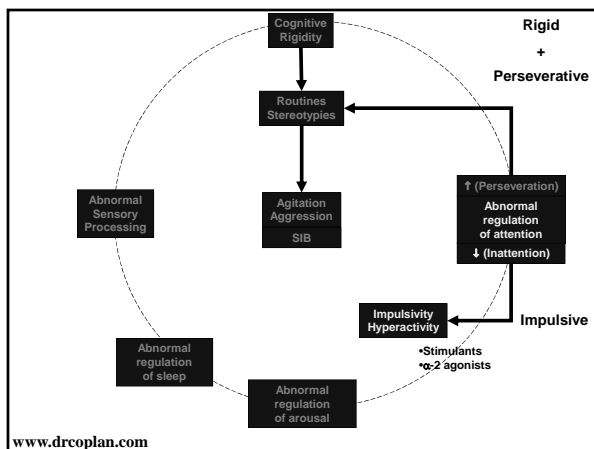
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Abnormal Regulation of Attention - 2

- **Inattention**

- Inability to focus
- Impulsive
- Distractible

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Inattention

- **Interventions**

- Limited stimuli
- Short work periods
- Stimulants, NRI's, alpha-2 agonists
 - Stimulants, NRI's → ↑Cognitive Rigidity
 - Try guanfacine first, OR
 - Start an SSRI, then add stimulant

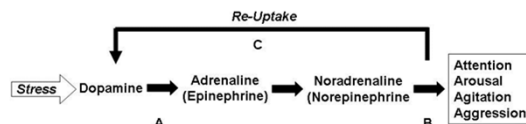
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Stimulants, NRI's

Generic Name(s)	Brand Name(s)	Comment
Amphetamine		FDA Schedule II
Dextroamphetamine	Dexedrine, Dextrostat	FDA Schedule II
Dextroamphetamine + amphetamine	Adderall	FDA Schedule II
Methylphenidate	Concerta, Ritalin, Metadate	FDA Schedule II
Dexmethylphenidate	Focalin	FDA Schedule II
Atomoxetine, Attentin	Strattera	Norepinephrine reuptake Inhibitor (NRI), not FDA Schedule II

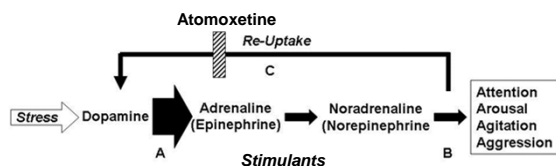
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Dopamine



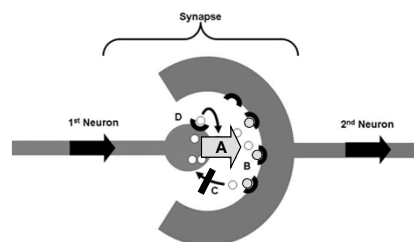
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Dopaminergic Drugs



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Dopamine promoting (dopaminergic) drugs



- A. Promote release of Dopamine & Norepinephrine (Stimulants)
- B. Mimic the action of Dopamine & Norepinephrine (Stimulants)
- C. Block re-uptake of Dopamine & Norepinephrine (Atomoxetine)

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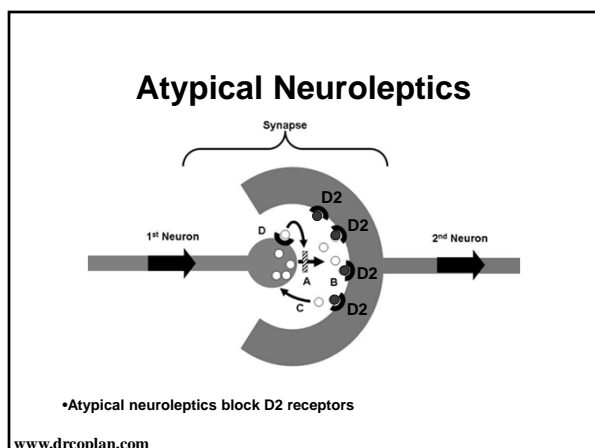
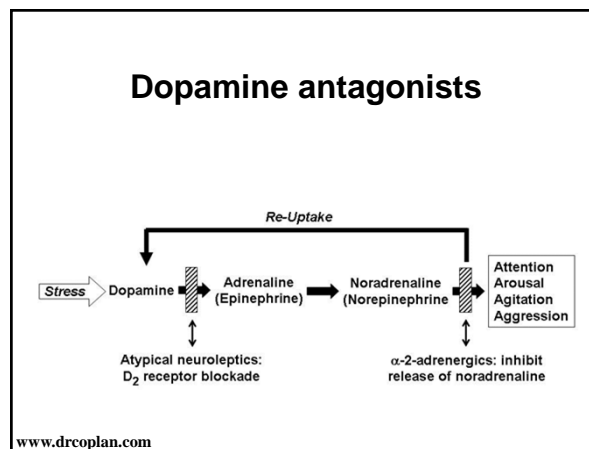
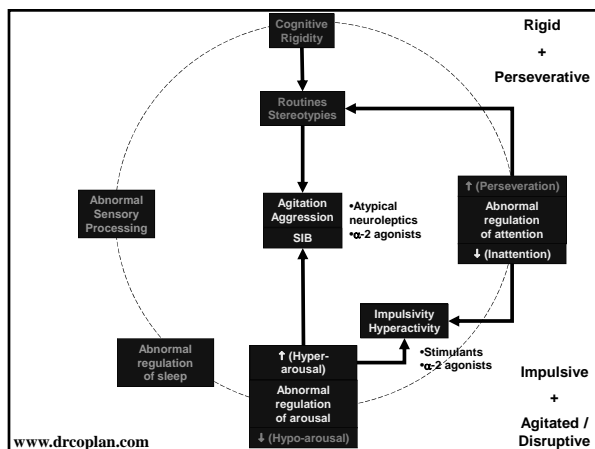
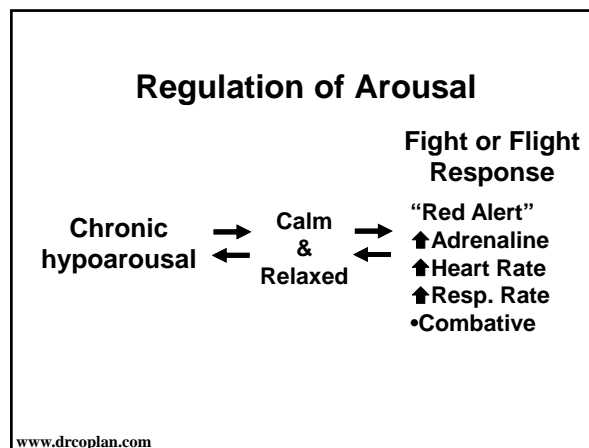
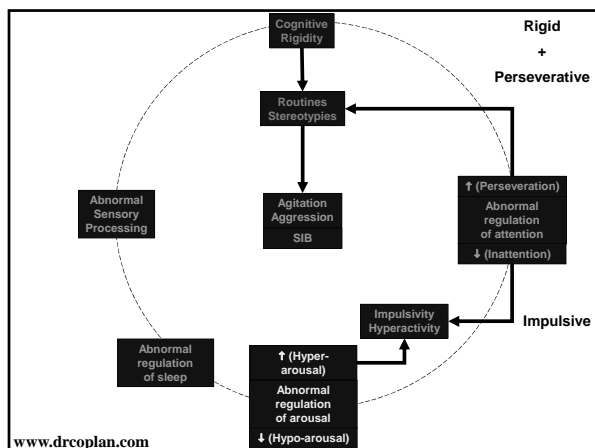
Inattention

- **Beware of anxiety or perseveration masquerading as inattention**
 - Perseveration on inner stimuli: "Inattentive"
 - Perfectionism: "Problems w. task completion"
 - Anxiety: "Rushes through work"

www.drcoplan.com



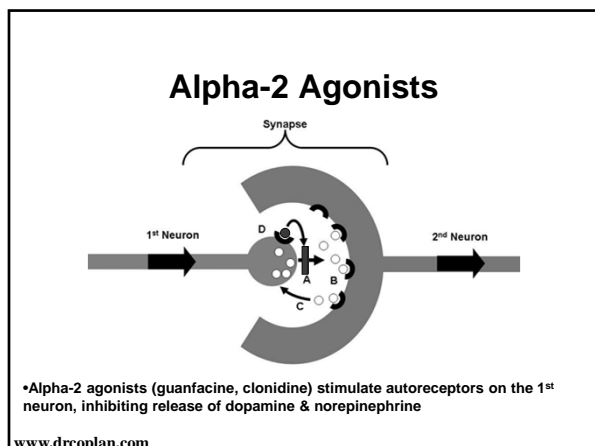
www.drcoplan.com



Atypical Neuroleptics

Generic Name	Brand Name	Comment
Aripiprazole	Abilify	Relatively less risk of weight gain
Clozapine	Clozaril	Causes bone marrow suppression
Olanzapine	Zyprexa	Greater risk of weight gain
Quetiapine	Seroquel	Greater sedation
Risperidone	Risperdal	<ul style="list-style-type: none"> • Greater risk of weight gain • Approved by FDA for treatment of agitation in children with ASD • Generic available
Ziprazidone	Geodon	Relatively less risk of weight gain

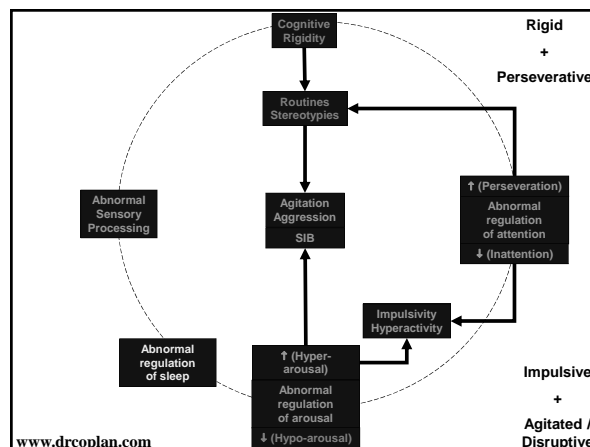
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Alpha-2 Agonists

Generic Name	Brand Name(s)	Comment
Clonidine	Catapres	More sedating than guanfacine
Guanfacine	Tenex, Intuniv	

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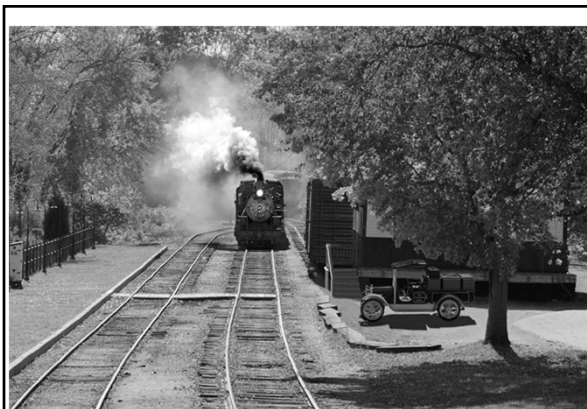
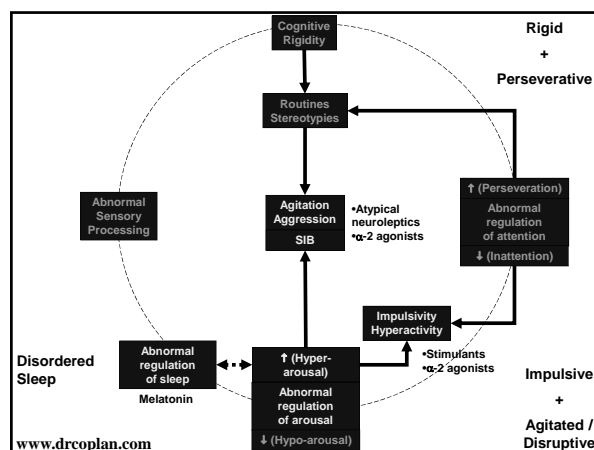
- ### Regulation of Sleep - 1
- **Melatonin**
 - Brain hormone
 - ↓ Metabolic rate (Heart, Temp)
 - “You’re sleepy now”
 - **Suppressed by light**
 - 24 hr cycle
 - Seasonal cycle
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- ### Regulation of Sleep - 2
- **Abnormal melatonin cycling**
 - Primary disorders of sleep
 - Blindness
 - ASD
 - **Symptoms**
 - Delayed onset of sleep
 - Shortened duration / frequent waking
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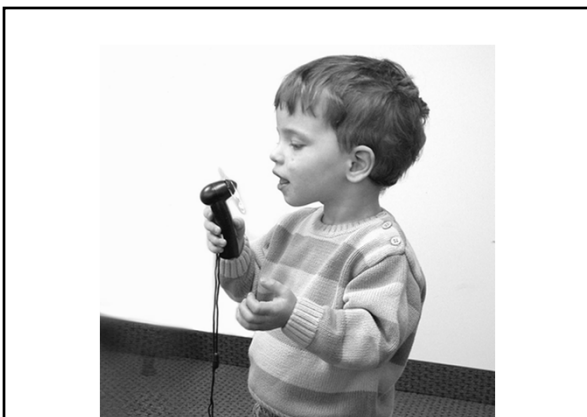
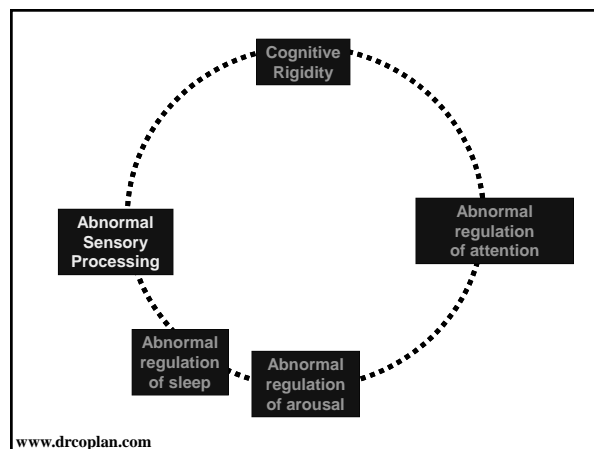
Regulation of Sleep - 3

- **Shared genetic control**
 - Regulation of sleep
 - Regulation of arousal
- **Family history of sleep disorder**

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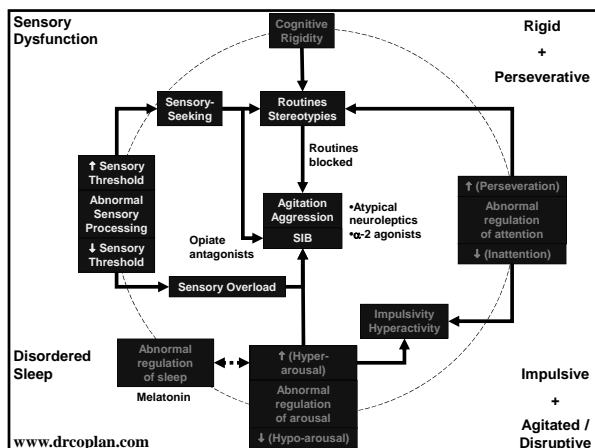
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Sensory Processing

- **Subjective Properties**
 - Familiar / Unfamiliar
 - Pleasant / Unpleasant
 - Strong / Weak
 - Internal / External
- **Sensory Input → Self-awareness**
- **Mirror Neurons → Empathy**

Mostofsky, S. and J. Ewen, *Altered Connectivity and Action Model Formation in Autism Is Autism*. Neuroscientist, 4/15/2011

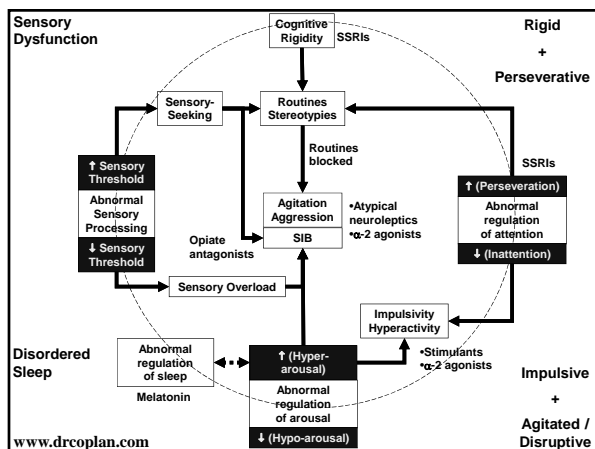
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The whole is greater than the sum of its parts

Max Wertheimer

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Summary

- **Why this child?**
 - Extrinsic factors:
 - Functional behavioral assessment (Escape, access, attention)
 - Family assessment (Are mom & dad in synch?)
 - Intrinsic factors
 - Cognitive Rigidity, Dysregulation of attention, arousal, sleep, or sensory processing
- **Family & Behavioral Intervention – Usually**
- **Medication: Sometimes**

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Summary

Directions for future research:

- **Better phenotyping of ASD**
 - Clinical
 - Genetic
- **Better drug studies**
 - Drug vs. Behavioral Therapy vs. Combination
 - Drug vs. Drug (not just drug vs. placebo)
 - Drug combinations (not just monotherapy)
 - Stimulant + SSRI, e.g.
 - Better outcome measures
 - Quality of Life
 - Long-term outcome
- **Brain / Behavior / Drug imaging**

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Thank you

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