Behavior management and psychopharmacology in children with autistic spectrum disorders

rev. 11/14/2012

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ABC Conference

11/16/2012

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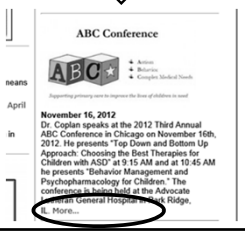

Learning Objectives

Participants will be able to:

- **Define cognitive rigidity and list 3 resulting maladaptive behaviors**
- **Define dysregulation of attention and discuss the 2 principle ways in which this manifests itself**
- **Define dysregulation of arousal, and discuss management strategies**

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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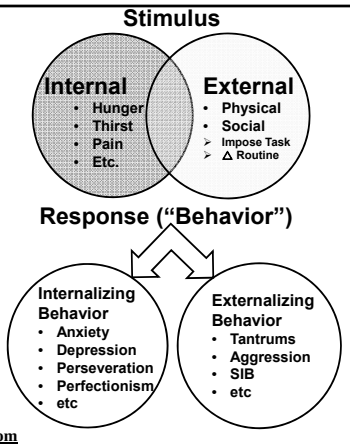

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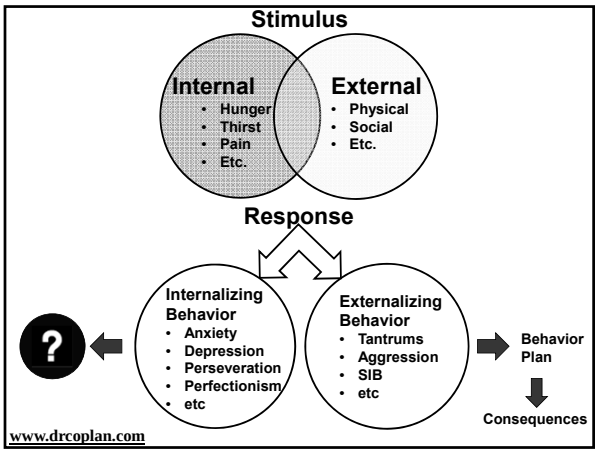

Behavior

- What is the child's developmental level?
- Is the behavior normal for the child's developmental level?
  - Tantrums / Noncompliance
  - "Impulsivity" / "Inattention"
  - Can the child de-center?

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Behavior

- What is the child's ability to communicate?
  - Does "disruptive" behavior serve a communicative function?
  - Or some other function?
    - Access
    - Escape
    - Self-calming
    - Attention
  - Or: No function?

Behavior

- Acute change or chronic?
- General health?
  - Vital signs, I&O, Level of consciousness
  - Pain?
- Anything new in child's life?
  - Medication
  - Family situation
  - School

Behavior Models

- Developmental Model
  - Certain behaviors are characteristic at certain ages/stages, and "unfold" with time (e.g. Piaget)
- Behaviorist Model
  - All behavior is the result of prior conditioning (e.g. Thorndike, Watson, Skinner, Lovaas)
    - Deny "development," "understanding"
    - "Behaviorist believe there is *nothing within to develop*" – JB Watson, 1928

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Behavior Analysis

(Functional Behavioral Assessment; FBA)

STIMULUS (the Antecedent)

⇩

RESPONSE (the Behavior)
(What function does the behavior serve?)

⇩

The Consequence
(Reinforcers & Aversives)

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Law of Effect

Animal Intelligence. Edward Thorndike, 1911

"Of several [possible] responses…to the same situation, those which are…closely followed by satisfaction to the animal will…be more likely to recur. Those which are…followed by discomfort to the animal will…be less likely to occur. The greater the satisfaction or discomfort, the great the strengthening or weakening of the bond"

Manipulating the Consequence for a given behavior feeds back on the probability that that behavior will recur.

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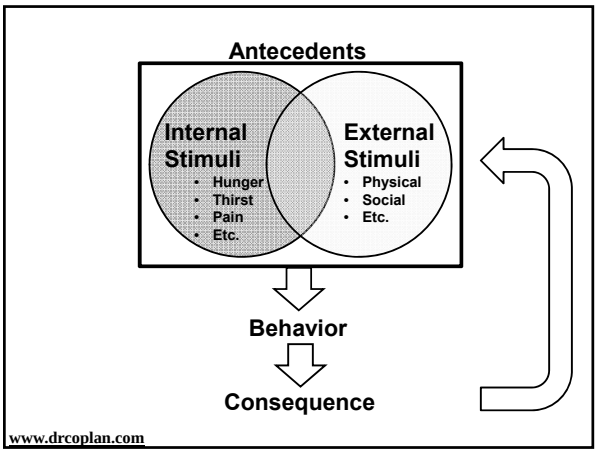

Consequences 1: Reinforcers

- **Reinforcers lead to an increase in frequency of the antecedent behavior**
  - **Positive Reinforcement (adds something)**
    - **Attention**
    - **Access to preferred object**
  - **Negative Reinforcement (removes something)**
    - **Escape from a task**
    - ***Negative Reinforcement is not punishment***

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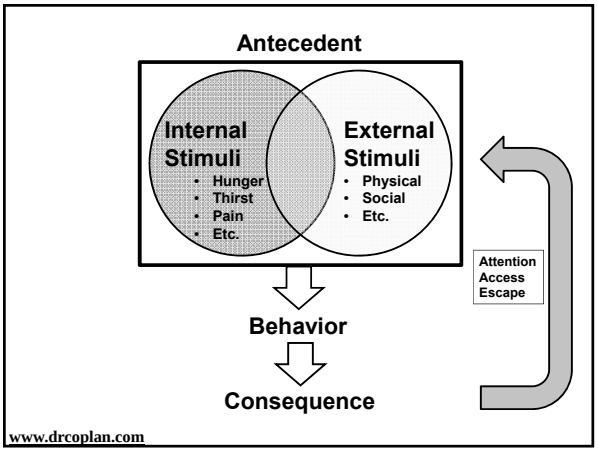

Consequences 2: Aversives

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

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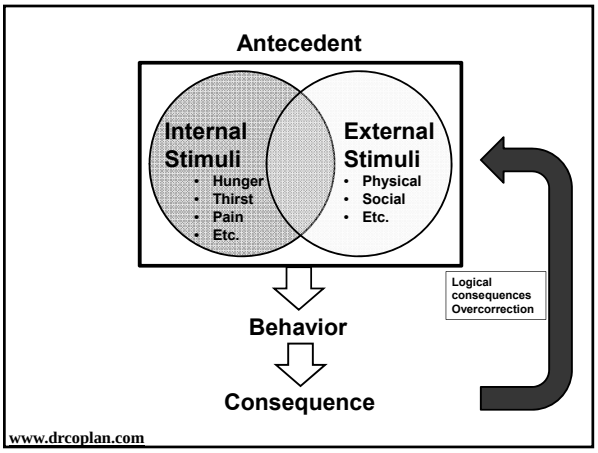

Food Selectivity

Negative and Positive Reinforcement of unwanted behavior

- **Parent removes non-preferred food ([-] reinforcement)**
- **Parent provides child with his/her preferred food ([+] reinforcement)**
- **Alternatives**
  - ***First* …..*Then* ("Premack Principle")**
  - **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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Disruptive Behavior: Function & Best Response

- **Attention**
  - **1-2-3 ➡ "Time Out" (T.O.)**
- **Access**
  - ***Never* grant access to desired object in response to disruptive behavior**
- **Escape**
  - ***Never* permit the child to escape from a task via disruptive behavior.**
    - **Walk child through task first, *then* ➡ T.O.**
    - **OR: Send child to T.O., and as soon as T.O. is complete, resume the task where you left off.**

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Token Economy: The next step beyond Time Out

- **Concretely specified behaviors**
- **Earn and Lose Points**
- **Points➡Access to preferred items**
  - **Preferred toys, Computer time, etc.**
  - ***NO access to preferred item at other times***
  - **"Extra" treats not as effective**
- **Works with children who understand rule-based play (CandyLand, Uno, etc.)**

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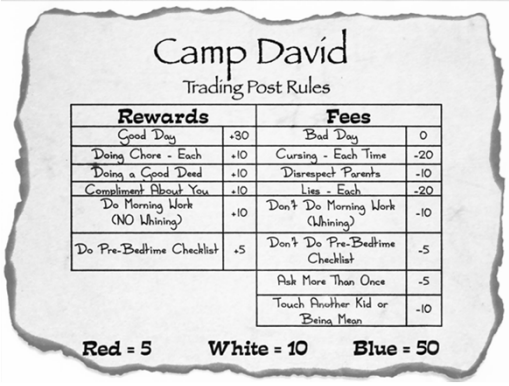

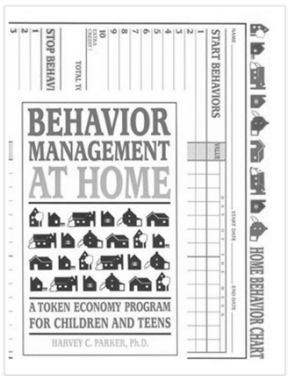

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But…..

Children with ASD have atypical responses to internal and external stimuli

- ***What good is Time Out if the child has no eye contact?***
- ***Obsessive behavior not the same as "ordinary" task refusal***

Not all behavior serves an external function

- ***Tourette Syndome (Tics, Coprolalia, Compulsive Touching)***
- ***Perseveration***

Or any social / behavioral function

- ***Seizures***

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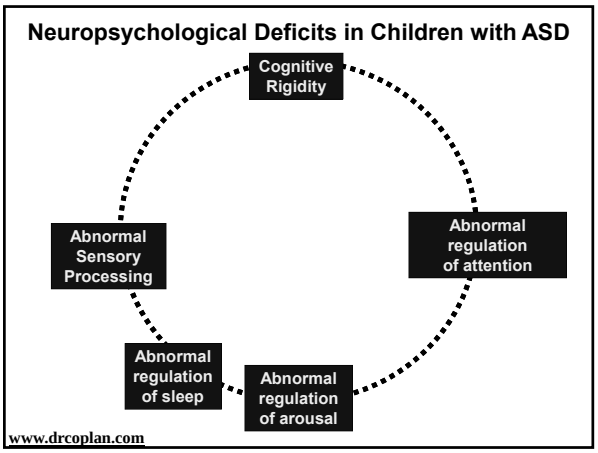
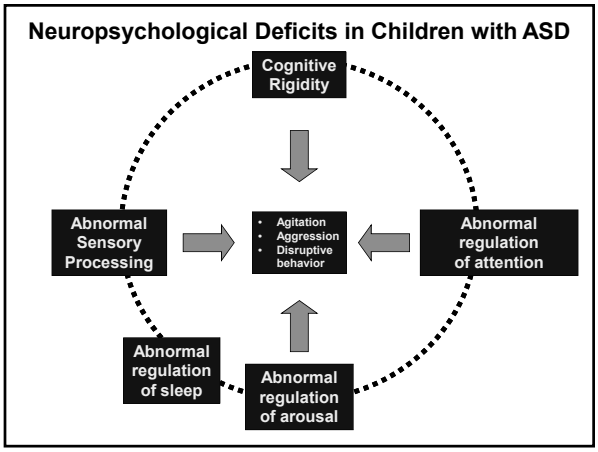
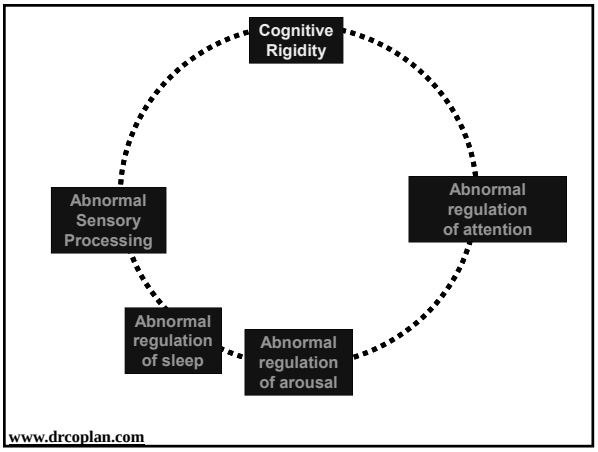
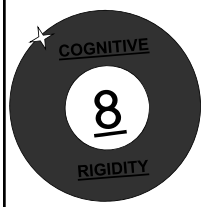






- Without a doubt
- Reply hazy, try again
- Signs point to NO
- Better not tell you now…

Cognitive Rigidity



"Externalizing Behaviors"

- **Inability to shift mental sets**
  - ***Insistently*** **repetitious behavior**
  - **Problems with unmet expectations, or changes in routine**
  - **Perfectionism**
  - **Compulsions**
  - **Obsessions**
- **(Anxiety)**
- **(Depression)**

"Internalizing Behaviors"

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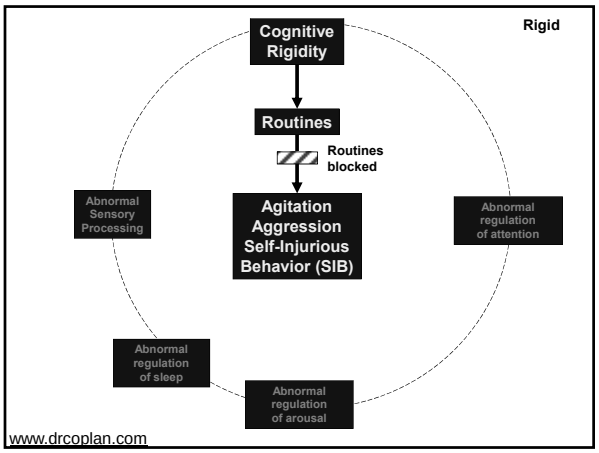


Changes in Routine

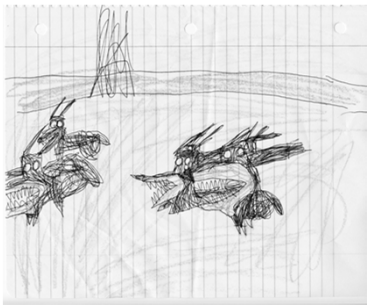
www.drcoplan.com *Rainman*, 1988

Perfectionism

Cognitive Rigidity

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

Anxiety



RD. 7 y.o. F, nl IQ, PDD-NOS & Anxiety. Father: GAD

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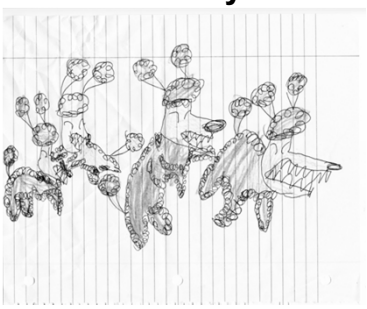
Anxiety



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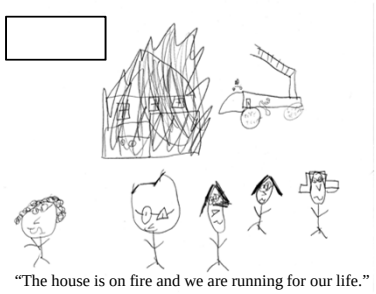
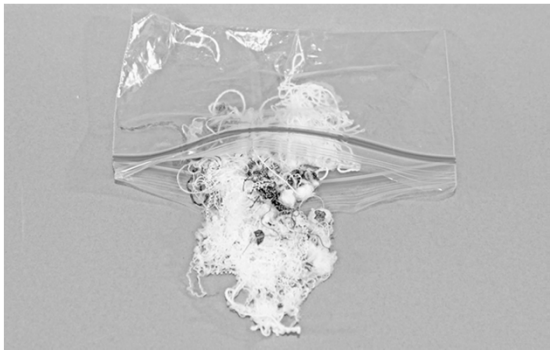


"The house is on fire and we are running for our life."

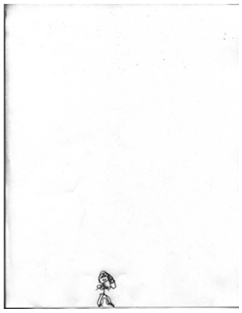
A.W.: 9 year old boy with PDD-NOS and normal IQ (MRN 11-07710



Joseph F: 15 y.o. boy asperger syndrome & chronic anxiety

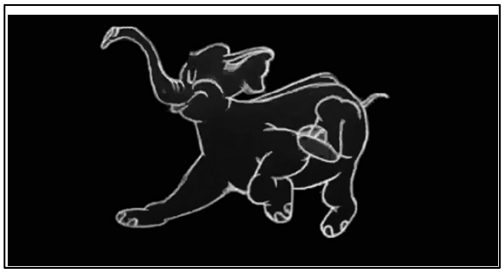
MRN: 05-0096

Depression



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

How do you kill a blue elephant?



Shoot it with a blue elephant gun.

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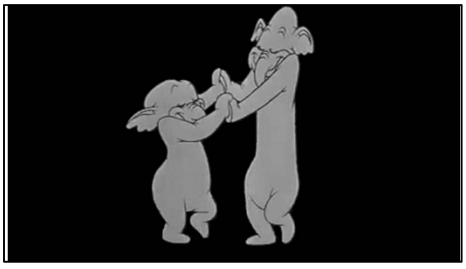
How do you kill a pink elephant?



Hold it by the trunk until it turns blue, then *shoot it with a blue elephant gun*.

Unaddressed internalizing behavior often comes out as externalizing behavior

Internalizing Behavior
- Anxiety
- Depression
- Perfectionism
- etc

→

Externalizing Behavior
- Task avoidance
- Tantrums
- Aggression
- SIB
- etc

→ **FBA Behavior Plan**

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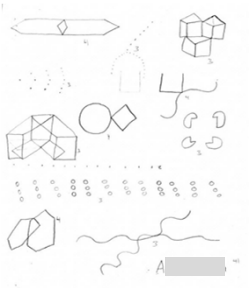
Anxiety, Perfectionism, and Self-Injurious Behavior



Standard Score: 138

A.D. : 9 y.o. girl with ASD (my MRN: 06-0227)

Throughout the session, "Alice" delivered a steady stream of self-deprecating comments, calling herself "stupid," or perseveratively asking if she was "fat." During the Bender, she anxiously and angrily twisted the eraser off the tip of the pencil, while declaring "Why do I keep making stupid mistakes?" As her stress level rose, she escalated to slapping herself, and then punching herself in the face.

"An ounce of prevention is worth a pound of cure"

Internalizing Behavior
- Anxiety
- Depression
- Perfectionism
- etc

~~→~~

Externalizing Behavior
- Task avoidance
- Tantrums
- Aggression
- SIB
- etc

→ **FBA Behavior Plan**

↘

Positive Behavior Support Plan:
- Proactively avert, or identify and dissipate the effects of cognitive rigidity (anxiety, perfectionism, hyper-self-criticism, etc.)

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Positive Behavior Support Plan for Cognitive Rigidity

- **Staff Awareness**
- **Visual Schedules**
  - **What am I supposed to be doing do *now*?**
  - **What am I supposed to do *next*?**
- **Relaxation Techniques**
  - **Mental Imagery**
  - **Isometrics**
  - **Deep Breathing**
  - **"Break" cards**
- **Cognitive Behavioral Therapy (CBT)**
- **SSRIs**

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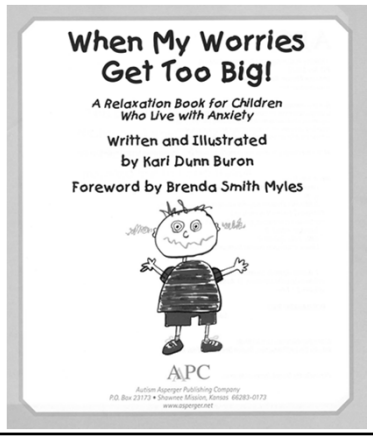

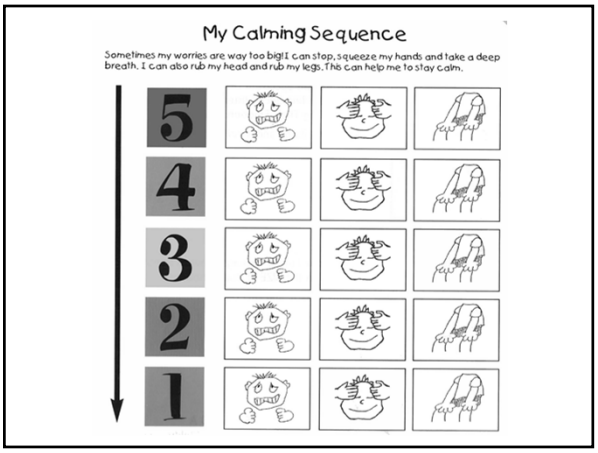

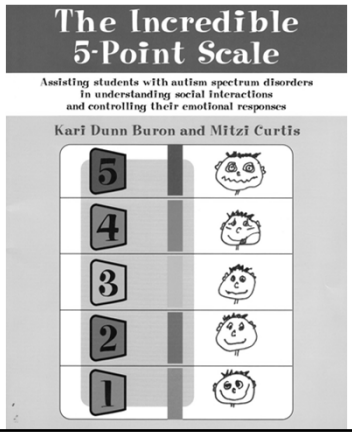

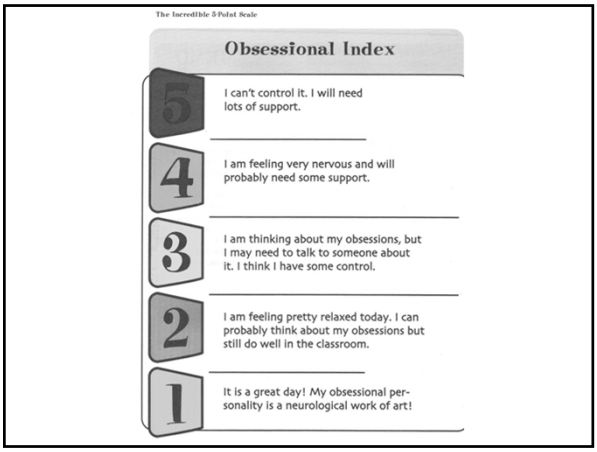

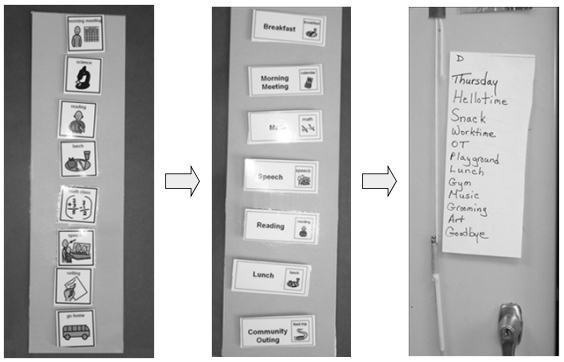

The Story of Billy's Box - 1

(or, why it's important to ID internalizing behavior)

- **8 y.o. boy with ASD and normal Nonverbal IQ**
- **Severe tantrums at school**
- **Antecedents:**
  - **TRANSITIONS**
- **Function?**
  - **Not attention, escape, access**
  - **"Biological" (i.e. just part of his ASD)?**

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The Story of Billy's Box - 2

(or, why it's important to ID internalizing behavior)

Q: "Billy – You're always getting in trouble at school. What's going on?"

A: "I'm afraid that if I hand in my work, I'll never get a chance to go back and make it perfect."

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The Story of Billy's Box - 3

(or, why it's important to ID internalizing behavior)

"Put your papers in the box, and we promise you will be able to go back later and work on them some more, if you want to."

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SSRIs in ASDs

- **Primary targets**
  - Cognitive Rigidity
    - Anxiety
    - Obsessive / Perfectionistic behavior
  - Depression
  - Stereotypies: Probably not
- **"Downstream" benefit:**
  - ↓ Disruptive Behavior
  - ↑ Quality of Life

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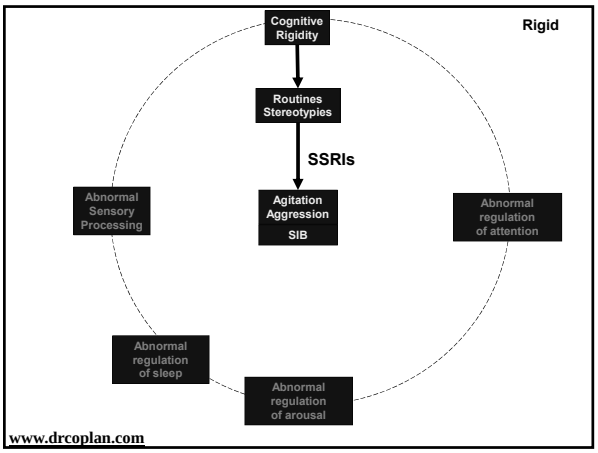

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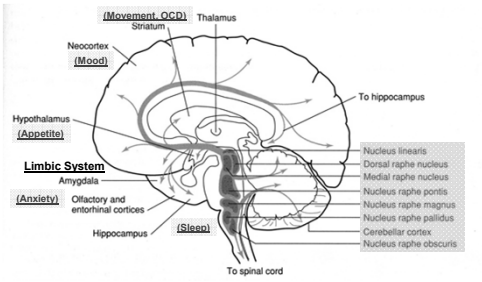
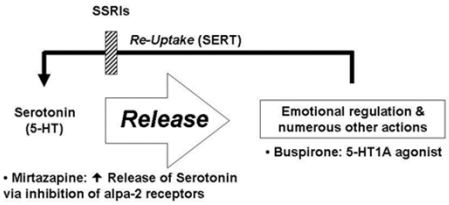
Serotonin (5 HT)



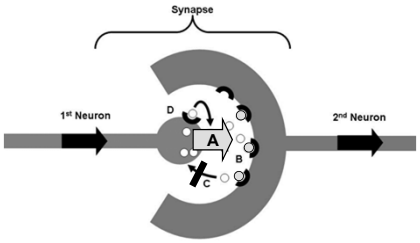
Nestler, *Molecular Neuropharmacology*, Fig 9.3

Serotonin-promoting (serotoninergic) drugs



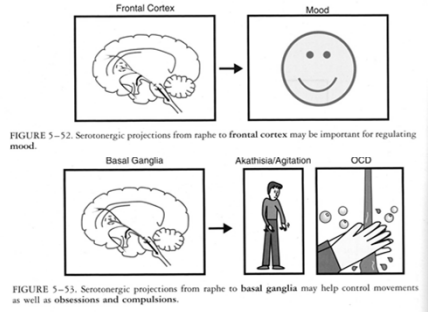
Selective Serotonin Reuptake Inhibitors block the re-uptake of Serotonin

Serotonin promoting (serotoninergic) drugs



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

Serotonin (5 HT) Pathways



Stahl, *Essential Psychopharmacology*, fig 5.52-3

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

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."

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

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

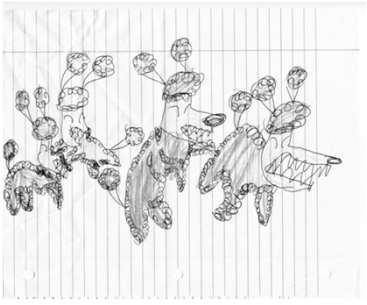
- Treatment-emergent symptoms
  - Citalopram: 1 child with new onset seizures (continued to have seizures after citalopram was stopped)
  - Fenfluramine: ↑ stereotypies; withdrawal, sadness; ↓appetite
    - "With monitoring, dose adjustment and time, all but one of these adverse effects were resolved"
  - Fluoxetine (Hollander 2005): 6 of 37 children had their dosage reduced due to agitation
    - 2 children in the placebo group also 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

Pharmacotherapy for anxiety disorders in children and adolescents

Ipser JC, Stein DJ, Hawkridge 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 bec/o side effects
  - "The overwhelming majority of evidence of efficacy was for the SSRIs, with the most evidence in paediatric OCD"

Anxiety



RD. 7 y.o. F, nl IQ, PDD-NOS & Anxiety. Father: GAD

www.drcoplan.com MRN: 07-0427

Anxiety after Rx with CBT & Escitalopram

RD. 9 y.o. F, nl IQ, PDD-NOS & Anxiety. Father: GAD

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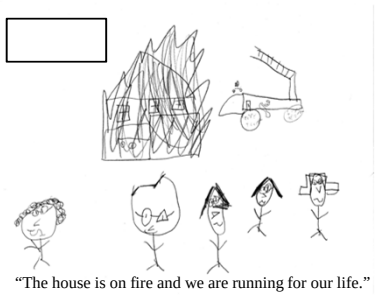
Anxiety



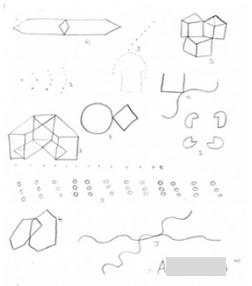
"The house is on fire and we are running for our life."

A.W.: 9 year old boy with PDD-NOS and normal IQ (MRN 11-07710

Fluoxetine 10 mg/d

A.W.: 9 year old boy with PDD-NOS and normal IQ (MRN 11-07710

Anxiety, Perfectionism, and Self-Injurious Behavior



Standard Score: 138

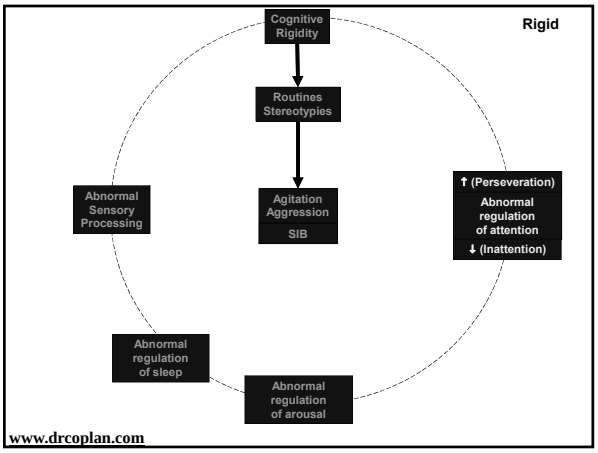
A.D. : 9 y.o. girl with ASD (my MRN: 06-0227)

Throughout the session, "Alice" delivered a steady stream of self-deprecating comments, calling herself "stupid," or perseveratively asking if she was "fat." During the Bender, she anxiously and angrily twisted the eraser off the tip of the pencil, while declaring "Why do I keep making stupid mistakes?" As her stress level rose, she escalated to slapping herself, and then punching herself in the face.

After one week on Sertraline

Sent: Thursday, May 31, 2012
To: James Coplan
Subject: amazing shift in A.D.
Importance: High

Dr. Coplan,
I "know" that it takes several weeks for SSRI's to "kick in" but the child I saw in my office today is simply a different child and the improvements are being noted across settings by mutiple adults. There was NO self abuse, NO negative self statements, an availability for interventions, just a complete transformation. We "fixed" mistakes, "re-did" errors, told jokes, and played together. The "core" Autistic symptoms are obviously still there - perseveration on bras, drawing, etc - but mood-wise there is no question that A. is already benefitting from the Sertraline... Impossible perhaps but really visibly clear...
Thank you very much.
S.S. Ph.D.



Regulation of Attention

Attend to stimulus #1 ⟷ Let go & Shift ⟷ Attend to stimulus #2

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Abnormal Regulation of Attention - 1

- **Perseveration**
  - Inability to "Let go and shift"
  - Gets "stuck"
  - *"Overattention Deficit Disorder"*
- **Compounds the effects of cognitive rigidity**

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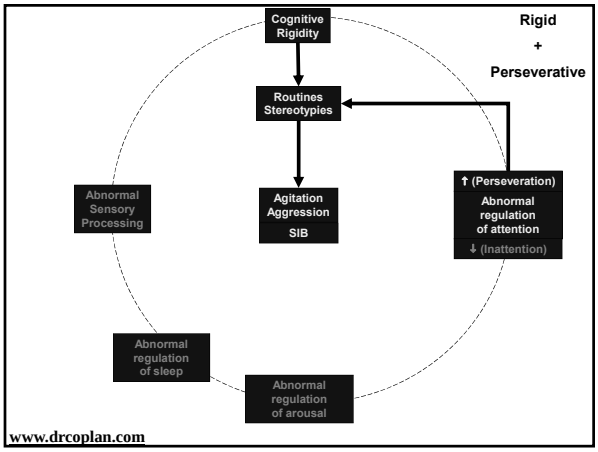

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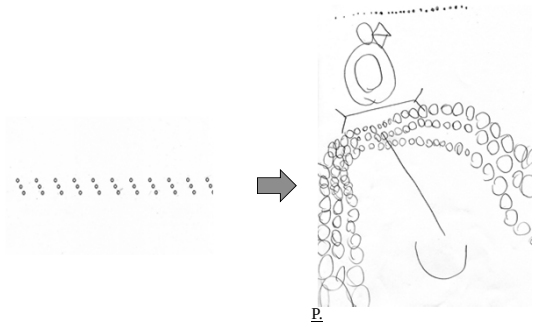
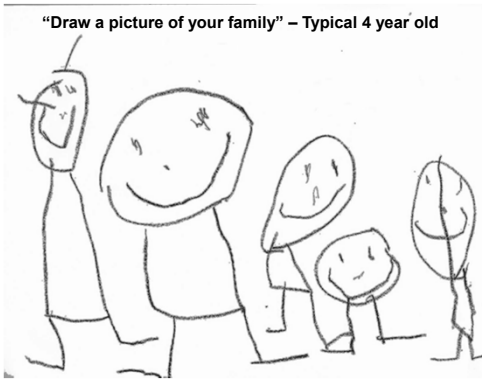
Perseveration



P.

"Draw a picture of your family" – Typical 4 year old



© J. Coplan 2010

"Draw a picture of your family" – 8 yr old with ASD

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Abnormal Regulation of Attention (Perseveration)

- **Interventions**
  - Verbal preparation for transitions
  - Visual Schedules
  - SSRIs (OCD: Proven; ASD: likely)

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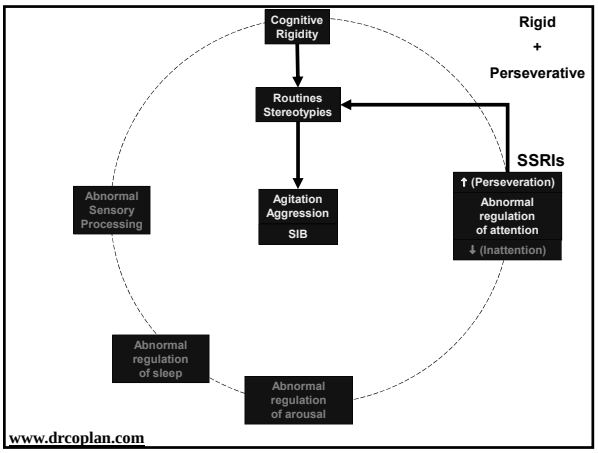

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Abnormal Regulation of Attention - 2

- **Inattention**
  - Inability to focus
  - Impulsive
  - Distractible

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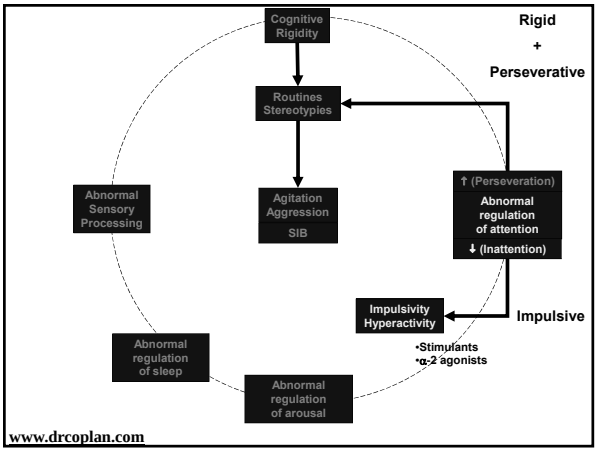

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Inattention

- **Interventions**
  - Limited stimuli
  - Short work periods
  - Medication
    - Stimulants (may ↑ anxiety / rigidity / agitation)
    - alpha-2 agonists

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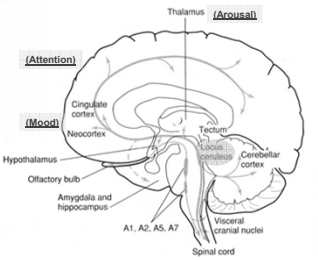
Noradrenergic pathways

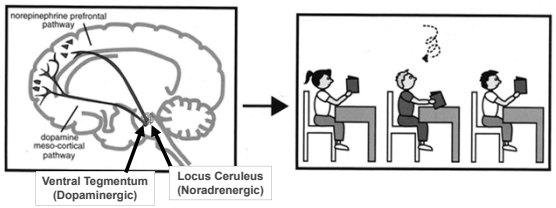
(Norepinephrine)



Locus Ceruleus ("blue spot"): Principal noradrenergic source in brain.

Nestler, *Molecular Neuropharmacology*, Fig 8.5

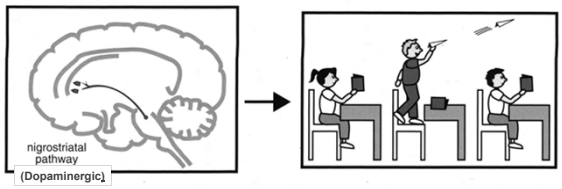
Inattention



Insufficient activation of frontal cortex ➔➔➔ Inattention

Stahl, *Essential Psychopharmacology*, fig 12.1

Hyperactivity

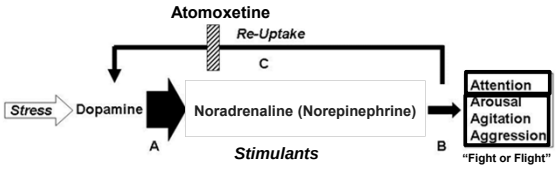


Stimulants in children with ADHD ➔ "Paradoxical" calming

Stahl, *Essential Psychopharmacology*, fig 12.1

Stimulants

(Dopaminergic; Noradrenergic; Sympathomimetic)



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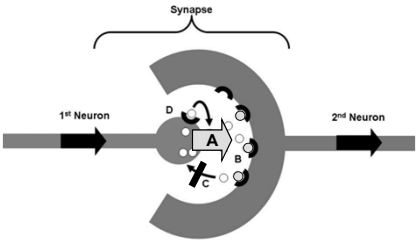
Stimulants

(Dopaminergic; Noradrenergic; Sympathomimetic)



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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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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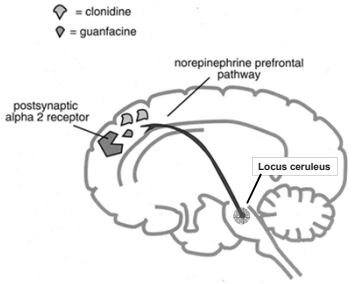
Alpha-2 agonists

(clonidine, guanfacine)



Stahl, *Essential Psychopharmacology*, fig 12.6

Alpha-2 Agonists

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

- Frontal cortex / Locus Ceruleus: post-synaptic alpha-2 receptors
- Sympathetic outflow (autonomic nervous system): Pre-synaptic autoreceptors →↓BP

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Clinical Pearl

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

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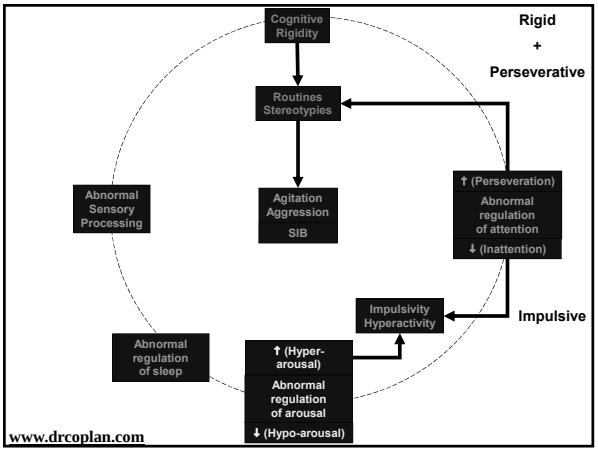

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"He is so hard to calm down when he gets upset….His emotional thermostat doesn't work"

Parent of an 8 year old with ASD

F. O. MRN 06-0208

Regulation of Arousal

Hypoarousal
- Lethargic

⇄ **Calm & Relaxed** ⇄ **Fight or Flight Response**

"Red Alert"
⬆Adrenaline
⬆Heart Rate
⬆Resp. Rate
•Combative

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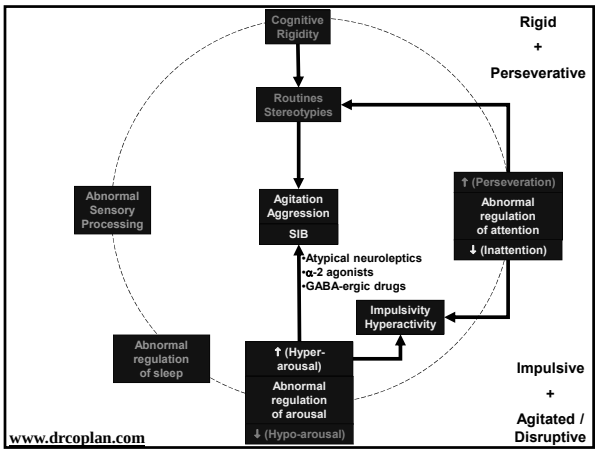
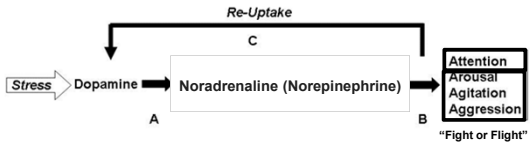


Dopamine

(Dopaminergic; Noradrenergic; Sympathomimetic)



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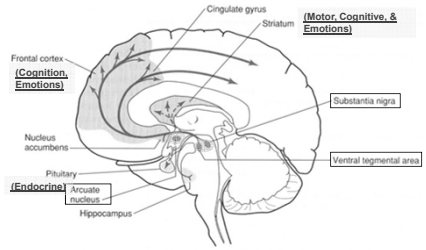
Dopamine

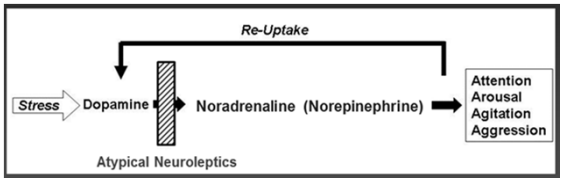


Substantia Nigra ("black stuff"), Ventral tegmentum, arcuate nucleus

Nestler, *Molecular Neuropharmacology*, Fig 8.6

Atypical Neuroleptics

(Dopamine Blockers)



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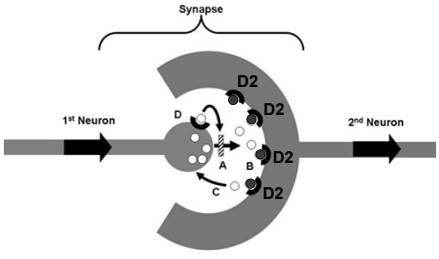
Atypical Neuroleptics



•Atypical neuroleptics block D2 receptors

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Atypical Neuroleptics

Generic Name	Brand Name	Comment
Aripiprazole	Abilify	• Relatively less risk of weight gain • FDA approved for Rx of ASD
Clozapine	Clozaril	• Bone marrow suppression
Olanzapine	Zyprexa	• Greater risk of weight gain
Quetiapine	Seroquel	• Greater sedation
Risperidone	Risperdal	• Greater risk of weight gain • FDA approved for Rx of ASD
Ziprazidone	Geodon	Relatively less risk of weight gain

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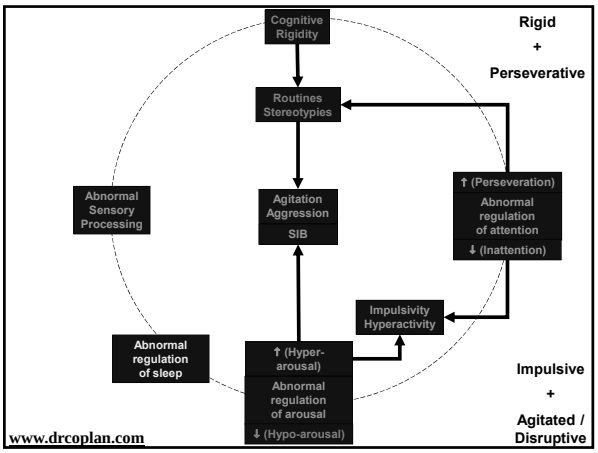

Regulation of Sleep - 1

- **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 wakening

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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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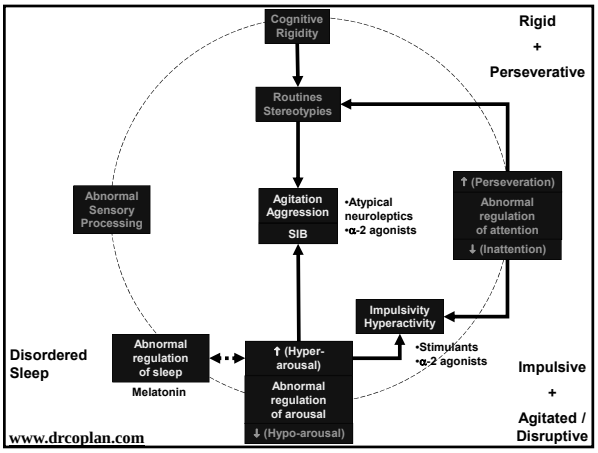

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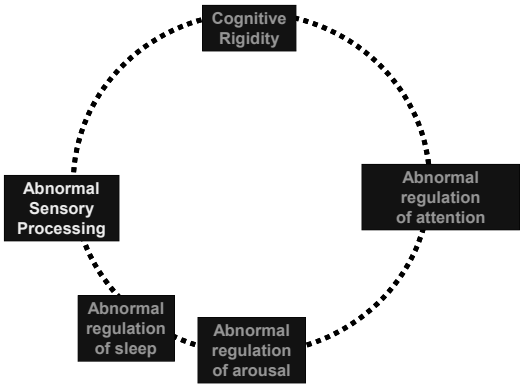

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Sensory Processing

- **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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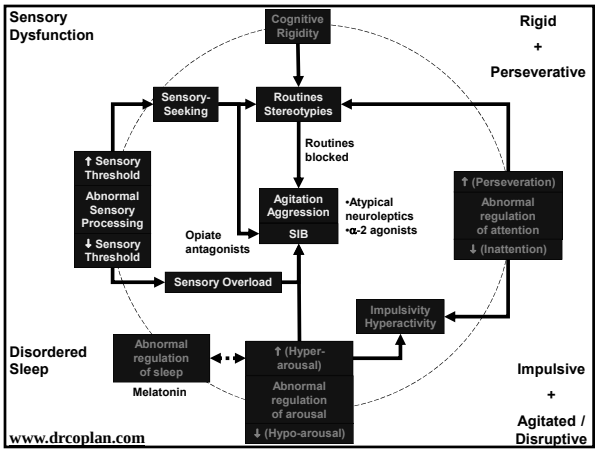

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The whole is greater than the sum of its parts

Max Wertheimer

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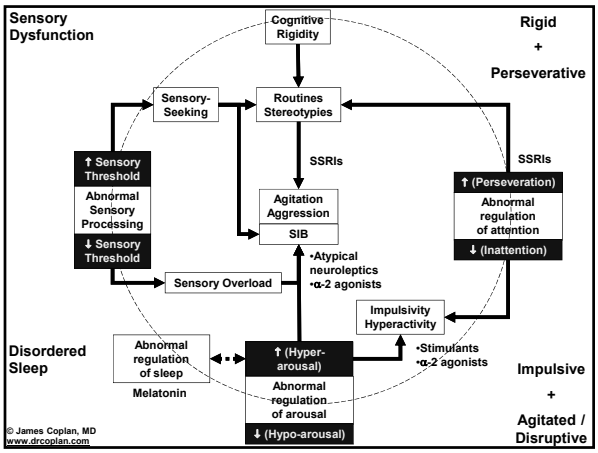

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Summary

- Why this child?
  - What is this child's developmental Level?
    - Is this stage-appropriate behavior?
  - Does the behavior serve a social function?
    - Escape, access, attention
  - Is the classroom placement appropriate?
    - Language level?
  - Does this behavior occur in other settings?
    - Family factors?
      - Parents consistent at home?
      - Parental psychopathology? (Anxiety, Depression, Alcohol)

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Summary

- Why this child?
  - Neuropsychological factors?
    - Cognitive Rigidity
    - Dysregulation of attention
    - Dysregulation of arousal
    - Sensory Seeking / Sensory Overload
- Behavioral Intervention – Usually
- Change in classroom setting – sometimes
  - Shift from rote to inferential learning (2nd - 3rd grade): challenge
- 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!