Behavior management and psychopharmacology in children with autistic spectrum disorders

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Autism™ NEW JERSEY

10/11/12

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**

"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"**

Behaviorism made simple

STIMULUS (the Antecedent)

↓

RESPONSE (the Behavior)

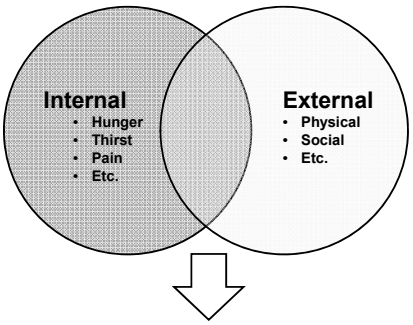
↓

The Consequence

Antecedents

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

Stimulus (The "Antecedent")



Response ("The Behavior")

Behaviorism made simple

STIMULUS (the Antecedent)

RESPONSE (the Behavior)

The Consequence

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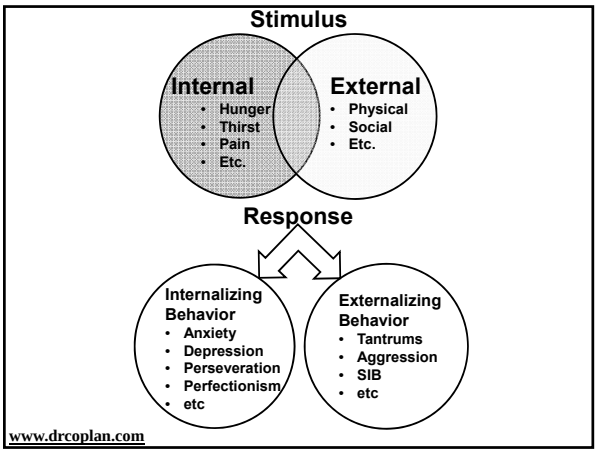

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Behavior

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

Behavior

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

Behavior

- What is the child's ability to communicate?
  - Does "disruptive" behavior serve a communicative function?

Behaviorism made simple

STIMULUS (the Antecedent)

RESPONSE (the Behavior)

The Consequence

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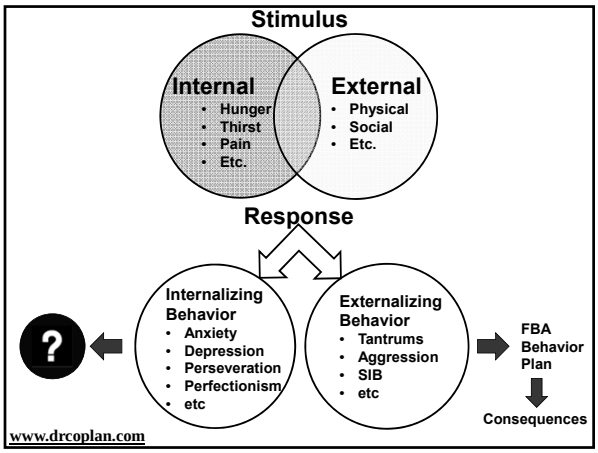

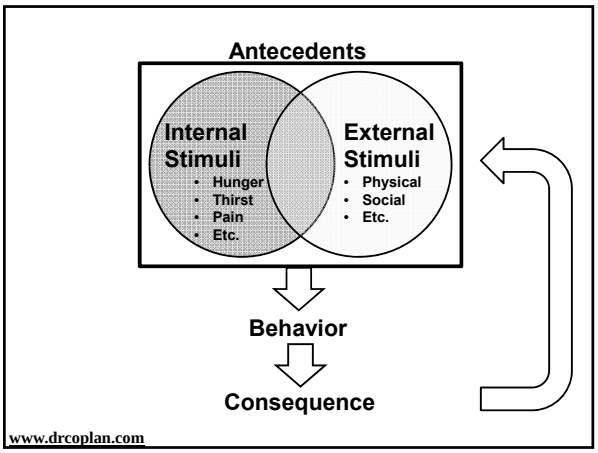

Law of Effect

Animal Intelligence. EdwardThorndike, 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.

Consequences

- **Reinforcers**
  - **Positive**
  - **Negative**
- **Aversives**

Consequences 1: Reinforcers

- **Reinforcers lead to an increase in frequency of the antecedent behavior**
  - **Positive Reinforcement (adds something)**
  - **Negative Reinforcement (removes something)**

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Positive Reinforcement

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

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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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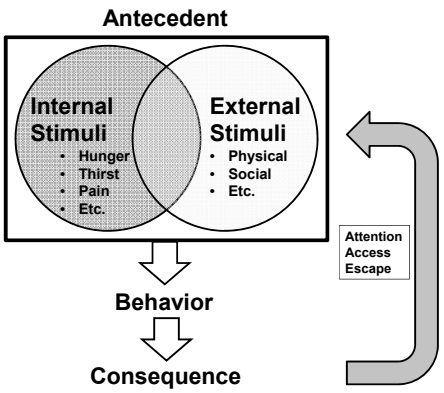

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Food Selectivity

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***
  - **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 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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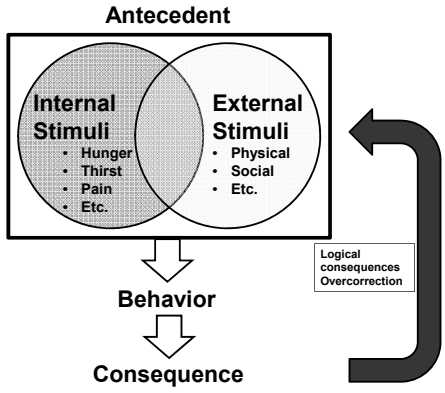

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Disruptive Behavior: Function & Best Response

- **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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Behavior Management Plan

Behavioral Intervention Plan

Student: Ethan Date of Birth:

School: Lower Pottsgrove Elementary Date of Meeting: 06/07/2012

A 1. Prevention strategies (antecedent):
1. Keep Ethan busy. During times he has to wait, provide alternative activities or sensory items to keep him engaged, thus reducing sensory motivated behaviors.
2. Use of Premack Principal (first/then) Use a visual and written "Must do" and "Can do" lists for Ethan, so that he knows what is expected to earn what he wants to do.
3. Use differential reinforcement of other or alternative behaviors (catch him being good and reward it!)
4. Provide non-contingent attention throughout the day for appropriate behaviors.
5. Use a high probability sequence when interferring behaviors are high (4 or 5 very quick requests to do simple things, followed by request to do task at hand).
6. Provide praise and activitiy reinforcement intermittently.
7. Provide sensory or movement breaks throughout instruction time.
8. Use antispetic bouncing:Provide Ethan with an appropriate escape such as drink or change in activity
9. Use broken record technique: repeat verbal directives until Ethan complies
10. Personal Care Assistant (up to 3 hours daily) to prompt/model/redirect Ethan to task

Behavior Management Plan

B 2. Replacement Behavior (functionally equivalent behavior):
1. Model and practice self- regulating strategies and appropriate listening skills
2. Instruct Ethan in expected and unexpected behaviors (ex: teach Ethan to fold or sit on his hands)
3. Teach Ethan to work for his break through use of token board for time on task.
4. Teach Ethan to to communicate his need for achange in activity or break (ex: "I want ___")

C 3. Consequences (reinforcement) for when the student performs the Replacement Behavior:
1. Differentially reinforce alternate (replacement) behaviors at a high rate
2. Give Ethan a penny for task completion or 3 minutes on task (gradually upping to 5, 10, 15 minutes).
3. Pair pennies with verbal praise
4. Tell Ethan "good job!" and give him a thumbs up when he is attending appropriately.
5. Give an activity break for every 5 pennies earned.

C 4. Consequences (procedures to follow) when the student performs the behavior of concern:
1. When Ethan engages in inappropriate behavior, give verbal and visual reminders of the expected behavior.
2. Model/have Ethan practice expected behavior.
3. Redirect Ethan back to task,employing the broken record technique.
4. Avoid giving an eye contact or verbal attention to inappropriate behaviors.
5. Give Ethan a thumb's down, while shaking your head no.
6. Use of time out ("thumbs down") chair if 1-5 does not work.

Behavior Management Plan

IEP ADDENDUM: **One to One Support Plan---Ethan K**

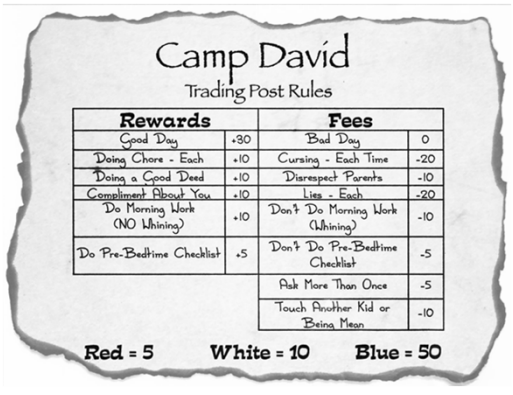
I. **Targeted IEP Goals:** Behavior goal: time on task without interfering behaviors

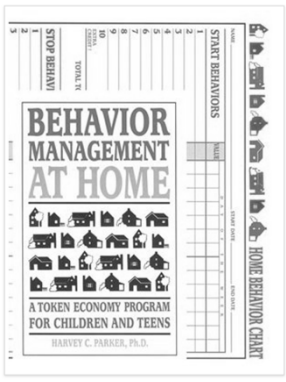
II. **Criteria for Acceptable performance:** Criteria for acceptable performance of targeted behaviors are addressed through IEP.

I. **Intervention Strategies**
- Positive reinforcement
- Differential reinforcement of Other/Alternate behaviors
- Follow SDI accommodations within the IEP

II. **Plan for Data Collection**
One to one assistant will complete weekly access logs.

III. **Role of the one-to-one assistant**
- Use strategies and consequences in Ethan's behavior plan
- Provide reinforcement for appropriate behavior
- Provide consequences (at discretion of classroom teacher) for inappropriate behavior
- Use visual, verbal, gestural prompts to redirect Ethan to back to task.
- Coach non-exceptional peers on extinction procedures and being appropriate role models.
- Receive training on the ipad applications that Ethan will be using in order to assist him.





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*

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Neuropsychological Abnormalities in Persons with ASD

Cognitive Rigidity
Abnormal Regulation of Attention
Abnormal Regulation of Arousal
Abnormal Regulation of Sleep
Abnormal Sensory Processing

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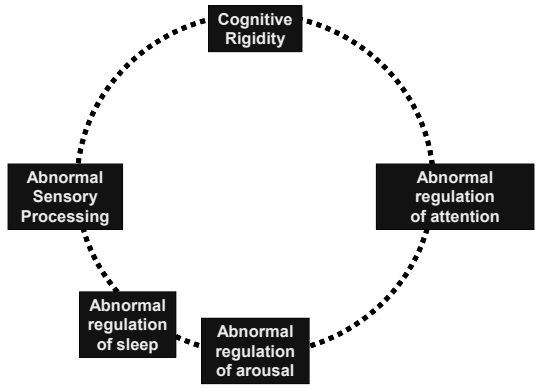
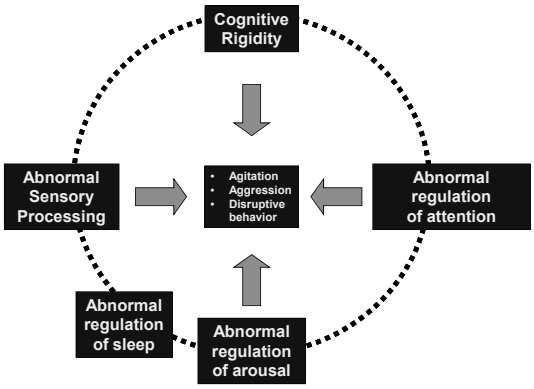
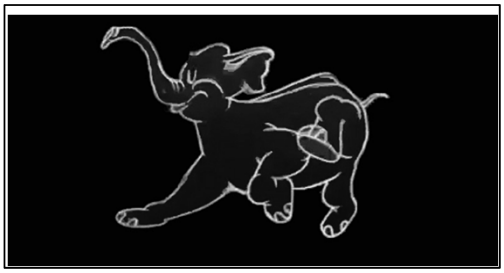
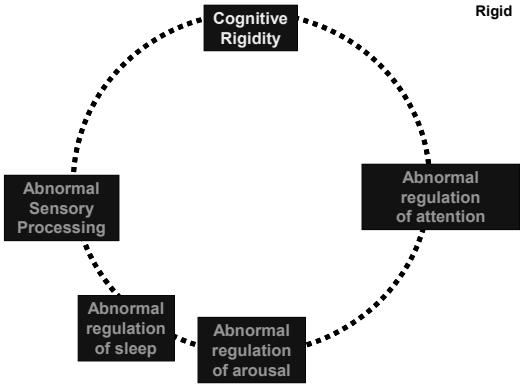
Neuropsychological Deficits in Persons with ASD



Neuropsychological Deficits in Persons with ASD







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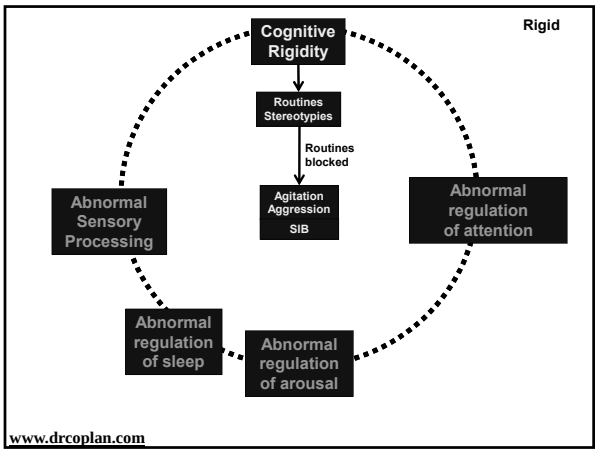
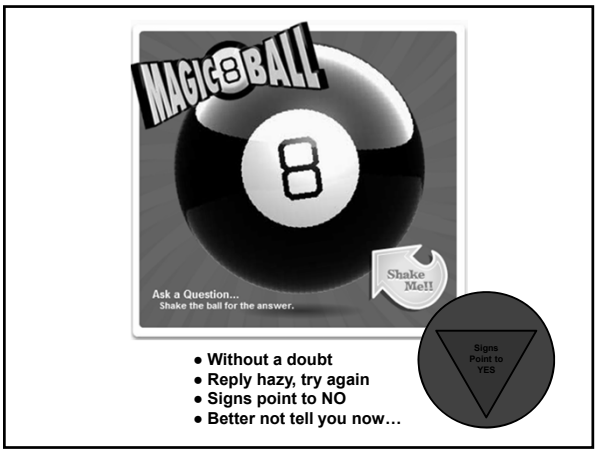
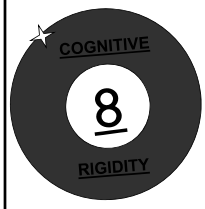




Cognitive Rigidity



"Externalizing Behaviors"

- **Inability to shift mental sets**
  - ***Insistently* repetitious behavior**
  - **Compulsions**
  - **Perfectionism**
  - **Obsessions**
- **(Anxiety)**
- **(Depression)**

"Internalizing Behaviors"

Cognitive Rigidity

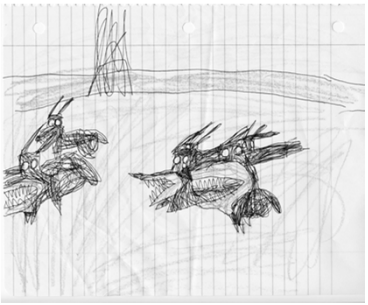
- ***Insistently* repetitious behavior**
- **Problems with changes in routine, transitions, unmet expectations**
- **Perfectionism / Perseveration**
- **Compulsions**
- **(Anxiety)**
- **(Depression)**

Perfectionism

Cognitive Rigidity

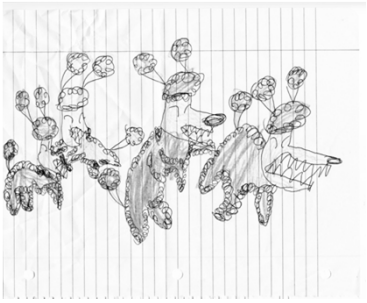
- ***Insistently*** **repetitious behavior**
- **Problems with changes in routine, transitions, unmet expectations**
- **Perfectionism**
- **(Anxiety)**
- **(Depression)**

Anxiety



RD. 7 y.o. F, nl IQ, PDD-NOS & Anxiety. Father: GAD
www.drcoplan.com MRN: 07-0427

Anxiety



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Anxiety

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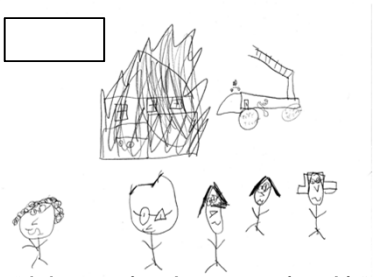
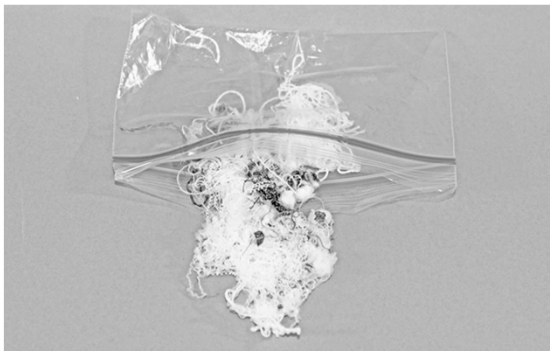
Anxiety



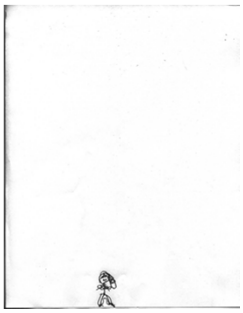
"The house is on fire and we are running for our life."

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



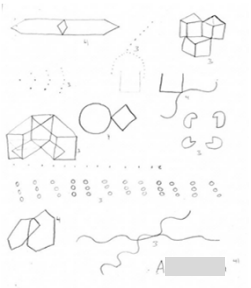
Joseph F: 15 y.o. boy asperger syndrome & chronic anxiety
MRN: 05-0096

Depression



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

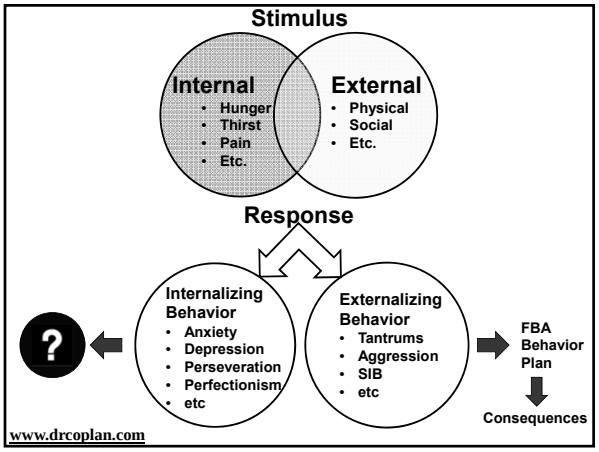
Anxiety, Perfectionism, and Self-Injurious Behavior



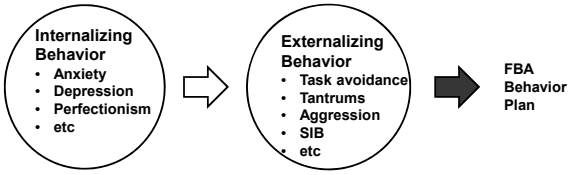
Standard Score: 138

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.



Unaddressed internalizing behavior often comes out as externalizing behavior



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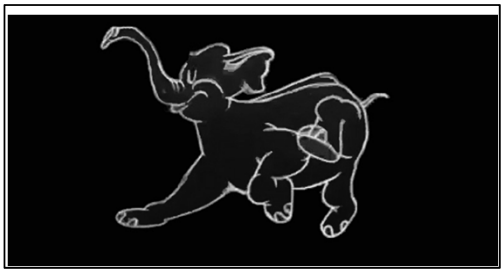
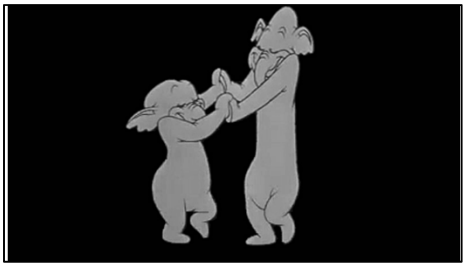
How do you kill a blue elephant?



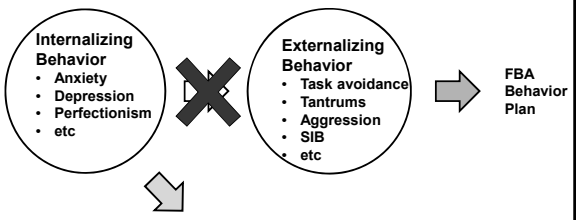
Shoot it with a blue elephant gun.

How do you kill a pink elephant?



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

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



Positive Behavior Support Plan:
Proactively avert, or identify and dissipate anxiety

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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)?

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."

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."

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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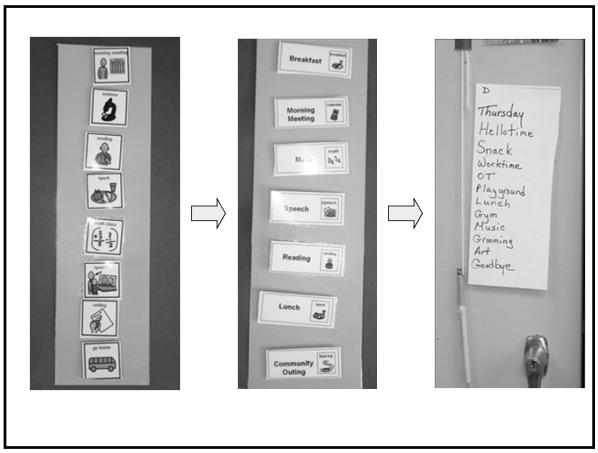

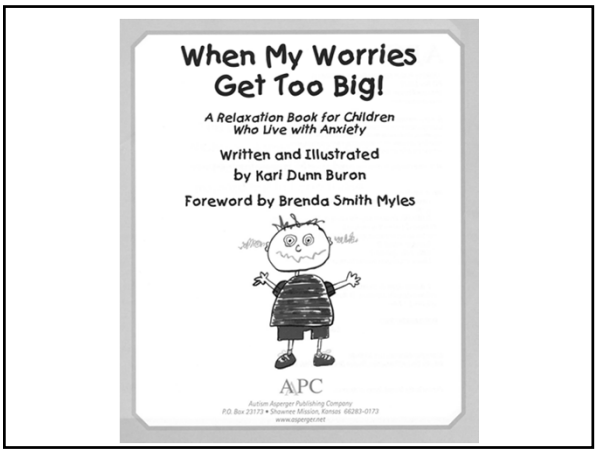

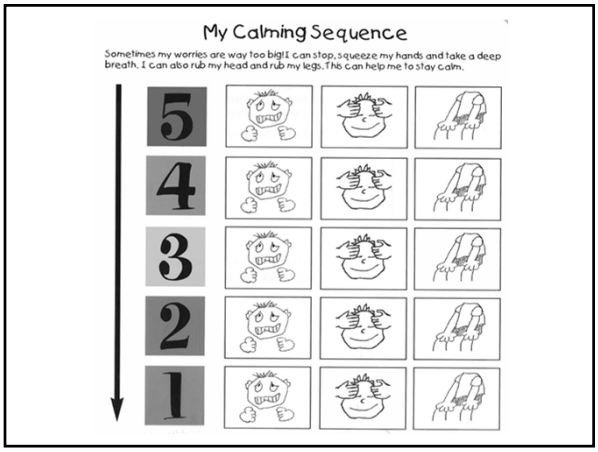

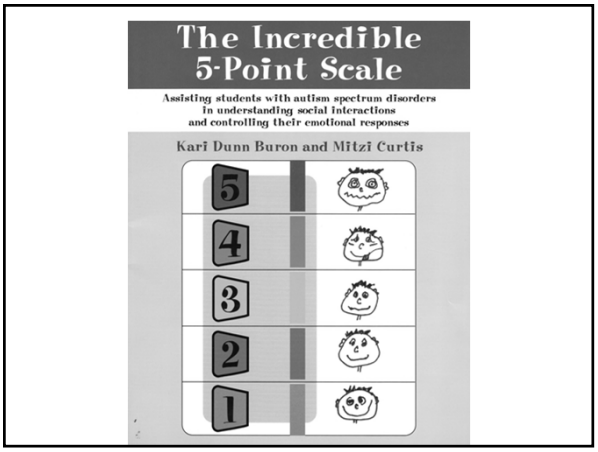

SSRIs in ASDs

- **Primary targets**
  - Cognitive Rigidity
    - Anxiety
    - Obsessions (thoughts)
    - Compulsions (behavior)
    - Perfectionism
  - Depression
  - Stereotypies: Probably not
- **"Downstream" benefit:**
  - ↓ Disruptive Behavior
  - ↑ Quality of Life

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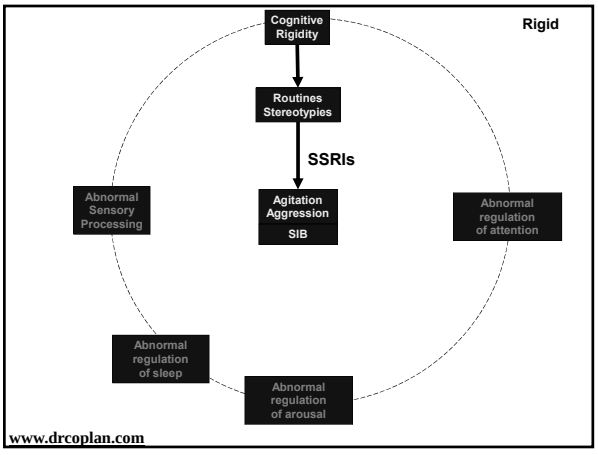

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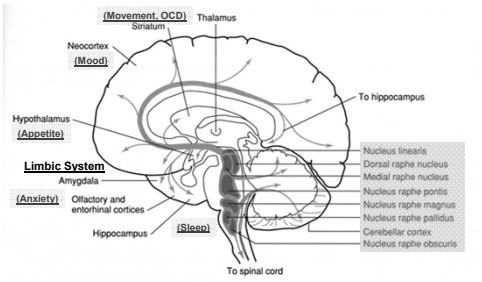
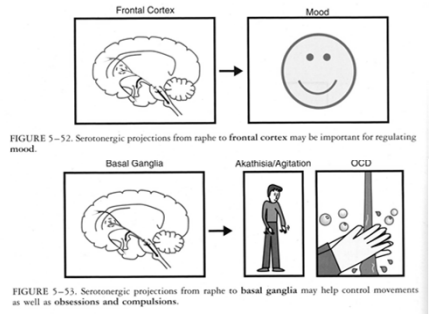
Serotonin (5 HT)



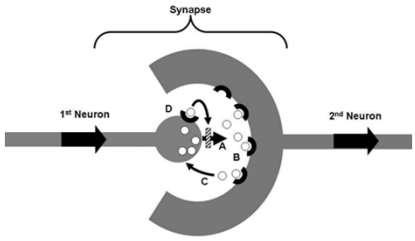
Nestler, *Molecular Neuropharmacology*, Fig 9.3

Serotonin (5 HT) Pathways



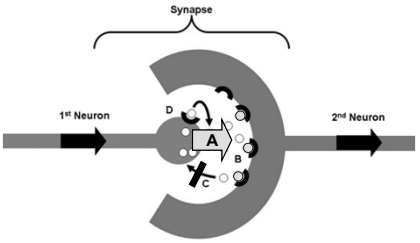
Stahl, *Essential Psychopharmacology*, fig 5.52-3

Mechanisms of Drug Action



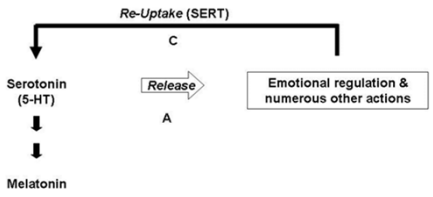
A: Release of transmitter by 1st neuron
B: Transmitter acts at receptor sites on 2nd neuron
C: Transmitter is taken up, and re-stored in 1st neuron
D: Autoreceptor on 1st neuron: detects release of transmitter

Serotonin 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



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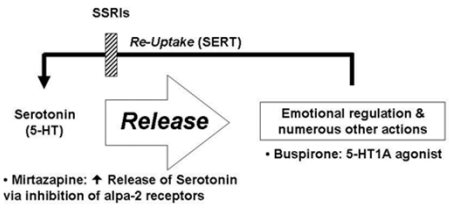
Serotonin-promoting (serotoninergic) drugs



Selective Serotonin Reuptake Inhibitors block the re-uptake of Serotonin

SSRIs in ASDs

- **Primary targets**
  - Cognitive Rigidity
    - Anxiety
    - Obsessions (thoughts)
    - Compulsions (behavior)
    - Perfectionism
  - Depression
  - Stereotypies: Probably not
- **"Downstream" benefit:**
  - ↓ Disruptive Behavior
  - ↑ Quality of Life

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SSRIs in ASDs

- **Side Effects**
  - Activation
    - Hyperactivity
    - Irritability
    - Insomnia
    - Agitation
  - Uncommon or irrelevant
    - GI dysfunciton
    - Sexual dysfunction
    - "Black Box" warning (suicidal mentation)

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Selective Serotonin Reuptake Inhibitors (SSRIs)

Generic Name	Brand Name	Comment
Fluoxetine	Prozac	• The first selective SRI
Fluvoxamine	Luvox	
Sertraline	Zoloft	• May be less activating
Citalopram	Celexa	• Prolonged QT interval
Escitalopram	Lexapro	• Prolonged QT interval
And others…		

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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

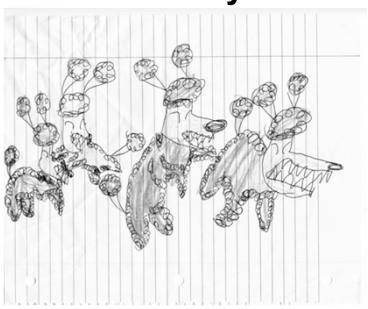
- Treatment-emergent symptoms
  - Citalopram: 1 child with new onset seizures (continued to have seizures after citalopram was stopped)
  - Fenfluramine: ↑ stereotypies; withdrawal, sadness; ↓appetite
    - "With monitoring, dose adjustment and time, all but one of these adverse effects were resolved"
  - 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

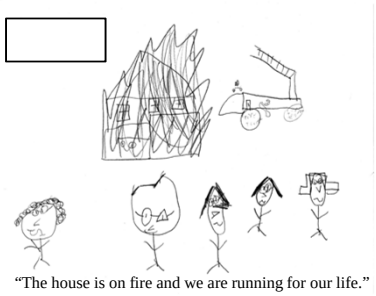
www.drcoplan.com MRN: 07-0427

Anxiety after Rx with CBT & Escitalopram

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

www.drcoplan.com MRN: 07-0427

Anxiety



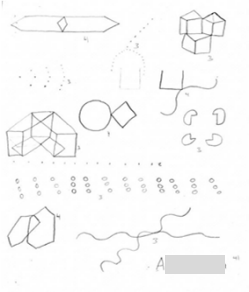
"The house is on fire and we are running for our life."

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

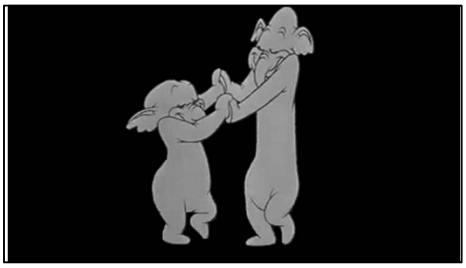
A.D. : 9 y.o. girl with ASD (my MRN: 06-0227)

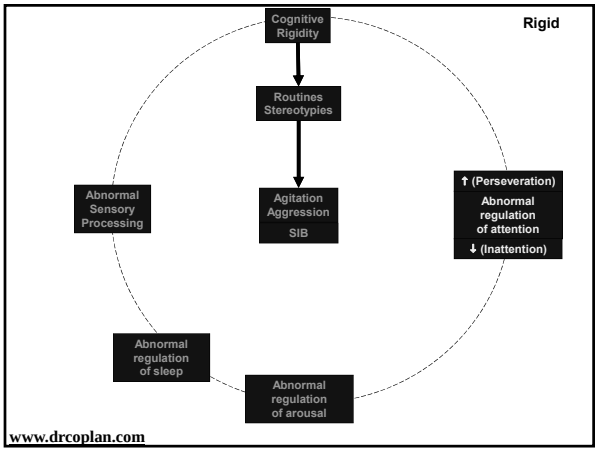
Throughout the session, "Alice" delivered a steady stream of self-deprecating comments, calling herself "stupid," or perseveratively asking if she was "fat." During the Bender, she anxiously and angrily twisted the eraser off the tip of the pencil, while declaring "Why do I keep making stupid mistakes?" 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

Let go & Shift

Attend to stimulus #1 ⟷ 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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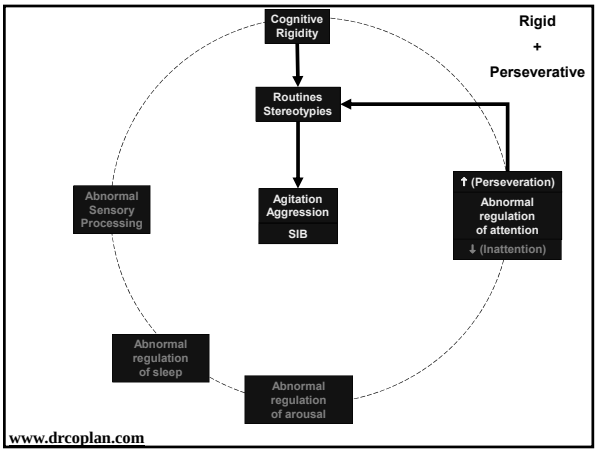
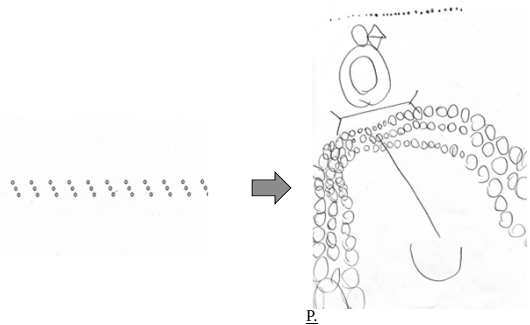
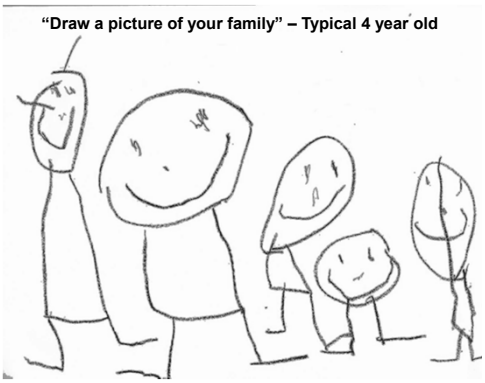


Perseveration



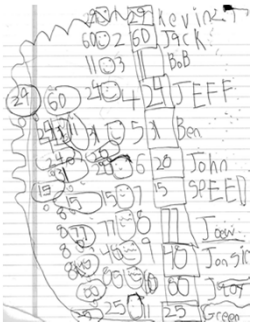
P.

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



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

Perseveration



BL; 8 yr old male, normal IQ; PPD-NOS

Abnormal Regulation of Attention (Perseveration)

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

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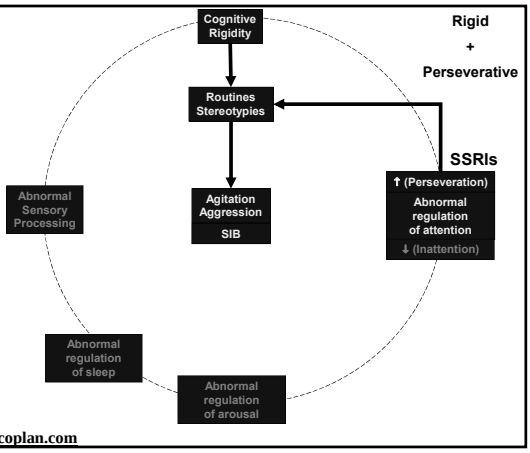

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Abnormal Regulation of Attention - 2

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

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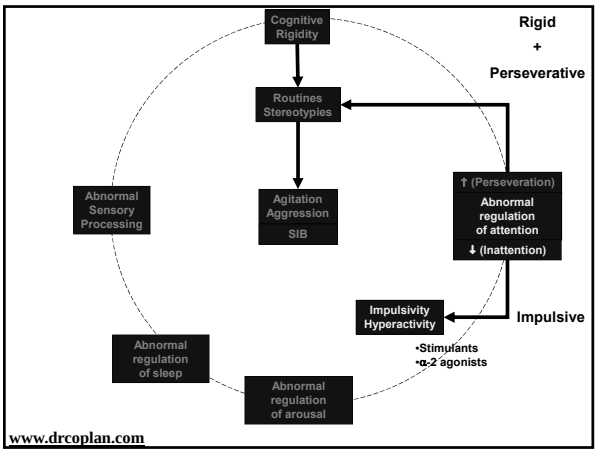

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Inattention

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

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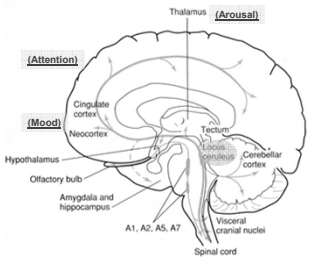
Noradrenergic pathways

(Norepinephrine)



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

Nestler, *Molecular Neuropharmacology*, Fig 8.5

Noradrenergic pathways

(Norepinephrine)

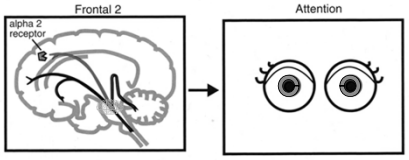
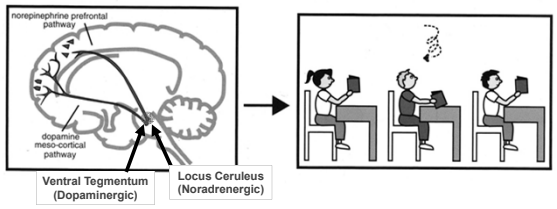


FIGURE 5–25. Other noradrenergic projections from the locus coeruleus to **frontal cortex** are thought to mediate the effects of norepinephrine on **attention**, concentration, and other **cognitive functions**, such as working memory and the speed of information processing. **Alpha 2** postsynaptic receptors may be important in transducing postsynaptic signals regulating attention in postsynaptic target neurons.

Stahl, *Essential Psychopharmacology*, fig 5.25

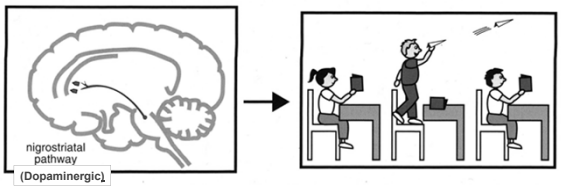
Inattention



Insufficient activation of frontal cortex ➔➔➔ Inattention

Stahl, *Essential Psychopharmacology*, fig 12.1

Hyperactivity

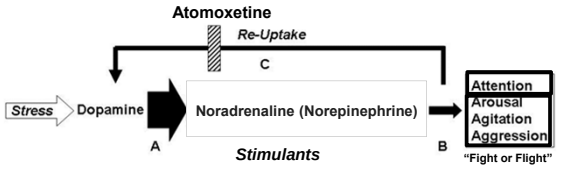


Stimulants in children with ADHD ➔ "Paradoxical" calming

Stahl, *Essential Psychopharmacology*, fig 12.1

Stimulants

(Dopaminergic; Noradrenergic; Sympathomimetic)



↑ Anxiety
↑ Cognitive Rigidity

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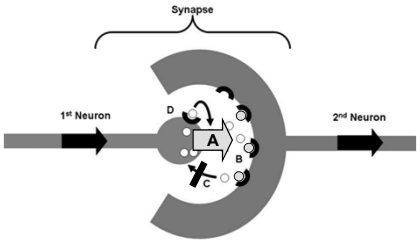
Stimulants

(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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Noradrenergic pathways

(Norepinephrine)

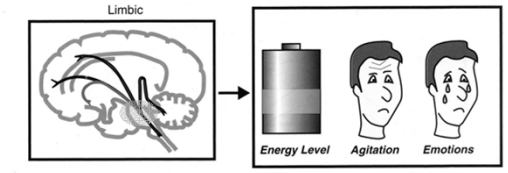

FIGURE 5–26. The noradrenergic projection from the locus coeruleus to **limbic cortex** may mediate emotions, as well as **energy**, fatigue, and psychomotor agitation or psychomotor retardation.

Excess Noradrenergic Activity ➔ Hypervigilance, Agitation

Stahl, *Essential Psychopharmacology*, fig 5.26

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
Lisdexamfetamine	Vyvanse	Metabolized to D-Amphetamine, Not FDA Sch. II
Atomoxetine, Attentin	Strattera	Norepinephrine reuptake Inhibitor (NRI), not FDA Schedule II

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References

(Stimulants)

Nickels, K., et al., Stimulant medication treatment of target behaviors in children with autism: a population-based study. J Dev Behav Pediatr, 2008. 29(2): p. 75-81.

Jahromi, L., et al., Positive Effects of Methylphenidate on Social Communication and Self-Regulation in Children with Pervasive Developmental Disorders and Hyperactivity. Journal of Autism and Developmental Disorders, 2009. 39(3): p. 395-404

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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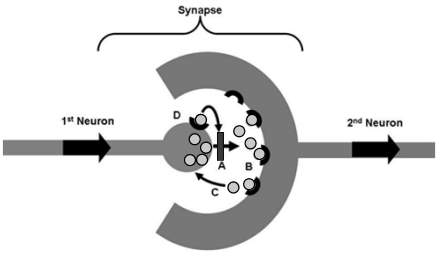
Alpha-2 Agonists



Alpha-2 agonists (guanfacine, clonidine)
- Pre-synaptic α2 receptors → ↓release of dopamine & norepinephrine → ↓BP
- Post-synaptic α2 receptors (Locus Ceruleus & Frontal Cortex) → ↑Attention

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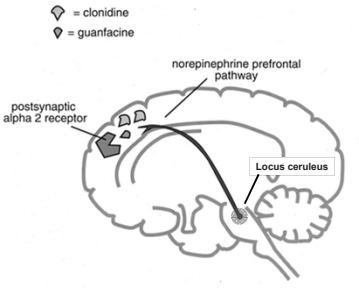
Alpha-2 agonists
(clonidine, guanfacine)



Stahl, *Essential Psychopharmacology*, fig 12.6

Alpha-2 Agonists

Benefits
- ↓ Agitation
- ↓ Hyperactivity
- ↑ Attention Span
- No exacerbation of anxiety / rigidity

Side Effects
- Sleepiness: Common
- Emotional Lability (crying) - occasional
- Hypotension (low BP) - rare

References
(alpha-2 agonists)

- Murray, M.J., Attention-deficit/Hyperactivity Disorder in the context of Autism spectrum disorders. Curr Psychiatry Rep, 2010. 12(5): p. 382-8.
- May, D.E. and C.J. Kratochvil, Attention-deficit hyperactivity disorder: recent advances in paediatric pharmacotherapy. Drugs, 2010. 70(1): p. 15-40.

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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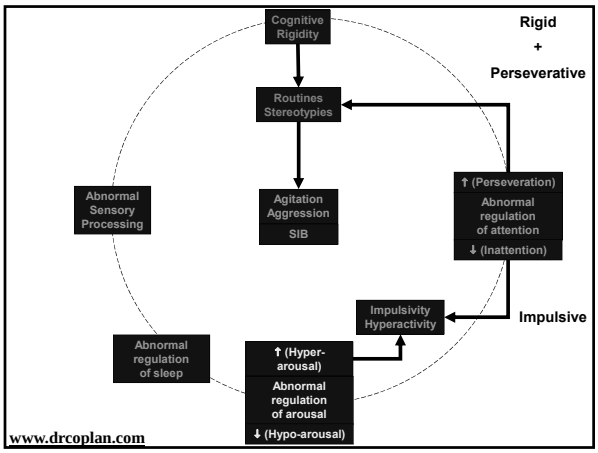

"He is so hard to calm down when he gets upset….His emotional thermostat doesn't work"

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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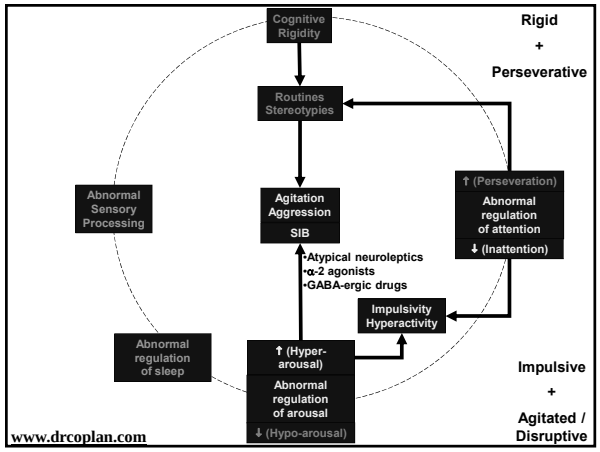
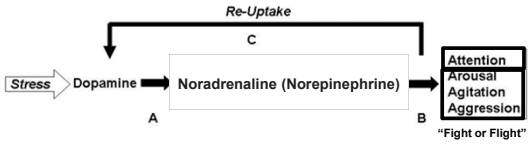


Dopamine

(Dopaminergic; Noradrenergic; Sympathomimetic)



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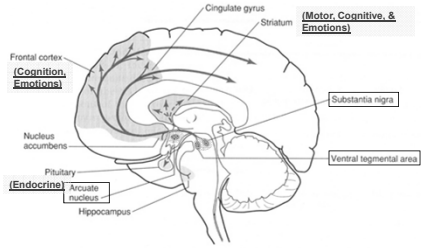
Dopamine

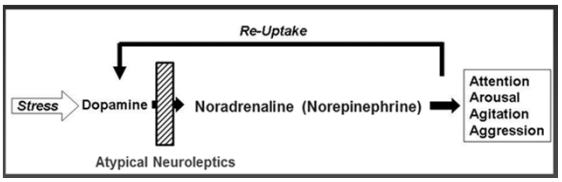


Substantia Nigra ("black stuff"), Ventral tegmentum, arcuate nucleus

Nestler, *Molecular Neuropharmacology*, Fig 8.6

Atypical Neuroleptics

(Dopamine Blockers)



Side Effects
Sleepiness (initially)
Weight Gain (common)
Diabetes (uncommon)
Movement Disorder (rare)

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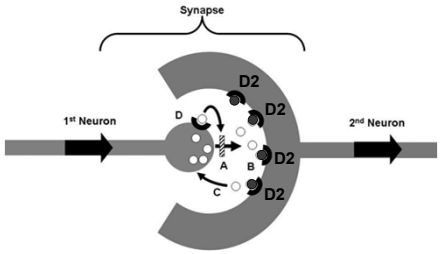
Atypical Neuroleptics



•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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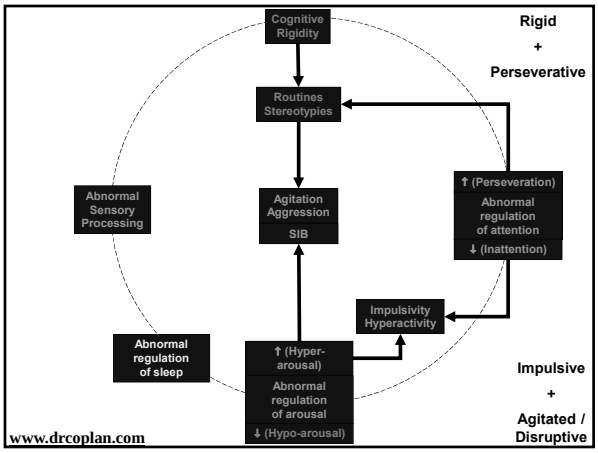
References

(neuroleptics, AEDs, GABA)

- Canitano, R. and V. Scandurra, *Psychopharmacology in autism: An update.* Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2011. 35(1): p. 18-28.
- Tuchman, R., AEDs and psychotropic drugs in children with autism and epilepsy. Mental Retardation & Developmental Disabilities Research Reviews, 2004. 10(2): p. 135-138.
- Wang, L.W., E. Berry-Kravis, and R.J. Hagerman, Fragile X: leading the way for targeted treatments in autism. Neurotherapeutics, 2010. 7(3): p. 264-74.



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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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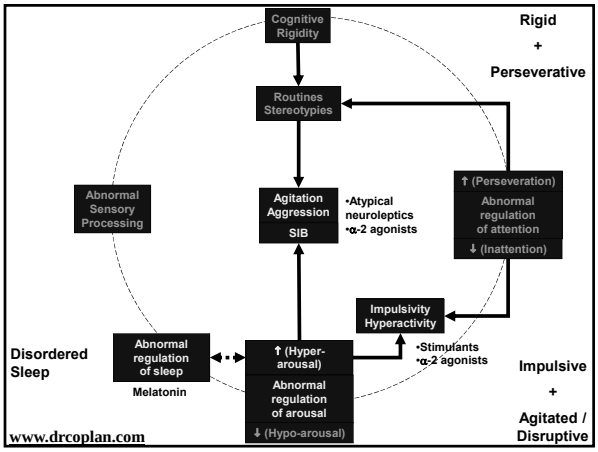
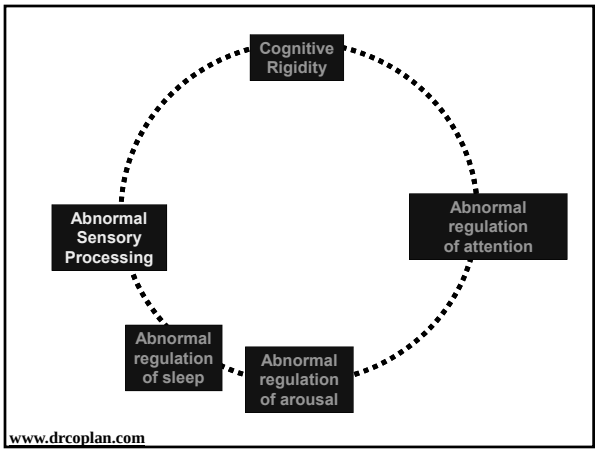


References

(Melatonin)

- Wright, B., et al., Melatonin Versus Placebo in Children with Autism Spectrum Conditions and Severe Sleep Problems Not Amenable to Behaviour Management Strategies: A Randomised Controlled Crossover Trial. J Autism Dev Disord, 2010.
- Miano, S. and R. Ferri, Epidemiology and management of insomnia in children with autistic spectrum disorders. Paediatr Drugs, 2010. 12(2): p. 75-84.
- Leu, R.M., et al., Relation of Melatonin to Sleep Architecture in Children with Autism. J Autism Dev Disord, 2010.



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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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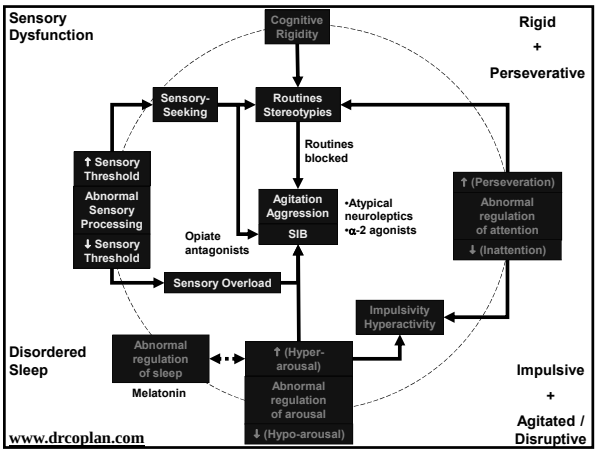

The whole is greater than the sum of its parts

Max Wertheimer

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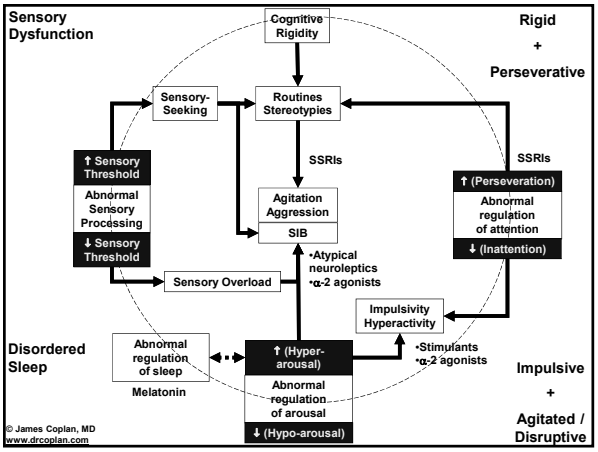

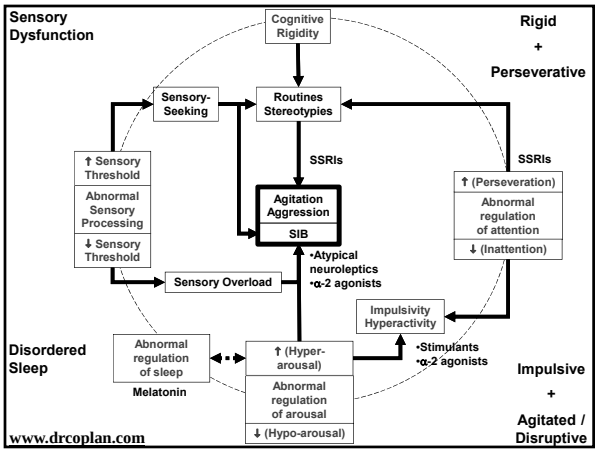

Summary

- **Why this child?**
  - 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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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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An ounce of prevention….

- Identify *internalizing* behaviors *before* they lead to *externalizing* behaviors
  - Behavior Management Plan that proactively seeks to avert or dissipate anxiety

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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