Behavior management and psychopharmacology in children with autism spectrum disorders

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Disclosures / References

- 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

Chapter 12: Behavior management and psychopharmacology

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

Outline / Basic Premises - 1

- Biologically driven behaviors / traits
  - Cognitive Rigidity
  - Dysregulation of Attention
  - Dysregulation of Arousal
  - Dysregulation of Sleep
  - Dysregulation of Sensory Processing
- Occur irrespective of environmental contingencies
- Do not serve a social function
- Specific behaviors / traits are tied to specific neurotransmitters / brain systems

Outline / Basic Premises - 2

- Socially driven behaviors
  - Occur in response to environmental contingencies
  - Serve a social function
    - Attention
    - Access to desired objects or activities
    - Escape from undesired activities
  - A-B-C Model
    - What is the Antecedent to the behavior?
    - What is the Behavior itself?
    - What are the Consequences for the behavior?

Outline / Basic Premises - 3

- Behavior analysis needs to take biological and environmental factors into account:
  - Underlying biological traits often provide the child with lots of opportunities to make unfortunate discoveries (viz: Tantrums or SIB are great ways to get attention or escape from tasks)
  - Intervention often requires both pharmacologic and behavioral measures
Children with ASDs, age 10+:
Neuropsychiatric Co-Morbidity

<table>
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<th>Condition</th>
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<th>PDD-NOS (n=374)</th>
<th>Aspergers (n=141)</th>
<th>Total (n=952)</th>
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<td>39%</td>
<td>38%</td>
<td>33%</td>
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<td>61%</td>
<td>14%</td>
<td>13%</td>
<td>16%</td>
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<td>Aspergers</td>
<td>6%</td>
<td>11%</td>
<td>4%</td>
<td>9%</td>
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<tr>
<td>Total</td>
<td>100%</td>
<td>86%</td>
<td>55%</td>
<td>95%</td>
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</table>

IAN Research Report #1 - May 2007
http://www.iancommunity.org/cs/ian_research_reports
Abnormal regulation of arousal
Abnormal regulation of attention
Abnormal regulation of sleep
Abnormal sensory processing

Cognitive Rigidity:
Changes in Routine / Unmet Expectations

Rainman, 1988

Cognitive Rigidity
(Difficulty shifting mental sets)

"Externalizing Behaviors"
- Insistently repetitious behavior
- Difficulty with unmet expectations
- Perfectionism
- Compulsions
  (Aggression, SIB)

- Obsessions
- (Anxiety)
- (Depression)
  "Internalizing Behaviors"

Perfectionism
Perfectionism

Joseph F: 15 y.o. boy Asperger Syndrome

Compulsions

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

Anxiety

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

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

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

Anxiety

BK; MRN 09-0605

“Standing in the Atlantic Ocean. The ocean has a very high surface, up to their mouth, so they can’t breathe.” Six year old boy with ASD and Anxiety.

Depression

KO; 10 yr old female, PDD-NOS, normal IQ

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.

Anxiety, Perfectionism, and Self-Injurious Behavior

A.D.: 9 y.o. girl with ASD (my MRN: 04-0227)

Standard Score: 138

How do you kill a blue elephant?

JH; 10 yr old male, PDD-NOS

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*.

Unaddressed internalizing behavior often comes out as externalizing behavior

“An ounce of prevention is worth a pound of cure”

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

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.”

Positive Behavior Support Plan for Internalizing Behavior

- 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

Self-centered
Inconscient
Of others
Non-compliant
Willfully disobedient
Stubborn
Rude
Unmotivated
Inattentive
Lazy
Disrespectful
Could do better if only he tried harder

Socially
Unaware
Rigid
Anxious
Perfectionistic

“We caution against the use of the word “stubborn” to characterize Ryan’s classroom behavior. Ryan’s task avoidance and non-adherence to teacher instruction reflect cognitive rigidity and anxiety, rather than “stubborn” behavior. Re-framing his actions will lead to more appropriate intervention, placing the focus on anxiety management and cognitive flexibility, rather than “compliance.”

Positive Behavior Support Plan for Internalizing Behavior

- Staff Awareness
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Positive Behavior Support Plan for Internalizing Behavior

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  - Deep Breathing
  - “Break” cards
- Cognitive Behavioral Therapy (CBT)
- SSRIs

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Selective Serotonin Reuptake Inhibitors (SSRIs)

- **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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Serotonin (5 HT)

Nestler, *Molecular Neuropharmacology*, Fig 9.3

Serotonin-promoting (serotoninergic) drugs

- **SSRIs in ASDs**
  - **Side Effects**
    - Activation
      - Hyperactivity
      - Irritability
      - Insomnia
      - Agitation
    - Uncommon or irrelevant
      - GI dysfunction
      - Sexual dysfunction
      - “Black Box” warning (suicidal mentation)

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### Selective Serotonin Reuptake Inhibitors (SSRIs)

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<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Comment</th>
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<tr>
<td>Fluoxetine</td>
<td>Prozac</td>
<td>The first selective SRI</td>
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<tr>
<td>Fluvoxamine</td>
<td>Luvox</td>
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<tr>
<td>Sertraline</td>
<td>Zoloft</td>
<td>May be less activating</td>
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<tr>
<td>Citalopram</td>
<td>Celexa</td>
<td>Prolonged QT interval</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Lexapro</td>
<td>Prolonged QT interval</td>
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<tr>
<td>And others...</td>
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### Selective serotonin reuptake inhibitors (SSRIs) for autism spectrum disorder (ASD).

**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.”

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### Pharmacotherapy for anxiety disorders in children and adolescents

**Ipsen JC, Stein DJ, Hawkeride S, Hoppa L. Cochrane Database of Systematic Reviews 2009, Issue 3.**

- **Studies reviewed:** 22 RCTs/ 2,519 participants
  - 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 due to side effects
    - “The overwhelming majority of evidence of efficacy was for the SSRIs, with the most evidence in paediatric OCD”

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**Anxiety**

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

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Anxiety after Rx with CBT & Escitalopram

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

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

Fluoxetine 10 mg/d

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

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 SSRIs 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 multiple 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.

5 Minute Break

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Regulation of Attention

Let go & Shift
Attend to stimulus #1

Attend to stimulus #2

Noradrenergic pathways (Norepinephrine)

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

Nestler, Molecular Neuropharmacology, Fig 8.5

Noradrenergic pathways (Norepinephrine)

Stahl, Essential Psychopharmacology, Fig 5.25

Abnormal Regulation of Attention - 1

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

Stahl, Essential Psychopharmacology, Fig 5.25

Stahl, Essential Psychopharmacology, Fig 5.25

“Draw a picture of your family” – Typical 4 year old

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Abnormal Regulation of Attention (Perseveration)

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

Abnormal Regulation of Attention - 2

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

- **Locus Ceruleus** (Noradrenergic)
- **Ventral Tegmentum** (Dopaminergic)

**Insufficient** activation of frontal cortex → → → Inattention

Stahl, Essential Psychopharmacology, fig 12.1

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**Stimulants, NRI’s**

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<tr>
<th>Generic Name(s)</th>
<th>Brand Name(s)</th>
<th>Comment</th>
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<tr>
<td>Amphetamine</td>
<td></td>
<td>FDA Schedule II</td>
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<tr>
<td>Dextroamphetamine</td>
<td>Dextrostat, Dexedrine</td>
<td>FDA Schedule II</td>
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<tr>
<td>Dextroamphetamine + amphetamine</td>
<td>Adderall</td>
<td>FDA Schedule II</td>
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<tr>
<td>Methylphenidate</td>
<td>Concerta, Ritalin, Metadate</td>
<td>FDA Schedule II</td>
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<tr>
<td>Dexamphetamine</td>
<td>Focalin</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Atomoxetine, Attentin</td>
<td>Strattera</td>
<td>Noradrenaline reuptake inhibitor (NRI), not FDA Schedule II</td>
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<tr>
<td>Lisdexamphetamine</td>
<td>Vyvanse</td>
<td>Pro-drug of D-amphetamine; not FDA II</td>
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**Alpha-2 Agonists**

<table>
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<tr>
<th>Generic Name</th>
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<th>Comment</th>
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<tbody>
<tr>
<td>Clonidine</td>
<td>Catapres</td>
<td>More sedating than guanfacine</td>
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<tr>
<td>Guanfacine</td>
<td>Tenex, Intuniv</td>
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</table>

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

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**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

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**Clinical Pearl**

- Beware of Cognitive Rigidity masquerading as ADHD
  - Perseveration on inner stimuli: “Inattentive”
  - Perfectionism:
    - “Problems w. task completion”
  - Anxiety:
    - “Rushes through work”
    - “Out of seat behavior”

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**Regulation of Arousal**

Hypoorousal
- Lethargic

Calm & Relaxed

Fight or Flight Response

“Red Alert”
- Adrenaline
- Heart Rate
- Resp. Rate
- Combative
“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

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**Dopamine**

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

Nestler, *Molecular Neuropharmacology*, Fig 8.6

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**Atypical Neuroleptics**

*Atypical neuroleptics block D2 receptors*

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

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**Nestler, Molecular Neuropharmacology**, Fig 8.6
Atypical Neuroleptics

<table>
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<tr>
<td>Aripiprazole</td>
<td>Abilify</td>
<td>• Relatively less risk of weight gain</td>
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<td>• FDA approved for Rx of ASD</td>
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<tr>
<td>Clozapine</td>
<td>Clozaril</td>
<td>• Bone marrow suppression</td>
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<tr>
<td>Olanzapine</td>
<td>Zyprexa</td>
<td>• Greater risk of weight gain</td>
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<td>Quetiapine</td>
<td>Seroquel</td>
<td>• Greater sedation</td>
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<tr>
<td>Risperidone</td>
<td>Risperdal</td>
<td>• Greater risk of weight gain</td>
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<tr>
<td>Ziprazidone</td>
<td>Geodon</td>
<td>• Relatively less risk of weight gain</td>
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Mood

JH, 10 yr old male, PDD-NOS

Depression, Anger (mood)

JH, 10 yr old male, PDD-NOS

Regulation of Sleep - 1

- Melatonin
  - Brain hormone
  - Metabolic rate (Heart, Temp)
  - “You’re sleepy now”
- Suppressed by light
  - 24 hr cycle
  - Seasonal cycle

Regulation of Sleep - 2

- Abnormal melatonin cycling
  - Primary disorders of sleep
  - Blindness
  - ASD
- Symptoms
  - Delayed onset of sleep
  - Shortened duration / frequent wakening
Regulation of Sleep - 3

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

Sensory Processing

- Subjective Properties
  - Familiar / Unfamiliar
  - Pleasant / Unpleasant
  - Strong / Weak
  - Internal / External
- Sensory Input ➔ Self-awareness
- Mirror Neurons ➔ Empathy
The whole is greater than the sum of its parts
Max Wertheimer

Prognosis & Family Genetics

Parents & Siblings of Children with ASDs: Neuropsychiatric Comorbidity

Anxiety D/O, TS, ASD

Generalized Anxiety D/O Poor Eye Contact (not ASD)

ASD with normal NV IQ Tourette Syndrome Anxiety

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Anxiety, OCD, ASD

Bipolar D/O, OCD, Anxiety D/O, ASD, “Processing D/O”

Bipolar D/O, Alcoholism, Anxiety D/O, ADHD, ASD

Bipolar D/O, Alcoholism, Anxiety D/O, ADHD, ASD

Adult outcomes for children who “lose the diagnosis”

Adults with ASD – Online Survey
The ABC's of Behavior Analysis

- What is the Antecedent?
- What is the Behavior?
- What is the Consequence?

Antecedents

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

Antecedents

- Internal:
  - Hunger
  - Thirst
  - Fatigue
  - Cognitive Rigidity
  - Dysregulation of Attention
  - Dysregulation of Mood / Arousal
  - Dysregulation of Sensory Processing
  - Other biological drivers

Behavior

- What, exactly, is the behavior?
  - "Topography"
    - Verbal
    - Physical
  - Frequency
  - Intensity
  - Duration
  - Timing
Behavior

- What is the child’s developmental level?
- Is the behavior normal for the child’s developmental level?
  - Tantrums / Noncompliance
    - 24 month old “striving for autonomy”
  - Cognitive Rigidity
    - 4 yr olds are “rule based” by nature
  - “Impulsivity” / “Inattention”
    - Attention span is a function of devel. level

- What is the child’s ability to communicate?
  - Does “disruptive” behavior serve a communicative function?

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

Consequences

- Reinforcers
  - Positive
  - Negative
- Aversives

Consequences 1: Reinforcers

- Reinforcers lead to an increase in frequency of the antecedent behavior
  - Positive Reinforcement (adds something)
    - Attention
    - Access to desired object / activity
  - Negative Reinforcement (removes something)
    - Escape from Task
    - Avoidance of punishment
      - “We drive within the speeding limit because we receive the negative reinforcement of not getting a speeding ticket”

Food Selectivity

- Parent removes non-preferred food([-] reinforcement)
- Parent provides child with his/her preferred food([+] reinforcement)
- Alternatives
  - First ….. Then (The Premack Principle)
  - Put refusal on extinction
  - The kitchen is closed between meals

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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

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.

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.)

Summary

Biological Drivers
Social Contingencies
Observable Behavior
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

- 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)

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

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

Summary

Services for adult “survivors” of childhood ASD

- Mental Health
  - Anxiety
  - Depression
  - Mood Disorders
  - Depression

- Vocational
- Workplace Social Skills
- Parent / Caregiver support
- Spouse / Partner support

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