A Rational Approach to Behavior Management & Psychopharmacology in Children with Developmental Disabilities

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Disclosures

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

• This presentation will include a discussion of off-label drug use.
“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”
Stimuli

Internal
• Hunger
• Thirst
• Pain
• Etc.

External
• Physical
• Social
• Etc.

Behavior
• “Internalizing”
• “Externalizing”
“Internalizing” Behavior

- Anxiety
- Depression
- Obsessiveness / Rigidity
- Perfectionism
“Externalizing” Behavior

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

Internal
- Hunger
- Thirst
- Pain
- Etc.

External
- Physical
- Social
- Etc.

Behavior
- “Internalizing”
- “Externalizing”
Behavior

• What is the child’s developmental level?

• Is the behavior normal for the child’s developmental level?
  – Tantrums / Noncompliance
  – “Impulsivity” / “Inattention”
Behavior

- 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
The ABC’s of Behavior Analysis

- What is the Antecedent?
- What is the Behavior?
- What is the Consequence?
Internal Stimuli
- Hunger
- Thirst
- Pain
- Etc.

External Stimuli
- Physical
- Social
- Etc.

Antecedents

Behavior

Consequence
Antecedents

- External:
  - Imposition of a task
  - Change in routine
  - Denial of access to object or activity
  - Other....
  - Or: No apparent external antecedent
The ABC’s of Behavior Analysis

- What is the Antecedent?
- What is the Behavior?
- What is the Consequence?
  - Reinforcers
    - Positive
    - Negative
  - Aversives
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 greater the strengthening or weakening of the bond”

Manipulating the Consequence for a given behavior feeds back on the probability that that behavior will recur.
Internal Stimuli
- Hunger
- Thirst
- Pain
- Etc.

External Stimuli
- Physical
- Social
- Etc.

Behavior

Consequence
Consequences 1: Reinforcers

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

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

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

Internal Stimuli
- Hunger
- Thirst
- Pain
- Etc.

External Stimuli
- Physical
- Social
- Etc.

Behavior

Consequence

Attention, Access, Escape
Food Selectivity

Positive and Negative Reinforcement of unwanted behavior

• Parent removes non-preferred food (negative reinforcement)
• Parent provides child with his/her preferred food (positive reinforcement)
• Alternatives
  – *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
Antecedent

**Internal Stimuli**
- Hunger
- Thirst
- Pain
- Etc.

**External Stimuli**
- Physical
- Social
- Etc.

Behavior

Consequence

Logical consequences
Overcorrection
Token Economy

• Concretely specified behaviors

• Earn and Lose Points (Tokens)

• Points ➔ Access to specified reward
  – Reward determined by child’s interests
    • Preferred toys
    • Computer time
    • Etc.
  – NO access to reward at other times
  – “Extra” treats not as effective
# Token Economy

**Camp David**

**Trading Post Rules**

<table>
<thead>
<tr>
<th>Rewards</th>
<th>Fees</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Good Day</strong></td>
<td><strong>Bad Day</strong></td>
</tr>
<tr>
<td>+30</td>
<td>0</td>
</tr>
<tr>
<td>Doing Chore - Each</td>
<td>Cursing - Each Time</td>
</tr>
<tr>
<td>+10</td>
<td>-20</td>
</tr>
<tr>
<td>Doing a Good Deed</td>
<td>Disrespect Parents</td>
</tr>
<tr>
<td>+10</td>
<td>-10</td>
</tr>
<tr>
<td>Compliment About You</td>
<td>Lies - Each</td>
</tr>
<tr>
<td>+10</td>
<td>-20</td>
</tr>
<tr>
<td>Do Morning Work (NO Whining)</td>
<td>Don’t Do Morning Work (Whining)</td>
</tr>
<tr>
<td>+10</td>
<td>-10</td>
</tr>
<tr>
<td>Do Pre-Bedtime Checklist</td>
<td>Don’t Do Pre-Bedtime Checklist</td>
</tr>
<tr>
<td>+5</td>
<td>-5</td>
</tr>
<tr>
<td></td>
<td>Ask More Than Once</td>
</tr>
<tr>
<td></td>
<td>-5</td>
</tr>
<tr>
<td></td>
<td>Touch Another Kid or Being Mean</td>
</tr>
<tr>
<td></td>
<td>-10</td>
</tr>
</tbody>
</table>

Red = 5      White = 10      Blue = 50
Disruptive Behavior: Function & Best Response

- **Attention**
  - 1-2-3 ➔ “Time Out”

- **Access**
  - *Never* grant access to desired object in response to disruptive behavior

- **Escape**
  - *Never* permit the child to terminate a task with disruptive behavior. Walk child through task first, *then* ➔ Time Out.
But.....

Children with disabilities often 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*
Neuropsychological Deficits in Persons with ASD

- Abnormal regulation of attention
- Abnormal regulation of arousal
- Abnormal regulation of sleep
- Abnormal Sensory Processing
- Cognitive Rigidity
Neuropsychological Deficits in Persons with ASD

- Abnormal regulation of arousal
- Abnormal regulation of sleep
- Abnormal regulation of attention
- Cognitive Rigidity
- Agitation
- Aggression
- SIB

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Abnormal regulation of arousal

Abnormal regulation of sleep

Abnormal Sensory Processing

Abnormal regulation of attention

Cognitive Rigidity
Cognitive Rigidity

• *Insistently* repetitious behavior
• Problems with changes in routine, transitions, unmet expectations
• Perfectionism
• (Anxiety)
• (Depression)
Abnormal regulation of arousal

Abnormal regulation of attention

Abnormal regulation of sleep

Abnormal Sensory Processing

Cognitive Rigidity

Routines Stereotypies

Routines blocked

Agitation Aggression

SIB

www.drcoplan.com
Cognitive Rigidity

- Insistently repetitious behavior
- Problems with changes in routine, transitions, unmet expectations
- Perfectionism
  - (Anxiety)
  - (Depression)
Anxiety
- Generalized Anx. D/O
- OCD / TS
- Phobias
- Selective Mutism

Depression

Cognitive Rigidity
- Difficulty changing mental sets
- Routines
- Transitions
- Repetitious behaviors
- Perfectionism

Atypicality
- Social:
  - Theory of Mind
- Language:
  - Pragmatics
  - Prosody
- Cognitive
  - Central Coherence
- Sensory/Motor:
  - Aversions / Attractions
  - Clumsiness

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Anxiety

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

RD. 7 y.o. F, nI IQ, PDD-NOS & Anxiety. Fam Hx: GAD
Depression

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

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Cognitive Rigidity

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

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Thursday
Hello time
Snack
Worktime
OT
Playground
Lunch
Gym
Music
Grooming
Art
Goodbye
When My Worries Get Too Big!

A Relaxation Book for Children Who Live with Anxiety

Written and Illustrated by Kari Dunn Buron

Foreword by Brenda Smith Myles

Autism Asperger Publishing Company
P.O. Box 23173 • Shawnee Mission, Kansas 66283-0173
www.asperger.net
My Calming Sequence

Sometimes my worries are way too big! I can stop, squeeze my hands and take a deep breath. I can also rub my head and rub my legs. This can help me to stay calm.
The Incredible 5-Point Scale
Assisting students with autism spectrum disorders in understanding social interactions and controlling their emotional responses

Kari Dunn Buron and Mitzi Curtis
Emily’s Anxiety Curve

- Feeling good: 1
- Tense: 2
- Mouthy: 3
- Swearing: 4
- Explosive: 5

<table>
<thead>
<tr>
<th>Emily thinks</th>
<th>Mrs. Olson thinks</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 hitting</td>
<td>hitting</td>
</tr>
<tr>
<td>4 running out of the room</td>
<td>swearing</td>
</tr>
<tr>
<td>3 swearing</td>
<td>mouthy</td>
</tr>
<tr>
<td>2 mad/tense</td>
<td>challenging</td>
</tr>
<tr>
<td>1 ok</td>
<td>working</td>
</tr>
</tbody>
</table>
SSRIs in ASDs

• Primary targets
  – Cognitive Rigidity
    • Anxiety
    • Obsessive / Perfectionistic behavior
  – Depression
  – ? Stereotypies

• “Downstream” benefit:
  – ↓ Disruptive Behavior
  – ↑ Quality of Life
Abnormal regulation of arousal
Abnormal regulation of attention
Cognitive Rigidity
Routines Stereotypies
SSRIs
Agitation Aggression
SIB
Abnormal Sensory Processing
Abnormal regulation of sleep
Abnormal regulation of attention
Abnormal regulation of arousal
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Neurotransmitters

A: Release of transmitter by 1\textsuperscript{st} neuron
B: Transmitter acts at receptor sites on 2\textsuperscript{nd} neuron
C: Transmitter is taken up, and re-stored in 1\textsuperscript{st} neuron
D: Autoreceptor on 1\textsuperscript{st} neuron: detects release of transmitter
Serotonin promoting (serotoninergic) drugs

A. Promote release of serotonin (Mirtazipine)
B. Mimic the action of serotonin at the 2\textsuperscript{nd} neuron (Buspirone)
C. Block re-uptake of serotonin (SSRIs)
Serotonin-promoting (serotonergic) drugs

Selective Serotonin Reuptake Inhibitors block the re-uptake of Serotonin

SSRIs

Re-Uptake (SERT)

Release

- Mirtazapine: ↑ Release of Serotonin via inhibition of alpa-2 receptors
- Buspirone: 5-HT1A agonist

Emotional regulation & numerous other actions
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

• Studies reviewed: 22 RCTs/2,519 participants
  o Short-term (average 11 wks)
  o Mean age 12 yrs
  o Drugs studied (versus placebo)
    o SSRIs: 15 (fluoxetine 6, fluvoxamine 2, paroxetine 3, sertraline 4)
    o SNRIs: 5, (clomipramine 3), venlafaxine 2)
    o Benzodiazepines: 2: (alprazolam 1, clonazepam 1)
    o Tricyclic antidepressants: 1 (desipramine)

• Meta-analysis
  o Response rate: Medication 59%; Placebo 31%
  o 7.3% of subjects treated with SSRIs withdrew because of side effects
  o “The overwhelming majority of evidence of efficacy was for the SSRIs, with the most evidence in paediatric OCD”
Dimensional predictors of response to SRI pharmacotherapy in obsessive–compulsive disorder


OCD Subtypes:

- “Aggressive” Obsessions & Checking Behavior (AGG)
- Sexual / Religious (SR)
- Contamination & Washing (CW)
- Symmetry & Exactness (SYM)
- Hoarding (HRD)
Dimensional predictors of response to SRI pharmacotherapy in obsessive–compulsive disorder


<table>
<thead>
<tr>
<th>Baseline demographical and clinical characteristics</th>
<th>Total</th>
<th>Clomipramine</th>
<th>Fluvoxamine</th>
<th>Fluoxetine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>165</td>
<td>62</td>
<td>79</td>
<td>24</td>
</tr>
<tr>
<td>Age</td>
<td>35.9 ± 11.0</td>
<td>35.1 ± 10.8</td>
<td>37.2 ± 11.7</td>
<td>34.0 ± 8.9</td>
</tr>
<tr>
<td>Gender</td>
<td>69 M</td>
<td>27 M</td>
<td>32 M</td>
<td>10 M</td>
</tr>
</tbody>
</table>
Result:

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

Analog of “Insistence on Sameness” / Meltdowns in ASD?
Dimensional predictors of response to SRI pharmacotherapy in obsessive–compulsive disorder

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

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

Protocol
• Fluox. or Placebo x 8 wk / 4 week “washout” / Fluox. or Placebo x 8 wk
• Mean dose 9.9 mg / d ( +/- 4.4 mg)
• Children's Yale-Brown Obsessive-Compulsion Scale (CY-BOCS)
• Clinical Global Improvement Scale-Autistic Disorder (CGI-AD)
• Fluoxetine Side Effects Checklist (FSEC)
Fluoxetine was superior to placebo in the treatment of repetitive behaviors by CY-BOCS (linear trend x treatment interaction $z=-2.075$, SE=0.407, $p=0.038$)
A Placebo Controlled Crossover Trial of Liquid Fluoxetine on Repetitive Behaviors in Childhood and Adolescent Autism


Fluoxetine was marginally superior to placebo on the improvement of the CGI change scores ($z=-1.907$, $SE=0.703$, $p=0.056$)
Fluoxetine did not significantly differ from placebo on treatment emergent side effects

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

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

Abnormal regulation of attention
- (Perseveration)
- (Inattention)

Routines & Stereotypies

Cognitive Rigidity

Agitation & Aggression
- SIB

Abnormal Sensory Processing

Abnormal regulation of sleep

Abnormal regulation of arousal

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Regulation of Attention

Attend to stimulus #1

Shift

Attend to stimulus #2
Abnormal Regulation of Attention - 1

- **Perseveration**
  - Inability to “Let go and shift”
  - Gets “stuck”
  - “Overattention Deficit Disorder”

- **Compounds the effects of cognitive rigidity**
Abnormal regulation of arousal

Abnormal regulation of attention
- Perseveration
- Inattention

Cognitive Rigidity

Routines Stereotypies

Abnormal Sensory Processing

Agitation Aggression
- SIB

Abnormal regulation of sleep

Abnormal regulation of arousal

↑ (Perseveration)
- Abnormal regulation of attention

↓ (Inattention)
Perseveration
“Draw a picture of your family” – Typical 4 year old
“Draw a picture of your family” – 8 yr old with ASD
Abnormal Regulation of Attention (Perseveration)

• **Interventions**
  – Verbal preparation for transitions
  – Visual Schedules
  – SSRIs (OCD: Proven; ASD: likely)
Abnormal regulation of arousal

Abnormal regulation of attention
- (Perseveration)
- (Inattention)

Cognitive Rigidity

Routines Stereotypies

Abnormal regulation of sleep

Abnormal Sensory Processing

Agitation Aggression
- SIB

Rigid + Perseverative

SSRIs

↑ (Perseveration)
Abnormal regulation of attention
↓ (Inattention)

Abnormal regulation of arousal

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Abnormal Regulation of Attention - 2

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

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

Abnormal regulation of attention
- Perseveration
- Inattention

Cognitive Rigidity

Routines Stereotypies

Abnormal Sensory Processing

Agitation Aggression
- SIB

Impulsivity Hyperactivity
- Stimulants
- α-2 agonists

Abnormal regulation of sleep

Abnormal regulation of arousal

↑ (Perseveration)
Abnormal regulation of attention
↓ (Inattention)

Impulsive

Rigid + Perseverative
Stimulants
(Dopaminergic; Sympathomimetic)

Stress ➔ Dopamine ➔ Adrenaline (Epinephrine) ➔ Noradrenaline (Norepinephrine) ➔ "Fight or Flight"

Re-Uptake

- Attention
- Arousal
- Agitation
- Aggression

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Dopaminergic Drugs

Atomoxetine

Stimulants

Stress → Dopamine → Adrenaline (Epinephrine) → Noradrenaline (Norepinephrine) → Re-Uptake

C

Attention
Arousal
Agitation
Aggression
Dopamine promoting (dopaminergic) drugs

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

<table>
<thead>
<tr>
<th>Generic Name(s)</th>
<th>Brand Name(s)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td></td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>Dxedrine, Dextrostat</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Dextroamphetamine + amphetamine</td>
<td>Adderall</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>Concerta, Ritalin, Metadate</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Dexamethylphenidate</td>
<td>Focalin</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Atomoxetine, Attentin</td>
<td>Strattera</td>
<td>Norepinephrine reuptake Inhibitor (NRI), not FDA Schedule II</td>
</tr>
</tbody>
</table>

Inattention

- Beware of anxiety or perseveration masquerading as inattention
  - Perseveration on inner stimuli: “Inattentive”
  - Perfectionism: “Problems w. task completion”
  - Anxiety: “Rushes through work”
# Alpha-2 Agonists

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

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Alpha-2 Agonists

• Alpha-2 agonists (guanfacine, clonidine) stimulate autoreceptors on the 1st neuron, inhibiting release of dopamine & norepinephrine

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References
(alpha-2 agonists)

Regulation of Arousal

Hypoarousal
• Lethargic

Calm & Relaxed

Fight or Flight Response
“Red Alert”
➡️ Adrenaline
➡️ Heart Rate
➡️ Resp. Rate
• Combative

Heart Rate
resp. Rate
Abnormal regulation of arousal

Abnormal regulation of attention
- Perseveration
- Inattention

Cognitive Rigidity

Routines Stereotypies

Abnormal Sensory Processing

Agitation Aggression
- SIB
- Atypical neuroleptics
- \( \alpha \)-2 agonists
- GABA-ergic drugs

Impulsivity Hyperactivity

\( \uparrow \) (Perseveration)
- Abnormal regulation of attention
\( \downarrow \) (Inattention)

\( \uparrow \) (Hyper-arousal)

Abnormal regulation of arousal

\( \downarrow \) (Hypo-arousal)

Impulsive
- Agitated / Disruptive

Rigid
- Perseverative

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Dopamine antagonists

Stress → Dopamine → Adrenaline (Epinephrine) → Noradrenaline (Norepinephrine)

Atypical neuroleptics: D₂ receptor blockade

α-2-adrenergics: inhibit release of noradrenaline

Re-Uptake

Attention
Arousal
Agitation
Aggression
Atypical Neuroleptics

- Atypical neuroleptics block D2 receptors

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### Atypical Neuroleptics

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>Abilify</td>
<td>Relatively less risk of weight gain</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozaril</td>
<td>Causes bone marrow suppression</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Zyprexa</td>
<td>Greater risk of weight gain</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Seroquel</td>
<td>Greater sedation</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Risperdal</td>
<td>• Greater risk of weight gain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Approved by FDA for treatment of agitation in children with ASD</td>
</tr>
<tr>
<td>Ziprazidone</td>
<td>Geodon</td>
<td>Relatively less risk of weight gain</td>
</tr>
</tbody>
</table>
References
(neuroleptics, AEDs, GABA)

Regulation of Sleep - 1

- **Melatonin**
  - Brain hormone
  - \(\downarrow\) Metabolic rate (Heart, Temp)
  - “You’re sleepy now”

- **Suppressed by light**
  - 24 hr cycle
  - Seasonal cycle
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
Abnormal regulation of arousal

Abnormal regulation of attention
- Perseveration
- Inattention

Cognitive Rigidity

Abnormal regulation of sleep
- Hypo-arousal
- Hyper-arousal

Routines Stereotypies

Agitation Aggression
- Atypical neuroleptics
- α-2 agonists
- SIB

Disordered Sleep
- Abnormal regulation of sleep
- Melatonin

Impulsivity Hyperactivity
- Stimulants
- α-2 agonists

Impulsive + Agitated / Disruptive

Rigid + Perseverative

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References
(Melatonin)

Abnormal regulation of arousal

Abnormal regulation of attention

Abnormal regulation of sleep

Abnormal Sensory Processing

Cognitive Rigidity
Sensory Processing

- **Subjective Properties**
  - Familiar / Unfamiliar
  - Pleasant / Unpleasant
  - Strong / Weak
  - Internal / External

- **Sensory Input ➔ Self-awareness**

- **Mirror Neurons ➔ Empathy**

Abnormal regulation of arousal

Abnormal regulation of attention
- Perseveration
- Inattention

Cognitive Rigidity

Abnormal regulation of sleep

Abnormal Sensory Processing
- Sensory Threshold

Sensory Dysfunction

Abnormal sensory processing

Agitation
- Impulsivity
- Hyperactivity

Impulsive / Disruptive

Routines
- Stereotypies

Sensory Overload

Melatonin

Atypical neuroleptics

α-2 agonists

Opiate antagonists

Rigid

Disordered Sleep

Agitation
- SIB

+ Impulsive

+ Disruptive

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The whole is greater than the sum of its parts

Max Wertheimer
Abnormal regulation of arousal

Abnormal regulation of attention
- Perseveration
- Inattention

Cognitive Rigidity

Sensory Processing
- Sensory Threshold
  - Hypo-arousal
  - Hyper-arousal

Sensory Overload

Agitation, Aggression
- SIB
  - Atypical neuroleptics
  - $\alpha$-2 agonists

Sensory-Seeking

Routines, Stereotypies

Impulsivity, Hyperactivity
- Stimulants
  - $\alpha$-2 agonists

Disordered Sleep
- Abnormal regulation of sleep
  - Melatonin

Rigid, Perseverative

Impulsive, Agitated / Disruptive

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Summary

**Why this child?**

- **Extrinsic factors:**
  - Functional behavioral assessment (Escape, access, attention)
  - Family assessment (Are mom & dad in synch?)

- **Intrinsic factors**
  - Developmental Level (stage-appropriate behavior)
  - Cognitive Rigidity, Dysregulation of attention, arousal, sleep, or sensory processing

**Family & Behavioral Intervention – Usually**

**Medication: Sometimes**
Summary

Directions for future research:

• **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**
Thank you
Stimuli

- **Internal stimuli**
  - Hunger
  - Thirst
  - Pain
  - Other...

- **External Stimuli**
  - Physical
    - Light, sound, touch, etc.
  - Social
    - Reinforcers (Positive & Negative)
    - Aversives
Behavioral Symptoms in ASD

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

Symptoms
- Routines, Stereotypies
- Perseveration / Inattention
- Agitation / Lethargy
- Insomnia
- Sensory seeking / avoidance
Abnormal regulation of arousal

Abnormal regulation of attention
- (Perseveration)
- (Inattention)

Cognitive Rigidity

Abnormal regulation of sleep

Abnormal regulation of arousal
- (Hypoarousal)
- (Hypoarousal)

↑ Sensory Threshold

↓ Sensory Threshold

Abnormal Sensory Processing

↑ Sensory Threshold

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Neurotransmitters

Dopamine
- Brain
  - Movement (Striatum)
  - Cognition (Cortex)
  - Emotion (Limbic System)
  - Endocrine (Hypothalamus, Pituitary)

Norepinephrine
- Brain:
  - Arousal (RAS)
  - Sleep/Wake
  - Working memory
  - Reward
- Sympathetic Nervous System:
  - Fight or Flight
    - Energy from glucose, fat
    - Heart Rate
    - Blood Pressure
    - Sweating
    - Dilated pupils

Epinephrine
- Brain: Role?
- Adrenal Glands
  - Fight or Flight

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Neurotransmitters

5-HT=Serotonin; DA=Dopamine; NE=Norepinephrine
SN=Substantia Nigra; VTA=Ventral Tegmentum; AN=Arcuate Nucleus; LC=Locus Ceruleus

Receptor Classes: D1.....D5
- Movement (Striatum / Basal Ganglia)
- Cognition, (Cortex)
- Emotion (Limbic system)
- Endocrine (Hypothalamus, Pituitary)

Receptor Classes: α1, 2; β1, 2, 3
- Arousal
- Sleep / Wake
- Working memory

Sympathetic Nervous System: Fight or Flight response

Epinephrine (Adrenaline) → Adrenal glands

Cerebral Cortex → Cerebellum
SN → VTA → AN
LC

Brainstem → Spinal cord

5-HT producing cells
Serotonin: The master neurotransmitter

Receptor Classes: D1,...,D5
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- Epinephrine (Adrenaline)
- Adrenal glands

Brainstem
- Cerebral Cortex
- Cerebellum
- SN VTA AN
- 5-HT producing cells
- LC
- Spinal cord

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Serotonin: The master neurotransmitter

Re-Uptake (SERT)

\[ \text{Serotonin (5-HT)} \rightarrow \text{C} \]

\[ \text{Release} \]

\[ \text{Melatonin} \]

Emotional regulation & numerous other actions