“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”

“Internalizing” Behavior

- Anxiety
- Depression
- Obsessiveness / Rigidity
- Perfectionism

“Externalizing” Behavior

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

• External / Social:
  – 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 great the strengthening or weakening of the bond”

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”*

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)

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 in public
- Over-correction
  - Must wash out soiled diaper (then discard)
  - If the child spills milk on purpose: child must mop the entire kitchen floor

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>Reward</th>
<th>Fees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good Day</td>
<td>0</td>
</tr>
<tr>
<td>Sleeping</td>
<td>4</td>
</tr>
<tr>
<td>Reading</td>
<td>10</td>
</tr>
<tr>
<td>Memory Tasks</td>
<td>20</td>
</tr>
<tr>
<td>Abnormal Sleep</td>
<td>30</td>
</tr>
<tr>
<td>Calm Down</td>
<td>35</td>
</tr>
<tr>
<td>Walking Dog</td>
<td>40</td>
</tr>
<tr>
<td>Drive Train</td>
<td>45</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 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

Neuropsychological Deficits in Persons with ASD

- Abnormal Sensory Processing
- Abnormal regulation of sleep
- Cognitive Rigidity
- Abnormal regulation of attention
- Abnormal regulation of arousal

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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. Fam Hx: GAD

Depression

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

Cognitive Rigidity

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

When My Worries Get Too Big!
A Relaxation Book for Children Who Struggle with Anxiety
Written and Illustrated by Karl Dunn Buron
Foreword by Brenda Smith Myles
The Incredible 5-Point Scale

SSRIs in ASDs

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

• “Downstream” benefit:
  – ▼ Disruptive Behavior
  – ▲ Quality of Life

Neurotransmitters

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

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"

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."

Pharmacotherapy for anxiety disorders in children and adolescents

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

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

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 p=2.075, SE=0.407, pR=0.038)
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/hemorrhage</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 sensory processing

Abnormal regulation of sleep

Rigidity

Perseveration

Abnormal regulation of attention

Attn shifting

Regulation of Attention

Attend to stimulus #1  ➔  Shift  ➔  Attend to stimulus #2

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Abnormal Regulation of Attention - 1

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

---

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 Attention - 2

- Inattention
  - Inability to focus
  - Impulsive
  - Distractable

Inattention

- Interventions
  - Limited stimuli
  - Short work periods
  - Medication
    - Stimulants, NRIs (may ↑ anxiety / rigidity / agitation)
    - α-2 agonists

Stimulants, NRIs

(Dopaminergic; Sympathomimetic)

Dopaminergic Drugs

SSRIs

Abnormal Regulation of Attention - 2

- Inattention
  - Inability to focus
  - Impulsive
  - Distractable

Inattention

- Interventions
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  - Short work periods
  - Medication
    - Stimulants, NRIs (may ↑ anxiety / rigidity / agitation)
    - α-2 agonists

Stimulants, NRIs

(Dopaminergic; Sympathomimetic)

Dopaminergic Drugs

SSRIs
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>Dexedrine, 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>Dexmethylphenidate</td>
<td>Focalin</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Atomoxetine, Attention</td>
<td>Strattera</td>
<td>Norepinephrine reuptake inhibitor (NRI), not FDA Schedule II</td>
</tr>
</tbody>
</table>

References (Stimulants)


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>

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

Atypical Neuroleptics

- Atypical neuroleptics block D2 receptors

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>
</tbody>
</table>
| Risperidone   | Risperdal  | - Greater risk of weight gain  
|               |            | - Approved by FDA for treatment of agitation in children with ASD  
|               |            | - Generic available |
| Ziprazidone   | Geodon     | Relatively less risk of weight gain |

References
(neuroleptics, AEDs, GABA)


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

References

(Melatonin)

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

Disordered Sleep

Sensory Dysfunction

Rigidity + Perseverative

Agitation Aggression SIB

Sensory Overload

Impulsivity Hyperactivity

Impulsive + Agitated / Disruptive

The whole is greater than the sum of its parts
Max Wertheimer

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 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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