AUTISM SPECTRUM DISORDER: EVIDENCE BASED TREATMENTS

Michelle M. Macias, MD, FAAP
Developmental-Behavioral Pediatrics
Medical University of South Carolina

Ashley Belt, M.Ed., BCBA
Board Certified Behavior Analyst
Lowcountry Autism Foundation
DISCLOSURES

- In the past 12 months, we have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.

- Dr. Macias does intend to discuss an unapproved/investigative use of a commercial product/device in the presentation, which will be disclosed at the time of discussion.
Learning Objectives

▸ Relate the current scientific support for educational, behavioral, and medical intervention strategies for youth with autism spectrum disorder.
Treatment Objectives

- Primary treatments are developmental and behavioral therapies.

- Decide what you are treating!
  - Core ASD Symptoms?
    - Social Reciprocity
    - Repetitive and restrictive behaviors ("RRB")
  - Coexisting Conditions?
    - Challenging/disruptive behaviors
    - Affective Disorders
    - Sleep disturbances
    - Seizure disorders
    - Others (GI, feeding problems)
What do we mean by “Evidence”?

- Factors to look for in a study:
  - Homogeneous case definition
  - Consistent dosing of product with consistent content
  - Valid outcome measure
  - Appropriate sample size
  - Placebo group
  - Double blind

- Hierarchy of evidence
  - Randomized, double blind placebo controlled prospective trial
  - Cohort studies
  - Case control studies
  - Case series
  - Retrospective data analysis
  - Anecdotal report

Grade BMJ, 2004
Power of the placebo

- Positive expectancy
- Participation affects caregiver behavior
  - Therapeutic impact of research participation
  - Parents looking for positive responses to a new treatment may be engaging their children in more activities to determine response
  - Sandler (2010) – Placebo as treatment for ADHD
Some Reviews that Grade the Evidence for Therapies for ASD:


Educational and Behavioral Interventions

- **ASD specific symptoms**
  - Communication, social relatedness, RRB

- **Coexisting developmental/learning problems**
  - Cognitive/adaptive, academic

- **Behavioral Challenges**
Approaches to Treatment

- Educational/Behavioral Interventions
  - Early Intervention programs
  - Intensive Behavioral Approaches: ABA, DTT, EIBI
  - Developmental models: DIR, Floortime, Denver
  - Integrated models: TEACCH, Denver, SCERTS
  - Speech and language therapy
  - Occupational therapy
  - Social skills instruction
Educational Interventions

Characteristics of successful models:

▸ Early, intensive, individualized
▸ Teach adaptive skills
▸ Work on generalizing and maintaining skills
▸ Address behavioral treatment
▸ Provide inclusion with supports
▸ Provide objective monitoring
Behavioral Interventions

- Applied Behavioral Analysis (ABA)
  - Discrete Trial Training (DTT)
  - Natural Environment Teaching (NET)
  - Errorless Learning
- Early Intensive Behavioral Intervention (EIBI)

- Teach new skills by breaking down into elements and reinforcing
  - Differential reinforcement of other behavior
  - Differential reinforcement of communication
  - Token economy
Developmental Interventions

- DIR™/Floortime™: Developmental, Individual Difference, Relationship Based
- Relationship-Development intervention (RDI)

*focus on teaching social communication, cognitive skills, emotional relationships*
Integrated Programs

- TEACCH: Treatment and Education of Autistic and Communication related handicapped Children
- ESDM: Early Start Denver Model
- SCERTS: Social Communication, Emotional Regulation, Transactional support
Speech-Language Therapy

- Designed to improve understanding of communication, use language effectively
- Includes:
  - Social communication interventions
    - Can include parent-mediated intervention
  - Picture Exchange Communication Systems (PECS)
  - Signing
Social Skills Instruction

- Both traditional and newer naturalistic behavioral strategies to teach social skills
- Joint attention training
- Social skills group interventions
- Peer mediated social intervention
Autism Spectrum Disorder Pharmacotherapy

- Goal is to reduce challenging behaviors and improve response to behavioral and educational interventions.
- Psychotropic medication use in ASD is common.
  - Frequency: studies range from 35-64%
  - Consistent findings: ↑ use with older age, presence of intellectual disability or psychiatric co-morbidity, Southern US
  - Stimulants, alpha$_2$ agonists, atypical antipsychotics, and SSRIs most common (depends on age).
Autism Spectrum Disorder Pharmacotherapy

- NO medications approved for core symptoms
- Medications often used to treat related sx, such as depression, anxiety, and aggression
- Stimulants, long acting alpha₂ agonists approved for ADHD
- Risperidone and aripiprazole are FDA approved for irritability
- Anxiety: only duloxetine FDA approved (others only for OCD)
- Depression: fluoxetine, escitalopram FDA approved
- Individuals with autism are often very sensitive to adverse effects (as are children with other disabilities), even at low doses.
Identify Target Symptoms

- ADHD type sx → Stimulants, ATX, alpha agonists
- Maladaptive behaviors/Aggression/Irritability → Stimulants, atypical antipsychotics
- Anxiety, depression → SSRIs, atypical antidepressants
- Repetitive behaviors and rigidity (OCD) → SSRIs, clomipramine
ADHD symptoms (Inattention, Hyperactivity)

- **Stimulants:**
  - 50% response rate (MPH), ES 0.29-0.54, greater improvement at higher doses
  - May benefit social communication, self-regulation
  - Side effects similar to youth without ASD, but more frequent (18% vs 3.5% dropout)

- **Alpha agonists:**
  - Guanfacine: 3 studies (RCT, open-label, retrospective) - effective in ↓ behavioral sx, response rates 27-50%.
  - Clonidine: 2 positive small crossover trials

- **Atomoxetine:** 2 studies (RCT) → improvement in ADHD sx

- **Risperidone:** ↓ hyperactivity, supported by open label and RCT
Treatment for Aggression: Systematic Review

- Antipsychotics have the largest efficacy for aggression (Effect Size for aggression 0.72)
- Stimulants have the next largest mean effect size (ES 0.60)
  - Both methylphenidate and amphetamines
- Mood stabilizers: highly varied results, largely inpatient studies (ES 0.47)
  - Lithium best (ES 0.63) and carbamazepine worst (ES 0.06)
  - 1 outpatient study with valproate, inferior to placebo (ES 0.13)
Aggression, Maladaptive/problem behaviors

- Antipsychotics have the largest efficacy for aggression (Effect Size for aggression 0.72)
  - Stimulants have the next largest mean effect size (ES 0.60) if ADHD sx present (MPH, AMPH)
- Risperidone, aripiprazole: Clinically significant improvement in irritability, self-injurious behavior
- Marginal evidence for benefit with other atypical antipsychotics, antiseizure drugs, psychostimulants (if no ADHD), naltrexone
- Alpha-2 agonists (clonidine) and N-acetylcysteine → some improvement, fewer SE than AA in small studies.
Antipsychotics: Evidence of Effect

- Various RCT of risperidone and aripiprazole

**Clinically significant improvement** in: irritability, hyperactivity

**Inconsistent** improvement in: anxiety, RRB, social withdrawal

**No improvements** in: social relatedness, communication/language, sensory problems

- 2009 RUPP study: risperidone + parent training superior to risperidone alone
Repetitive behaviors and rigidity

- Selective Serotonin Reuptake Inhibitors (SSRIs) use based on similarity between repetitive behaviors of ASD and symptoms of OCD.
  - Best evidence is for fluoxetine (Hollander 2005)
  - Negative citalopram study (STAART 2009), but used for anxiety
  - Negative fluvoxamine study (2000)
- Clomipramine (seratonin selective TCA): inconsistent findings (better for OCD).
- Buspirone (anxiolytic, partial serotonin agonist): improved ADOS RRB score (2.5 mg BID)*
- Valproate: positive small RCT (2005)

*Are repetitive behaviors in ASD fundamentally different from behaviors in OCD?*

*Chugani et al. J Pediatr 2016*
<table>
<thead>
<tr>
<th>Agent</th>
<th>Targeted symptom(s)</th>
<th>Potential adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atypical antipsychotic agents</strong> (e.g., risperidone*, aripiprazole*, olanzapine)</td>
<td>Aggression</td>
<td>Weight gain</td>
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<tr>
<td></td>
<td>Hyperactivity/inattention</td>
<td>Metabolic syndrome</td>
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<td></td>
<td>Repetitive behavior</td>
<td>Tardive dyskinesia</td>
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<td></td>
<td>Sleep disturbance</td>
<td>Extrapyramidal symptoms</td>
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<td>Increased salivation</td>
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<td></td>
<td>Sedation</td>
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<tr>
<td><strong>Stimulants</strong> (e.g., methylphenidate, dextroamphetamine, dexmethastrimide)</td>
<td>Hyperactivity/inattention/impulsivity</td>
<td>Decreased appetite</td>
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<td>Difficulty falling asleep</td>
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<td></td>
<td>Irritability</td>
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<td></td>
<td>Social withdrawal</td>
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<td><strong>Selective serotonin reuptake inhibitors</strong> (e.g., fluoxetine, fluvoxamine, sertraline, paroxetine, etc)</td>
<td>Aggression</td>
<td>Potential increased risk of suicidal ideation</td>
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<tr>
<td></td>
<td>Anxiety</td>
<td>Behavioral activation</td>
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<td></td>
<td>Depression</td>
<td>Imoritality</td>
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<td>Repetitive behavior</td>
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<td><strong>Alpha-2-adrenergic agonists</strong> (e.g., guanfacine, clonidine)</td>
<td>Aggression</td>
<td>Sedation</td>
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<td></td>
<td>Hyperactivity/inattention</td>
<td>Fatigue</td>
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<td>Sleep disturbance</td>
<td>Irritability</td>
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<td>Constipation</td>
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<td>Hypotension</td>
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<td>Rebound hypertension if discontinued abruptly</td>
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<td><strong>Anticonvulsant mood stabilizers</strong> (e.g., lamotrigine)</td>
<td>Aggression</td>
<td>Mood lability</td>
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<tr>
<td></td>
<td>Hyperactivity/inattention</td>
<td>Fatigue</td>
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<td>Repetitive behaviors</td>
<td>Insomnia</td>
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<td>Sleep disturbance</td>
<td>Diarrhea</td>
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<td></td>
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<td>Weight gain</td>
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<tr>
<td></td>
<td></td>
<td>Increased appetite</td>
</tr>
<tr>
<td><strong>Atomoxetine</strong></td>
<td>Hyperactivity/inattention</td>
<td>Potential increased risk of suicidal ideation</td>
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<td></td>
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<td>Irritability</td>
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<td></td>
<td></td>
<td>Gastrointestinal symptoms</td>
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<td></td>
<td></td>
<td>Fatigue</td>
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<tr>
<td><strong>Melatonin</strong></td>
<td>Sleep disturbance</td>
<td>Difficulty waking</td>
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<td></td>
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<td>Daytime sleepiness</td>
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<tr>
<td><strong>Mood stabilizer</strong> (e.g., lithium)</td>
<td>Aggression</td>
<td>Weight gain</td>
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<tr>
<td></td>
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<td>Nausea</td>
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<td>Frequent urination</td>
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* Approved by the US Food and Drug Administration for the treatment of aggression and irritability in children with autism spectrum disorders.

Data from:
Sleep

- Sleep problems are highly prevalent in ASD (44-83%)
  - Evidence of abnormal melatonin regulation in ASD
- Sleep hygiene, behavioral management 1\(^{st}\) line
- Limited data to support diphenhydramine, clonidine (small + study)
- Melatonin
  - Clinical studies have shown some benefit
  - Meta-analysis: \( \uparrow \) duration by 73 min, \( \downarrow \) sleep onset latency by 66 min
  - Recommendations: start with 0.5, \( \uparrow \) max 10 mg 1 hr before bedtime
- Iron
  - Some data suggest low serum ferritin levels may contribute to symptoms of restless sleep
ABA: Learning Objectives

- Basic principles of ABA
- Behavior and why it happens
- Quick tips of the trade
Applied Behavior Analysis (ABA)

“The science in which tactics derived from the principles of behavior are applied to improve socially significant behavior and experimentation is used to identify the variables responsible for improvement in behavior.” Cooper, Heron & Heward, 2007

First and foremost, ABA is a science and a discipline devoted to understanding and improving human behavior.
Know your ABCs

- **Antecedent**: what happened before the behavior occurred? (i.e.: working independently in a quiet space; “sit down”)
- **Behavior**: what was the individual doing? (i.e.: hitting, biting, kicking, ran away, flop, crying with tears, etc.)
- **Consequence**: How did you respond to the behavior? (i.e.: redirect, gave preferred item, first/then, continued to say “sit down”, provided prompts, etc.)

<table>
<thead>
<tr>
<th>Antecedents</th>
<th>Behavior</th>
<th>Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bag of chips on the table</td>
<td>“Chips”</td>
<td>Mom hands the child the bag of chips</td>
</tr>
<tr>
<td>Touched a client with the flu</td>
<td>Wash hands with warm water and soap</td>
<td>Germs removed from hands</td>
</tr>
</tbody>
</table>
Reinforcement and punishment

- **Reinforcement**: A stimuli that comes after a behavior and increases the future likelihood of that behavior reoccurring.

- **Punishment**: A stimuli that comes after a behavior and decreases the future likelihood of that behavior reoccurring.

- Naturally occurring
- Individualized
# Reinforcement and Punishment

<table>
<thead>
<tr>
<th>Positive (+) think of adding</th>
<th>Reinforcement</th>
<th>Punishment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A preferred item/activity is GIVEN after the behavior, making the behavior more likely to reoccur.</td>
<td>An aversive stimulus is GIVEN after the behavior, making the behavior less likely to reoccur.</td>
<td></td>
</tr>
<tr>
<td>Negative (-) think of subtraction</td>
<td>An aversive stimulus is REMOVED after the behavior, making the behavior more likely to reoccur.</td>
<td>A preferred item/activity is REMOVED after the behavior, making the behavior less likely to reoccur.</td>
</tr>
</tbody>
</table>
Bribery

- *Bribery is giving the child something during the problem behavior.*

- For example, you are taking your child to the grocery store and he/she begins to scream. The bribe would be saying, “If you stop crying, I will get you a candy bar.” The child stops screaming. Did it really work?
Motivation

▸ Why we do what we do

▸ This can affect what stimuli acts as a reinforcer

▸ We can manipulate motivation by using two basic ABA principles:
  ‣ Satiation
  ‣ Deprivation
Extinction

- *Previously reinforced responses that are no longer reinforced*
  - *Vending machine*
- Extinction bursts
- Spontaneous recovery
Define the behavior

- Make it measurable, observable and clear
  - My definition and your definition of a behavior can be very different
- Prioritize
  - focus on one or two behaviors at a time
- Collect baseline data (scatterplot; time sampling, frequency, duration)
Functions of behavior

- Sensory
- Escape/Avoidance
- Attention
- Tangible

Multiple functions are more than likely occurring
The Mand

- *The component of communication that teaches the child the meaning of communication*
  - It motivates the child to communicate
- *Everyone communicates, even individuals without communication systems.*
- *How do you teach?*
  - Start with teaching only a couple of requests at first.
    - Items and activities (go, up, banana, etc.)
      - Avoid teaching generalized requests (more, eat, etc.)
  - Requests should be easy and effortless for the child (gesture toward preferred item, one worded responses, etc.)
  - Teach using the child’s favorite item/activity, but know that this item/activity should only be given to the child once he/she has made that request for the item/activity.
  - Put those items that the child is requesting for somewhere out of reach in order to motivate the child to make those requests.
Demands

- **Simple, clear and to the point**
  ("shoes")

- **Prompt (hand over hand, gesture, model, visual cues)** more challenging tasks

- **Be careful of wording**

  - "Are you ready to clean up?"

- **Only place demands if you expect follow through.**

  - Don’t tell a child to clean up, if in the end you are the one cleaning up the mess.
Visual schedules

- **Daily Visual Schedules** (activities that will occur that day)
- **Activity Visual Schedules** (typically related to a behavior chain (i.e. steps to brushing teeth, getting dressed, etc.))
- Schedule preferred activities to go after non-preferred activities rather than the other way around. For instance, first the child must brush his/her teeth, then play on the iPad.
Transitions

- Use a “promise reinforcer” during transitions from preferred to non-preferred activities
Give choices

- *Choices help motivate the child to follow through with the initial direction*

- *YOU are in control of what choices are given*
  - Should we wear the green or blue shirt today?
  - Did you want French fries or Cheetos with your sandwich?

- *There will be times when a choice is not available (going to school, the doctor, etc.)*
Visual timers

- Help prep for a transition
- 1 minute, 30 seconds, 10 seconds
- might cause more anxiety in the individual
  - remove the timer altogether or limit the warning to just one 10 second timer
Be proactive

- **provide frequent attention**
  - Set a timer that goes off every 30 minutes or an hour to prompt you to provide attention (you are playing so nicely, wow, look at you!)
    - The more frequent, the better
    - MotivAider, Repeat Timer (app store)

- **make tasks easy by providing assistance**

- **sensory diet – consult with the child’s OT if applicable**

- **teach communication skills**
Make a trade

▶ **Telling the child “no” or “not right now”**
  ▸ “No, you can’t have French fries right now, but you can have Cheetos or Cheez-Its?”

▶ **Giving up preferred items/activities**
  ▸ “We are all done swinging, but we can go down the slide or jump on the trampoline.”

▶ **Having to wait**
  ▸ “The French fries are not ready, let’s go watch Mickey Mouse while we wait!”
Change your reaction

- **Be careful with your reactions to problem behavior**
  - Avoid too much eye contact and extra verbiage ("It will be okay," "Calm down")
  - Instead use non-vocal cues
- **Be consistent with your reactions**
  - Avoid threats
Survival mode...

- *If you know that you cannot wait the behavior out, then reinforce quickly.*
  - *It’s better to come to a decision quickly and consider what you can handle that day*

- *Think back to extinction…*
  - The quicker we can reinforce the behavior, the less likely the child will learn to engage in that problem behavior for a long duration or even engage in additional, harmful problem behavior.

- *It reinforces the quick, more accepting problem behavior (crying, whining, etc.)*
One last tip…

▸ Give yourself a break and take it one day at a time.

▸ “A failure is not always a mistake, it may simply be the best one can do under the circumstances. The real mistake is to stop trying.”

B.F. Skinner
Resources

- [http://www.pattan.net/Videos/](http://www.pattan.net/Videos/)  
  - ABA Training Videos  
    - Search via parent, teacher, or therapist
- [https://www.marybarbera.com](https://www.marybarbera.com)  
  - Parent training (currently a wait list)
- [http://www.behaviorbabe.com](http://www.behaviorbabe.com)  
  - More about ABA
- [http://www.iloveaba.com/p/free-resources.html](http://www.iloveaba.com/p/free-resources.html)
Resources, continued

- AAP: http://www.aap.org/cocwd
- Autism Speaks: http://autismspeaks.org
- CDC: http://www.cdc.gov/ncbddd/autism/index.html
- http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143565.htm
- http://nccam.nih.gov/
- http://www.aap.org/healthtopics/complementarymedicine.cfm
- http://www.aap.org/sections/chim/ClinicianResources.html
- http://autism.healingthresholds.com/
Selected References


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