Psychotropic Medication Review

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When to try medication?

- After all other behavioral and environmental interventions have been tried
- Cannot treat social or communication deficits with medication- educational and behavioral interventions are the mainstays of treatment
- But may be useful to treat specific symptoms and comorbid conditions such as attention problems and mood disorders

It is important to establish the function of behavior

Behavior = Communication !!!

- To obtain something
- To seek attention
- Avoidance
- Escape: behavior (e.g. tantrum) serves to remove a demand placed on the child

Why use psychotropic medication for children with ASDs?

- Anxiety
- Depression, irritability and volatile mood
- Stereotypies and perseveration
- Hyperactivity/impulsivity
- Inattentiveness/distractibility
- Aggression
- Self-injurious behavior
- Sleep disorders

Medication is not a life sentence

- Medication trials should be long enough to see if there is a positive, negative, or no effect -the time needed depends on the medication
- Generally a low-dose is tried first and gradually increased
- If response is not optimal after an adequate trial, a different medication should be tried

Monitoring response to medication

- Identify specific target symptoms
- Important to track changes from baseline, by gathering data before and after the medication is started
- Important to not make more than one change at once
- Gather information from multiple sources if possible
- May be helpful to use a visual representation (eg thermometer) for emotion or mood
- A child may be more eloquent using media other than verbal expression (eg writing or drawing)

Anxiety

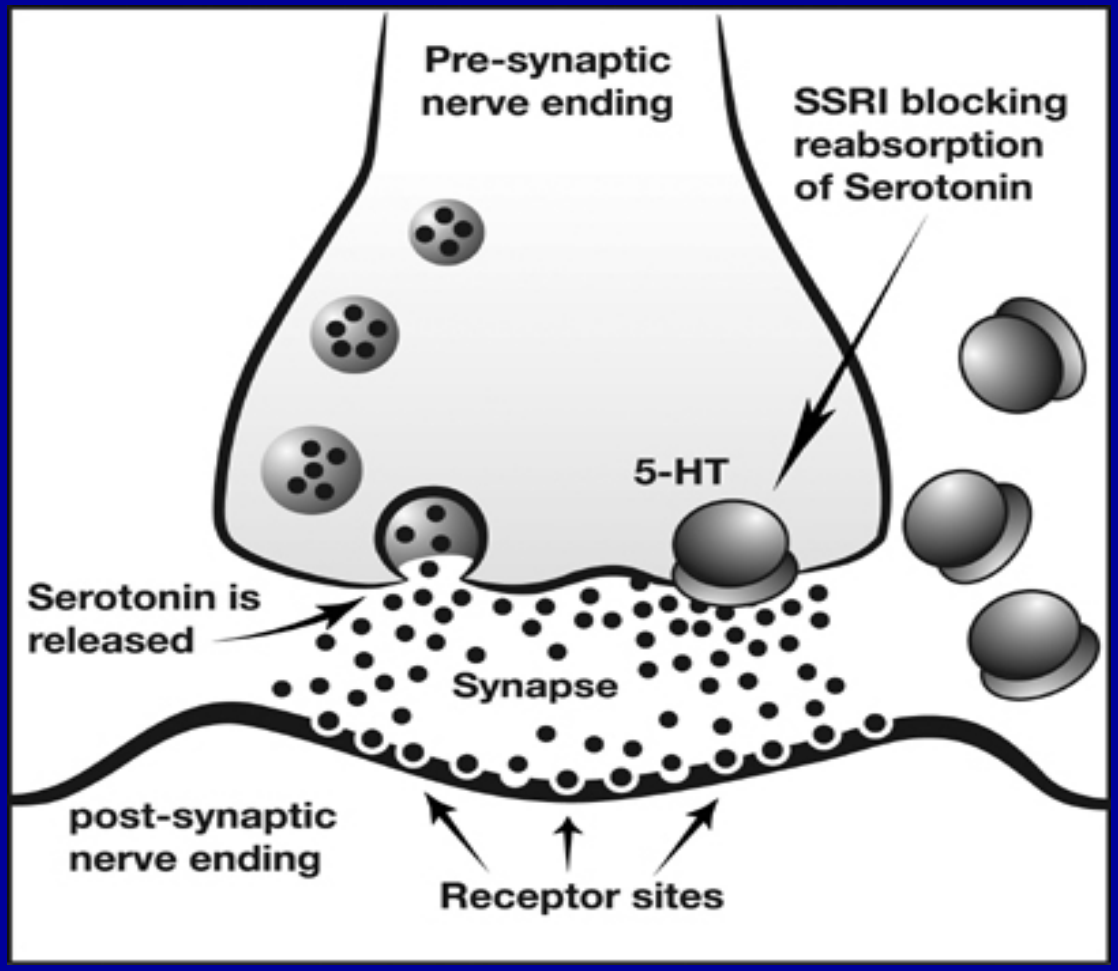
- Children with ASDs generally prefer predictability, and can be quite rigid, with high levels of anxiety
- Causes of anxiety
  - Change in routine
  - Not getting a demand met
  - Sensory overload
  - Social situations
  - Specific phobias: bugs, fire-alarms

Addressing anxiety

- Advance warning of upcoming events or schedule changes
  - Visual schedules
  - Social stories http://www.thegraycenter.org/
  - Sensory supports
- Allow downtime (? time for self-stim)
- Balance need for structure with practicing flexibility
- Cognitive Behavioral Therapy
- Omega 3 fatty acids
- Medication

Medication used for anxiety

- SSRIs (Selective Serotonin Uptake Inhibitors)
  - Most commonly used, non-addictive
  - Generally safe: side effects usually mild- most commonly include agitation, irritability, giddiness, increase impulsivity, appetite increase or decrease, sleep disruption, increased bruising and nose bleeds, increased urination
  - Concern about suicidal thinking is more in children with depression, less problematic than originally thought but medications continue to have a “Black Box Warning”
  - Serotonin Syndrome: rare, fever, rigidity, mental status changes, avoid concurrent DM cold medicine use (eg dextromethoraphan)


Pre-synaptic
nerve ending
SSRI blocking
reabsorption
of Serotonin
5-HT
Serotonin is
released
Synapse
post-synaptic
nerve ending
Receptor sites

SSRIs

- Fluoxetine (Prozac)-long-lasting, minimal chance of suicidal thinking
- Sertraline (Zoloft)
- Fluvoxamine (Luvox)
- Citalopram (Celexa)
- Venlafaxine (Effexor)
- Paroxetine (Paxil)- no longer recommended due to short duration of action leading to increased risk of suicidal thinking

Benzodiazepines

- Ativan (lorazepam)
- Klonopin (clonazepam)
- Valium (diazepam)

- Addictive potential limits use
- Useful on a short-term basis (eg dentist)
- Side effects: sedation, dizziness, mood changes, low blood pressure, respiratory depression

Depression and mood disorders

- Common in older and higher-functioning children- diagnosis can be difficult due to flat affect, little expression of emotion
- Consider family history
- Look for a change from baseline, or change in functioning
- Consider stressors
- Consider seasonal affective issues
- Counseling if higher-functioning
- Omega 3s
- Medication: SSRIs, wellbutrin, possibly tricylics or atypical neuroleptics

Stereotypies and repetitive behavior: behavioral intervention

- How “interfering” is the behavior?
- Functional assessment
- For physical stereotypies: label the behavior, teach a replacement behavior, give hand fidget, reinforce alternative behavior or decreased target behavior
- For sameness behaviors: build variation into daily schedule
- CBT (Cognitive-Behavioral Therapy): exposure and response-prevention, for higher-functioning children

Obsessive compulsive disorder versus autism

- Compulsive behavior in OCD is driven by obsessions: eg fear of germs, need to check locks, while repetitive behaviors in autism are more automatic and unconscious
- People with OCD feel distressed by their obsessions (though less true in children) while people with ASDs may find comfort in their repetitive behaviors
- Counting, touching and sameness behaviors are more common with ASDs, while washing and checking are more common in OCD

Medication for stereotypies

- SSRIs are often used – may be more helpful if the behavior seems anxiety-driven, and if there are broader anxiety issues
- Study results are mixed- some showed improvement in global functioning and in symptoms associated with anxiety and repetitive behaviors. Side effects were generally mild, but increased activation and agitation occurred in some subjects. Some did not show benefit over placebo (eg for Celexa in 2009)

Overactive, impulsive, inattentive, and distractible behavior

- Over half of children with ASDs have ADHD symptoms
- Impairment in functioning (academic, activities of daily living, social, safety) may be due in part to ADHD symptoms and executive dysfunction, as well as to autism
- If possible, should have ADHD assessment with standardized questionnaires (eg Conners or Vanderbilt) esp. if higher functioning
- Need to consider context of behavior- may not be paying attention because has no interest in topic…hyperactivity may be sensory in nature

ADHD: DSM-IV Criteria

Inattention: 6 or more symptoms for at least 6 months to a degree that is maladaptive and inconsistent with developmental level

- Poor attention to details, makes careless mistakes
- Difficulty sustaining attention to tasks or play
- Does not seem to listen
- Does not follow through on instructions, fails to finish tasks
- Difficulty organizing tasks and activities
- Avoids or dislikes tasks that require sustained mental effort
- Loses things
- Easily distracted by extraneous stimuli
- Forgetful in daily activities

DSM-IV Criteria (continued)

Hyperactivity-impulsivity: 6 or more symptoms for at least 6 months to a degree that is maladaptive and inconsistent with developmental level

HYPERACTIVITY

- **Fidgets or squirms**
- **Leaves seat in classroom**
- **Runs about or climbs excessively**
- **Difficulty playing quietly**
- **"On the go"**
  or as if "driven by a motor"
- **Talks excessively**

IMPULSIVITY

- **Blurts out answers**
- **Difficulty waiting turn**
- **Interrupts or intrudes on others**

DSM-IV Subtypes of ADHD

- Predominantly Inattentive Type
  - At least 6 of 9 symptoms
- Predominantly Hyperactive-Impulsive Type- At least 6 of 9 symptoms
- Combined Type- 6 or more symptoms each of hyperactivity and inattention

DSM-IV Criteria (continued)

- Symptoms must be present before age seven years (some debate about this)
- Symptoms must be present in two or more settings
- There must be clinically significant impairment in social, academic or occupational functioning

There is often impairment in executive function

- Sustaining and shifting attention
- Inhibition of inappropriate behavioral or emotional responses
- Working memory
- Time perception
- Foresight and planning
- Ability to flexibly switch among problem-solving strategies
- Emotional control
- Maintaining appropriate activation and arousal
- Self-monitoring

Treatment of ADHD symptoms in children with ASDs

- Consider classroom placement/supports
- Consider sleep patterns
- Treat as would any child with ADHD
- Collect data before and after starting medication from teachers (Clinical Attention Problem Scales- www.dpeds.org under Screening and Assessment)
- Best evidence for stimulants, Strattera, risperidone, and alpha-agonists

Medications available for ADHD

- Stimulants
  - Ritalin, Concerta, Metadate (methylphenidate)
  - Focalin (dexmethylphenidate)
  - Dextrostat, Dexedrine (dextroamphetamine)
  - Adderall (mixed amphetamine salts)
  - Vyvanse
- Alpha agonists
  - Tenex (guanfacine)
  - Clonidine
- Selective Norepinephrine Reuptake Inhibitor: Atomoxetine (Strattera)
- Others: Wellbutrin, tricyclic antidepressants, atypical neuroleptics, Provigil, amantadine

Psycho-stimulants

- Work by blocking re-uptake of dopamine at the synapse
- In recent studies of psychostimulants, around 50% of children with ASDs and ADHD symptoms showed positive clinical responses (lower than non-autistic children with ADHD)
- Overall, there may be a decreased response rate and increased chance of side effects compared to children with ADHD without autism
- Start with stimulants unless contraindications

  (glaucoma, substance abuse, poor growth)
- Several medication and dose changes may be needed
- Start low and titrate up to good effect
- Consider starting on a weekend (so can see effect/side effects)

Types of stimulants

Methylphenidate-based

- Short-acting (3 to 5 hours):
  - Methylin (tablet, solution, chewable tablet), Ritalin
- Longer-acting (8 to 10 hours):
  - Generic: methylphenidate SR or Methylin ER
  - Metadate ER, Metadate CD: biphasic release (30% initial release)
  - Ritalin LA: biphasic release (50% initial release)
- Longest acting:
  - Concerta: Duration 10 to 12 hours;
- Daytrana patch: put on in the morning, 12 hour duration when worn for 9 hours, can cause skin irritation

Methylphenidate (continued)

- Focalin (dexmethylphenidate): purified right-handed form of methylphenidate so twice as strong (so use lower dose). Duration 3-4 hours
- Focalin XR: Duration 8 to 10 hours

Amphetamine-based

- **Dexedrine/Dextrostat** (dextroamphetamine): Duration 3-4 hrs
- **Dexedrine Spansules**, Duration = 6-8 hrs
- Adderall (mixed salt amphetamine), 4 to 6 hours
- **Adderall XR,** 10 to 12 hours
- Monitor fruit juice, vitamin C and acidic food intake with Dexedrine, Adderall – can reduce efficacy
- **Vyvanse** (lisdexamfetamine dimesylate), 10-12 hours, acidity of food does not matter

Stimulant use: positive effects (data from typically-developing children)

- Most powerful effects are on core symptoms of ADHD and social and classroom behavior, more modest effects on intelligence & achievement test scores
- Improvements shown in:
  - Inattention, impulsivity, hyperactivity
  - Impulsive aggression
  - Noncompliance
  - Social interactions and peer relations
  - Short-term memory, verbal and non-verbal learning, vigilance and reaction time.
  - Academic efficiency and academic accuracy
- Protective effects shown against the development of anxiety and mood disorders, disruptive behavior and grade retention

Stimulant use: side effects

Side effects of stimulants

- Appetite suppression
- Sleep disruption
- Headaches and stomach aches
- Tics (1% to 3% transiently)
- Irritability and sadness (up to 20%)
- Mild elevations of Heart rate and blood pressure
- Theoretic lowering of seizure threshold, but several studies have shown no worsening of seizures by stimulant use in children with well-controlled seizure disorders

Stimulant use: side effects

- Possible effect on growth: especially during the first 1 to 2 years of treatment, may be catch-up growth later- study results are mixed. Important to monitor growth.
- Rebound effect usually 4 to 6 hours after administration (for short-acting)
  - Always consider when symptoms occur in relation to administration

Cardiac Risk of Stimulants:
Conclusions of FDA Pediatric Psychopharm. Advisory Panel (2006)

- No increased risk of sudden death in healthy patients with ADHD treated with stimulants
- Risk for sudden death in children with preexisting structural cardiac abnormalities, treated with stimulants for ADHD, is lower than risk posed by strenuous exercise
- Screen for cardiac symptoms like fainting or palpitations; and family history of cardiac rhythm problems. EKG and Cardiology eval if concerns.
- Careful use of stimulants is possible in the context of structural, rhythmic or blood pressure concerns

Other non-stimulant ADHD medications

Atomoxetine (Strattera)

- Works best for children with anxiety and ADHD. Lasts 24 hours
- Less effect on appetite and sleep than stimulants.
- Can cause emotionality and irritability
- Side effects are common: mood swings, irritability, anorexia (14%), headache, stomach upset, constipation, dizziness, sleepiness

Guanfacine (Tenex)

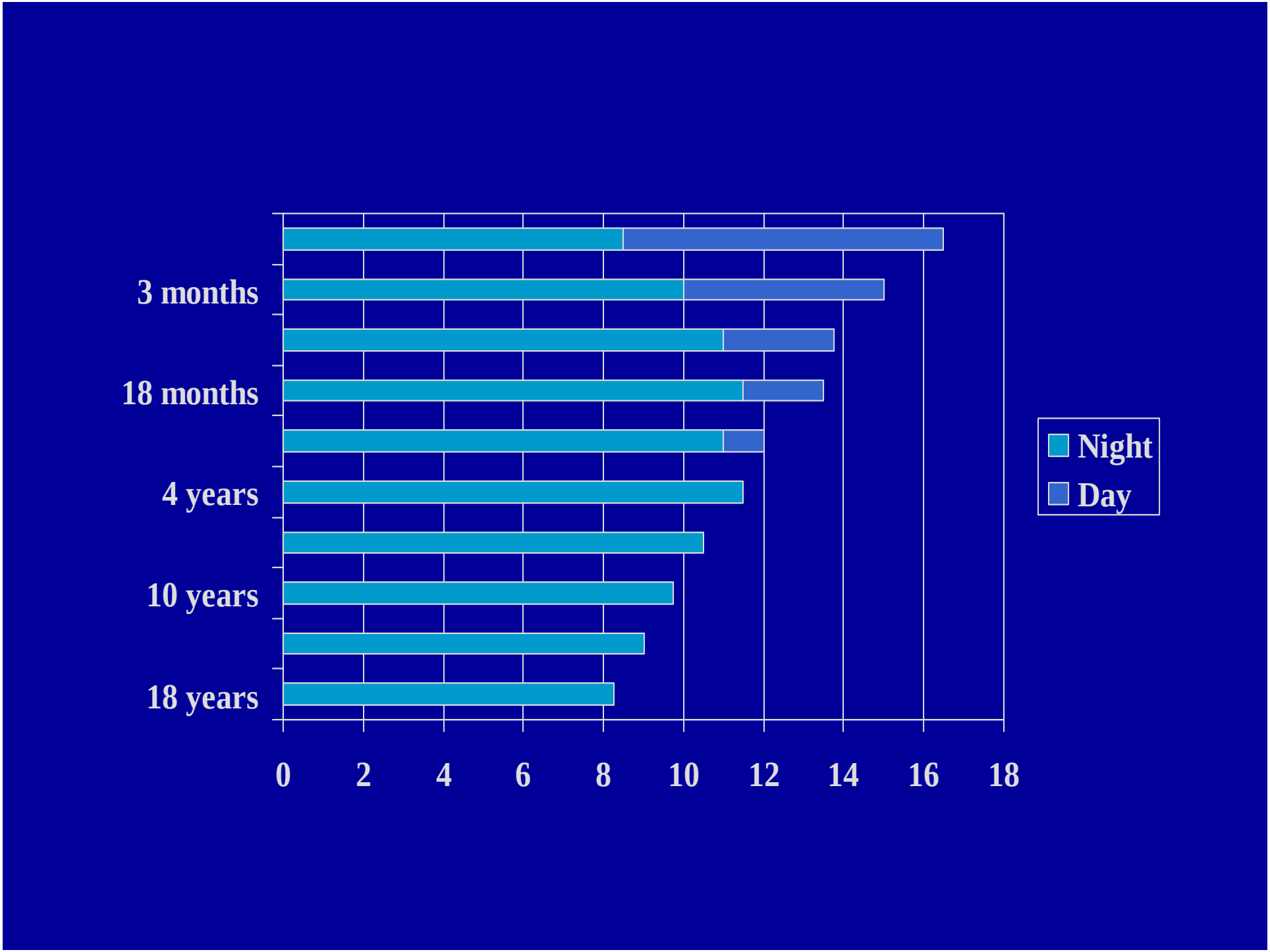
- Side effect: low blood pressure, dizziness, headache, **sedation**, sleep disruption, constipation, stomach ache' nausea, decreased appetite, dry mouth
- Can improve hyperactivity, impulsivity, aggression, inattention, cognition, social behavior and tics
- May not see full effect until 4-6 week after starting
- Useful as an adjunct to stimulants for afternoon use, or if there is problematic appetite suppression on stimulants
- **Intuniv**: new long-acting form of guanfacine, lasts 24 hours, not covered by MaineCare

Clonidine

- Similar to guanfacine, but has more side effects, chiefly sedation, so is used more for sleep than for daytime symptoms
- Useful for ADHD with comorbid tic disorders, PTSD, aggression or difficulty sleeping
- Side effects: constipation, sleepiness, low , hypotension, bradycardia, weight gain, irritability, depression, nightmares, dry mouth

Sleep

- Studies vary but between 53-78% of children with an ASD present with sleep issues
- This compares to 26-32% for typically developing children
- Not a clear association to having a co-morbid diagnosis of an intellectual disability
- Increased incidence is by parent report but has also been confirmed in studies using actigraphy and polysomnography


3 months
18 months
4 years
10 years
18 years
0
2
4
6
8
10
12
14
16
18
Night
Day

Most common sleep issues in ASD

- Sleep onset
- Sleep maintenance
  - Children with ASDs tend to not wake more frequently than typically developing children but are awake for longer (up to 2-3 hours) and engage in more disruptive behavior at that time
  - Remember part of sleep maintenance is based on social cues
- Sleep duration
- Can be worsened or caused by less than ideal bedtime routines or bedtime associations so need to consider standard sleep hygiene recommendations first

Melatonin

- Melatonin is a neurohormone whose major role is to organize circadian physiology- particularly sleep-wake cycle and core body temperature rhythms
- Primarily regulated by light/dark but meals and social cues may reinforce this effect
- May also be a true genetic difference in the secretion of Melatonin in patients with ASDs

Melatonin

- May be helpful for children with a true circadian rhythm disturbance but behavioral explanations and strategies should be attempted first
- Dosing 0.5 mg-3 mg
  - Lower dosing may be more effective
  - 2 actions of sedating and adjusting clock so may take up to 2 weeks to fully trial a dose
  - Theoretical side effects of effect on puberty and decreased sz threshold but actually tolerated in actual use

Other for sleep

- Valerian Root
  - Studies mixed on effectiveness, dosing somewhat unclear, most studies side effects similar to placebo
- Clonidine
  - Typically 0.05 mg to 0.2 mg
  - Primarily for difficulties falling asleep- may get rebound waking
- Benedryl (Diphenhydramine)
  - 12.5-25 mg, sometimes used short term to regulate sleep and work on sleep hygiene
  - Side effects- for some children opposite effect, nausea, vomiting, blurred vision

Self-injurious behavior (SIB)

- Lack of environmental stimulation (boredom)
- Reinforced by social attention, access to preferred items, or avoidance or escape from undesired activities
- May provide sensory input (provide endogenous endorphins)

How to approach SIB

- Functional assessment: description of the behavior, situations in which the behavior is most and least likely to occur, antecedents, and consequences
- **Reinforcement**: appropriate behavior is reinforced, SIB is ignored
- **Extinction:** no longer providing reinforcement for a response that was previously reinforced (eg planned ignoring)
- **Protective equipment**: can serve as extinction for sensory input
- **Functional communication training**
- **Punishment**: time out, water mist, restraint
- **Medication**: atypical neuroleptics (risperidone), SSRIs, clonidine, ?naltrexone

Risperidone in autism

- Risperidone is approved for treatment of irritability associated with ASD in children ages 5 to 16 years
- 2 well-designed short-term (8 week) studies showed significant improvements in irritability, stereotypy, social withdrawal, lethargy, hyperactivity and noncompliance.
- Benefits were maintained up to 6 months, with improvements in adaptive functioning (communication, daily living and social skills)

Risperidone:adverse effects

- Increased appetite and Obesity
  - Weight gain can be 20 or 30 lbs
  - Risk of increased cholesterol and blood sugar
- Sleepiness
- Constipation
- Increased salivation or dry mouth
- Movement disorders
  - Tremor vs. dystonia vs. tardive dyskinesia

Other atypical neuroleptics

- Aripriprazole (Abilify) and ziprasidone (Geodon) have shown promise in small trials of patients with ASDs
- Limited clinical trial experience failed to support quetiapine (Seroquel) or clozapine. Limited data for olanzapine.
- Other side effects:
  - **Abilify: Risk of activation or agitation approx 25%**
  - **Geodon: risk of arrythmias**

Other medications

- Buproprion (Wellbutrin)
  - Studies show mixed results for ADHD, can help depression
  - Weaker effects than stimulants
  - Adverse effects: seizures (0.4%) , tics, rash, insomnia, increased urination
  - Start with Wellbutrin 75mg, ½ tab bid, to tid, then Wellbutrin XL 150
- Tricyclic antidepressants
  - 15 studies showing efficacy. Especially useful for ADHD with comorbid depression or enuresis
  - Side effects: cardiac conduction effects, interval prolongation, seizures, sedation, weight gain, anxiety, irritability, overdose risk. EKGs essential.