Starting Early:
Promoting emotional and behavioral well-being in early childhood

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Partnership Access Line

Disclosures

• No conflicts of interest
Background

• 25% lifetime prevalence of mental or behavioral disorders worldwide (WHO 2001)

• ~1 in 5 children under the age of 18 in the US have a diagnosable mental illness (Report of the Surgeon General 1999)
  • Only ~25% receive treatment

• Up to 10% of children 2-5 demonstrate mental health impairment (Egger HL and Angold A JCPP 2006)

Prevalence
Accessing Evidence-based Treatments

• Poor dissemination
• Complicated health-care systems
• Workforce shortages
  • Rates utilization unknown
  • As of 2012, 8300 child psychiatrists serving 15 million children (AACAP 2013)
  • <1000 developmental pediatricians, avg wait >6mos. (Jimenez J Dev Behav Pediatr 2017)

Ages 0-5: A unique opportunity

• A period of rapid brain changes
• Radical cognitive, linguistic, motor and socioemotional development
• Frequent encounters with health professionals
Evidence-based treatments do exist

• Ages 0-3
  • Family-centered parent-child (dyadic) treatment
  • NO studies of safety/efficacy of psychopharmacological treatments for infants and toddlers

• Ages 4-5
  • Family-centered parent-child (dyadic) treatment
  • Medications*
Prenatal Maternal Mental Health

- >50% postnatal depression begins prior to birth
  - Pregnancy complications
  - Non-live birth
  - Low birthweight
  - Preterm Birth
  - Increased risk of child mental health concerns.

Prenatal Maternal Mental Health: Specific Conditions

- Depression
- Severe Anxiety
- Bipolar Disorder
- Schizophrenia
- Eating Disorders
- Substance Use Disorders
Prenatal Maternal Depression and Anxiety

- Cognitive Deficits
- Mood
- Anxiety
- Behavioral difficulties in childhood, adolescence, adulthood (Stein A et al. Lancet 2014)
- Paternal psychological distress associated with behavioral and emotional difficulties in offspring at 36 mos (Kvalevaag AL et al. Pediatrics 2013)

Prenatal Environmental Factors

- Alcohol exposure
  - Growth retardation, characteristic facies, developmental delays, both externalizing and externalizing symptoms (Behnke et al. Pediatrics 2013)
- Illicit Substances
  - Behavioral problems, developmental delay (Behnke et al. Pediatrics 2013)
- Smoking
  - ADHD, Conduct Problems (Joelsson P et al. BMC Psych 2016)
Prenatal Environmental Factors

• Maternal Stress
  • Dysregulation of the HPA axis in offspring incl. altered infant cortisol and higher resting cortisol in adolescents (Lewis AJ et al. BMC Medicine 2014)

• Diet
  • High intake of highly processed foods during pregnancy predicts externalizing problems at age 5 (Jacka FN et al. JAACAP 2013)
Year 1

- Infant–caregiver dyad becomes primary focus
- Infant development of internal models of relationships

Postnatal Period

- Assess for psychosocial adversity
  - Food Insecurity
  - Community Violence
  - Home environment
- AAP recommends universal screening for maternal depression
  - Patient Health Questionnaire-2
  - Edinburgh Postnatal Depression Screen
Postpartum Depression

- “Baby Blues” common
  - Present in first month
  - Typically resolve without formal treatment
- Severe/prolonged symptoms may reflect postpartum depression
  - Up to 10% of mothers during first 3 months (Earls MF Pediatrics 2013)
  - Can present initially as anxiety
  - Reassurance, referral (OB, PCP, Psychiatrist)
  - Delusions, paranoia, hallucinations, mania?
    - **MEDICAL EMERGENCY**

Year 1: Social-emotional Milestones

- 3 months: social smile
- 7-9 months: focused attachment behaviors
  - Selective comfort seeking from primary caregiver
    - Physical Exam
    - Immunizations
  - Separation distress
  - Stranger anxiety
“EBCD”

• Explore the environment
• Build relationships
• Cultivate development
• Develop parent confidence

Year 1: An opportunity to intervene

• Use the well child visit to reinforce nurturing caregiving through positive feedback
• Concerned about parent-child relationship?
  • Referral to adult mental health provider
  • Referral to infant-parent mental health provider
<table>
<thead>
<tr>
<th>Evidence based treatments</th>
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<tbody>
<tr>
<td><strong>Nurse Family Partnership</strong></td>
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<tr>
<td>• 28 wks gestation – 24 mos.</td>
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<tr>
<td>• Home nursing visits beginning in pregnancy</td>
</tr>
<tr>
<td>• Improved well-being, academics, health, decreased risk-taking behaviors</td>
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<tr>
<td><strong>Parents as Teachers</strong></td>
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<tr>
<td>• 0-5 yrs</td>
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<tr>
<td>• Home visiting program by parents for parents</td>
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<tr>
<td>• Improved cognitive development, school readiness, 3rd grade achievement</td>
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<tr>
<td><strong>Video Interaction Project</strong></td>
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<tr>
<td>• 0-36 mos</td>
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<tr>
<td>• Videotaped review of 5 min parent-child interaction as part of well-child visit</td>
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<tr>
<td>• Improved interaction quality, cognitive devel, decreased stress</td>
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<tr>
<td><strong>Video Interaction for Positive Parenting</strong></td>
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<tr>
<td>• 12-36 mos</td>
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<tr>
<td>• 5 session in-home intervention with video review, coaching</td>
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<tr>
<td>• Increased maternal sensitivity, secure attachment rates</td>
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**Evidence based treatments, cont’d**

| **Attachment Biobehavioral Catchup** |
| • 0-48 mos |
| • Foster parent intervention |
| • Increased secure attachment rates, normalization of diurnal cortisol release patterns. |
| **Infant Parent Psychotherapy** |
| • 12-36 mos |
| • Dyadic treatment for families who have experienced trauma |
| • Increased rates secure attachment. Decreased trauma sx, behavioral problems. |

Olds D 2010
Mendelsohn AL et al. J Dev Behav Pedia. 2007
• Expanded opportunities to promote well-being and identify children at risk
• Observe how the child organizes their feelings when stressed
  • “Attachment Behaviors”
Toddlerhood

Circle of Security®
Parent Attending To The Child’s Needs

Attachment Theory

- John Bowlby (1907-1990)
- Mary Ainsworth (1913-1999)
  - The Strange Situation Procedure (SSP) (Ainsworth MD Child Dev 1970)

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HOSPITAL • RESEARCH • FOUNDATION
The Strange Situation

https://www.youtube.com/watch?v=QTsewNHUHU
Attachment Styles

• Secure (~60%) (Ainsworth MD Child Dev 1970)
• Insecure (~40%) (Ainsworth MD Child Dev 1970)
  • Insecure-ambivalent
  • Insecure-avoidant
• Disorganized

• Research classification, NOT DISORDER

Attachment Disorders

• Reactive Attachment Disorder
  – Inhibited, withdrawn toward caregivers
  – Persistent social and emotional disturbance
  – CONTEXT: Extremes of insufficient care
    • Rare: 10% of those with severe early neglect
• Disinhibited Social Engagement Disorder
  – Inappropriately interacts with unfamiliar adults
  – Tends to be clinically stable over time
    • Rare: 20% of those with severe early neglect

Why is this important?

- Children with insecure/disorganized attachment can have problems regulating emotions and understanding mental states of others later in life
- Associated with circumstances in which parent cannot adequately attend to child’s needs
  - Postpartum depression, substance abuse, mental illness, trauma/loss, institutionalization

Tips for well-child visit

- Impractical and unsafe to attempt SSP in the office
- Observe for warning signs, refer if overt
- Ensure that all possible measures being taken to support consistent, loving caregiving.
- Refer parent for mental health treatment if indicated
- “Catch the child being good.”
- Suggest pleasant one on one activities
Evidence based treatments

- **Video Interaction for Positive Parenting**
  - 12-36 mos
  - 5 session in-home intervention with video review, coaching
  - Increased maternal sensitivity, secure attachment rates

- **Attachment Biobehavioral Catchup**
  - 0-48 mos
  - Foster parent intervention
  - Increased secure attachment rates, normalization of diurnal cortisol release patterns.

- **Infant Parent Psychotherapy**
  - 12-36 mos
  - Dyadic treatment for families who have experienced trauma
  - Increased rates secure attachment. Decreased trauma sxss, behavioral problems.

- **Mothers Toddlers Program**
  - 12-36 mos
  - Dyadic treatment for substance-involved mothers and child
  - Improved mentalization capacity, attachment-based caregiving.

- **Circle of Security**
  - 13-88 mos
  - Combines group process approach with video review
  - Increased rates secure attachment, changes in externalizing/internalizing behaviors, caregiver mentalization.


Autism Spectrum Disorder

- Signs emerge in the second year of life
  - Delay in language
  - Delay in social reciprocity

- DSM-5 Diagnosis
  - Social communication impairments
  - Restrictive, repetitive patterns of behavior

- ~1 in 68 children in the US (Developmental Disabilities Monitoring Network Surveillance Year. 2014)
ASD: What to do if you suspect

• Slam dunk? Make the diagnosis!
• Unclear? Refer for formal evaluation (ADOS)
  • Long waits
• Encourage parent to apply for DDA services
  • Age 0-3: Developmental Delay
  • Age 4+: Dx, onset prior to 3, Adaptive fn <69, FSIQ<84
• Applied Behavior Analysis
• Speech Therapy
• Occupational Therapy

Behavioral Problems

• Developmentally appropriate
  • “Terrible 2s” (and 3s)
• Parent Psychoeducation
• Encourage “positive parenting practices”
Positive Parenting

- Positive reinforcement for positive behaviors
  - Specific praise
  - Smiling/high-fiving
  - Describing what the child did that was pleasing
  - “Time in”
- Avoidance of positive attention for negative behaviors
  - Active ignoring (as long as behaviors not unsafe)
- Consequences
  - Immediate, and consistent!
  - Delivered in neutral tone
  - Time out
    - Quiet, non-distracting, non-entertaining space
    - 1 min per year of life

Evidence based treatments

<table>
<thead>
<tr>
<th>Program</th>
<th>Age/Typology</th>
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<tr>
<td>New Forest</td>
<td>30-77 mos, Children with ADHD</td>
</tr>
<tr>
<td>Incredible Years</td>
<td>3-8 yrs, Children with CD, ODD, ADHD</td>
</tr>
<tr>
<td>Triple P</td>
<td>36-48 mos, Children at high risk with parental concerns about behavioral difficulties, Online version (2-9y)</td>
</tr>
<tr>
<td>Parent Child Interaction Therapy (PCIT)</td>
<td>2-7 yrs, Children with clinical level disruptive behavior symptoms</td>
</tr>
<tr>
<td>Helping the Noncompliant Child</td>
<td>3-8 yrs, Children with noncompliant behaviors</td>
</tr>
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Other things to watch for in toddlers

• Anxiety
• Severe Inhibition
• Symptoms associated with trauma exposure

• Helpful Screeners:
  • Ages and Stages: Social Emotional (2-60mos)
  • Brief Early Childhood Screening Assessment (18-60mos)
  • Baby-Pediatric Symptom Checklist (0-18 mos)
Preschool: social-emotional milestones

- Seeks to please friends
- Engages in fantasy play
- More likely to agree to rules
- Enjoys singing/dancing/acting
- More independent

Preschool: 3-5yrs

- Emotional and behavioral impairments emerge with slightly greater fidelity
  - Autism Spectrum Disorder
  - Oppositional Defiant Disorder
  - Attention-Deficit/Hyperactivity Disorder
  - Posttraumatic Stress Disorder
  - Major Depressive Disorder
  - Anxiety Disorders
  - Sleep Disorders

Preschool ADHD Treatment Study (PATS)

- NIMH funded multi-center randomized crossover efficacy trial
- 3-5.5 yo with severe ADHD unresponsive to 10 week parent training intervention
- 37/279 patient parents said behavioral treatment resulted in satisfactory improvement.

Source: Greenhill et al. JAACAP 2006.

PATS continued

- Stimulants generally effective
  - N= 147
  - Effect size = 0.4-0.8
  - Optimal dose ranges 2.5mg PO BID – 7.5mg TID
- Lower doses provided better balance of benefits and side effects
- Lower response rates compared to older children
  - ES in MTA (7-9 y/o) = 0.5-1.3
- Higher rates of side effects
  - 30% incidence; 8% dropped out due to SEs, vs 4% in MTA.

Sources: Greenhill et al. JAACAP 2006, MTA Cooperative Group Arch Gen Psychiatry 1999.
ADHD diagnosis is stable over time - 89.9% still meeting diagnostic criteria

Patients with comorbid ODD or conduct disorder had higher rates of ADHD.

Girls experienced a steeper symptom decline (but girls’ baseline symptoms more severe).

Some indication of long-term benefit based on parent ratings

PATS at 6 years


Atomoxetine

• 5-6 y/o
• 8 week double blind placebo-controlled RCT, N = 101
• ADHD-IV ratings improved, ES = 0.6-0.8.
• No significant difference on CGI measures
• 25-33% experienced significant side effects.

Kratochvil CJ et al 2011
Anything else?

- **No** other large studies of safety or efficacy of psychopharmacological treatments for children under 6.
- Risperidone has FDA approval down to 5 for irritability and aggression in autism.
- Adderall and Dexedrine have FDA approval down to age 3, but tend to be less well tolerated than methylphenidates.
- In 2014, over 100,000 atypical antipsychotic and antidepressant rx written for children under 3 y/o in the US.

Summary

- Parental mental illness and psychosocial adversity are early risk factors
- Early assessment of parent-child relationship is important
- Early intervention should focus on improving the parent-child relationship
- Data supporting the use of psychiatric medications in children under 6 is limited.
Questions?

PARTNERSHIP ACCESS LINE
866-599-PALS (7257)
Monday-Friday, 8am-5pm
www.seattlechildrens.org/PAL

Break: 10 minutes
Suicidality in Primary Care

Nick Weiss, M.D.
April 28, 2018

Disclosures

- Dr. Weiss is a Partnership Access Line consultant. He also works in private practice and on the Seattle Children’s Hospital Psychiatry and Behavioral Medicine Unit (PBMU).
- He has no financial conflicts of interest to report.
Epidemiology

Suicidal Ideation, Suicidality, Self-Harm

Suicide Rates for Teens Aged 15-19
Self-Harm

- Lifetime prevalence for non-suicidal self-injury in the United States has been reported as 21.2-28%.
Suicide Completion Rates

- Ages 5 to 11: 1 per 1 million
- Ages 10-14: 1 per 100,000
- Ages 15-19: 7-8 per 100,000

Means of Completed Suicide

- Hanging and Firearms >90%
- Overdose ~7%
- Other Means (Cutting) <3%
Self-Harm Is Associated with Elevated Suicide Completion Risk

Predisposing Risk Factors for Suicide

- Psychiatric disorders
- Substance use disorders
- Previous suicide attempt or self-harm
- Family history of suicide attempts (5x) and completion
- History of physical or sexual abuse
- Impulsivity
- Social isolation
- Male
- White or Native American
Precipitating Factors

• Interpersonal problems: breakups and family fights
• Disciplinary problems
• Bullying
• Profound loss
• Access to means
• Alcohol and drug use
• Exposure to suicide

Screening
1. In the past few weeks have you wished you were dead?
2. In the past few weeks have you felt that you or your family would be better off if you were dead?
3. In the past week have you been having thoughts of killing yourself?
4. Have you ever tried to kill yourself?
5. Are you having thoughts of killing yourself right now?
Brief Suicide Safety Assessment

1. Praise patient
2. Consider measures (PHQ-9, SCARED, CRAFFT 2.0)
3. Interview patient alone & with caregiver(s)
4. Assess protective factors
5. Make a safety plan
6. Determine disposition
7. Provide resources

SAFETY TRUMPS CONFIDENTIALITY

Ask Your Questions Directly

- “Are you having thoughts of killing yourself right now?”
- “Do you have a plan to kill yourself?”
- “What is your plan?”
- “If you were going to kill yourself, how would you do it?”
- “Have you ever tried to kill yourself?”
- “Did you want to die?”
Assessment Acronym: Is Path Warm

- Ideation
- Substance abuse
- Purposelessness
- Anxiety
- Trapped
- Hopelessness
- Withdrawal
- Anger
- Recklessness
- Mood changes

Intervention
High Risk: to ED

- Planned or recent attempt with a lethal method
- Attempt that included steps to avoid detection
- Inability to openly and honestly discuss suicide attempt and what precipitated it
- Inability to discuss safety planning
- Lack of alternatives for adequate monitoring and treatment
- Severe psychiatric disorders underlying suicidal ideation and behavior
- Agitation
- Impulsivity
- Severe hopelessness
- Poor social support

Lower Risk: Next Steps

- Validation, letting them know that you’ll help
- Inform appropriate people
- Brainstorming on coping skills, replacement behaviors
- Help family identify precipitants, begin problem solving, implement appropriate supervision
- Means reduction
- Safety planning
- Close follow-up
- Medications?
What is a Safety Plan?

- Written list of warning signs, coping strategies and resources developed collaboratively with the youth
- Includes contact information for social supports and professional supports
- Often includes reasons for living
- Many templates on-line
- “MY3” App
- NOT A NO HARM CONTRACT
Resources

- ASQ
  - Search: Ask Suicide Screening Questions
- AAP Guidance on Suicide and Suicide Attempts in Adolescents
  - Search: Suicide and Suicide Attempts in Adolescence
- National Suicide Prevention Lifeline: 800.273.TALK(8255)
- Safety Plan Template and Instructions:
  - Search: Developing Effective Safety Plans for Suicidal Youth
- 24/7 Crisis Text Line: Text “HOME” to 741-741
- County Crisis Line

Questions?
Break: 20 minutes

Psychotropic Medications for Challenging Behaviors and Co-occurring Psychiatric Disorders In Autism

David Camenisch, MD/MPH
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PAL Consultant
Objectives

- Epidemiology of co-occurring psychiatric disorders in ASD.
- Guidelines and strategies that guide pharmacotherapy for challenging behaviors related to autism and common co-occurring psychiatric disorders.
- Improve their knowledge base regarding use of medication for challenging behaviors and co-occurring psychiatric disorders in children with autism through review of the evidence base and case-examples.

Psychotropic Trends in ASD

- No medications are effective in treating core symptoms of ASD
- Medication are commonly used in ASD
  - 80% of adults
  - 45% of children (Aman et al. 2003)
- Use of medications increases with age
- Once medications are used, they are more commonly continued
- Polypharmacy is the rule, not the exception (Tsiouris, 2013)
- Atypical antipsychotics, SSRIs, and stimulants most commonly used (Esbensen et al. 2009)
General Considerations

• ASD is a neurodevelopmental “substrate” for other learning, behavioral and emotional challenges
  • enhances likelihood of co-occurring mental health conditions
  • influences effectiveness of “standard” medication treatments
  • Influences rates of side effects and pharmacokinetics

General Considerations (cont.)

• Atypical manifestations of mental and physical disorders in ASD population
  • Self-injury, irritability, aggression, bizarre movements and behaviors
  • Overlap of ASD features and symptoms of other mental health disorders often delays recognition and treatment of co-occurring conditions (Bakken, 2010)
Psychiatric Comorbidities in Autism

• **Intellectual Disability** – 31.6% (CDC)
• **Anxiety Disorders** – 50% (Rodgers J. Curr Dev Disorder Rep. 2018)
• **Depressive Disorder** –
  • 31% - primary care sample (Saqr et al. Autism. 2018)
  • 4X life-time risk (Hudson CC. Jrnl Abnl Child Psych. 2018)
• Bipolar Disorder
• ADHD
• **Disruptive Behavior Disorders**
• Psychotic Disorders – ASD is risk factor
  • Catatonia
• Obsessive-Compulsive Disorder

Presence of co-morbidities increases level of disability burden on families and healthcare expenditures.

In some cases, co-occurring psychiatric issues are responsible for the majority of the disability (e.g. higher functioning ASD and anxiety)

Contributes to high rates of psychotropic use in ASD – 80% of children with co-occurring diagnosis are on psychotropic medications
Symptom-driven versus diagnosis-driven treatment

- Core symptoms
  - Repetitive behaviors, restricted interests or activities (B.)
  - Social communication and social interaction deficits (A.)
- Common co-occurring behaviors
  - Irritability (aggression, tantrums, mood lability, SIB)
  - Hyperactivity
  - Sleep problems
  - Self-injury
- Common psychiatric co-morbidities
  - Anxiety
  - Depression
  - ADHD

Things to Think About When Considering Medications

- What is the potential risk or impact of behaviors? (harm to self, harm to others, loss of placement, etc.)
- What is the level of behavioral support available?
- Could medication support or augment other interventions?
- Are there psychiatric or medical co-morbidities that need to be considered?
- What is parental level of comfort?
- What is your level of comfort?
How does this distinction affect medical decision making?

- Helps set expectations for response to medication
- May influence timeline for treatment and follow-up
- In some cases, may impact dosing
- Important part of conversation about role of non-medication treatments
- Highlights importance of “active” medication management – no “set and forget it.”

Challenges in advancing psychopharmacology

- Lack of widely accepted diagnostic tools for co-occurring psychopathology (anxiety, psychosis)
- Difference of opinion on whether to focus on co-morbid diagnosis (anxiety, depression) OR symptoms domains (aggression)
- Debate about etiology of specific behaviors (e.g. repetitive behaviors)
Challenges in advancing psychopharmacology (cont.)

- Phenotypic and genotypic heterogeneity in ASD population
- High placebo response rates
- Logistical and financial challenges of multi-site trials
- Lack of validated and normed outcome measures

Repetitive Behaviors/Restricted Interests

- Core symptom of ASD (B. Criteria)
- Multiple etiologies (stereotypy, physical discomfort, anxiety, emotional distress)
- Tend to wax and wane
- Consider degree of impairment and level of distress
- More aggressive treatment indicated if involves self-injury
Medications and Repetitive Behaviors

• Risperidone
• Aripiprazole (Abilify)
• Valproic Acid/Divalproex sodium
• Selective serotonin re-uptake inhibitors (SSRIs) - citalopram, fluoxetine, clomipramine

Atypical Antipsychotic Medications

• Use of risperidone (Risperdal) and aripiprazole (Abilify) are supported by evidence and experience
• In foundational studies, improvement in RRBs was a secondary outcome measure
• It is hard to predict who will benefit – no predictive phenotype
Atypical Antipsychotic Medications (cont.)

- Improvement may through indirect mechanism (e.g. mediating hyperactivity, improvement in cognitive and/or behavioral rigidity, etc.)
- Improvement can be seen in other areas (adaptive functioning, hyperactivity, social withdrawal and communication) (Politte et al. 2014)

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Medications examined = citalopram, fluoxetine, fluvoxamine and clomipramine
- Not effective for repetitive behaviors (Cochrane, 2010)
- High rates of adverse events
- Meta-analysis found small but significant effect size disappeared with inclusion of unpublished studies. (Carrasco et al. Pediatrics. June 2012)
- SSRI use for co-occurring disorders that may manifest at repetitive behaviors (anxiety, OCD, depression) should be considered on case by case basis.
Case study: Wally

- 15 y/o
- ASD – severity level 3 (A. and B. criteria), w/ language impairment, w/ intellectual impairment
- Treatment targets = anxiety, repetitive self-injury, “impulsivity”
- Came to me on high dose sertraline and delayed release guanfacine (Intuniv) twice a day
- Parents did not want to consider an atypical antipsychotic
- RRBs waxed and waned
- With time, behavioral support and improved functional communication has done well

Social Withdrawal/communication

- Risperidone
- Naltrexone
- Lamotrigine
- Oxytocin
Oxytocin

- Insufficient evidence to recommend at this point
- Area of active research so stay tuned
- Timing and dose may important (e.g. impact on up/down regulation of OT receptors at critical times)
- Alternative ways of stimulating endogenous OT are being explored
- Response impacted by timing, gender, trauma, genetics and ??? vasopressin/DDAVP

Irritability

- Risperidone and aripiprazole
  - Best evidence (and FDA approval) for irritability not RRBs)
- Haloperidol
- Alpha-agonists *
- Olanzapine (side effects)
- Divalproex sodium/valproic acid
- Quetiapine
- Lamotrigine
**Risperidone (Risperdal)**

- FDA approval (2006) for irritability (not RRBs) in ASD
- 2 large DBRCTs (McCracken et al. NEJM 2002; Shea. Pediatrics 2004)
- Response rates 57-72% (Politte et al, 2014)
- Can also effective for reducing repetitive behaviors and hyperactivity
- Can see decreases in frequency and severity of episodes

**Risperidone (Risperdal) (cont)**

- Low dose (1-2 mg) is typically effective
- High rates of side effects - sedation, weight gain, hyperglycemia, dyslipidemia
- Periodic efforts to lower dose and stop should be part of ongoing care.
Aripiprazole (Abilify)

- FDA approval (2009) for irritability in ASD
- May also reduce repetitive behaviors
- Not as clearly effective in decreasing frequency of aggressive episodes
- Does not have clearly favorable metabolic side effect profile relative to risperidone (similar to risperidone in one head-to-head trial) (De Hert et al. Euro Psych 2011)

Aripiprazole (Abilify) (cont)

- Activation/aggression is more common as side effect versus risperidone
- Unique mechanism – partial D2 agonist; selective 5-HT1A agonist; 5-HT2A antagonist
- Weight gain more likely to be an issue in medication naïve, younger and higher baseline weight (Mankowski et al. J Child Adol Psychopharm. 2013)
Case study: Gavin

- 18 y/o
- ASD – Level 3 (x2), w/ language impairment, w/ intellectual impairment
- Treatment targets = aggression, sensitivity to sounds, behavioral rigidity
- Came to me on quetiapine and clonidine
- History of treatment with paroxetine
- Partial response to quetiapine
- He has done well with addition of very low dose of Haldol

Hyperactivity

- Risperidone, aripiprazole
- Methylphenidate
- Atomoxetine
- Alpha-agonists*
- Naltrexone
- Amphetamines
- Amantadine
Methylphenidate

- Good evidence of benefit for hyperactivity in children with ASD (RUPP, 2005)
- Lower response rates than neuro-typical children
- Higher rates of adverse events (AE) – aggression, emotional outbursts, paradoxical activation
- Higher rates of side effects - insomnia, decreased appetite
- Tolerability improves with higher cognitive function

Methylphenidate (cont)

- Start with short-acting preparations
- Long-acting preparations better tolerated
- Due to multi-factorial nature of executive function deficits, frequent re-evaluation is recommended
- As with ADHD w/o ASD, non-ADHD negative behaviors can improve
Atomoxetine

- Norepinephrine re-uptake inhibitor
- Dosing and response similar to non-ASD populations
- Typically better tolerated than stimulants
- Can take awhile to achieve full effect
- Most common side effects include fatigue, nausea and decreased appetite
- Response improved when combined with parent training but did separate from placebo as stand alone treatment (Handen B, King B. In process)
- Can be effective for co-occurring anxiety for some

Alpha-agonists

- Some evidence for improving impulsivity (clonidine) and hyperactivity (guanfacine) in ASD
- Often tried for before anti-psychotics (for both irritability and hyperactivity) because of favorable SE profile
- Improvement in target behaviors can improve general functioning
- Effective sleep aide – direct and indirect effects
- Can take several weeks to months for full affect
Case study: Ethan

- 12 y/o
- ASD – Level 2-3 (x2), w/o language impairment, w/o intellectual impairment
- Treatment targets = ADHD, anxiety, sleep disturbance, eating/feeding issues; question of depression
- Several MPH class trials with irritability at fairly low doses
- Has done well on amphetamines for ADHD
- Did not respond to clonidine or Remeron; activation on citalopram
- Parents did not want to try SGA
- Has done extremely well on lamotrigine

Glutamatergic Agents

- N-acetyl cysteine (NMDA modulator) – 1 small RTC; improved irritability (Hardan A et al. Arch Gen Psych. 2009)
- NMDA antagonists (amantadine, memantine)
  - did not show improvement in multiple RDBPC trials
  - Some promise as adjunct to risperidone
Cannabis

- Unscientific “case studies”
- Scientific Basis – altered endocannabinoid signaling in mice with gene abnormality linked to autism and mouse model of Fragile X syndrome
- Erroneous information in mainstream media, internet and online advocacy groups (Mothers for the Medical Marijuana Treatment of Autism, Mothers Advocating Medical Marijuana for Autism)

Cannabis (cont.)

Why not “just try it?”
- It is illegal to give to minors (even CBD oil has enough trace THC to be considered Schedule I by DEA)
- Untested
- Increases risk of psychosis (ASD already confers risk)
- Unrecoverable loss of IQ related to cannabis use in adolescence
- Potential negative impacts on sleep, mood, anxiety, memory and executive function
ADHD and ASD

- Can compound developmental deficits and behavioral challenges related to ASD
- Gating deficits and stimulus management can compound and mimic ADHD symptoms
- Remember to advocate for and encourage non-medication strategies at school - social skills deficits, organizational and study skills, test accommodations

ADHD and ASD (cont)

- Range of ADHD medications can be effective
- Long-acting preparations better tolerated
- Symptoms can persist into adulthood (Johnston, 2012)
  - ADHD alone - fast and inaccurate on attentional switching
  - ASD with ADHD - slower in response (reduced processing speed)
Anxiety and ASD

- Very common (50%)
- Generalized anxiety and social anxiety are most common (Caamano, 2013)
- Further worsens social communication deficit
- Can be hard to distinguish between repetitive motor symptoms (e.g. compulsions) and RRBs due to autism
- Cognitive and behavioral rigidity attributed to ASD can mask anxiety (especially in younger children)
- Full range of anxiety medications (SSRIs, antihistamines, benzodiazepines) can be effective but SE are common

Depression and ASD

- More common in higher functioning ASD – increased psychological awareness; more opportunities to experience impact/limitations of ASD
- ASD can mask and compound symptoms – social withdrawal, constricted affect, irritability
- Consider developmentally appropriate CBT
Depression and ASD (cont)

SSRIs are most common medication
• Often effective
• Start low and go slow
• Dose range not terribly different with non-ASD populations
• Treatment response less consistent compared to non-ASD
• High rates of activation and other SE (GI)

Suicide and ASD

• ASD is an independent risk factor for suicide attempts
• ASD is a risk factor for depression
• Suicidal behavior and attempts can be masked by repetitive self-injury
• Communication deficits can delay identification

Suicide and ASD (cont)

- Cognitive deficits can influence understanding of death, expression of SI (as unhappiness) and risk assessment
- Probably more common in higher function
- Lack of peer, parent and self-acceptance are common factors
- Co-occurring psychiatric issues, bullying and abuse are risk factors – similar to non-ASD

Psychosis and ASD (Bell et al. Br Jrnl Psych. 2018)

- ASD confers risk of psychosis
  - ASD present in 30-50% of children diagnosed with severe psychotic disorders (Rappaport et al. JAAACP. 2009)
- Both ASD and psychosis are “overlapping” spectrum constructs
- Share physical and genetic vulnerabilities
- No standardized tools to evaluate psychosis in ASD
- More overlap with negative than positive symptoms
Psychosis and ASD (cont)

- Psychosis often misdiagnosed during times of stress/transition
- ASD deficits in ToM, social functioning and rigid thinking make increase paranoid thinking; reports of hallucinations and impaired reality testing
- Symptom based treatment approach is recommended
- Children with ASD are twice as likely to experience treatment failure when AAP prescribed for psychotic symptoms (Downs J et al. Jnl Clin Psych. 2017)

Sleep Dysfunction and ASD

- 44-83% of children with ASD experience sleep problems
- Huge impact on individual and family function
- Evidence of abnormalities in melatonin synthesis and release
- Insomnia is most common (initial and middle insomnia)
Sleep Dysfunction and ASD (cont.)

- Less common: night terrors, sleep apnea (obstructive and central), RLS and or parasomnias
- Sleep issues have significant impact on daytime behaviors that may be focus of treatment and source of disability
- Medications for behavioral and psychiatric issues can impact sleep
- Sleep medications can impact medical issues (seizures, GI function, OSA)

Medications for sleep

- **Melatonin** - large empirical base; studies less consistent; facilitates transition to sleep; increase TST and can improve daytime behaviors; parent report > actual improvement; homeopathic versus hypnotic dosing; rebound may exacerbate middle insomnia
- **Anti-histamines** - (diphenhydramine, hydroxyzine, doxylamine) no studies; safe and effective; SE common
Medications for sleep (cont)

- **Alpha-agonists** - no studies; rarely used if sleep is only issue; BP/CV effects are most common SE
- **Trazodone** - no studies in pediatric ASD populations; SE common; risk of priapism harder to manage due to communication deficits.
- **Atypical Anti-psychotics** NOT recommended exclusively for sleep
- **Gabapentin** (Neurontin)

Summary

- There are no medication treatments for core symptoms of ASD
- Medications should be used with appropriate non-medications strategies
- Strongest evidence is for risperidone and aripiprazole targeting irritability and hyperactivity.
- For hyperactivity alone, methylphenidate; alpha-agonists and atomoxetine are reasonable alternatives.
- SSRIs are not effective for repetitive behaviors and rates of activation are high.
Environmental Risk Factors for ASD

- Valproic acid
- Prenatal rubella
- Misoprostol (ulcer treatment)
- Chlorpyrifos (insecticide)
- Pollution (proximity to freeways)
- Agricultural pesticides
- Increased paternal age
- Maternal use of SSRIs (Mezzacappa et al. JAMA Peds. 2017)
- Prenatal Ultrasound (Rosman et al. JAMA Peds. 2018)
- Pre-gestational/Gestational Diabetes + Obesity (Li et al. Pediatrics. 2016)
- Herpes Simplex 2 (Mahic et al. mSphere. 2017)

Primary Care Recommendations for Genetic Testing in ASD

- Heritability estimates in ASD exceed 80%
- 25-40% of ASD cases have identified genetic abnormality
- Yield of different genetic tests
  - High resolutions karyotype – 5%
  - Micro-array – 10%
  - Exome sequencing – 25%
- Risk in subsequent off-spring (de novo/no genetic cause)
  - One sibling w/ ASD – 10-20% (Ozonoff. 2011)
  - Two siblings w/ ASD – 16-35%