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Pediatric Symposium: 2020 Targeted Topics

Sessions available on-demand until December 31, 2020

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Prescribing Considerations for Children with Intellectual Disabilities and Developmental Disabilities

Dawn Garzon Maaks PhD, CPNP-PC, PMHS, FAAN, FAANP
University of Portland
School of Nursing

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Disclosures

- I have no personal disclosures
- This discussion includes non-FDA approved therapies

Learning Objectives

At the end of the session the learner will be able to:

1. Identify the current guidelines for the diagnosis of intellectual disorders (ID) and developmental disorders/autism (DD)
2. Integrate knowledge of the current evidence for the use of pharmacologic modalities for the treatment of mental health issues in children with ID and DD into primary care
3. Integrate knowledge of the current evidence for the management of sleep disorders in children with ID and DD into primary care.

Intellectual Disorders

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Intellectual disorders (ID)

- Individuals with ID have altered intellectual functioning which impacts their ability to receive, process and store information in a retrievable way
  - Impacts day to day function and ability to complete tasks
- Previously known as mental retardation
- New DSM V diagnostic criteria involves more than just IQ
- Estimated to affect 1% of the population

(Siegel et al., 2020)

DSM V Criteria

- Current intellectual deficits of ≥2 standard deviations below the population mean
- Also has concurrent deficits in at least 2 domains of adaptive functioning:
  - Conceptual skills (language, reading, writing, math, reasoning, knowledge, and memory
  - Social skills (empathy, social judgment, interpersonal communication skills, the ability to make and retain friendships, and similar capacities)
  - Practical skills (self-management in areas such as personal care, job responsibilities, money management, recreation, and organizing school and work tasks)

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DSM V Criteria

Performance in the lowest 3% of a person's age and cultural group, or an IQ of 70 or below.	• Multimodal
Standardized, culturally appropriate, psychometrically sound measures across 3 domains.	• Clinical and standardized intelligence assessment
Symptoms begin during the developmental phase.	• Not a specific age- may be missed milestone or behavioral problems
The individual's functioning is inappropriate for their age, development, & sociocultural background	• How to they cope with activities in daily life? • Are they able to achieve developmentally appropriate independence?

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Causes

- Prenatal, natal and postnatal causes
  - Genetic- Down syndrome, Rett syndrome, fragile X. Can also include genetic defects which damage the brain structures (tuberous sclerosis, neurofibromatosis)
  - Inborn errors of metabolism which result in the accumulation of neurotoxic elements or inappropriate nutrients for CNS function
  - Prenatal malnutrition, placental insufficiency, substance exposure (fetal alcohol syndrome), maternal illness (ex. Hypothyroidism, rubella, CMV, parvovirus B19)
  - Delivery- anoxia/hypoxia, prematurity, hypoglycemia, cerebral hemorrhage
  - Post-natal- injuries or illnesses that cause brain damage (ex. lead poisoning, TBI, meningo/encephalitis, brain tumor, surgery), chemo, radiation
  - Severe child abuse, environmental deprivation, and neglect

(Siegel et al., 2020)

Psych comorbidities

- Three times higher than nonaffected peers
- Serious behavioral problems 2.5-4x more common
- ODD, ADD, ASD, anxiety, depression, schizophrenia, BPD
- Make their experience of the world worse

(Siegel et al., 2020)

Medical co-morbidities

- Seizure disorders
- Constipation
- Sleep disorders (2x more common)
- Pain disorders which go undetected- menstrual cramps, tooth decay, injury
- Hearing/visual impairment (30%)
- Motor impairments that increase inattention and hyperactivity

(Siegel et al., 2020)

Assessing behavioral problems

- Is it serving a function?
  - Escaping a situation
  - Gaining attention/time with favored person
- Are they ill or in pain?
- Is it anxiety or frustration from communication difficulties?
- Are they being asked to perform at a level beyond their ability?
- Is it a sensory integration issue?
- Is their routine off?
- Are they feeding off adult stress, anxiety, etc.?
- Are norm referenced diagnostic psych tests listed in CPG (Siegel et al, 2020)

Treatment

- Focuses on symptoms management and not disease amelioration
- Psychosocial interventions are critical and first line
  - Psychotherapy and CBT
  - Communication therapy
  - Educational interventions
  - Social/caregiver support
  - Applied behavioral analysis

Psychopharmacologic agents

- Appropriate to treat comorbidities
  - Best evidence supports use of MPH and risperidone
- None are FDA approved for use in ID
- Atypical antipsychotics can help with aggression, stereotypies, irritability, ODD and violence
  - Scare evidence for all but risperidone
  - SE more common- akathisia (up to 13%) tardive dyskinesia (up to 20-34%) if chronically used
  - Neuroleptic malignant syndrome may be harder to diagnose
- MPH can help with inattention and hyperactivity
  - Effect sizes are generally lower than in non-affected peers
- Alpha 2 agonists can be considered
  - Worries with side effect monitoring and somnolence

(Siegel et al., 2020; Molina-Ruiz et al., 2017)

- Antianxiety medications may help with aggression, stereotypies and self-harm
- SSRIs are considered safest but no evidence to show superiority
  - Most evidence available for fluoxetine, sertraline, paroxetine
- Do not use benzodiazepines
  - Heightened sensitivity might cause behavioral disinhibition worsening
- Lithium is approved in 12+ for BPD and ID and is treatment of choice for psychosis associated with Prader Willi
- Valproic acid may help BPD with rapid cycling (more common in ID)

(Siegel et al., 2020; Molina-Ruiz et al., 2017)

Psychopharmacologic agents

Sleep disorders

- 80% of children have disrupted sleep- screen at each visit
- First-line approach should always be sleep hygiene, sleep regularity, and behavioral approaches
- No FDA approved choices
- Melatonin
  - Safe and well researched
  - 1-3 mg initial to maximum of 10mg
  - If not response to 6mg, poor likelihood of response with higher doses
  - Helps with sleep induction but not maintenance
  - Demonstrated best for ASD
  - Parasomnias
- Clonidine
  - 25-50 mcg HS
  - Titrate up 25 mcg to no 5-10 mcg/kg/d

Blackmer & Feinstein. Management of sleep disorders in children with neurodevelopmental disorders. Pharmacotherapy 2016; 206: 84-98.

Sleep disorders

- Trazodone- older than age 5 years
  - Atypical antidepressant
  - 2 mg/kg/dose to 50mg
  - Max dose 150mg
  - Associated with priapism and do not use in individuals with Rett syndrome because of risk of QT prolongation
- Iron supplementation
  - Helps with periodic limb movements
  - Higher risk for IDA because of picky eating and sensory integration issues
  - Recommendation based on clinical experience vs hard data (Blackmer & Feinstein,)
  - 1-2 mg/kg/day

Sleep disorders

- Antihistamines- diphenhydramine and hydroxyzine
  - Widely used by parents, limited information in this population
  - Do cause anticholinergic effects so use in caution with other medications
  - Some children have paradoxical excitation

Fragile X

- Increased risk for anxiety, impulsivity, self-injurious behavior and aggression.
- All treatment off-label
- Ekert et al. Data from 25 clinics, 415 patients
  - 37% had adverse effects from medication- mostly weight gain and sedation
  - Most common used are atypical antipsychotics (aripiprazole and risperidone), SSRIs, sedating anxiolytics, and stimulants

Eckert et al. Pharmacologic interventions for irritability, aggression, agitation and self-injurious behavior in Fragile X syndrome: An initial cross-sectional analysis. J Autism Develop Disord 2019; 49-4595-4602

Autism

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Autism

- DSM 5: one single diagnosis
  - Asperger Syndrome and PDD NOS are no longer listed
  - Core deficits in social communication/interaction and restrictive/repetitive behavior patterns
    - Difficulty understanding others' intent, unusual social communication, abnormal eye contact, hypo or hyper reactivity to stimuli, rigidity, difficulty processing visual and auditory communication.
    - Perseverative behaviors (may be compulsions), stereotypies (echolalia, hand flapping) often when struggling to understand others
  - If no intellectual disorder, may not be diagnosed until social difficulties are evident in school setting.
- Get care for developmental delay as soon as possible and not waiting for official diagnostic evaluation.
  - Older children can be referred to school for language and cognitive eval
  - Refer to get formal diagnostic evaluation

(Hyman SL, et al., 2020)

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Common Comorbidities

- Sleep disorders*
- Feeding problems- esp. food refulsal
- GI disorders- esp. constipation, diarrhea, reflux
- Obesity
- Anxiety*
- Wandering
- Seizures
- Aggression
- Attention Deficit Hyperactivity Disorder

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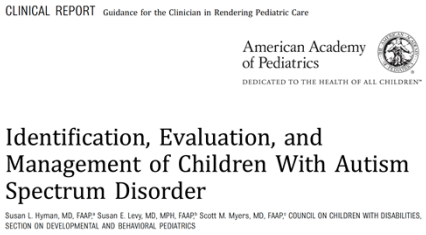
Statement about medications and ASD

- CPG states medication should only be used if:
  - Determined is not a behavior of refusal or distress
  - Rule-out of medical conditions- reflux, constipation
  - "Treatable medical conditions and behavioral factors assessed and intervention does not address the symptoms of concern"


CLINICAL REPORT Guidance for the Clinician in Rendering Pediatric Care

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Identification, Evaluation, and Management of Children With Autism Spectrum Disorder

Susan L. Hyman, MD, FAAP,[a] Susan E. Levy, MD, MPH, FAAP,[b] Scott M. Myers, MD, FAAP,[c] COUNCIL ON CHILDREN WITH DISABILITIES, SECTION ON DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS

(Hyman SL, et al., 2020)

Autism and ADHD

- High comorbidity (about 50%)
- Signs of inattention might be due to language issues
- Flight may happen if overwhelmed (looks like impulsivity and oppositionality)
- Must consider anxiety as a contributing factor
- The same medicines used for ADHD symptoms in those without ASD are appropriate for use in kids with ASD
- Consider atomoxetine if comorbid anxiety is a worry- helps with hyperactivity but less for inattention
- Half are treatment for irritability, aggression, hyperactivity, anxiety and oppositionality (Lamy et al., 2020)

(Hyman SL, et al., 2020)

Autism and aggression

- Risperidone and aripiprazole are only FDA approved options for irritability and aggression
- Do improve tantrum frequency, aggression in episodes and self-injurious behavior.
- Second generation antipsychotics may not help with high functioning ASD patients
- Ziprasidone and quetiapine may be more weight neutral
- Some evidence that second-generation long acting injectable (aripiprazole, risperidone and paliperidone) increase compliance, are effective and lower treatment cost

Lamy et al, 2020

Mood and repetitive behaviors

- SSRIS used frequently with limited evidence base
- Most evidence is for fluoxetine
- Fluvoxamine may help with behavior and aggression- also helps with OCD

Lamy et al, 2020

On the horizon

Lamy et al, 2020

- Fecal transplants and probiotic supplementation shows promise for GI dysfunction and may help reduce core symptoms
- Immunomodulators being studied now- increasing evidence of immune system dysfunction and ASD
- Memantine (GABA modulator) may help with memory and decrease aggressive behaviors
- CBD

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