

# PSYCHIATRIC COMORBIDITY IN AUTISM SPECTRUM DISORDER

Pediatrics TeleECHO

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# INTRODUCTION

- University of Utah Neurobehavior HOME Program
- Medical school U of U. Residency (Triple Board) at Brown
- No disclosures to report



# OBJECTIVES

- Week 1: Anxiety & Depression vs Week 2: Irritability/Aggression and ADHD
- Review DSM criteria ASD & changes
- Challenges of assessing comorbidity
- General treatment approach
- Review co-morbidity Anxiety & Depression and specific treatment.
- Questions and case discussion

# DSM-5 Criteria for ASD

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by *all* of the following, currently, or by history:

1. Deficits in social-emotional reciprocity to failure to initiate or respond to social interactions..
2. Deficits in non-verbal communication used for social interaction.
3. Deficits in developing, maintaining, and understanding relationships.

B. Restricted, repetitive patterns of behavior, interests, activities as manifested by at least two of the following, currently or by history:

1. Stereotyped or repetitive motor movements, use of objects, or speech.
2. Insistence on sameness, inflexible adherence to routine.
3. Highly restricted, fixated interests that are abnormal in intensity or focus
4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment.

C. Symptoms must be present in early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies).

D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of functioning.

E. Not better explained by Intellectual Disability or Global Delay

# DSM-5 Autism Spectrum Disorder

## Severity Levels:

- 1. Requiring support
- 2. Requiring substantial support
- 3. Requiring very substantial support

## Specifiers:

- With or without accompanying intellectual impairment
- With or without accompanying language impairment
- Associated with a known medical or genetic condition or environmental factor
- Associated with another neurodevelopmental, mental, or behavioral disorder
- With Catatonia

# Changes from DSM-IV-TR to DSM-5

- No longer sub-categories (Autistic Disorder, Asperger Syndrome, PDD-NOS, Disintegrative Disorder)
  - *Spectrum instead of separate identities*
  - *No consistent biological features distinguish Asperger Syndrome from Autism*
- DSM-IV: symptoms divided into three areas (social reciprocity, communication, and restricted & repetitive behaviors). DSM-5 rearranged into two areas: A) social communication/interaction, and B) restricted & repetitive behaviors. Dx based on symptoms, currently or by history.
- Though symptoms must begin in early childhood, *they may not be recognized until social demands exceed capacity.*
  - *Social camouflaging*
- Atypical sensory processing was included as part of area B
- Severity (level of required support) and specifiers
- Addition of Social (Pragmatic) Communication Disorder.

# The Challenge

- 75% of children with ASD require treatment for emotional, physical, or behavioral problems.
  - *Up to 72% meet criteria for at least one psychiatric disorder.*
- One of the most challenging disorders for patients, families, and providers.
  - *You are the front line. Take a deep breath...*
  - *Thank you*
  - *Importance of knowing resources*

Leyfer, O.T. et al. (2006). Comorbid Psychiatric Disorders in Children with Autism: Interview Development and Rates of Disorders. *J Autism Dev Disord*, 36:849-861

Jean Frazier. Medical & Psychiatric Comorbidities in ASD. Grand Rounds at Brown University 5/11/16.

# Rates of Psychiatric Disorders

- Significant variation across studies
- Methods for assessing cases differs
  - *Chart reviews or counting from existing databases (clinical sample vs state/national registry vs parent groups vs school districts)*
  - *Informant based*
  - *Direct patient evaluation (structured interview)*
- Sample differences
  - *Clinic vs population derived, age ranges, inclusion or exclusion criteria [i.e. based on Intellectual Disability], number of subjects*
  - *Some of the early studies included only subjects referred for psychiatric treatment.*
- Lack of Validated Rating Scales & “Gold Standard”



# Rating Scales - assessment or treatment response

## General population

- Child Behavior Checklist
- Vanderbilt ADHD Rating Scale
- Diagnostic Interview Schedule for Children
- Clinical Global Impressions Scale

## Specifically designed

- Aberrant Behavior Checklist (ABC)
- Developmental Behavior Checklist
- Behavior Problems Inventory
- Children's Yale-Brown Obsessive Compulsive Scale Modified for Pervasive Developmental Disorder

## Intellectual Disability Scales

- Psychiatric Assessment Schedule for Adults with Developmental Disabilities
- Diagnostic Assessment for the Severely Handicapped

## Modification of SADS for Autism

- Autism Comorbidity Interview Present & Lifetime (ACI-PL)

# Difficulty in psychiatric assessment

The internal emotional state:

- *How to access & understand*
  - Up to 50% are non-verbal. Those with adequate language have a variety of other types of communication impairment
- *Alexithymia*
- *Theory of Mind Impairment*
- *Deficits in complex information processing & executive functioning*

Are the difficulties due to effects of the core features of ASD, life experience, or comorbid psychiatric disorders superimposed?

Lord, C. & Paul, R. (1997). Language & communication in autism. D. J. Cohen & F. R. Volkmar, Handbook of autism & pervasive developmental disorders (2nd Ed) New York.

Baron-Cohen, S. (1995). *Learning, development, and conceptual change. Mindblindness: An essay on autism and theory of mind*. Cambridge, MA, US: The MIT Press

South M and Rodgers J (2017) Sensory, Emotional and Cognitive Contributions to Anxiety in Autism Spectrum Disorders. *Front. Hum. Neurosci.* 11:20. doi: 10.3389/fnhum.2017.00020

# Diagnostic Overshadowing

- The tendency to overlook symptoms of mental health problems and attribute them to being part of ‘having Autism Spectrum Disorder’
  - *But this can go the other way!*
    - especially in Psychiatry

# Why does it matter?

- When problematic behaviors are recognized as manifestations of a comorbid psychiatric disorder, rather than just isolated behaviors, more specific treatment is possible.
  - *Specific treatment generally more effective*
  - *May help cover treatment*
  - *When thinking about planning & provision of services*
  - *Research can then better study psychopharmacology*
    - And may be better able to help the search for genes that increase risk of ASD
  - *Could help elucidate brain mechanisms*
  - *Identifying a disorder or illness can take pressure off of relationships*
    - High caregiver burden

# Formulation

- Biopsychosocial
- Multi disciplinary
  - *Behavioral*
  - *Educational*
  - *Medical*
  - *Pharmacological*

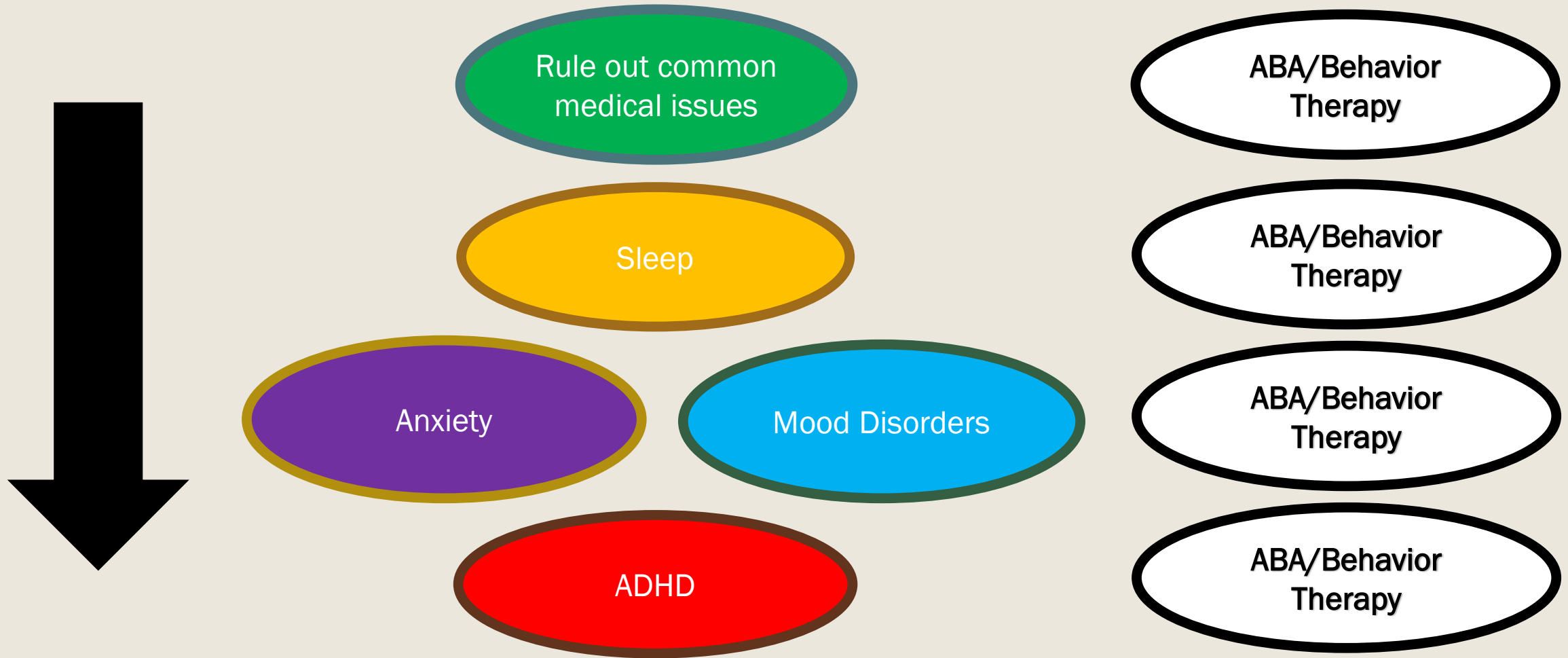
Questions to ask:

- Are there neurovegetative symptoms of mood disorders?
- Are there episodes?
- Is this a distinct qualitative or quantitative change, *from baseline*, in emotion or behavior?
- Is this a new emotion or behavior?
- Is there a strong FHx of psychiatric disorders?
- Medical comorbidity?

# Treatment

- Treat psychiatric symptoms, psychiatric disorders, or certain behaviors associated with ASD?
- ABA Therapy
- Parent Training
- Medication management
- Speech Therapy
- Occupational Therapy
- Physical Therapy
- Social Skills groups
- CBT
- Other (family therapy)

# Treatment Hierarchy



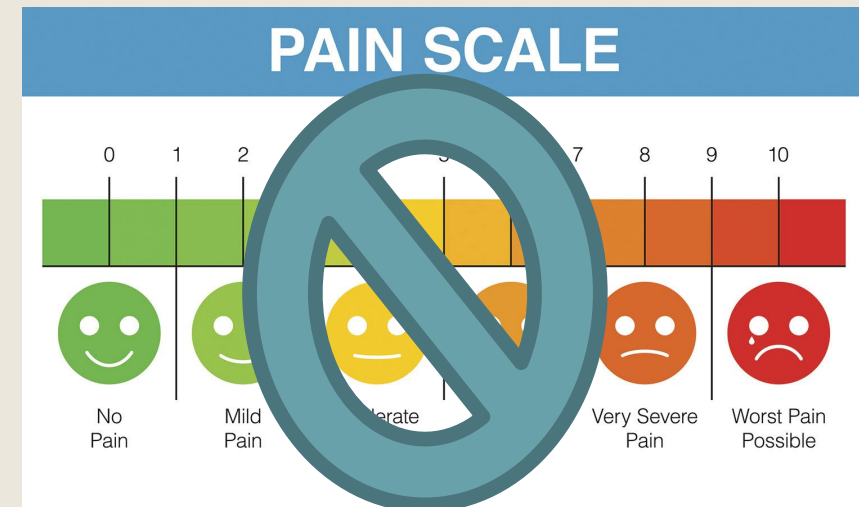
Mahajan R, Bernal MP, Panzer R, et al. Clinical practice pathways for evaluation and medication choice for attention-deficit/hyperactivity disorder symptoms in autism spectrum disorders. *Pediatrics*. 2012;130 Suppl 2:S125-138.

Modification of Algorithm created by Todd Levine M.D. Dept Child Psychiatry Brown University. 2015

# Missed medical problems\* may drive surface features that resemble psychiatric disorders.

- Gastrointestinal
  - *Constipation*
  - *GERD*
  - *Celiac disease*
- Allergies
- Seizures
- Pain
  - *Dental*
  - *Headache*
  - *Ear ache*
  - *Musculoskeletal*
- Sleep Disorders
  - *PLMD, RLS, and OSA*

\* Complicated by unusual pain tolerance



Medical Comorbidities in Autism Spectrum Disorder. A Primer for Health Care Professional & Policy Makers. 2nd Edition: July 2014. Prepared by Treating Autism, ESPA Research, Autism Treatment Plus

C. S. Allely, "Pain Sensitivity and Observer Perception of Pain in Individuals with Autistic Spectrum Disorder," The Scientific World Journal, vol. 2013, Article ID 916178, 20 pages, 2013. <https://doi.org/10.1155/2013/916178>.

# ABA Therapy

Method: build functionally useful behaviors and reduce maladaptive ones

Focus: small, measurable units of behavior are taught systematically

Goal: build on simple responses into complex and fluid combinations of age-appropriate responses

Evidence of effectiveness:

- Higher scores on standardized tests of language, cognition and adaptive skills
- Strongest predictor of optimal outcome





# ABCs and Functions of Behavior

- Antecedent
- Behavior
- Consequence

## Functions

1. Escape or Avoidance
  - *task demand, prompt at school, sitting at doctor's office*
2. Attention
3. Gain Access
  - *interrupt desired activity or not allowed to have what they want*
4. Sensory Stimulation

# General Principles of Psychopharmacology in ASD

- Start with drugs that have less risk adverse effects before moving to atypical antipsychotics.
- “START LOW[ER] AND GO SLOW[ER]”
- Medications generally less tolerated
  - *SSRIs: pre-pubertal children more likely to become **activated** (excessive emotional arousal & resultant behavioral change [aggression, hyperactivity, pacing, restlessness, agitation])*
  - *Start on weekend (especially stimulants)*
  - *Benzodiazepines and disinhibition; Benadryl and paradoxical excitation*
  - *Warn of potential side effects*
- Often maximum benefit achieved at lower doses
- Frequent follow-up, especially after initiation
- Consider a treatment hierarchy
- Most trials off label

# Sleep Problems



- 44-83% in children with ASD
  - *Initiating, sustaining*
  - *Early morning awakenings*
  - *Restless*
  - *Bedtime resistance*
  - *Co-sleeping*
  - *OSA, PLMD, RLS*
- High burden on families

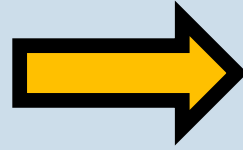
Percent of parents responding their child had problems on a specific PCQ question by good sleeper–poor sleeper<sup>1</sup>.

PCQ question	Good sleeper ( <i>n</i> = 1200)	Poor sleeper ( <i>n</i> = 584)	Total ( <i>n</i> = 1784)
Language use and understanding	60.6	69.5	63.5
Compulsive behavior	32.2	47.6	37.2
Anxiety	40.9	61.2	47.5
Sensory issues	41.2	63.2	48.4
Aggression	20.3	37.3	25.9
Hyperactivity	41.7	66.8	49.9
Attention span	56.1	77.7	63.2
Mood swings	25.7	47.8	32.9
Eating habits	44.8	57.9	49.1
Social interactions	53.9	75.4	60.9
Self-stimulatory behavior	36.2	55.1	42.4
Self-injurious behavior	9.9	23.5	14.4

<sup>1</sup> All scales were significant between good sleepers and poor sleepers at  $p < 0.001$ .

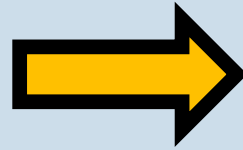
# Treatment for Insomnia

- Melatonin
  - 1 to 6 mg PO qHS
  - sleep initiation



- Well studied & tolerated

- Clonidine
  - 0.025 to 0.2 mg



- Tolerance

- Trazodone
  - 25 to 200 mg



- Priapism risk

- Mirtazapine
  - 3.75 to 15 mg



- Increased appetite

- Don't forget sleep hygiene!



- Limit screen time; regular routine

# ANXIETY

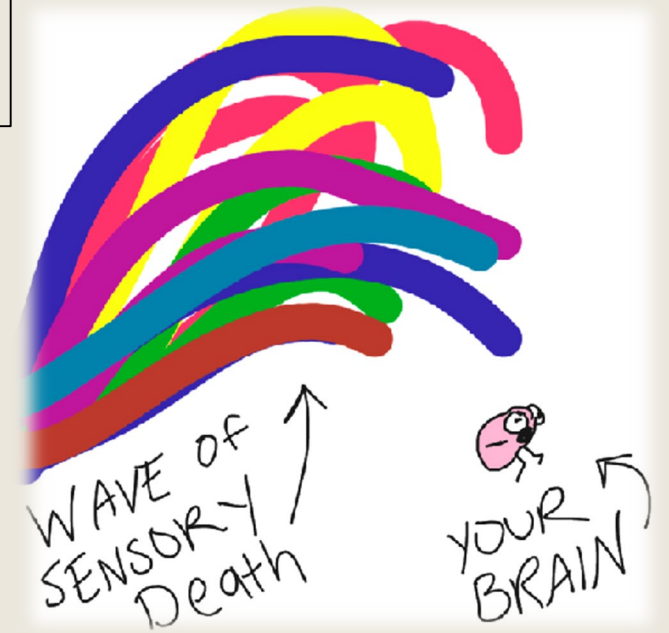
- Among the most common presenting problems for children & adolescents with ASD.
- Prevalence rates from 11 to 84%.
  - *Most have it around 50%*
- Simple Phobias most common
  - *Social phobia*
- Generalized Anxiety Symptoms
  - *Appearing tense, restless*
- Obsessive-Compulsive Disorder
  - *Preoccupations/restricted behaviors part of Autism versus obsessions or compulsions.*
    - Pleasure/regulating versus fear based
    - Distress when a behavior is interrupted?

Ghaziuddin, M. Asperger syndrome: Associated Psychiatric and Medical Conditions. Focus on Autism and Other Dev Dis. 2002, 17:138-44

White S, Oswald D, Ollendick T, Scahill L. Anxiety in Children & Adolescents with Autism Spectrum Disorders. Clin Psychol Rev. 2009 Apr;29(3):216-29

# CONCEPTUALIZING ANXIETY

- Inability to tolerate uncertainty?
- Atypical Sensory Impairment?
  - *Link between sensory processing -> anxiety -> repetitive behaviors*
  - *When the sensory world becomes “too real”*
- Dysfunction of the Autonomic Nervous System, HPA Axis, & size of Amygdala
- Direct manifestation of social disability?
  - *Many patient acutely aware of their disconnectedness*



# ASSESSING FOR ANXIETY

- Distress related to transitions
  - *What is life like moment to moment?*
  - *“Not comfortable in their own skin”*
- Significant difficulty minor changes in routine
- Not able to enjoy the moment
  - *From one future event to another*
- Outwards signs
  - *Pacing, sweaty hands, face flushed, tremulous*
  - *Skin picking*
  - *Increased repetitive behaviors*
- Elevated HR or BP
- Consider environment
- Scales: lack consensus tool





# MEDICATIONS FOR ANXIETY

- Sertraline (Zoloft):
  - < 12 yrs: start at 6.25 mg or 12.5 mg
  - > 12 yrs: start at 25 mg
  - Range 25-150 mg qday; however up to 200 mg can be effective.
- Buspirone (Buspar):
  - start 2.5 mg BID. Titrate in 2.5 to 5 mg/day qweek.
  - Range: 2.5 mg BID to 15 mg BID
- Mirtazapine (Remeron): 3.75 mg qHS, can increase by 3.75 mg up to 15 mg
- Guanfacine (Tenex):
  - start 0.25 mg BID or 0.5 mg qHS. Titrate in 0.5 mg increments to 1 mg BID or 1 mg TID [if weight > 40 kg].
  - ER (Intuniv) in 1 mg intervals. Can increase weekly by 1 mg. 1-4 mg common therapeutic doses. Limited by sedation, hypotension, bradycardia

# OTHER ANXIETY TREATMENTS

- Consider CBT if higher functioning
  - *Coping skills vs exposure based treatments*
    - Mixed literature about *habituation*
    - Importance of caregiver involvement
- Sensory strategies
  - *Noise blocking headphones, deep pressure, joint compressions, massage, weighted vests/blankets, swinging, regular stimming*
- Social stories
- Visual schedules
- Pet therapy
  - *Emotional support animals, equine therapy*
- Improve functional communication

# MAJOR DEPRESSIVE DISORDER



- Rates in studies vary from 0.9 to 11%.
- Directly correlated with higher level of baseline functioning, more self-awareness of impairment, and higher IQ.
- Reports increase with age (chronologic & emotional)
- Victimization & family conflict correlated with
- Change from baseline

Besides DSM criteria, also consider: aggression, mood lability, hyperactivity, decreased self-care, change in function, changes in core symptoms of ASD, increased compulsions, and increased self-injurious behavior.



Diagnostic Manual-  
Intellectual Disability:

A Clinical Guide for Diagnosis  
of Mental Disorders in Persons  
with Intellectual Disability

# DM-ID

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NADD Press

# MAJOR DEPRESSIVE EPISODE

DSM-5 Criteria	Adapted Criteria
Five or more symptoms during the same 2-week period and at least one of the symptoms should be either (1) depressed mood or (2) loss of interest or pleasure.	<b>Four</b> or more symptoms. (3) Irritable mood
Depressed mood most of the day, nearly every day.	Or irritable. Rarely smiles or laughs, cries or appears tearful. <b>Increase in repetitive or ritualistic behavior.</b> Onset or increase in agitated behaviors (assault, SIB, screaming, property destruction).
Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day.	No adaptation. Refuses preferred activity, more withdrawn, lost response to reinforcers.
Weight loss or gain, or decrease or increase in appetite nearly every day.	No adaptation. More obsessive about food, stealing food, agitation during mealtime.

# Major Depressive Episode (continued)

DSM 5 Criteria (continued)	Adaptations
Insomnia or hypersomnia nearly every day	No adaptation
Psychomotor agitation or retardation	No adaptation. Paces, up & down from seat, slowed movements, decreased talking, vocalizes much more or less than usual.
Fatigue or loss of energy	No adaptation. Appears tired, refuses or becomes agitated about activities that require physical effort
Feelings of worthlessness or excessive guilt	No adaptation. Negative self-statements. May seek excessive reassurance that she/he is a good person
Decreased concentration	No adaptation. Change with ABA therapy, at school, or other programs?

# Major Depressive Episode (continued)

DSM 5 Criteria (continued)	Adaptations
Suicidal ideation	No adaptation. Might talk about death, someone who has died, or perseveration
Symptoms cause clinically significant distress in functioning.	No adaptation. Individual may lose residential placement, get expelled from school
Episode not attributable to the physiological effects of a substance or to another medical condition.	Almost any physical pain may cause difficulty with focus, sleep, eating, and psychomotor agitation. Thyroid, UTIs, OM, cellulitis, constipation, GERD, migraines, drug side effects.

# Medications for Depression

- Selective Serotonin Reuptake Inhibitors
  - *Fluoxetine (Prozac)*
  - *Sertraline (Zoloft)*
  - *Citalopram (Celexa)*
  - *Escitalopram (Lexapro)*
- Norepinephrine & Dopamine Reuptake Inhibitor
  - *Bupropion: Contraindicated in patients with seizure disorders*
- Alpha2 & 5-HT2/5-HT3 antagonist
  - *Mirtazapine*
- Serotonin Norepinephrine Reuptake Inhibitors
  - *Venlafaxine (Effexor)*
  - *Duloxetine (Cymbalta)*



# Other Depression Treatments

- Consider CBT if higher functioning
  - *Behavioral activation*
- Parent Training (if increased SIB part of depression)
- Sensory diet via OT:
  - *Hypo responsive*: jump on mini-trampoline, swinging, and resistive physical work, such as swimming and use of playground equipment
- Rule out bullying
- Light therapy
- In some cases treatment refractory sx's
  - *TMS or ECT*

Questions?  
Cases?