Not Just a Checklist – Pediatric Diagnosis and Management of Autism Spectrum Disorder

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Disclosure

- Financial relationships with industry within the last 12 months:
  - None

- Off label uses:
  - Stimulant medication as a treatment for hyperactivity and disinhibition in children with autism spectrum disorder

In the DSM Era (since 1980), Rather Than a Medical Diagnosis Autism Has Become A Checklist

Diagnostic & Statistical Manual of Mental Disorders

- Published by the American Psychiatric Association
- Criteria for and inclusion of specific disorders change over time with each new publication of the DSM
- Autism did not appear in the DSM until the DSM-III in 1980
  - Criteria for autism have gotten easier to meet over time
    - Prevalence of autism has increased over time

Changing DSM Criteria Over Time

- **DSM-III:**

"Pervasive lack of responsiveness to other people, gross deficits in language development, and bizarre responses to various aspects of the environment"

Changing DSM Criteria Over Time

- DSM-IV:

"**Qualitative impairments** in social interaction, qualitative impairments in communication **(including delays in language development)**, and **restricted, repetitive and stereotyped** behaviors, interests, **and** activities"

Changing DSM Criteria Over Time

- DSM-5:

"**Persistent deficits** in social communication/social interaction and restricted, repetitive patterns of behavior, interests, **or** activities"

In the DSM Era, Rather Than a Medical Diagnosis Autism Has Become A Checklist

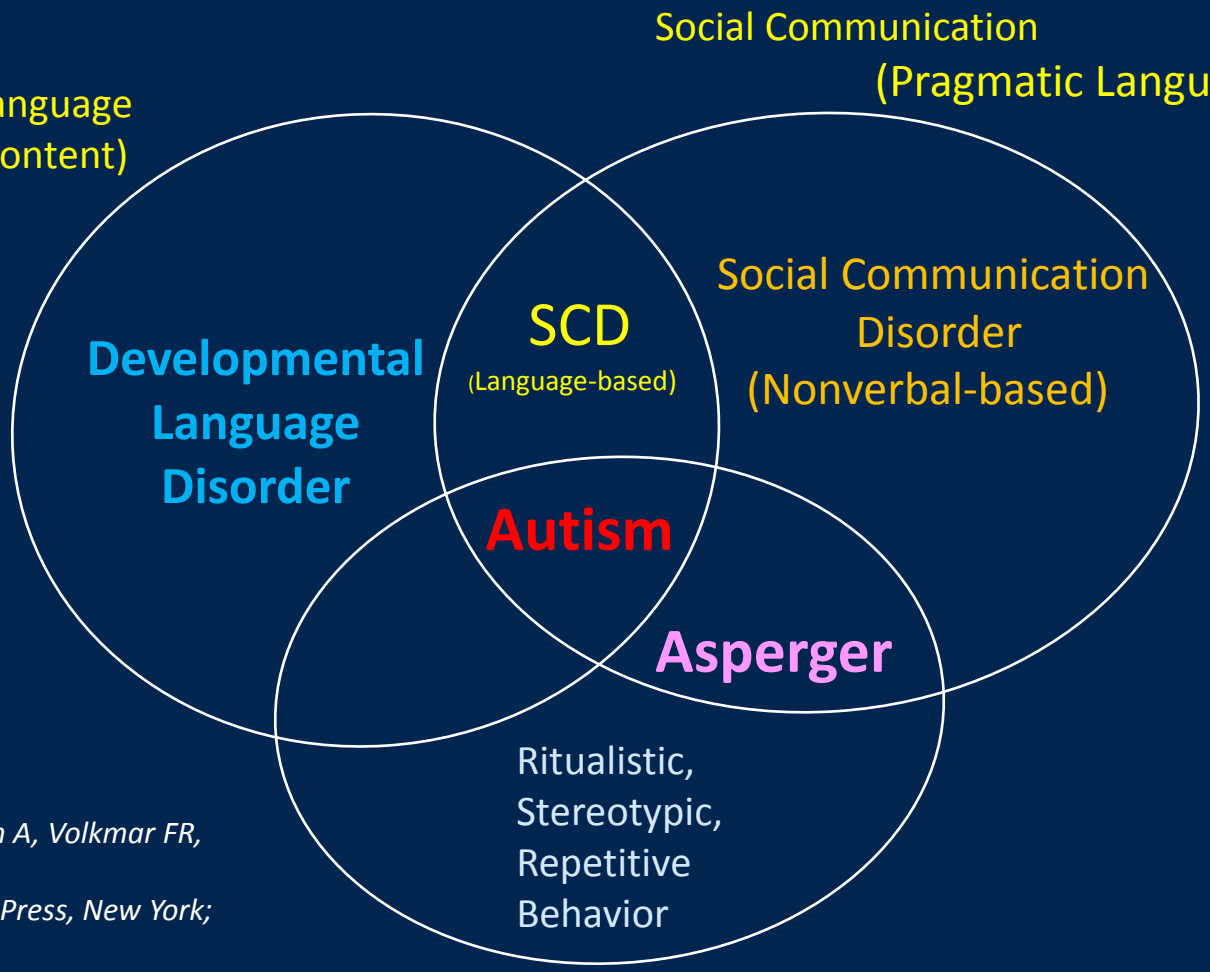
- DSM-IV: Pervasive Developmental Disorders (PDD)
- At least 6 of 12 items
  - 2 from column A (impairment in social interaction)
  - 1 from column B (impairment in communication)
  - 1 from column C (repetitive/stereotypic behaviors)
- Diagnoses: Autistic Disorder, Asperger Disorder, PDD-NOS

To the DSM-5, Autism is Still a Checklist

- DSM-5:
  - 3/3 items for deficits in social communication and social interaction
  - 2/4 items for restricted, repetitive patterns of behavior, interests, or activities

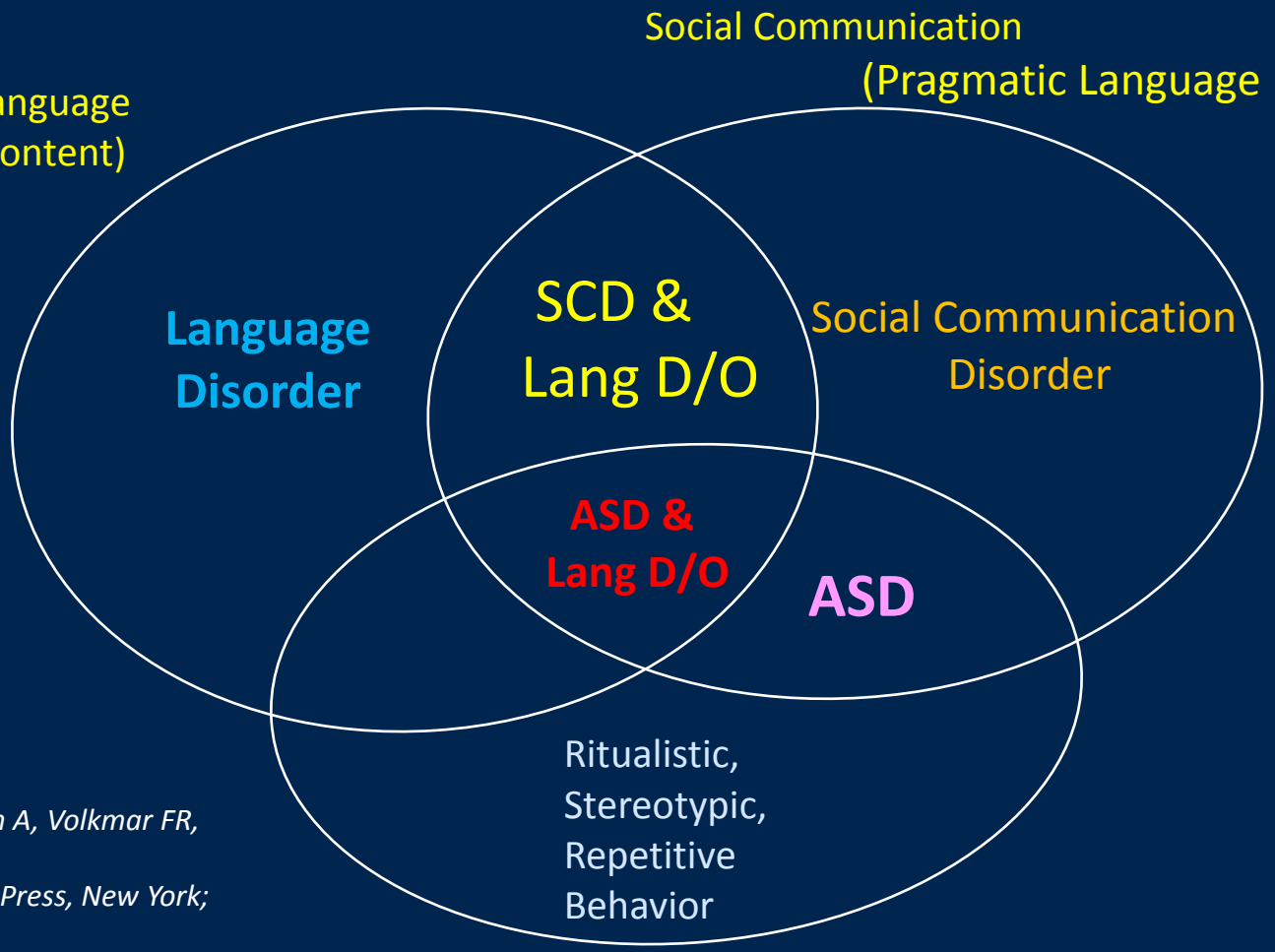
- Diagnosis: Autism Spectrum Disorder
  - Specify:
    - With or without language disorder
    - With or without intellectual disability
    - Associated with known medical or genetic condition
    - Severity level: Requiring support; Requiring substantial support; Requiring very substantial support

DSM-IV: Pervasive Developmental Disorders



Adapted from: Bishop DVM. In Klin A, Volkmar FR, Sparrow SS, editors. Asperger Syndrome. The Guilford Press, New York; 2000: p 273.

DSM-5: Autism Spectrum Disorder



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Goal

- Understand autism as a medical diagnosis within the spectrum and continuum of pediatric developmental-behavioral disorders, **NOT AS A CHECKLIST**

Objectives

- Identify children with autism spectrum disorders based on their presenting developmental-behavioral profiles
- Identify evidence-based behavioral, educational, therapeutic, and medical interventions for children with autism spectrum disorders
- Describe the medical laboratory workup of children with autism spectrum disorders

AAP Developmental Screening Recommendations

- Standardized screening at well child visits at:
  - -9 months: Developmental Screening
  - -18 months: Developmental + Autism Screening (MCHAT)
  - -24 or 30 months: Developmental + Autism Screening (MCHAT)

Myth: Primary Pediatric Health Care Professionals Are Missing Most Children with Developmental Concerns

- Palfrey JS, et al (1987)*
  - Only 28.7% of children who required special educational services were identified before they reached school at 5 years of age.
  - Subsequently, perception developed that primary pediatric health care providers are to blame for missing the vast majority of children with developmental-behavioral disorders.**
  - This has led to mandated use of parent-completed developmental and behavioral screening questionnaires and an erosion of confidence in primary pediatric health care professionals' clinical skills.**

*Palfrey JS, et al. *J Pediatr*.1987;111(5):651–659

**Voigt RG and Accardo PJ. Mission Impossible? Blaming Primary Care Providers for Not Identifying the Unidentifiable. *Pediatrics* 2016;138(2):e20160432.

Reality: Only Lower Prevalence, Higher Severity Developmental Disorders Can Be Reliably Identified Prior to School Age

Developmental-Behavioral Disorder	Age/Grade of Reliable Identification	Prevalence	Reliably Identifiable Before School Age?
Severe ID (IQ < 50) CP	1 year	0.4% 0.4%	Yes
Mild ID (IQ < 70) ASD	3 years	1.6-2.6% 1.7%	Yes
Slower Learning/Global Learning Disabilities (IQ 70-89)	Kindergarten to 1st grade	23%	No
Specific Learning Disabilities/ADHD	1st to 4th grades	5-10%	No

- Thus, the vast majority of children with developmental concerns have milder severity conditions that CANNOT BE RELIABLY IDENTIFIED BEFORE SCHOOL AGE!

Is Pediatric Clinical Judgment So Bad??

- US Department of Education's goal:
  - Provide EI services to at least 2% of children < 3 years*
- In 2002: 2.2% of US children < 3 years receiving EI*
- In 2010: 2.8% of US children < 3 years receiving EI**
- In 2015: 2.95% of US children < 3 years receiving EI***
  - **With 2.95% of children from 0-3 years of age being served by EI, it appears most likely that most children who can be reliably identified by 3 years of age *are* being identified!**

*US Department of Education. FY 2007 program performance plan; 2006. Available at: www.ed.gov/about/reports/annual/2007plan/allprogs.pdf.
**Rosenberg SA, et al. Pediatrics 2013; 131: 38-46
***The Early Childhood Technical Assistance Center. Part C National Program Data. Available at: http://ectacenter. org/ partc/ partcdata. asp.

AAP Algorithm for Autism Screening

- AAP recommends autism-specific screening at 18 months
  - Study of M-CHAT screening of 3793 children at 16-30 months –
    - **PPV only 0.11***
  - Study of M-CHAT screening of general population sample of 18 month olds –
    - **PPV only 0.015****

*Kleinman JM. Robins DL. Ventola PE, et al. *J Autism & Devo Dis* 2008; 38(5):827-839

** Sternberg N, Bresnahan M, Gunnes N, et al. *Paediatr Perinat Epidemiol* 2014**; 28: 255-262**

Meyer Center Faculty Developing New Autism Screener

Clinical Resource for Autism Prediction

C.R.A.P.®

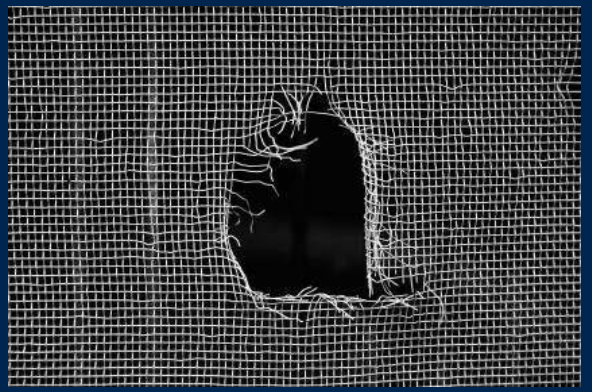
MCHAT vs CRAP®

	MCHAT	CRAP®
Cost	Free	$0.25
Positive Predictive Value	0.11	0.015

Clinical Resource for Autism Prediction:

PPV = 0.015

"Evidence" for Autism Screening?
(Don't ask the USPSTF)



- "The USPSTF concludes that the **current evidence is insufficient** to assess the balance of benefits and harms of screening for autism spectrum disorder (ASD) in young children for whom no concerns of ASD have been raised by their parents or a clinician."

If Not Checklists, Then What???

Years of medical training/ accumulated clinical experience & clinical judgment versus a checklist….

If Not Checklists, Then What?

- **Medical Training:**

  -History + Examination = Diagnosis

- **Developmental-Behavioral Concerns:**

Developmental History + **Neurodevelopmental Exam** = **Developmental Diagnosis**

Medical Model of Developmental Diagnosis

- Chief complaint
  - Failed developmental screen
- Developmental history
  - Identify pattern of developmental delay (static, acute, progressive)
  - Identify delay, dissociation, deviation
- Neurodevelopmental exam
  - Confirm developmental history
- **Make developmental diagnosis within the spectrum & continuum of developmental-behavioral disorders**

Developmental History

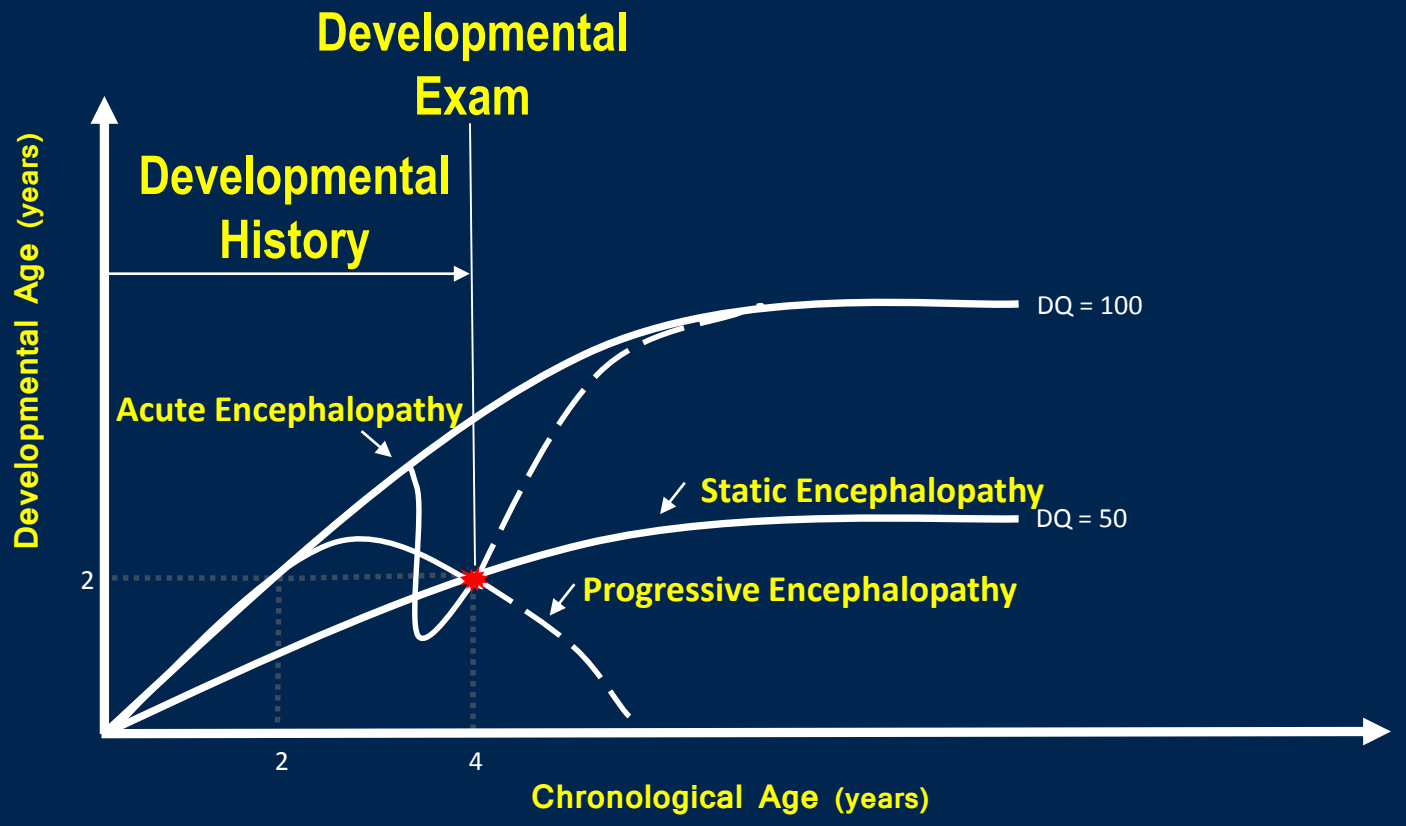
- History of developmental milestone acquisition within each developmental stream

- Parents are best historians when developmental history focuses on milestones that are **memorable** and milestones that were **attained more recently**

- **Functions of Developmental History:**

1. **Identify pattern of developmental delay**
   - **Static, Acute, Progressive**
2. **Identify markers of atypical development**
   - Delay, Dissociation, Deviation

Patterns of Developmental Delay



Developmental Delay

- Significant lag in one or more streams of development

- **Most commonly represented by a more global delay affecting all streams of development**

Developmental Dissociation

- Difference between developmental rates of two streams of development, with one stream significantly more delayed
- Dissociation is atypical compared to more global developmental delay

Developmental Deviation

- Deviation from the sequence of typical milestone acquisition within a stream of development
- Acquiring higher level developmental milestones before accomplishing lower level developmental milestones
- Development or behavior that is atypical at any age

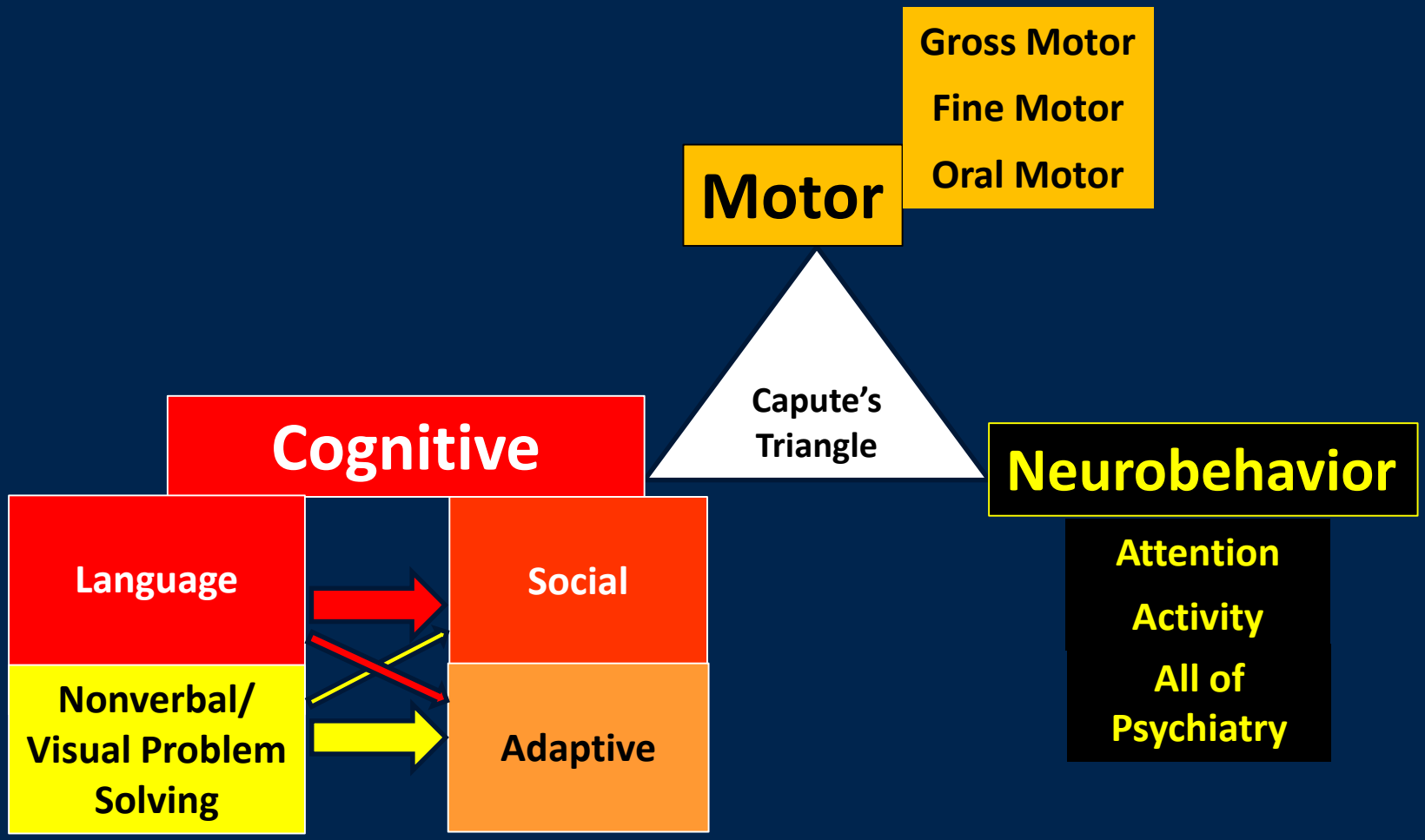
Developmental Deviation

- 2 year old boy fails a developmental screen ("not talking")
  - Gross Motor: Walked at 1 year; ran at 18 months; just started to jump
  - Visual Perceptual/Fine Motor/Adaptive: Intentionally released objects before 1 year and scribbled soon after 1 year. Copies strokes but not circle. Recognized all letters of the alphabet at 18 months
  - Speech/Language: Began babbling at 1 year; currently has a 10 word vocabulary but does not use a specific "Mama" and "Dada"; Use multiword phrases by repeating phrases from videos; does not use gestured language; just started following gestured commands

Neurdevelopmental Exam

- Performed to confirm the developmental history

Developmental Diagnosis: Capute's Triangle



Key Neurodevelopmental Principles

- **Spectrum of disability within each stream**
  - Mild disabilities predominate over severe disabilities
  - The more severe the developmental-behavioral disability, the earlier it can be reliably identified
    - Children with autism spectrum disorders are usually not noticed to behave appreciably differently from typically developing children until after 12 to 18 months of age
    - Children with milder cases of autism spectrum disorders might not be reliably identified until older ages (when social demands exceed their social abilities)

Key Neurodevelopmental Principles

- **Continuum of disability across streams**
  - Presenting developmental complaint most often just the “tip of the iceberg”
  - Diffuse/global developmental-behavioral difficulties more common than dissociated/deviated development
  - Dissociation/deviation in one stream more commonly associated with dissociation/deviation in other streams

Key Neurodevelopmental Principles

- **Delay, dissociation, and deviation reflect atypical CNS processing (connectivity)**
  - -The more delayed, dissociated, and deviated the development, the more atypical the development is
  - -The more atypical the development is, the more atypical the behavior should be expected to be
  - -The atypical neurobehavior observed in autism spectrum disorder is accompanied by atypical delayed, dissociated, and deviated cognitive development/central processing

SPECTRUM OF GLOBAL DEVELOPMENTAL DELAY

Mild Cognitive Delay/ Slow Learning DQ/IQ ≤ 89

Behavior commensurate with cognitive abilities

Motor skills commensurate with cognitive abilities

23% of the population

Increasing Delay

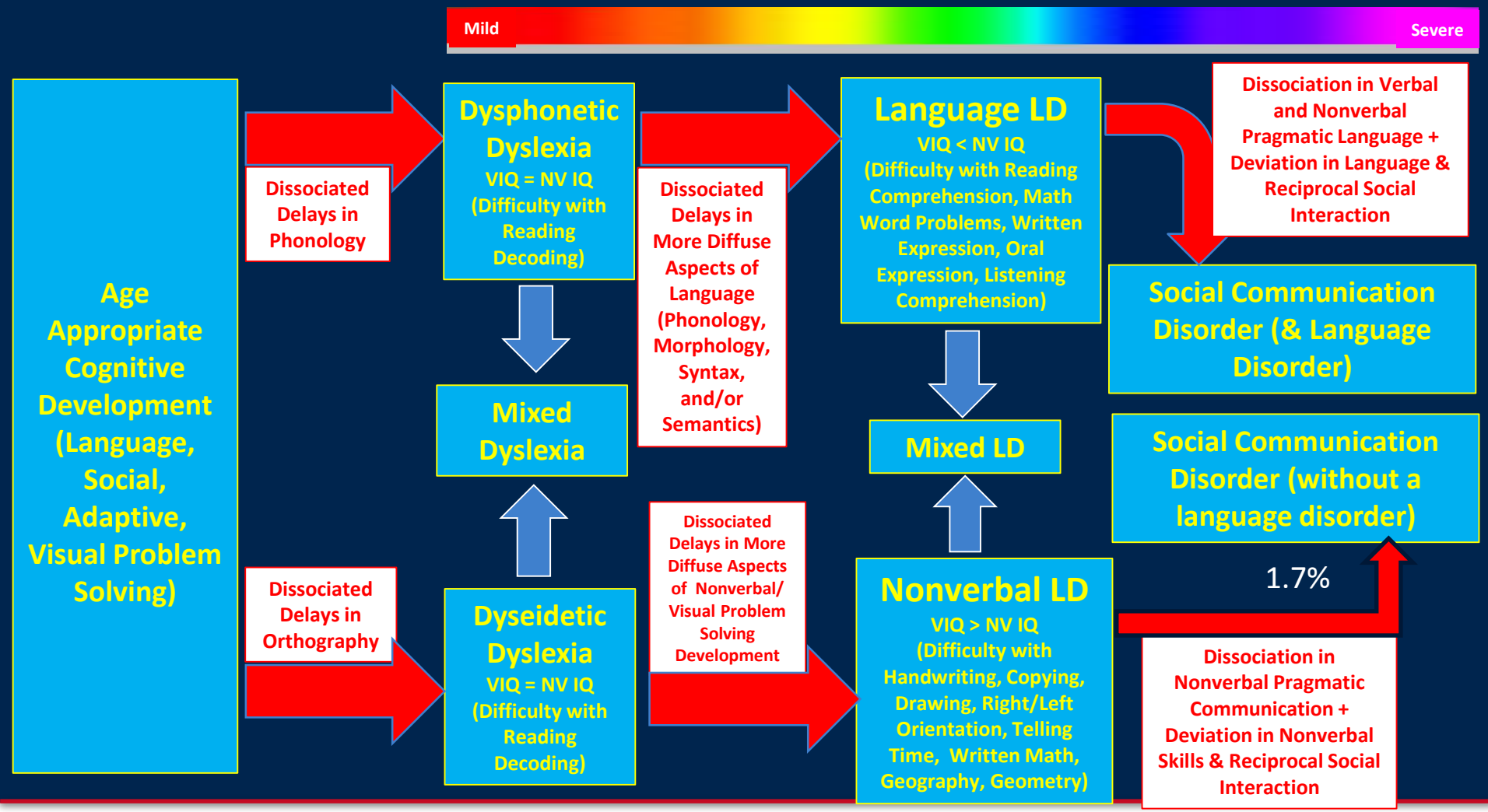
Global Cognitive Delay/Intellectual Disability DQ/IQ < 70

Behavior commensurate with cognitive abilities

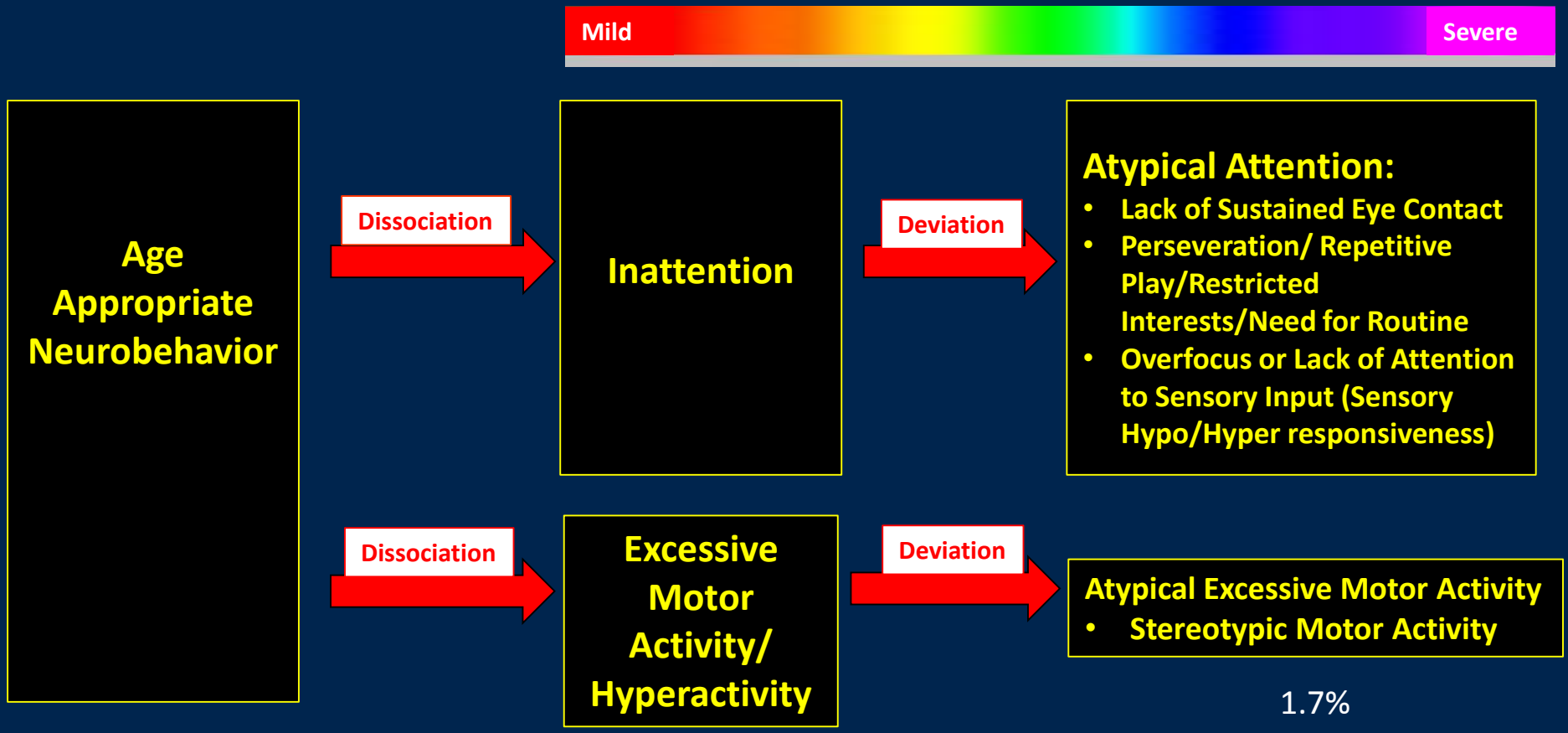
Motor skills commensurate with cognitive abilities

2-3% of the population

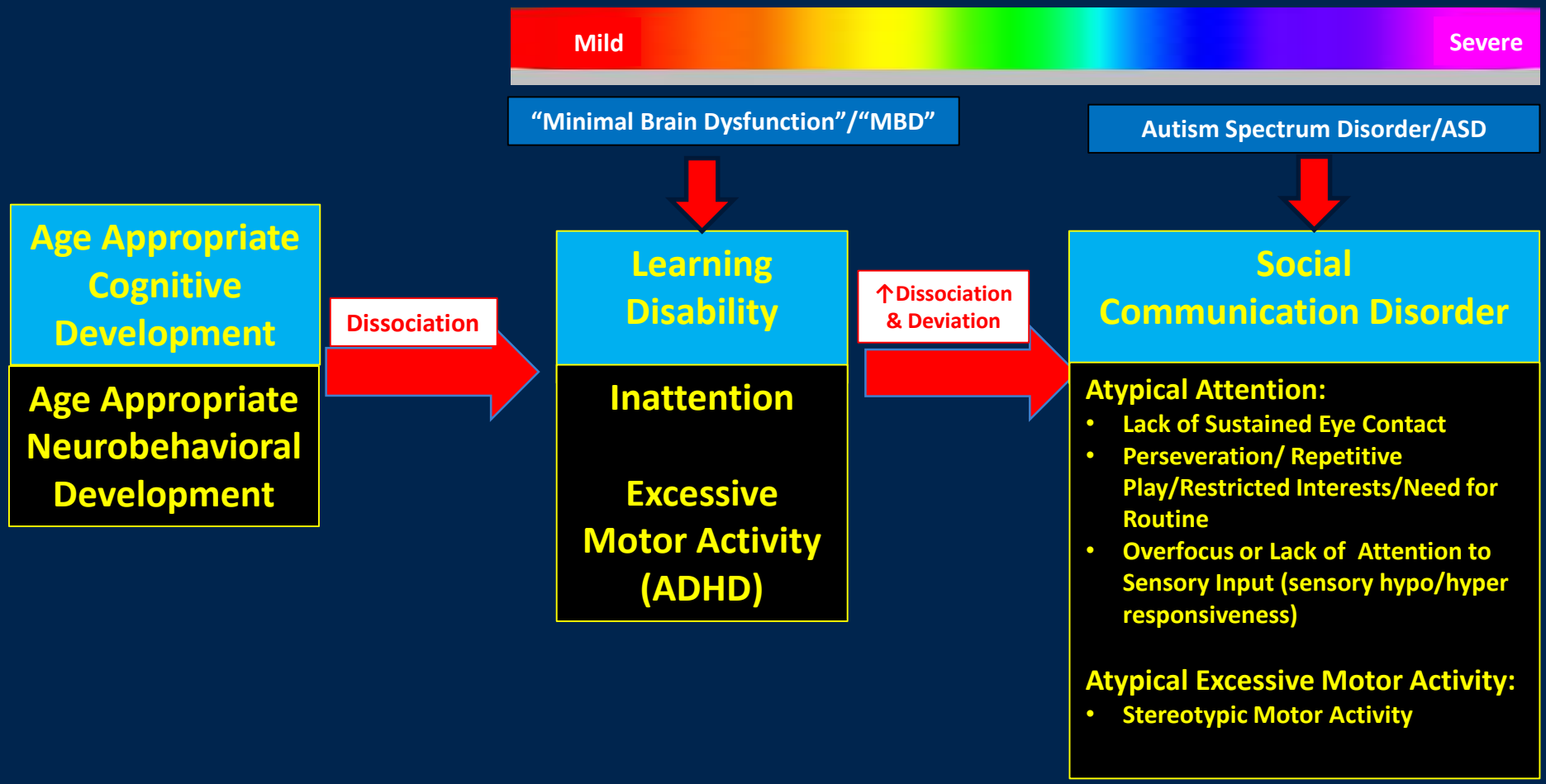
SPECTRUM OF COGNITIVE DISSOCIATION & DEVIATION



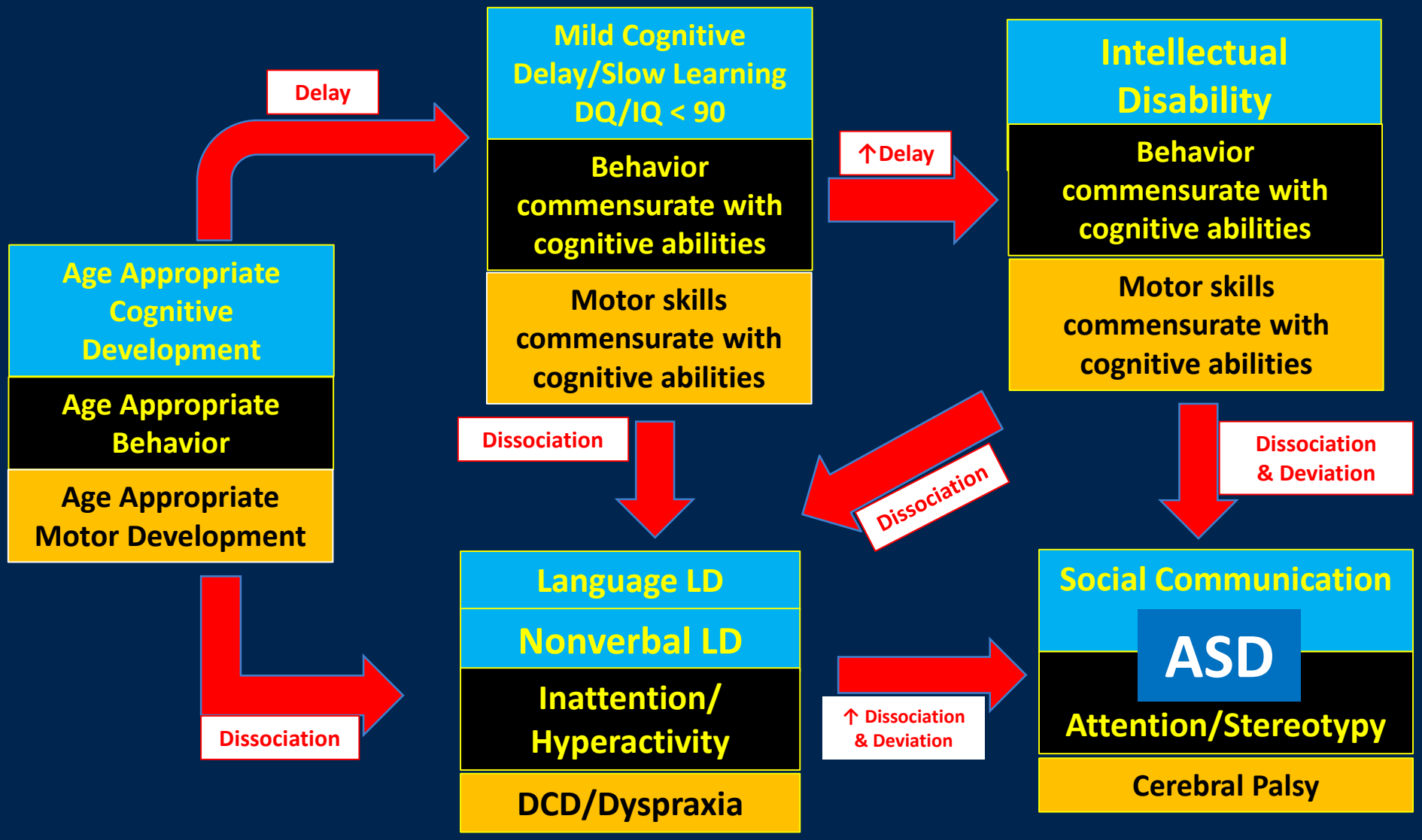
SPECTRUM OF NEUROBEHAVIORAL DISSOCIATION & DEVIATION



CONTINUUM OF COGNITIVE & NEUROBEHAVIORAL DISSOCIATION AND DEVIATION



Spectrum and Continuum of Developmental Disabilities



Early Intervention/Special Education

- National Research Council, Committee on Educational Interventions for Children with Autism. *Educating Children with Autism*. Lord C, McGee JP, eds. Washington, DC: National Academies Press; 2001

- National Autism Center (2015). *Findings and conclusions: National standards project, phase 2*. Randolph, MA. www.nationalautismcenter.org

Early Intervention

- **Refer to EI as soon as a diagnosis of autism is suspected**

- Services should include intensive direct and consultative language, behavioral, and social skills interventions

- Provide a minimum of 25 hours per week
  - -Individualized
  - -Highly structured
  - -Systematically planned
  - -Developmentally appropriate

Early Intervention

- Priorities of focus:
  - Functional spontaneous communication
  - Social instruction delivered throughout the day in various settings (typical peers, home)
  - Cognitive development
  - Play skills
  - Proactive approaches to atypical and challenging behaviors.

- Generalization and maintenance of newly learned skills in natural environments as important as the acquisition of new skills.

Evidence-Based Intervention

- Applied Behavioral Analysis (ABA)
  - Strongest empirical support in the published, peer-reviewed research literature
  - Method to teach, reinforce, and maintain new skills and desirable behaviors
  - Method to extinguish problematic maladaptive behaviors (self-injury; aggression)

Other Educational/Therapeutic Interventions

- Developmental models
  - Focus on remediation of fundamental deficits in pivotal developmental skills
  - Early Start Denver Model: Developmental + ABA techniques

- Structured teaching (TEACCH)
  - Focus on improving skills and modifying environment to accommodate deficits
  - Emphasis on visual schedules, physical/task organization

Other Educational/Therapeutic Interventions

- Social Skills Instruction (e.g. “Social Stories”)
  - Address initiating social interactions, responding to social overtures, minimizing stereotyped behavior
- Speech and Language Therapy
  - Goal to promote verbal and nonverbal communication
  - Augmentative communication/PECS

Other Educational/Therapeutic Interventions

- Occupational Therapy
  - Address associated fine motor deficits and delays in activities of daily living
  - No evidence for “sensory integration therapy” (See AAP Policy Statement June 2012)
- Physical Therapy
  - Address associated gross motor deficits

Response to Intervention

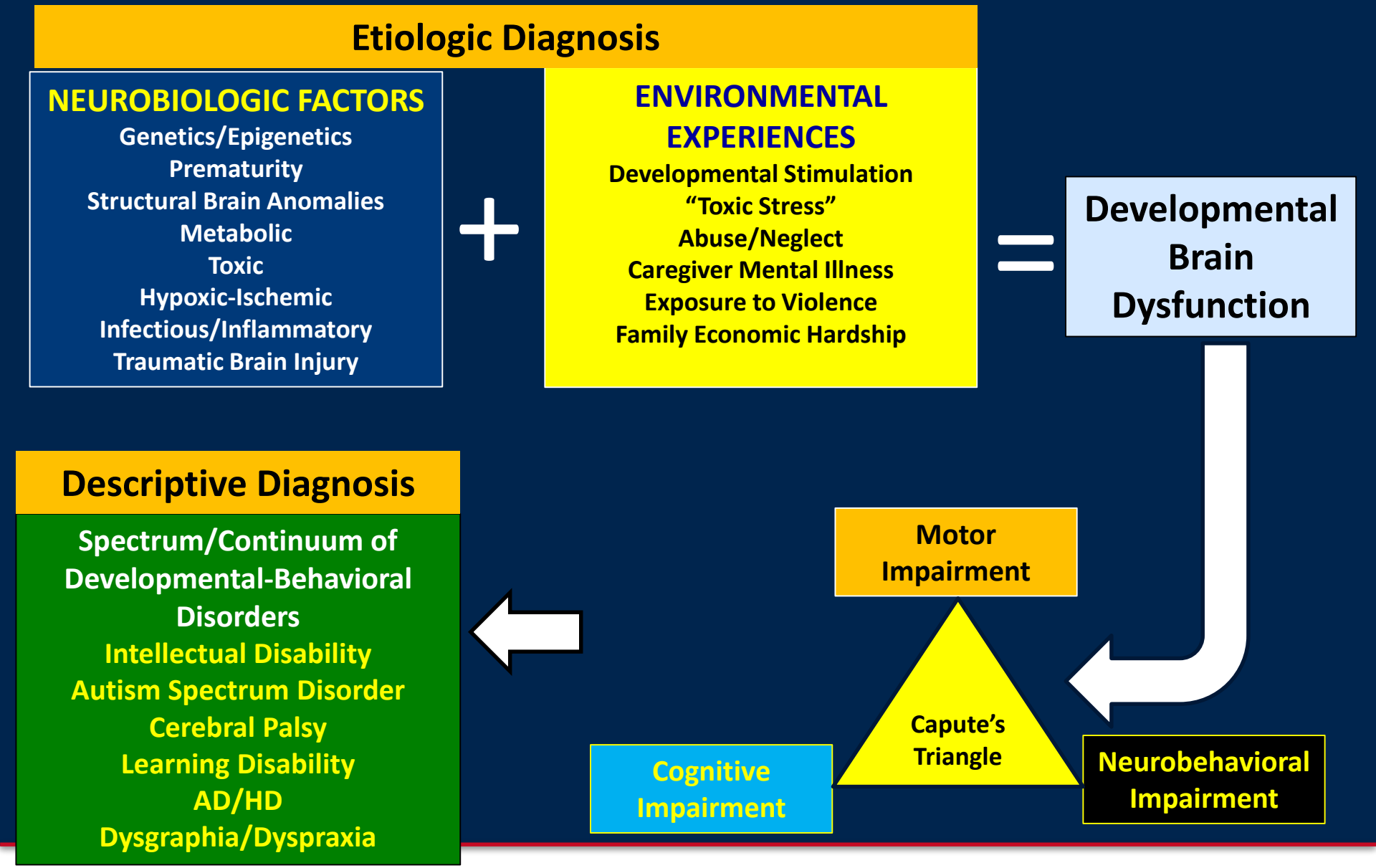
- Outcomes extremely variable
  - Up to 25% may no longer meet criteria for ASD*
  - Others show very slow gains
- Possible predictors of improved outcomes
  - Higher IQ/Receptive language
  - Better imitation skills
  - Milder autism symptoms
  - Increased intensity of **early** behavioral interventions

*Helt M. Neuropsychol Rev. 2008; Dec;18:339-66.

Why Consider Laboratory Testing to Establish a Medical Diagnosis?

- Peace of mind for families in knowing cause of developmental difficulties
- Prevent other associated medical problems
- Provide specific genetic counseling for families
- Eliminate need for further unnecessary (standard and nonstandard) testing

Etiologic and Descriptive Diagnoses for Developmental-Behavioral Disorders



Medical Workup

- Consider in all children with autism spectrum disorders
  - -Audiology assessment
  - -Fragile X DNA analysis
  - -Chromosome microarray analysis

Medical Workup To Consider with Specific Indications

- Neurocutaneous findings: Tuberous Sclerosis, NF1 (MRI)
- Cleft palate, toe syndactyly: SLO (↑7-dehydrocholesterol)
- Marked macrocephaly, skin hamartomas: PTEN hamartoma syndromes
- Deceleration of head growth, hand wringing: Rett (MECP2)
- Progressive pattern of developmental delay, decompensation with mild illness, failure to thrive, hypotonia, hypertonia, ataxia, nystagmus, epilepsy, severe/profound intellectual disability, macrocephaly, coarse facial features, hepatosplenomegaly: Metabolic studies
- Isolated language regression; Concern about seizures (20-35%): EEG
- Mouthing non-food items/pica: Lead, iron, zinc

Medical Conditions That May Exacerbate Maladaptive Behaviors*

- GI: constipation, esophagitis
- Sleep disorders
- Anxiety/depression
- Malnutrition/side effects of dietary supplements
- Allergies: atopic dermatitis, conjunctivitis
- Headaches
- Corneal abrasion
- Dental: abscess, caries, impaction, trauma
- ID: OM, otitis externa, pharyngitis
- Sprains, occult fractures

*Myers SM. *Pediatr Ann* 38: 42-49, 2009

Psychopharmacology

- Risperidone /Aripiprazole
  - Only meds with FDA-approved labeling specific to autism (Risperidone > 5 yr and Aripiprazole > 6 years)
  - For treatment of irritability, including aggressive behavior, deliberate self injury, and temper tantrums

- Hyperactivity/impulsivity*
  - Methylphenidate

*Research Units on Pediatric Psychopharmacology (RUPP) Autism Network. Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. *Arch Gen Psychiatry*. 2005;62:1266-1274.

Psychopharmacology

- Psychotropic meds for children with ASD typically not as effective compared to treating same target behaviors in children without ASD
  - -Fewer with positive response
  - -Decreased magnitude of positive response
  - -More side effects
- "Start low, go slow"

Unproven Therapies

- Dietary/vitamin supplements
- Restrictive diets
- Chelating agents
- Facilitated Communication
- Auditory Integration Therapy
- Music Therapy
- Sensory Integration Therapy
- Swimming with dolphins
- Antifungals, antivirals, antibiotics
- IVIG
- Craniosacral therapy
- Hyperbaric oxygen
- Interactive metronome
- Transcranial magnetic stimulation
- Secretin

Unproven Therapies

- Take advantage of:
  - Lack of evidence-based biomedical treatments for neurodevelopmental disabilities
  - Desire to “do something”
  - Natural course of neurodevelopmental disabilities
  - Waxing & waning course of behavioral problems
  - Cognitive Dissonance
  - Placebo Effect
    - Need for randomized, double-blind, placebo-controlled trials, just like for any other medical treatment

“Keeping an open mind is a virtue – but not so open that your brains fall out”

James Oberg (in Carl Sagan, The Demon Haunted World: Science as a Candle in the Dark. Ballantine Books (1996)

Potential Harm of Nonstandard Therapies

- Side effects
  - Including death (chelation)
- Financial Cost
  - Not covered by insurance
- Time Cost
  - Lost family time
  - Time away from evidence-based interventions
- Emotional Cost
  - False Hope
  - Parental Guilt

Conclusions

- Autism spectrum disorder is a developmental diagnosis within the spectrum of developmental disabilities, not a simple checklist
- Children with autism spectrum disorder most commonly present with an atypical developmental profile (dissociated delays and deviation)
  - Atypical development (dissociation/deviation) is usually accompanied by atypical behavior

Conclusions

- Early intervention should begin as soon as autism is even suspected
- Medical Workup: Audiology evaluation, DNA for Fragile X, CMA should be considered in all children with ASD
- ABA has most evidence in treatment of ASD
- Beware of non-evidence based interventions that may take advantage of desperate parents who would try anything to help their children