

DEVELOPMENTAL MEDICINE: Making (Developmental) Diagnoses & Evidence-Based (Medical) Interventions

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I do intend to discuss unapproved/investigative uses of a commercial product/device in my presentation.

Unapproved/Investigative uses will be identified as they occur in the presentation.

I have/have not used artificial intelligence in the development of this presentation.

Objectives

- At the conclusion of this activity, learners will be able to:
 - Identify both neurobiological and environmental risk factors for delays in development
 - Apply the basic pediatric neurodevelopmental principles that underlie the spectrum and continuum of developmental-behavioral diagnoses
 - Recommend evidence-based psychopharmacological interventions for children with developmental disabilities, when indicated
 - Counsel families of children with developmental disabilities about the plethora of non-evidence-based interventions that are widely available, but despite their popularity, have not been evaluated as treatments for children with developmental disabilities in terms of either their safety or efficacy

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Poll Everywhere

- Which of the following has the ***lowest odds*** of happening?
 - A. Getting bitten by a shark
 - B. Getting struck by lightning
 - C. Winning the national Powerball Lottery
 - D. Getting an appointment with a board-certified developmental-behavioral pediatrician

**ACGME-
Mandated
DBP
rotations
for > 25
years**

Summary of Pediatric Gumbeaux 5/9/2024: Neurodevelopmental Assessment

- 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**
-
- **Make etiological diagnosis**
 - Physical Exam/Medical laboratory workup: **Focus on neurological exam, dysmorphic features, neurocutaneous features, growth parameters**

Coming Attraction: Fall 2024
Pediatric Gumbeaux



Case: 4 year old with “Hyperactivity”

- Developmental History
 - Static pattern of globally delayed developmental milestones
 - Gross Motor DQ's = 75%
 - Visual-Motor Problem Solving DQ's = 75%
 - Speech/Language DQ's = 50%
- Neurodevelopmental Exam
 - Gross motor = 3 years (DQ = 75%)
 - Visual-motor problem solving = 3 years (DQ = 75%)
 - Speech/Language = less than 9 months to 24 months (DQ = 47%)
- Developmental Diagnosis?
 - Globally delayed developmental milestones with dissociated and deviated language

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Etiologic & Descriptive Diagnoses for Developmental Disorders

Etiologic Diagnosis

**NEUROBIOLOGICAL
FACTORS**

+

**ENVIRONMENTAL
EXPERIENCES**

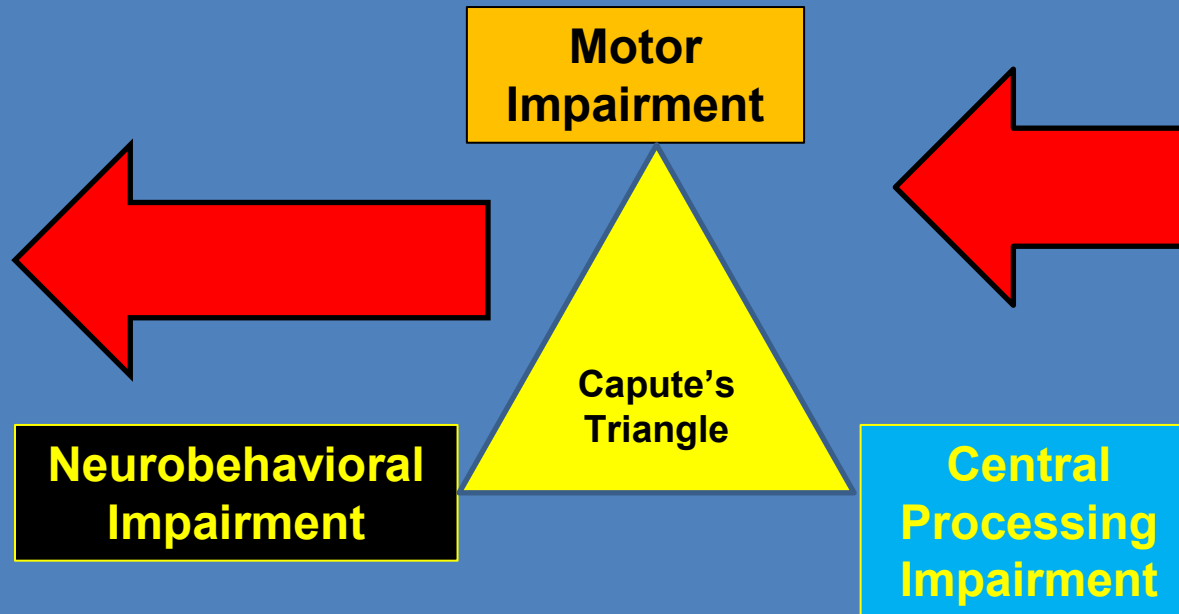
=

**Developmental
Brain
Dysfunction***

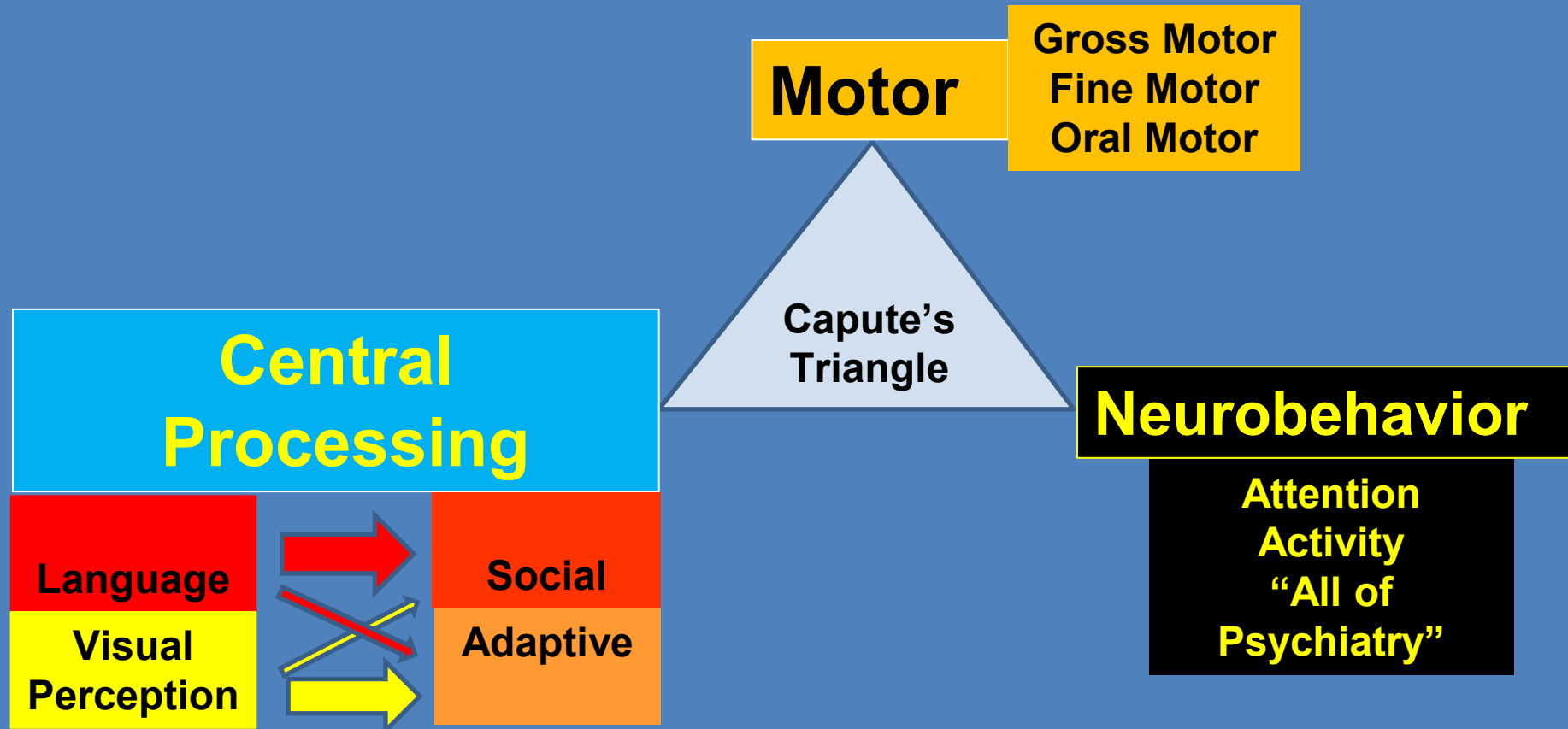
*Moreno-DeLuca A, Myers SM,
et al. *Lancet Neurol* 2013
Apr;12(4):406-414

Descriptive Diagnosis

**Spectrum/Continuum
of
Developmental-
Behavioral
Disorders**



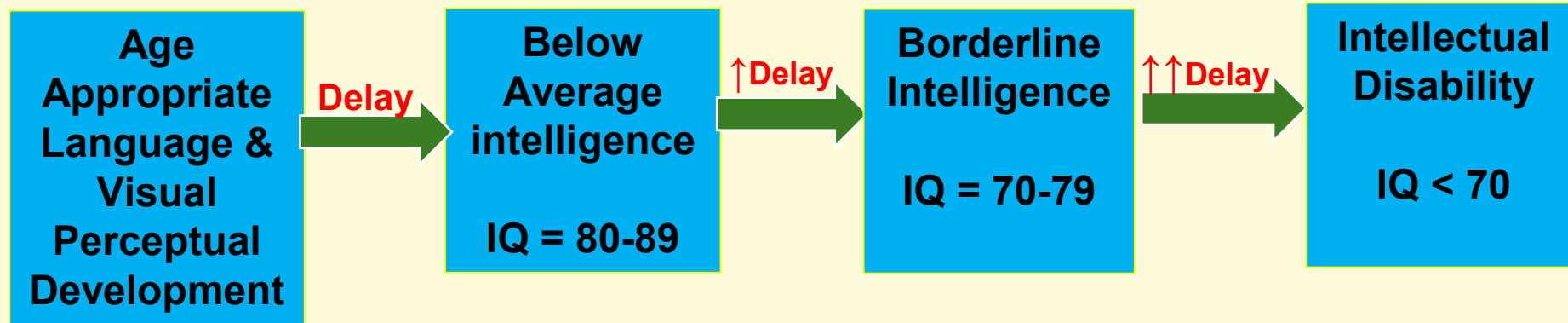
Developmental Diagnosis: Capute's Triangle



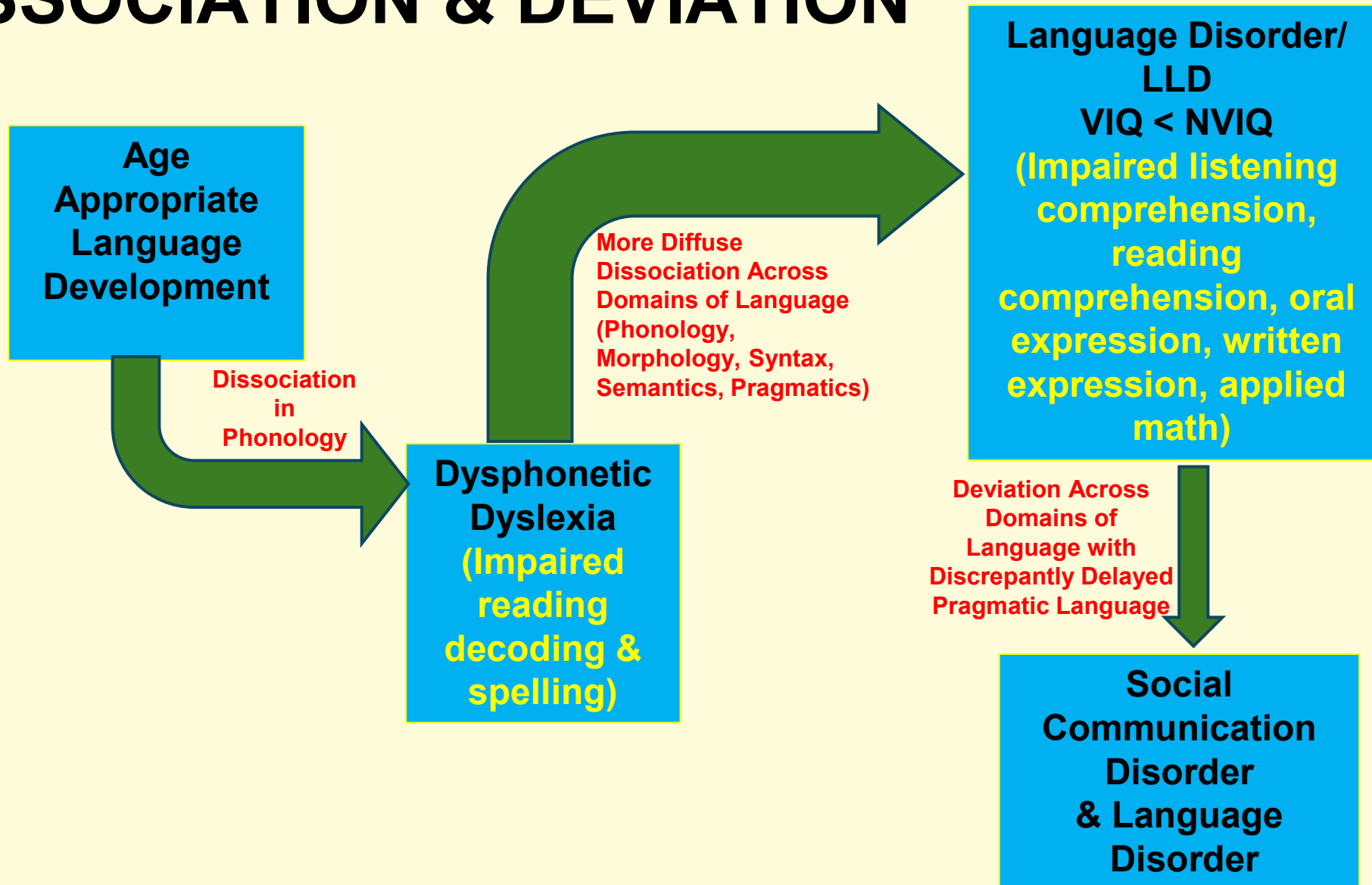
Key Neurodevelopmental Principle #1

- **Spectrum of disability
within each developmental
stream**

SPECTRUM OF GLOBAL CENTRAL PROCESSING (LANGUAGE & VISUAL PERCEPTUAL) DELAY



SPECTRUM OF LANGUAGE DISSOCIATION & DEVIATION



SPECTRUM OF VISUAL PERCEPTUAL DISSOCIATION AND DEVIATION

Age
Appropriate
Visual
Perceptual
Development

Mild Dissociation
Involving Specific
Visual Perceptual
Domains

Dyseidetic Dyslexia
(Impairment in
Reading Decoding
& Spelling) or
Dyscalculia
(Impairment in math
calculation)

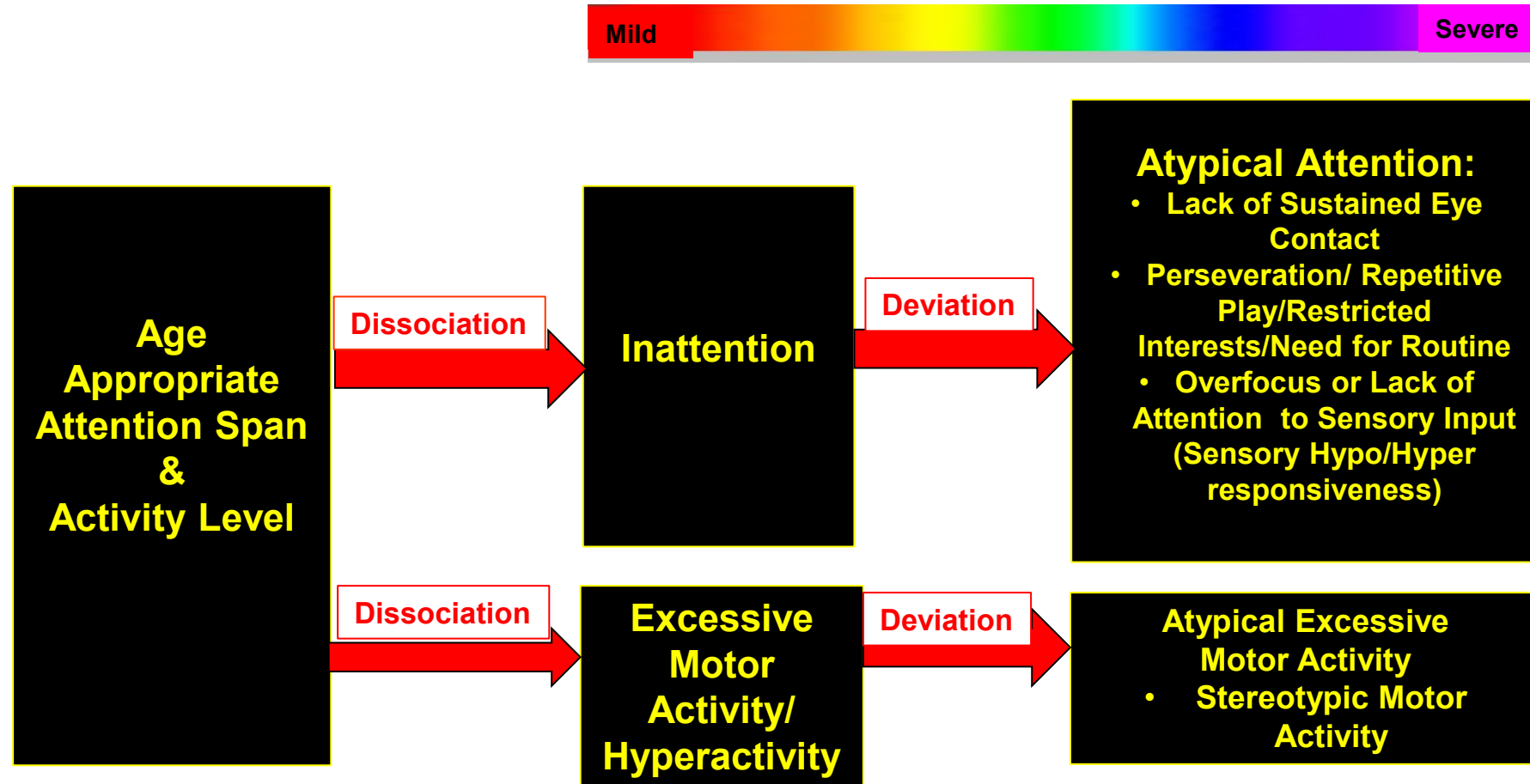
More Diffuse Dissociation Across
Domains of Visual Perception
(Visual Discrimination, Visual
Memory/Sequential Memory,
Spatial Relationships, Form
Constancy, Visual Figure Ground,
Visual Closure)

NVLD
VIQ > NVIQ
(Impairments in
Copying/Drawing/Writing,
Math
Computation/Reasoning,
Right/Left Orientation,
Telling Time,
Geography/Geometry)

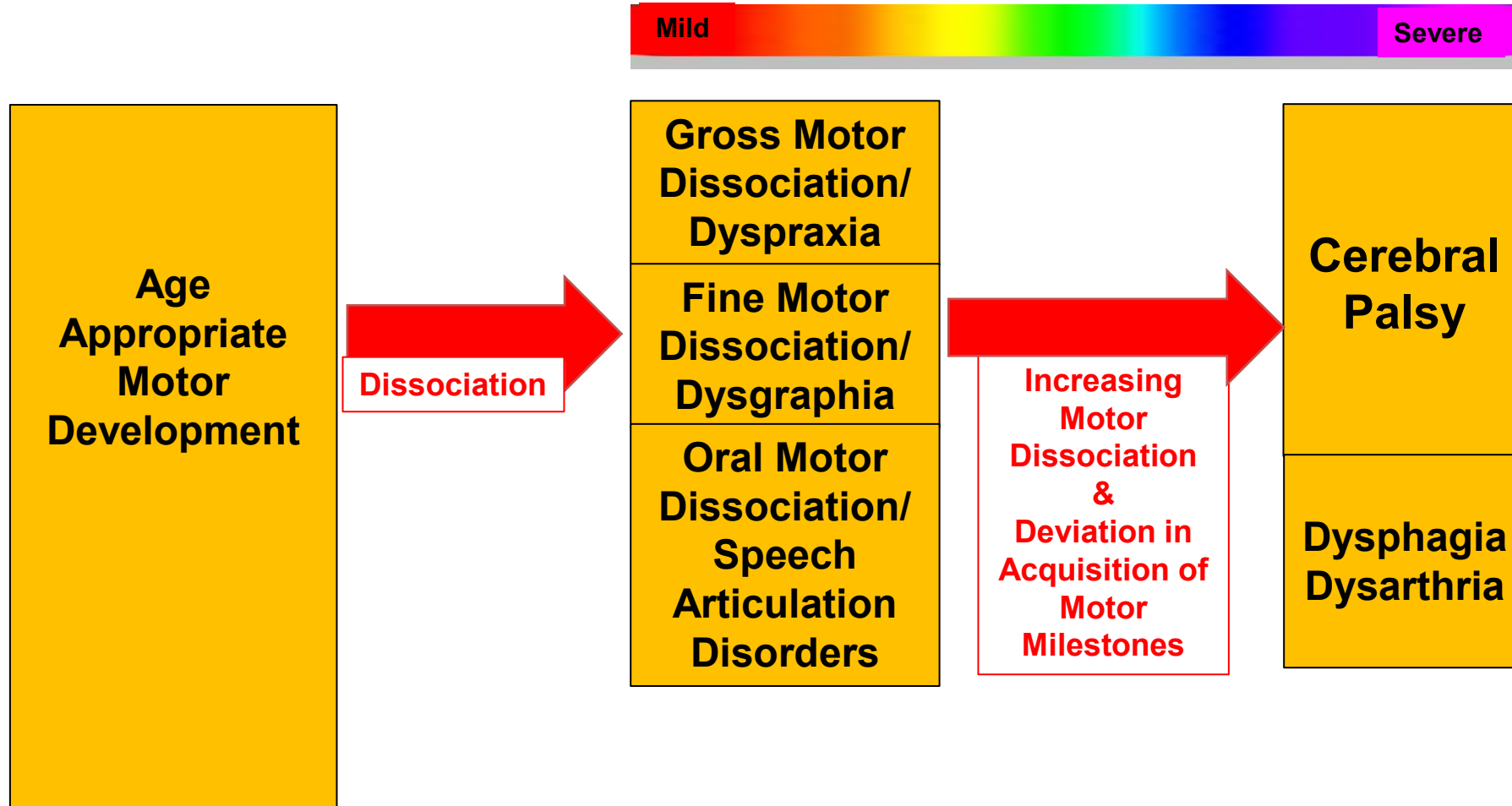
Deviation Across
Domains of Visual
Perception with
Discrepantly Delayed
Visual Perception of
Human Relations
(Nonverbal
Communication)

**Social
Communication
Disorder**
(without a Language
Disorder)

SPECTRUM OF NEUROBEHAVIORAL DISSOCIATION & DEVIATION



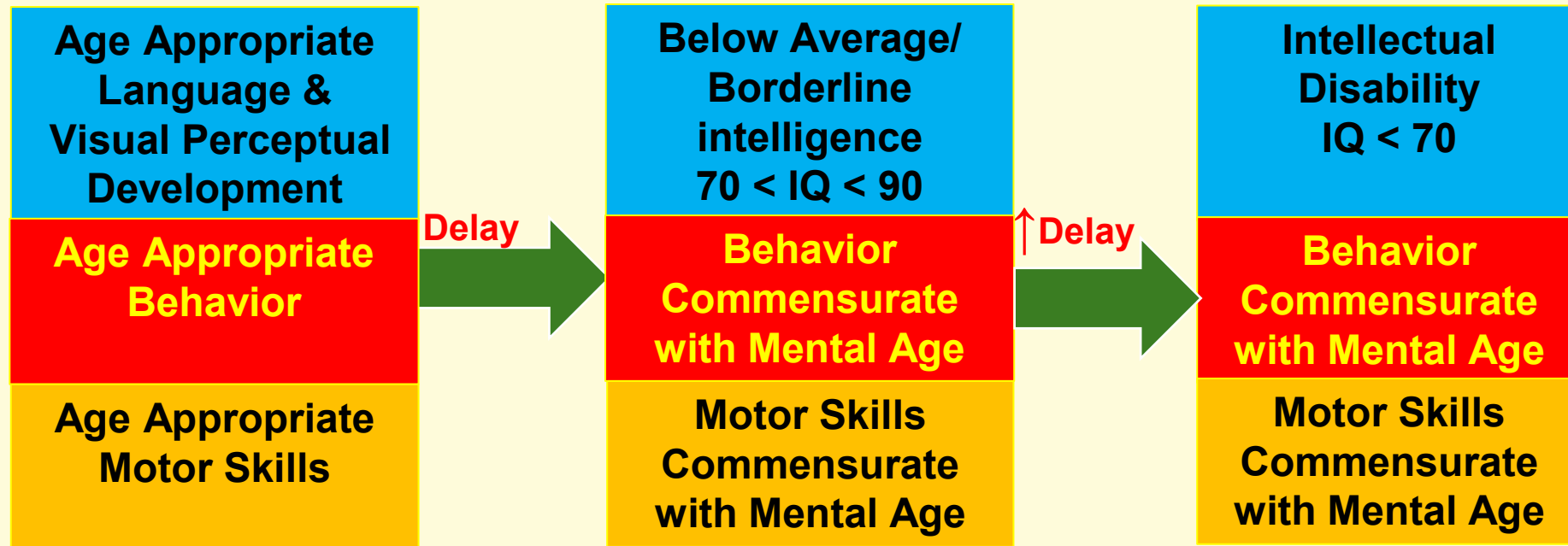
SPECTRUM OF MOTOR DISSOCIATION & DEVIATION



Key Neurodevelopmental Principle #2

- **Continuum of disability
across developmental
streams**

SPECTRUM/CONTINUUM OF GLOBAL DEVELOPMENTAL DELAY

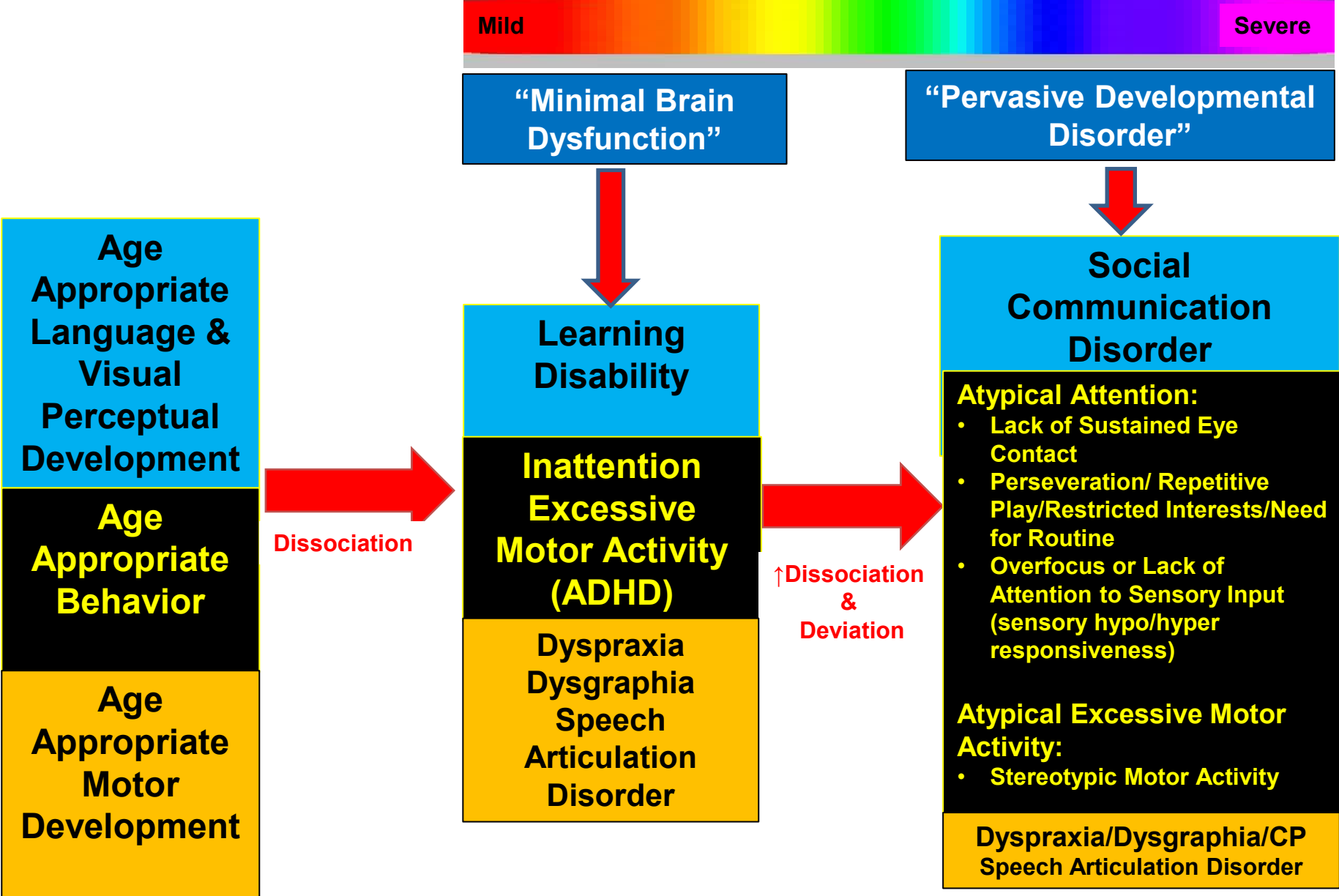


Key Neurodevelopmental Principle #3

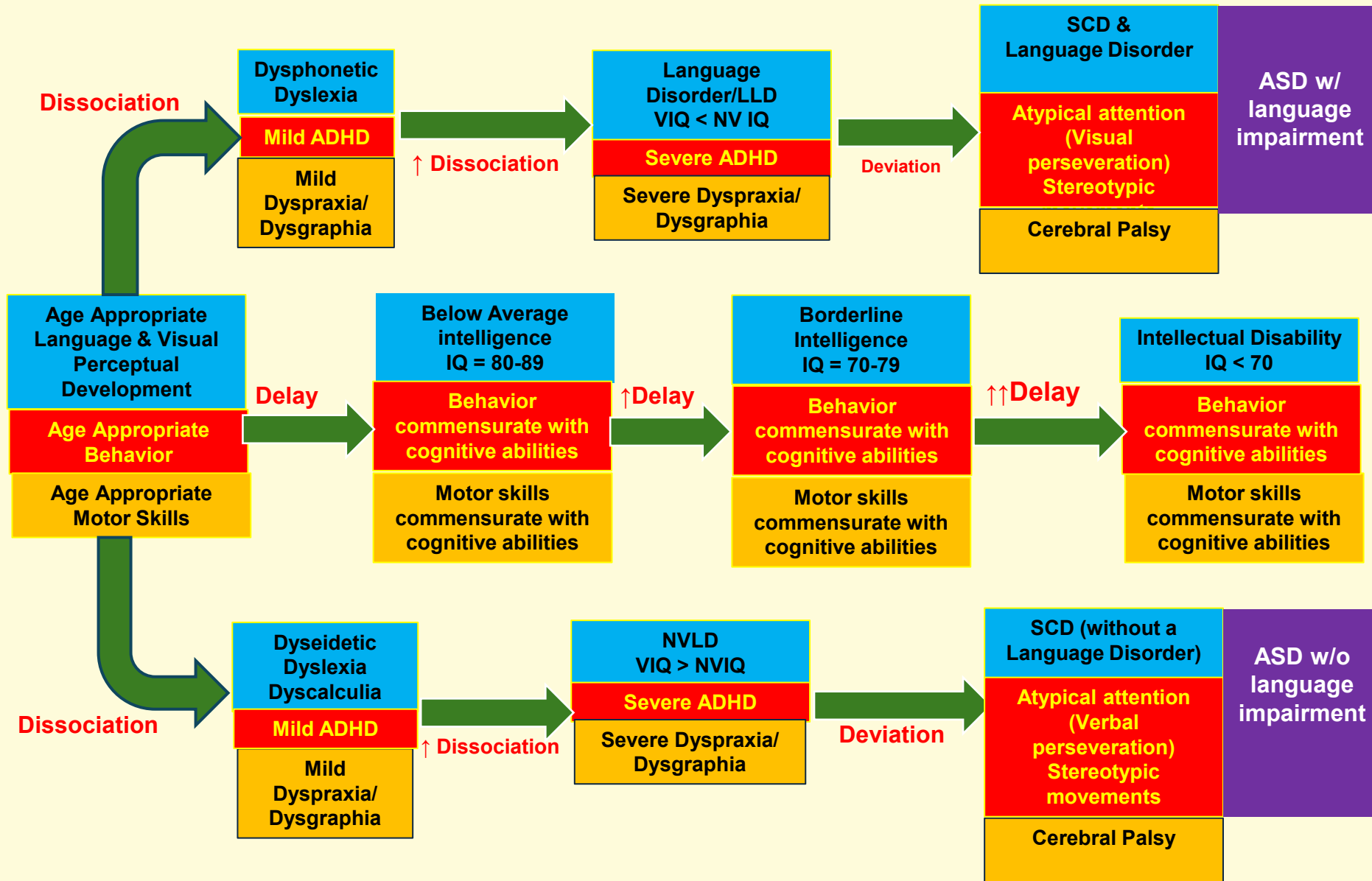
- **Increasing dissociation & deviation reflect increasingly atypical development**



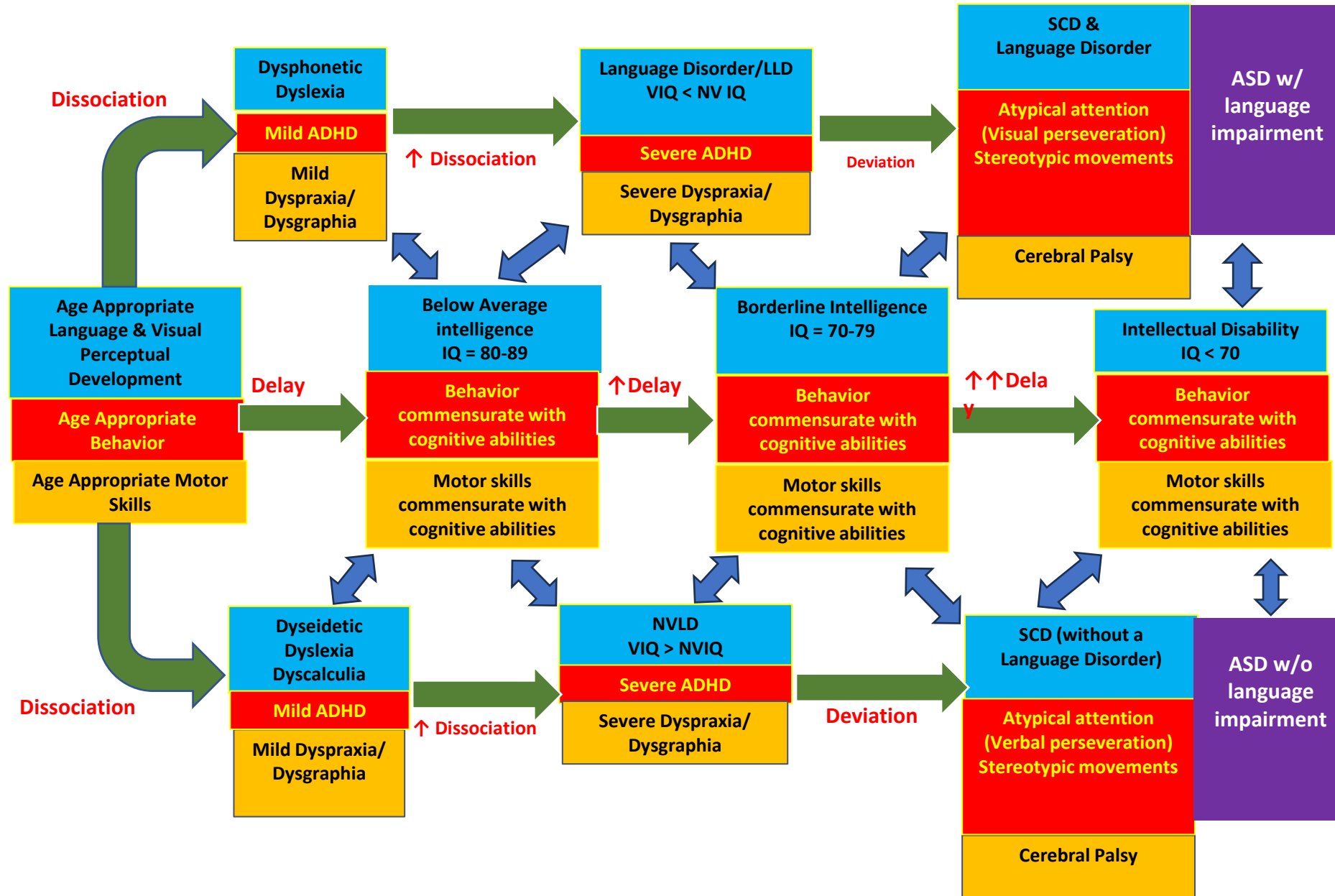
SPECTRUM/CONTINUUM of DEVELOPMENTAL DISSOCIATION/ DEVIATION



SPECTRUM & CONTINUUM OF DEVELOPMENTAL DISABILITIES

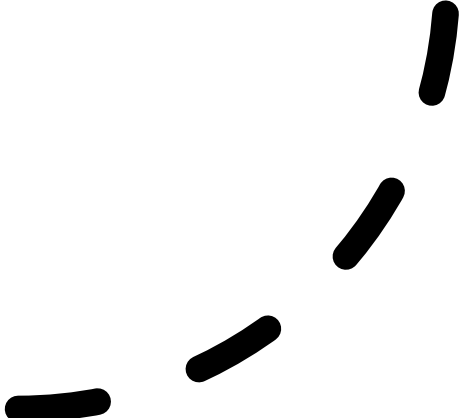


SPECTRUM & CONTINUUM OF DEVELOPMENTAL DISABILITIES

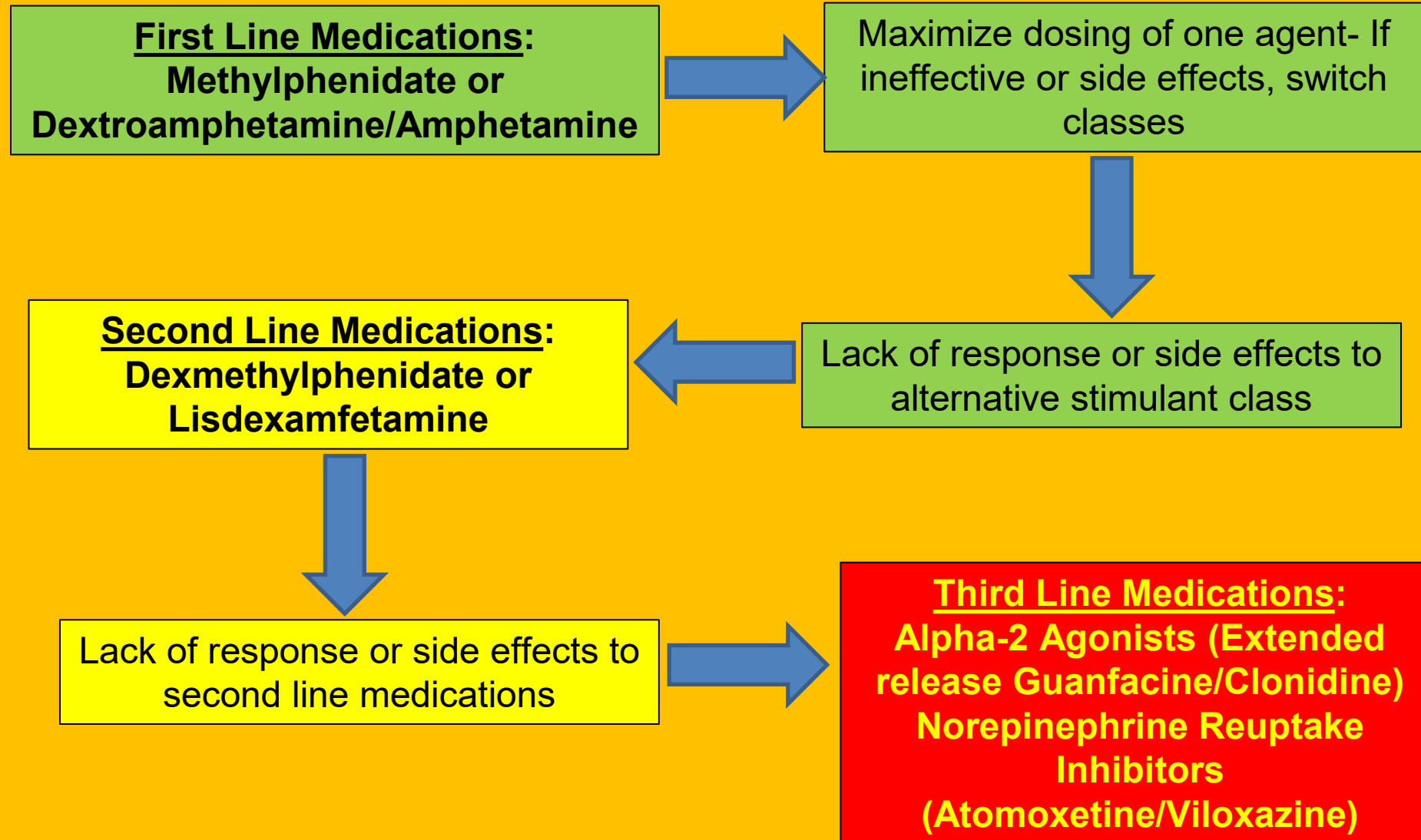


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Developmental Medicine Themes

- **First, do no harm**
 - **Practice evidence-based medicine**
- 
- A decorative graphic consisting of several thick, black, curved dashes arranged in a roughly circular pattern in the bottom right corner of the slide.

FDA-Approved Medications for ADHD in Children (≥ 6 yr)



The ADHD Medication Guide©

- Developed by Andrew Adesman, MD
- Available at: <https://www.adhdmedicationguide.com>

Effect
Size

Stimulants > Alpha-2 Agonists/NRIs

Side
Effects

Stimulants < Alpha-2 Agonists/NRIs



Evidence-Based Treatment of Pediatric Anxiety/Depression

- **Psychotherapy**
 - Cognitive Behavioral Therapy (CBT)
- **Medication**
 - Selective Serotonin Reuptake Inhibitors (SSRIs)
 - Serotonin & Norepinephrine Reuptake Inhibitors (SNRIs)

FDA-Approved Use of SSRI's & SNRI's in Children

Medication	FDA-Approved Age	FDA-Approved Diagnosis	Starting Dose	Maximum Daily Dose
Fluoxetine (Prozac)	7 years & older 8 years & older	OCD MDD	10 mg	60 mg
Fluvoxamine (Luvox)	8 years & older	OCD	25 mg	200 mg
Sertraline (Zoloft)	6 years & older	OCD	25 mg	200 mg
Escitalopram (Lexapro)	7 years & older 12 years & older	GAD MDD	5 mg	20 mg
Duloxetine (Cymbalta)	7 years & older	GAD	30 mg	60 mg

GAD: Generalized Anxiety Disorder; OCD: Obsessive-Compulsive Disorder; MDD: Major Depression Disorder

SSRI & SNRI Side Effects

**FDA Black
Box
Warning**

**Activation
GI
Bleeding**
(if taken with NSAID,
Anticoagulants)
Withdrawal

**Serotonin
Syndrome**

Psychopharmacology in Developmental Medicine: Complex Circumstances

0

Preschoolers

Intellectual
Disability
(ID)

Autism

Before Considering Psychotropic Meds in Preschoolers, ID, Autism



Is behavior
inappropriate
for
developmental
level?

Is behavior
impairing
across
settings?

Is behavior
secondary to
demands &
expectations
that exceed
developmental
abilities?

Child with disability in regular classroom



Accommodations & Modifications

of all assignments, materials, texts, pacing, testing, & grading



Mismatch between demands/expectations for performance and underlying developmental abilities



STRESS
(Anxiety & Frustration)

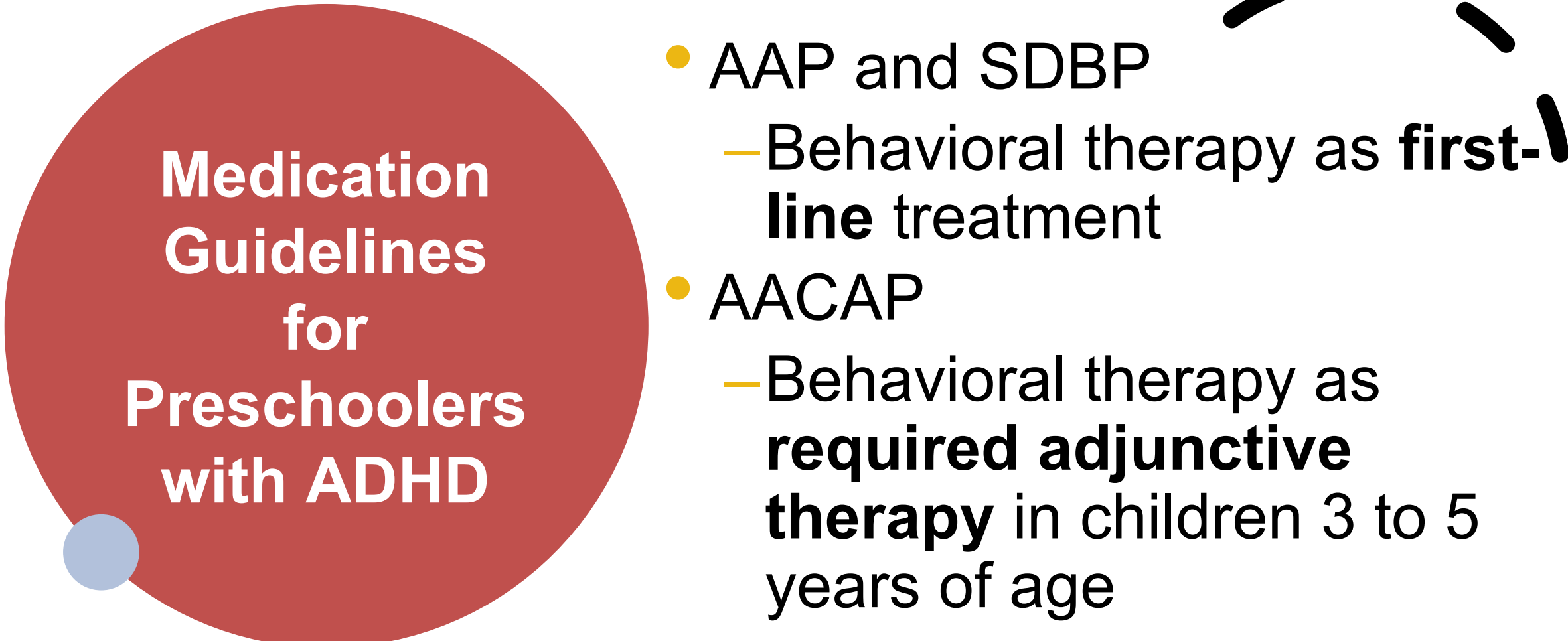


FLIGHT

Secondary Inattention
Task avoidance
Passive resistance
Social withdrawal
Low self esteem
School negativity

FIGHT

Secondary Impulsivity/Hyperactivity
Attention seeking
Acting out
Oppositional
Aggressive
Elopement from stressful situation



Medication Guidelines for Preschoolers with ADHD

- AAP and SDBP
 - Behavioral therapy as **first-line** treatment
- AACAP
 - Behavioral therapy as **required adjunctive therapy** in children 3 to 5 years of age

Coyle JT. *JAMA* 2000; 283(8): 1059-1060

- Editorial Board of *Journal of Child & Adolescent Psychopharmacology*
 - 80% reported **no/very rare** prescribing of psychotropic medications to children < 5 years

Psychotropic Meds Not As Effective in Preschoolers, ID, Autism



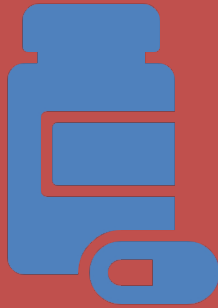
↓ With a positive response

↓ Magnitude of positive response

↑ Side effects

“Start low, go slow”

ADHD Meds in Preschoolers



- **FDA Approved:**
 - Dextroamphetamine approved starting at 3 years.
- **Not FDA Approved**
 - **AAP:**
 - Recommends Methylphenidate for < 6 years
 - **2021 DBPNet Study***
 - “Improvement”: Stimulants = 78%; Alpha-2 Agonists = 66%
 - **2023 Systematic review & Meta-analysis****
 - Immediate-release Methylphenidate, Extended-release Methylphenidate, Lisdexamfetamine

*Harstad E, et al. *JAMA* 2021;325(20):2067-2075

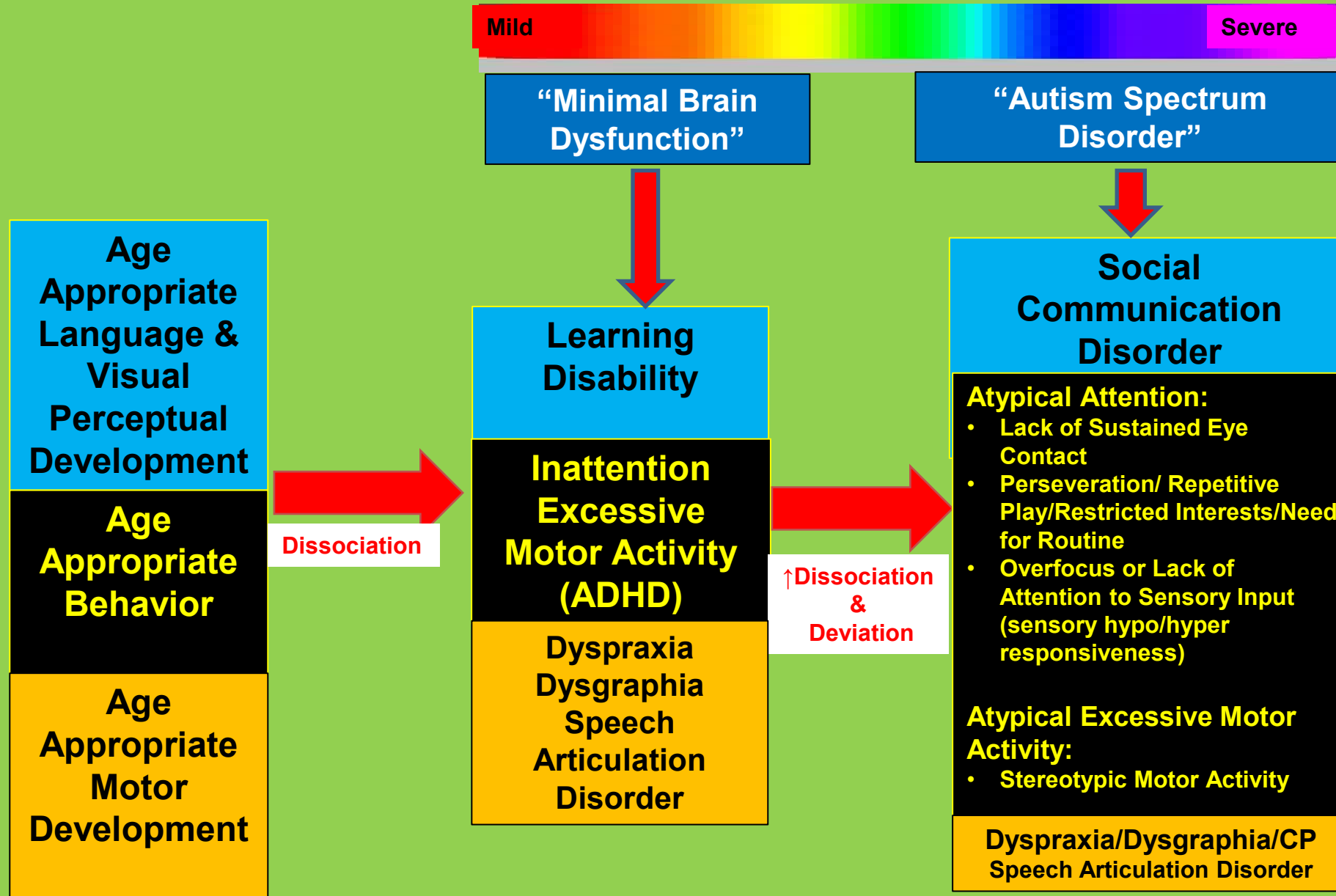
**Sugaya LS, et al. *JCPP Adv* 2023 Feb 25;3(3);e12146. PMID 37720577



Autism & ADHD

- **DSM-IV**
 - ADHD and Autism mutually exclusive
- **DSM-5**
 - ADHD can be diagnosed in autism
- **Neurodevelopmental Model**
 - All with Autism have Atypical Attention

Neurodevelopmental Model of Autism



Autism/ID:
Treatment for
Disinhibition/
Hyperactivity

- Behavioral intervention
 - Parent Training in Behavior Management
 - ABA
- School supports and accommodations
- **No FDA-approved medications**



Evidence-Based (but not FDA-approved) ADHD Meds in ID/Autism



Intellectual
Disability:
Methylphenidate*

Autism:
Methylphenidate
Guanfacine ER**

*Simonoff E, et al. *J Child Psychol Psychiatry Allied Discip.* 2013;54:527–535)

**Research Units on Pediatric Psychopharmacology (RUPP) Autism Network:
Arch Gen Psychiatry. 2005;62:1266-1274 & *Am J Psychiatry* 2015;172:1197-206

Additional Stimulant Med Side Effects



Preschool:
Irritability
Tearfulness

Intellectual
Disability:
Social
Withdrawal

Autism:
Accentuate
differential
auditory and
visual
attention
span

ID/Autism & Psychiatric Comorbidities



Disruptive
behavior

Anxiety/OCD

Depression/Mood
Disorders



**ID/Autism
&
Disruptive
Behavior**

- **Disruptive behaviors**
 - Irritability
 - Tantrums
 - Oppositional/defiant
 - Aggression
 - Self-injury
 - Elopement

- GI: constipation, esophagitis
- Sleep disorders
- Side effects of dietary supplements
- Allergies: atopic dermatitis, conjunctivitis

Step 1

**Don't Forget
Medical Conditions
That May Exacerbate
Maladaptive
Behaviors***

- Headaches
- Corneal abrasion
- Dental: abscess, caries, impaction, trauma
- ID: OM, otitis externa, pharyngitis
- Sprains, occult fractures

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

Step 2

- Make sure that behavior is inappropriate for developmental level & impairing across settings

- Make sure that behavior is not secondary to demands & expectations that exceed developmental abilities

❖ Parent
Management
Training
(PMT)

Step 3

Evidence-Based
Treatment

❖ Applied
Behavioral
Analysis
(ABA)

Risperidone > 5 years

Step 4

Medications with FDA-approved
labeling specific to autism

Aripiprazole > 6 years

Atypical Antipsychotics

	Starting Dose	Maximum Dose
Risperidone (> 5 years)	0.25 mg	3 mg
Aripiprazole (> 6 years)	2 mg	15 mg

Atypical Antipsychotics: Side Effects

Sedation

Weight gain

- Hyperlipidemia
- Glucose intolerance
- Diabetes

Extrapyramidal symptoms

(Acute Dystonia, Tardive Dyskinesia)

Gynecomastia

Dry mouth or hypersalivation

Constipation

Neuroleptic malignant syndrome

(fever, muscle rigidity, altered mental status, autonomic dysfunction)



**ID/Autism:
Anxiety/
Depression**

- Signs/symptoms of anxiety/depression overlap with autism
- Nonverbal: Trouble communicating emotions
- Treatment
 - ⦿ Adapted Cognitive Behavioral Therapy (BIACA)
 - ⦿ **No FDA-approved medications**



Autism & Anxiety/ Depression

- Systematic reviews of RCTs:
 - No evidence for use of anti-anxiety, antidepressant, or mood stabilizing meds in autism*

*Deb S, et al. *BJPsych Open* 2021; Oct 1:7(6):e179, 1-15.doi: 10.1192/bjo.2021.1003.

*Limbu B, et al. *BJPsych Open* 2022; 8:e52, 1-12. doi: 10.1192/bjo.2022.18

Autism & OCD

- **OCD:** Ego-dystonic intrusive thoughts (obsessions) & rituals (compulsions)
- **Autism:** Ego-syntonic restricted/repetitive behaviors (perseveration)
- **SSRIs not associated with improvement in restricted, repetitive behaviors in Autism***

**J Am Acad Child Adolesc Psychiatry.* 2021;60(1):25-45.

Autism/ID & Anxiety/Depression

- **# of DBPs = 803***
- **# of Child Psychiatrists = 10,597****

*American Board of Pediatrics, *Data and Workforce*. Available at <https://www.abp.org/content/data-and-workforce>. Accessed January 17, 2024

**American Academy of Child and Adolescent Psychiatry. *Workforce Issues*. Available at: https://www.aacap.org/aacap/Resources_for_Primary_Care/Workforce_Issues.aspx. Accessed July 17, 2022.

Auditory Integration Therapy
Sensory Integration Therapy
Facilitated Communication
Swimming with dolphins
Interactive metronome
Craniosacral therapy
Tinted lenses/Optomeric
visual training
Patterning
EEG biofeedback

Autism “Treatments” Without Evidence

Restrictive diets
Dietary/Vitamin
supplements
Chelating agents
Antifungals, antivirals,
antibiotics
IVIG
Hyperbaric oxygen
Secretin
Polypharmacy

See Association for Science in Autism Treatment
<https://asatonline.org/>



Why are Families Attracted to Unproven Therapies for Developmental Disabilities?

- Lack of evidence-based biomedical treatments
- Desire to “do something”
- Natural course of DD
- Waxing & waning behavior
- Cognitive Dissonance
- Placebo Effect

Potential Harm of Non-Evidence- Based Therapies

- **Side effects**
 - Including death
 - Chelation (cardiac arrhythmias)
 - Withholding immunization (meningitis/encephalitis)
- **Financial Cost**
 - Not covered by insurance
- **Time Cost**
 - Lost family time
 - Time away from evidence-based interventions
- **Emotional Cost**
 - False Hope
 - Parental Guilt

Case: 4 year old with “Hyperactivity”

- Developmental Diagnosis?
 - Globally delayed developmental milestones with dissociated and deviated language (GM = 3 years; VMPS = 3 years; Language < 9 to 24 months)
 - Diagnosis: Autism spectrum disorder with a language impairment and globally delayed developmental milestones
- Is behavior developmentally inappropriate?
- Is behavior impairing across settings?
- Is behavior due to demands/expectations that exceed abilities?
- Have evidence-based behavioral interventions been attempted?
- Psychotropic medication trial?

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Review of Content

- 3 markers of developmental concern (Delay, Dissociation, Deviation)
- 3 primary developmental streams (Central Processing, Neurobehavior, Motor)
- 3 primary neurodevelopmental principles:
 - Spectrum of disability within each stream
 - Continuum of disability across streams
 - Increasing dissociation & deviation reflect increasingly atypical development

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Action Items

- Beware of behavioral problems due to mismatch between demands & expectations and developmental abilities
- Psychotropic meds for Preschoolers/Intellectual Disability/Autism
 - Fewer with positive response
 - Decreased magnitude of positive response
 - More side effects
 - **START LOW, GO SLOW**
- Beware of non-evidence-based interventions that may take advantage of desperate parents who would try anything to help their children

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References and additional reading

1. **Voigt RG** (editor), Macias MM, Myers SM, Tapia CD (associate editors). *AAP Developmental and Behavioral Pediatrics*, 2nd ed. Itasca, IL: American Academy of Pediatrics; 2018.
1. **Voigt RG** (editor), Macias MM, Myers SM, Chan B (associate editors). *AAP Developmental and Behavioral Pediatrics*, 3rd ed. Itasca, IL: American Academy of Pediatrics; (in preparation)

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