

Neuropsychiatry of Developmental Disorders: Principles & Practice

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Disclosures

Neither I nor my spouse has any relevant financial relationships with any commercial interest.

Learning objectives

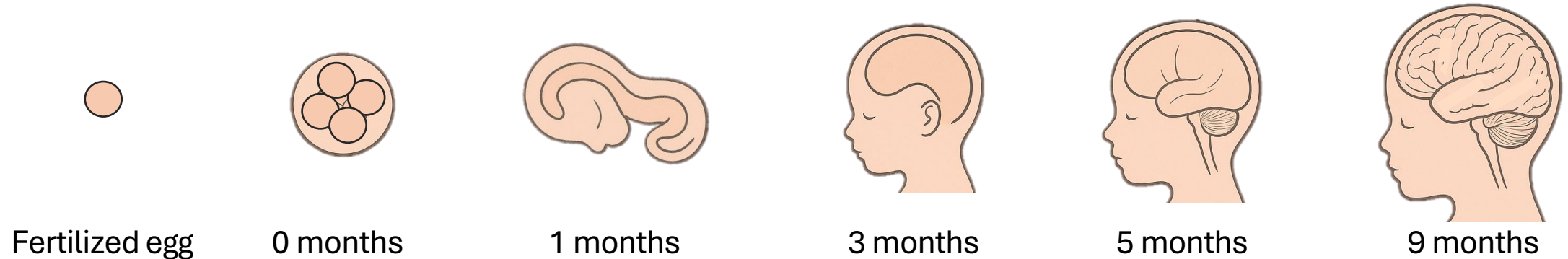
Principles:

- Understand the origins of developmental brain disorders
- Describe the core features of autism spectrum disorder & common neuropsychiatric manifestations

Practice:

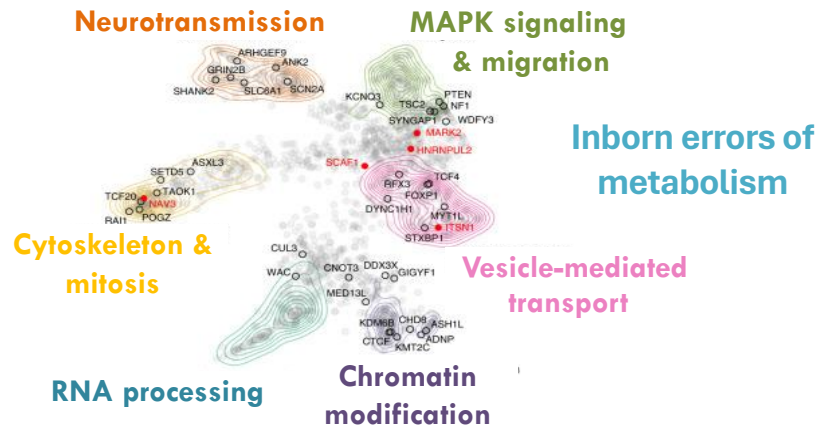
- Approach to evaluating & addressing "change in behavior"
- Interventions for neuropsychiatric symptoms in adults with autism spectrum or other neurodevelopmental disorders

Development Brain Disorders: Prenatal origins



Pathogenic Gene Variant(s)

Environmental Events (in utero)



Prenatal or Neonatal stroke

Nutritional deficiencies

Specific infections
(e.g., toxoplasmosis, rubella, CMV, VZV, HSV, Zika)

Placental insufficiency or injury

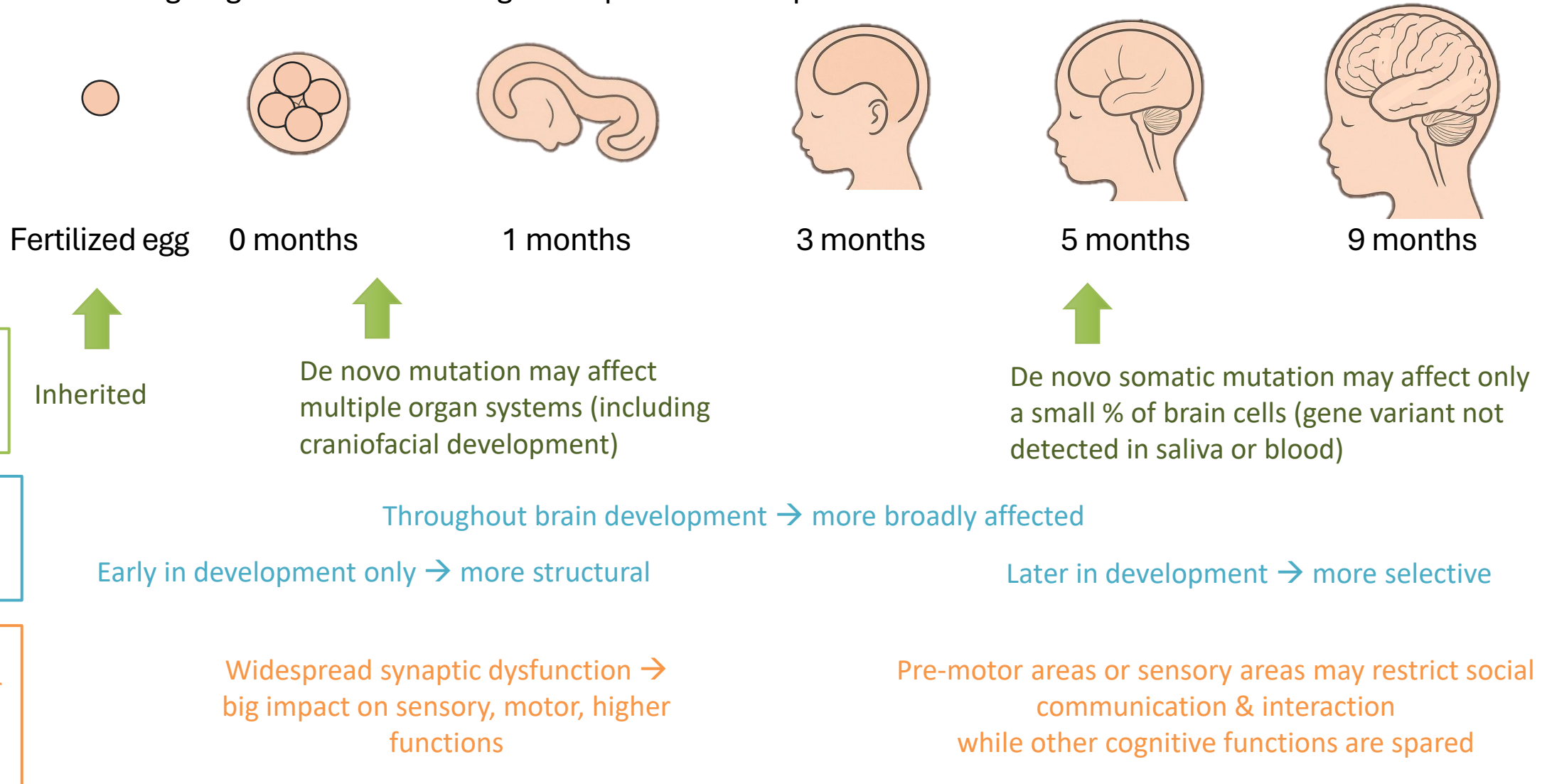
Toxins & Teratogens
(e.g., alcohol, isotretinoin)



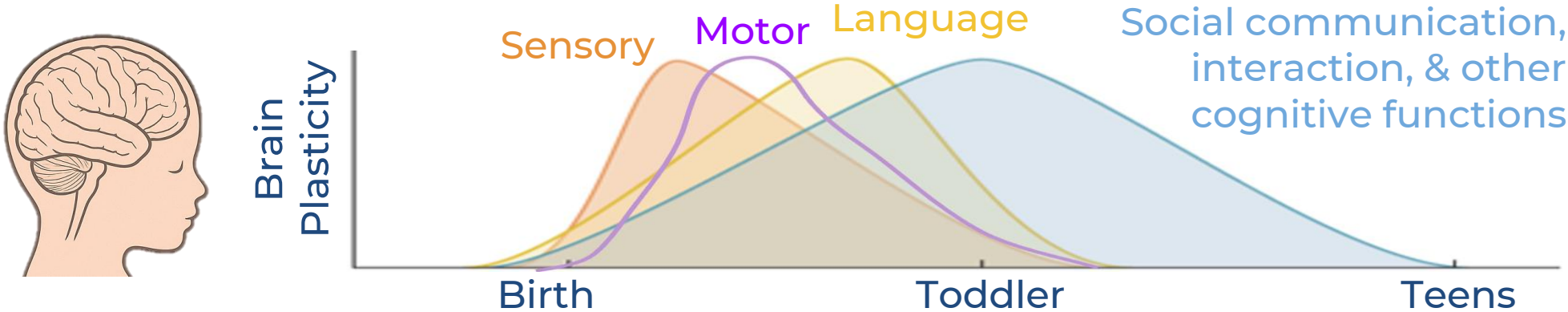
Zhou, et al. (2022) *Nat Genetics*

Development Brain Disorders: Prenatal origins

Developmental timing of gene mutation and gene expression is important

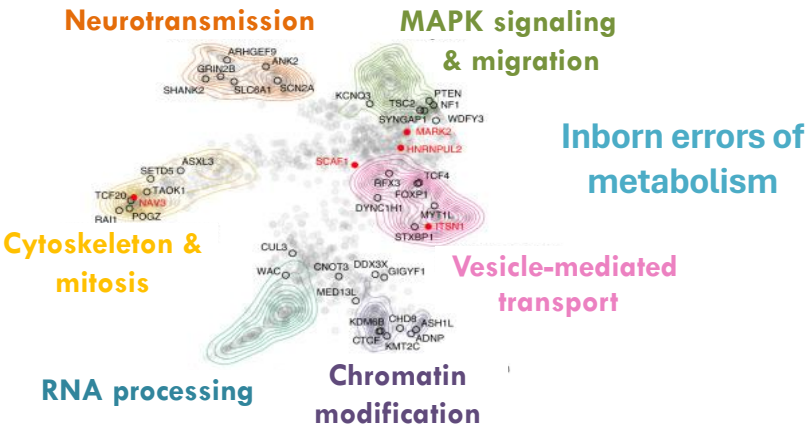


Developmental Brain Disorders: Postnatal development



Pathogenic Gene Variant(s)

Environmental Events (postnatal)

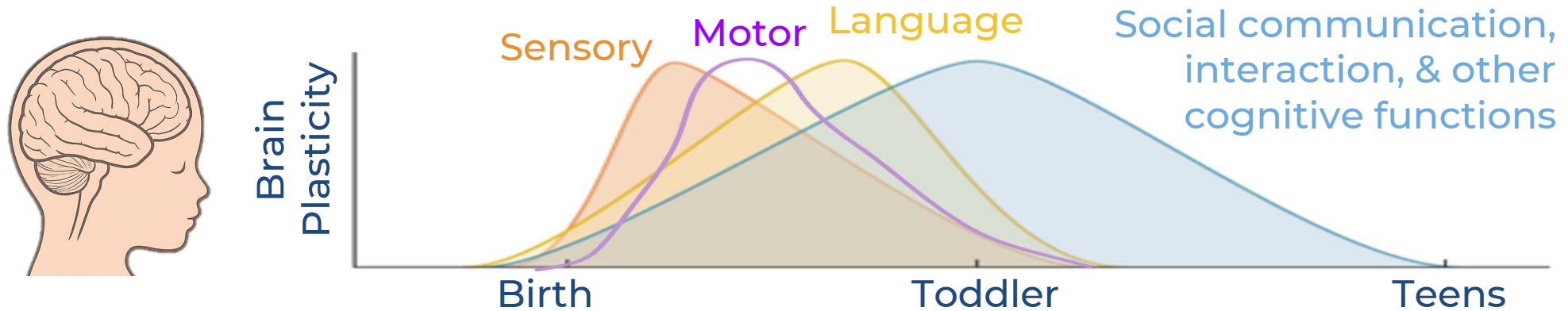


- Stroke or traumatic brain injury
- Nutritional deficiencies
- Infection, auto immune, neuroinflammatory
- Brain tumors
- Neurometabolic, neurodegenerative
- Epilepsy



Zhou, et al. (2022) *Nat Genetics*

Developmental Brain Disorders: Postnatal development



Move toward understanding development brain disorders in the context of what brain circuits are affected (rather than silo'ing "co-occurring conditions").

- 25yoF with autism spectrum disorder (ASD), intellectual disability (ID), and epilepsy → 25yoF with SCN1A-related development disorder that causes ASD, ID, epilepsy, & migraine
- Avoids "exceptionalism" (e.g., ASD vs. ID vs. epilepsy genes) and promotes understanding that gene variants alter brain developmental trajectories in different ways. How a person's brain networks form in early life will support (or not support) different behavioral patterns.

What is autism spectrum disorder (ASD)?

- ~~First description by Leo Kanner in 1943 & Hans Asperger~~

Difficulties with
Social Communication
& Social Interaction

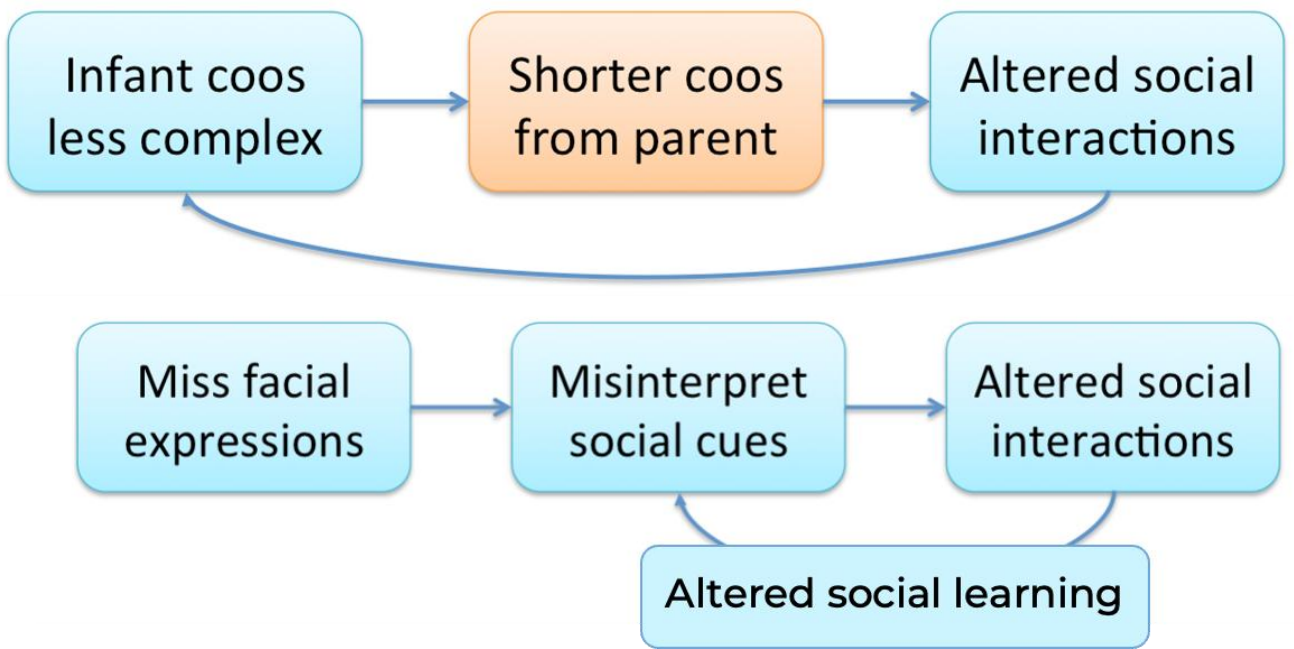
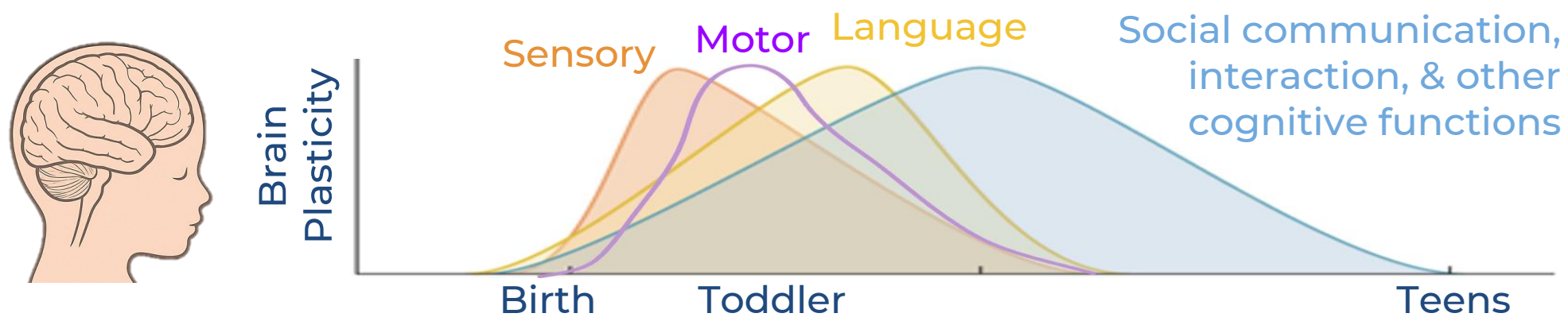
- Social reciprocity
- Non-verbal comm.
- Relationships

Restricted,
Repetitive
Interests or
Behaviors

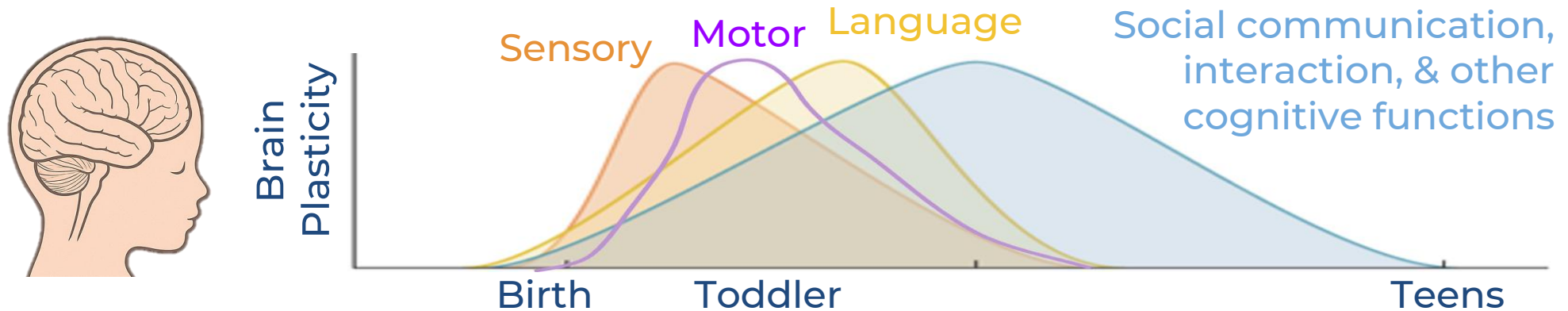
Disturbances in
Sensory
Perception

- First described by Dr. Grunya Efimovna Sukhareva, Russian child psychiatrist, in 1925 (in Russian)
- Her case series (in German) described **6 boys in 1926 & 5 girls in 1927** with autistic tendencies. She described:
 - talking in stereotypic ways
 - lack of facial expressiveness & expressive movements
 - flattened affective life
 - keeping apart from their peers
 - strong interests pursued exclusively
 - sensory sensitivities to specific noises or smells

Altered trajectories of social development in ASD



Altered trajectories of social development in ASD



Gender (or even perceived gender) influences social interactions starting very early in life.



Pink "girl" clothes



Blue "boy" clothes

Many people with ASD have strong desire for social interaction & empathy

See more at Green et al., 2019 Curr Psychiatry Rep

Altered trajectories of language & social communication

EXPRESSIVE LANGUAGE

SOCIAL PERCEPTION

- THEORY OF MIND
- ANTICIPATE LISTENER'S INTERESTS
- CONGRUENT NONVERBAL COMMUNICATION

MOTOR OUTPUT

- ECHOLALIA
- SCRIPTING

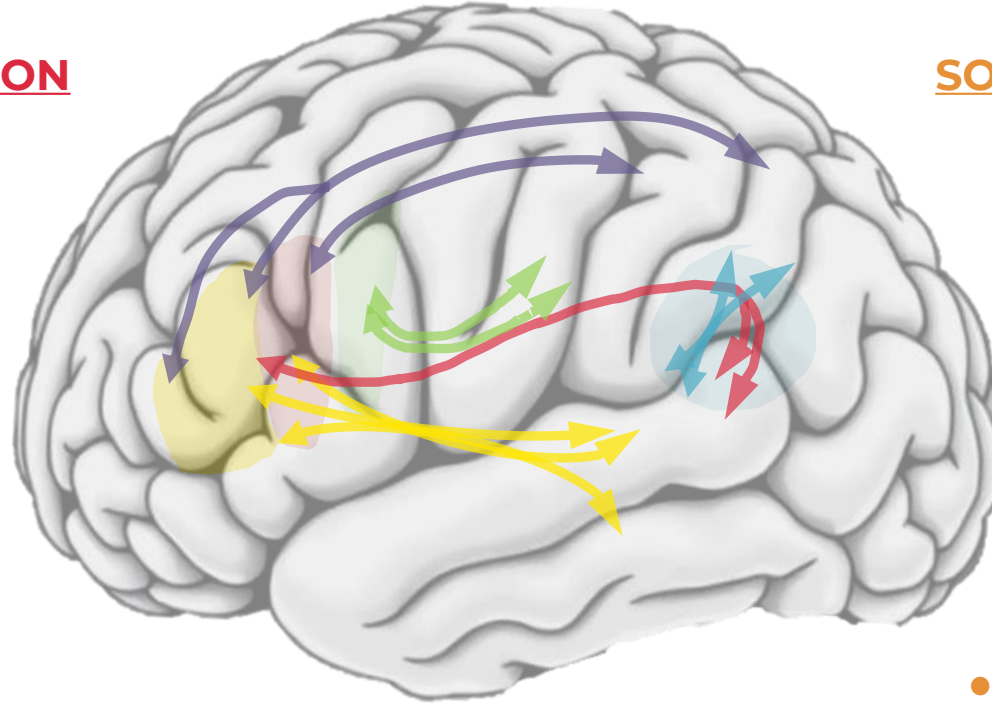
RECEPTIVE LANGUAGE

SOCIAL PERCEPTION

- INTEREST IN / AWARENESS OF SOCIAL WORLD
- THEORY OF MIND

SENSORY PERCEPTION

- ATTENDING TO SOCIAL CUES
- READING SOCIAL CUES



- **DISTRACTING MOVEMENTS OR SENSATIONS**
 - **DISTRACTING SENSORY STIMULI**
- **ADAPTATION TO DEMANDS OF ENVIRONMENT**
 - **ACTIONS MAY BE MORE EFFECTIVE THAN WORDS**

Altered trajectories of sensory processing & perception

Sound



Smell & Taste



Watch "Carly's Cafe" to see
her sensory experience
[https://www.youtube.com/
watch?v=KmDGvquzn2k](https://www.youtube.com/watch?v=KmDGvquzn2k)

Touch



Vision



Infants distinguish between social & non-social sounds already at 4 months & videos at 4-6 months



Social sound



Non-social sound



Social video

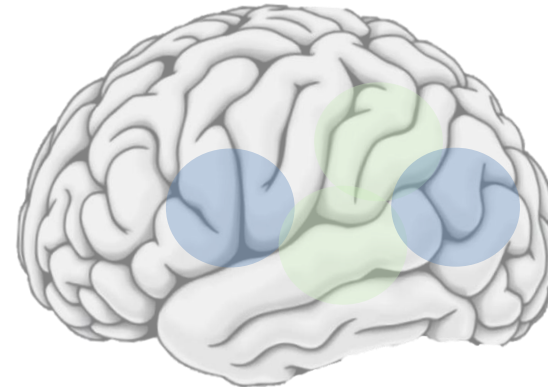


Non-social video



Blasi et al. (2015) Cortex

Infants later diagnosed with ASD did not show same preference for social sounds & sights over non-social



Lloyd-Fox et al. (2018) EIJN

Many sources for repetitive behaviors & restricted interests

Stimming &
sensory seeking



Tics OCD
Anxiety ADHD
Tardive dyskinesia
Seizures Catatonia

**Positive vs.
negative
valence**

**Responses
to external
or internal
stimuli**

**Behaviors
related to
co-occurring
conditions**

Self-injurious behaviors



Head banging

Skin picking or biting

Aggressive behaviors
toward others

Common neuropsychiatric manifestations in ASD

Cognitive & Behavioral

- **Language impairments**
- **Social interaction challenges**
- **Sensory sensitivities**
- **Surprising cognitive profile!**
- **Sleep difficulties**
- Attention
- Executive functioning
- Impulsivity

Mood

- Irritability
- Anxiety
- Depression
- Catatonia
- Mood lability

Actions & movements

- Stereotypies
 - Stimming
 - Sensory seeking
 - Anxious
- Self-injurious
- Self expression
 - Emotion
 - Communication
- **Incomplete control over motor system**
- **Motor apraxia**
- Seizures
- Tics

Consult question: 40yoM with ASD with expressive language impairment p/w new aggressive behaviors



- Lives at group home and rides in a shared van to a day program
- No history of aggressive behaviors; however, a few months ago started hitting other riders (when those riders were misbehaving)
- When mom drives him to day program in her car, no aggression
- Psychiatrist associated with group home starts aripiprazole daily

Key features from history:

- Aggressive behavior is new & context specific → clue to root cause

Formulation:

- Increase in irritability leads to intolerance of others' behaviors he previously tolerated

Plan:

- Look for source of irritability → many routine medical problems missed in non-speaking adults

Outcome:

- Broken molar on dental exam
- Treating tooth → no more aggression
- **Aripiprazole does not treat broken teeth!**

Clinical practice approach: Greet the patient first!



**Minimize time
in the waiting
room**



**Introduce yourself to
patient first, then
caregivers**



**Ask patient if
wants to be
examined first**



**Wait for patient
verbal response
(> 1 min)**

**Ask caregivers about
special fears or
sensitivities**

**Simplify instructions.
Allow extra time to
process.**

**Observe responses
carefully.
Avoid surprises.**

**Be flexible! Adjust
clinical style to patient's
cognitive, sensory, &
emotional needs**

Clinical practice: Behavior as a form of communication

Change in behavior:

Change in sleep patterns

Hitting head

Change in appetite

Pushing, hitting others

Spending more time alone

Refusing routines

Loss of joy in special interests

Increased tantrums with transitions

DISCOMFORT

ANXIETY

IRRITABILITY

Clinical practice: Ask caregivers how limited or non-speaking adult communicates discomfort

Pointing
Increased vocalizations
Less active



Retreats to room



Easily frustrated

Decreased flexibility
Refuse routines
More rigid routines

What types of discomfort have they reported in the past?

Do they show altered pain perception?

Ability to speak $\neq$ Ability to report discomfort

Many have very high pain threshold

Clinical practice: Look for common medical problems

Timing, frequency & associated symptoms provide clues to common illnesses

Sleep records (24 hr) & Medication administration
(e.g., quetiapine, caffeine)

Keeping diary of timing, duration, associated symptoms, environmental changes

Use family history as a guide
(e.g., migraine, allergy)

Screen for problems by age & season



Seasonal allergies

Wisdom teeth

Daylight Savings

Spring Equinox

**Ask about common conditions.
Look/listen for nasal congestion.**

Constipation (can be severe, get KUB)

Sinusitis due to cold or allergies

GERD

Headaches

(Make differential, test, & treat, empirically if needed)

Adults with ASD at higher risk for many medical problems

16X
Seizures

3X
Constipation

1.7X
Sleep problems

1.5-2X
GERD

Adults with expressive language impairments often have common problems such as **headaches or allergies** go unrecognized &/or don't receive over-the-counter p.r.n. (as needed) medication!

Higher risk for:

- Autoimmune disease
- Cardiovascular disease
- Diabetes
- Obesity
- Endocrine disorders
- Other CNS disorders
- GI disorders
- Pulmonary disease
- Anemia
- Nutrition concerns
- Vitamin D deficiency
- Osteoarthritis
- Hearing impairment
- Vision (7.8x)

Kaiser study with 1507 adults with ASD compared with adults without ASD (Croen et al, 2015)

Acknowledgments

Many thanks to my teachers:
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MGH Lurie Center
Lexington, MA



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Boston, MA

 **Brigham and Women's Hospital**
Founding Member, Mass General Brigham

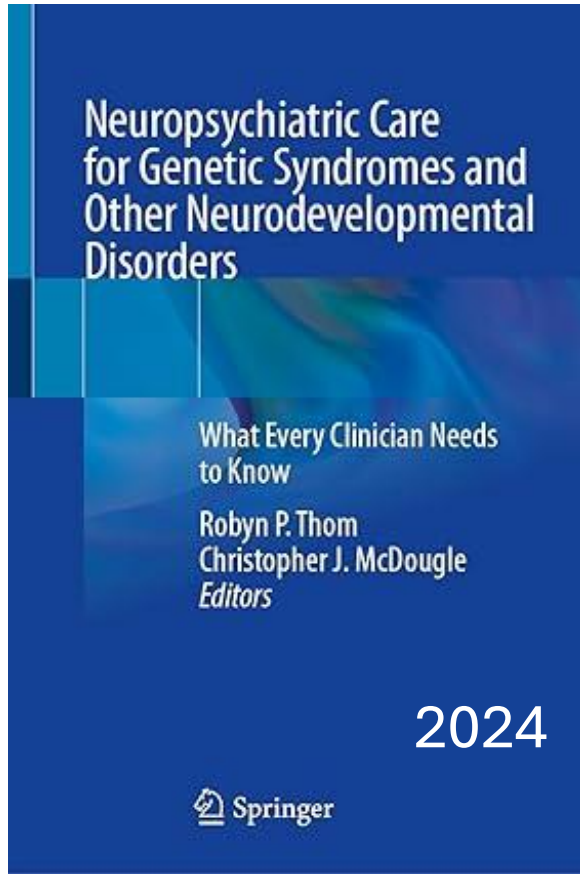
 **HARVARD MEDICAL SCHOOL**
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Many thanks to the organizers:

Neuropsychiatry:
a Comprehensive
Update 2025

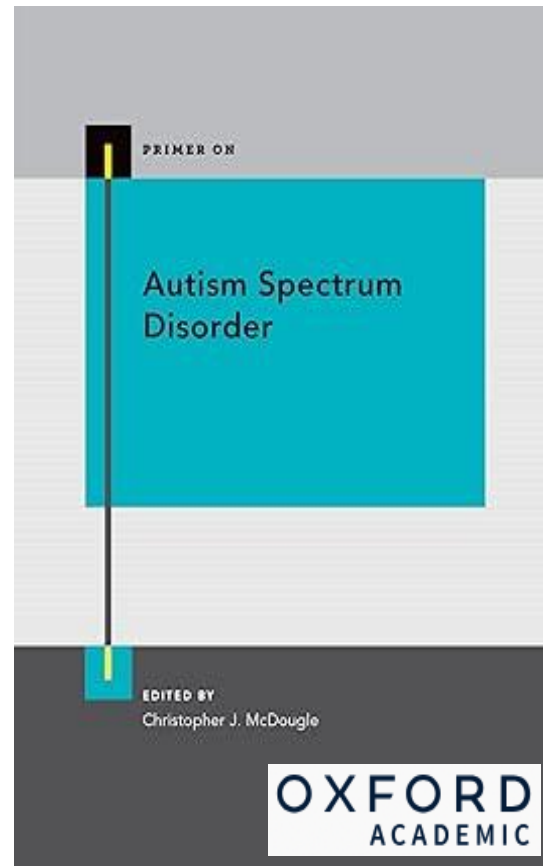


Resources



Available at Springer Nature*

* <https://link.springer.com/book/10.1007/978-3-031-76269-7>



McDougle (editor),
2nd edition coming soon!

 **Brigham and Women's Hospital**
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TEACHING HOSPITAL



<https://adult-autism.health.harvard.edu/>



**Clinical Care for
Autistic Adults**
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Self-paced online CME course

<https://learn.hms.harvard.edu/programs/clinical-care-autistic-adults>

Resources

Approach to care for adults with ADHD for neurologists!



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Neurology[®]
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COMMENTARY

December 17, 2024



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Check for updates

Do I Have ADHD? Diagnosis of ADHD in Adulthood and Its Mimics in the Neurology Clinic

Susanna B. Mierau

[AUTHORS INFO & AFFILIATIONS](#)

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- Zhou et al., 2022, Integrating de novo and inherited variants in 42,607 autism cases identifies mutations in new moderate-risk genes. Nat Genet.
- Green et al., 2019, Women and Autism Spectrum Disorder: Diagnosis and Implications for Treatment of Adolescents and Adults. Curr Psychiatry Rep.
- Manter et al., 2025, Pharmacological treatment in autism: a proposal for guidelines on common co-occurring psychiatric symptoms. BMC Med.
- Thom & McDougle CJ, 2023, Repetitive Thoughts and Behaviors in Autism Spectrum Disorder: A Symptom-Based Framework for Novel Therapeutics. ACS Chem Neurosci



ASD-related medication trials ([ADHD](#), [SSRIs](#))

- [Arnold et al., 2005 Arch Gen Psych](#)
- [Harfterkamp et al., 2012 JAACAP](#)
- [Scahill et al., 2015 Am J Psychiatry](#)
- [Zhou et al., 2021 JAACAP \(review\)](#)
- [King et al., 2009 Arch Gen Psych](#)
- [Hiroto & King, 2023 JAMA \(review\)](#)

Questions re: leucovorin

- [See discussion at Vogel 2025 Science](#)

Additional slides (if needed for Q&A panel)

Look for common co-occurring conditions

ADHD - 25%

- Hyperactivity
- Impulsivity
- Distractibility
- Inattention
- Fidgeting
- Requires frequent redirection
- Apologetic or remorse when repeats inappropriate behavior
- Emotional dysregulation
- Frequently snacking or requesting food

Depression - 25%

- Loss of interests & skills
- More time alone
- Refusal to leave home

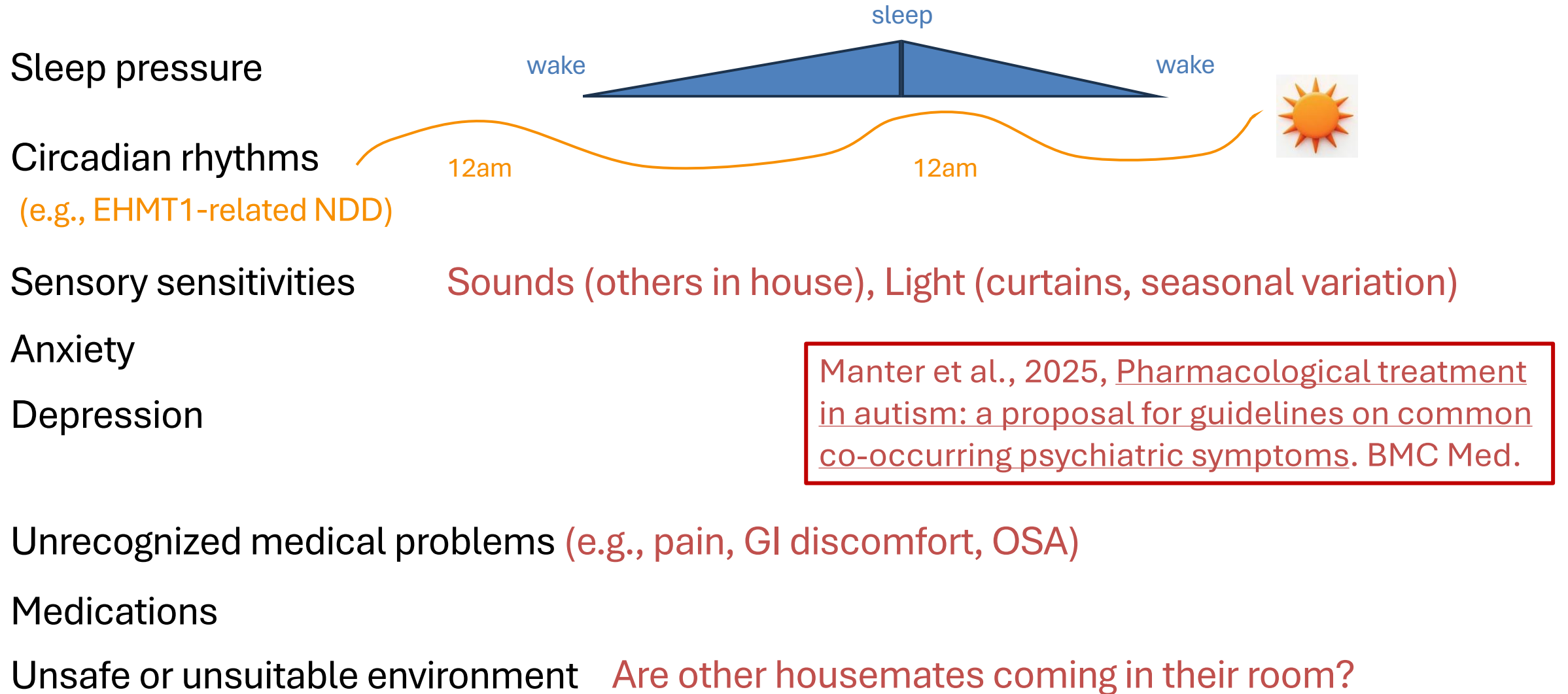
Anxiety - >20-30%

- Routine refusal
- Difficulty with transitions
- Avoidance behaviors
- Crying or other distress
- Stay near caregiver
- Anxiety-related tremors
- ↑ Repetitive behaviors
- Self-injurious behaviors (skin pick, hair pull, biting)
- Intermittent catatonia

OCD - 9%

- Handwashing/germ fears more responsive to SSRIs
- Tapping/intense routines can be ASD (w/o OCD)

Many sources for sleep difficulties in ASD



ADHD & ASD can have common co-occurring features

Feature	ADHD	ASD
Anxiety	Anxiety often used to ↑ attention (e.g., saving hard tasks for last minute). Anxiety also arises from fear of failure, inconsistency.	Anxiety in new situations, or in anticipation of new, due to difficulty with social interaction &/or sensory.
OCD-like symptoms	Can get distracted by negative thoughts or worries, easily jump to next “worse case” in mind.	Can have a certain “rightness” to movements, position of items, etc.
Repetitive movements	Fidgeting, moving around in seat, restlessness, need to be on the go	Certain movements can have a “rightness” &/or provide comfort
Altered response to sensory environment	Can get easily distracted by external stimuli. Some may need stimulation (e.g., brown noise) to focus on certain tasks. Novelty is very interesting.	Difficulty ignoring non-relevant sensory stimuli. Sensory overload can cause significant distress.

Notes on medications for neuropsychiatric disorders

- **Stimulant medication for ADHD**

- **Start with long-acting** in the morning
- Identify behaviors we expect to increase or decrease with treatment
- Titrate over a few days
- If anxious behaviors appear or agitation, lower to previous dose or treat other conditions first (e.g., poor sleep, anxiety)

- **Non stimulant medication for ADHD**

- **Atomoxetine** can disrupt sleep for some people (even though "non stimulant")
- **Extended release guanfacine** improves irritability in children, not shown in adult
- **Bupropion** can be helpful for adults (off-label indication, but commonly used), can lower seizure threshold

- **Watch for overactivation or agitation**

- **SSRIs at higher doses** can lead to activation including increased energy level, impulsivity, hyperactivity and insomnia (including trazodone, especially at ≥ 150 mg nightly)
- **Mirtazapine** can also switch to being activating (instead of sedating) at higher doses, can also lead to weight gain
- **Quetiapine** can cause agitation due to anti-cholinergic effects & cause urinary retention, especially at higher doses

Manter et al., 2025, Pharmacological treatment in autism: a proposal for guidelines on common co-occurring psychiatric symptoms. BMC Med.