

# Autism: An Overview of the Current Research and Science

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**Preserving Science through  
Research & Discourse.**

**Defending Humanity with  
Integrity & Truth.**

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REVIEW

## The Neuroimmunology of Autism

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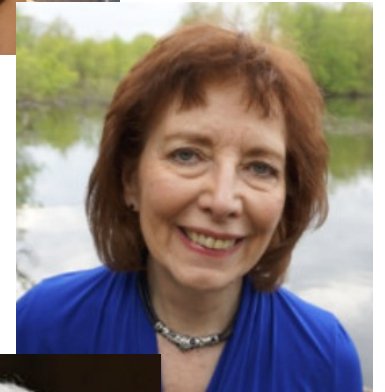
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Alterations and maladaptations of the immune system remain some of the most *controversial* concepts in autism spectrum disorder (ASD).

Nonetheless, intensifying evidence confirms that much of what ASD involves is related not to a static encephalopathy-based model of autism

but rather to the consequences of *environmental insult* and complex and dynamic psychological and physiological processes involving the *interdependence* of the nervous, immune, and host microbiome.

Taking a neuroimmunological perspective, we highlight the need for a *multi-scale, holistic approach* to understanding and developing future therapeutic modalities to address the core symptoms of ASD that go beyond the current reductionist and “magic-bullet” medical paradigm.

Keywords: Autism spectrum disorder · Immune system · Neuroimmunology · Gut-brain axis · Bioregulatory systems medicine

# Timeline – Diagnosis

## 1910s

Eugen Bleuler introduces the term “autism” as one of the symptoms of schizophrenia



## 1940s

Kanner and Asperger publish systematic case reports; lay foundation for distinction from childhood schizophrenia



## 1920s

Sucharew develops fundamental description of autism spectrum symptoms



## 1980s

DSM-III clarifies distinction between autism and childhood schizophrenia



## 1994 / 2013

DSM-IV and DSM-5 adopt “autism spectrum disorder (ASD)” as a dimensional neurodevelopmental disorder

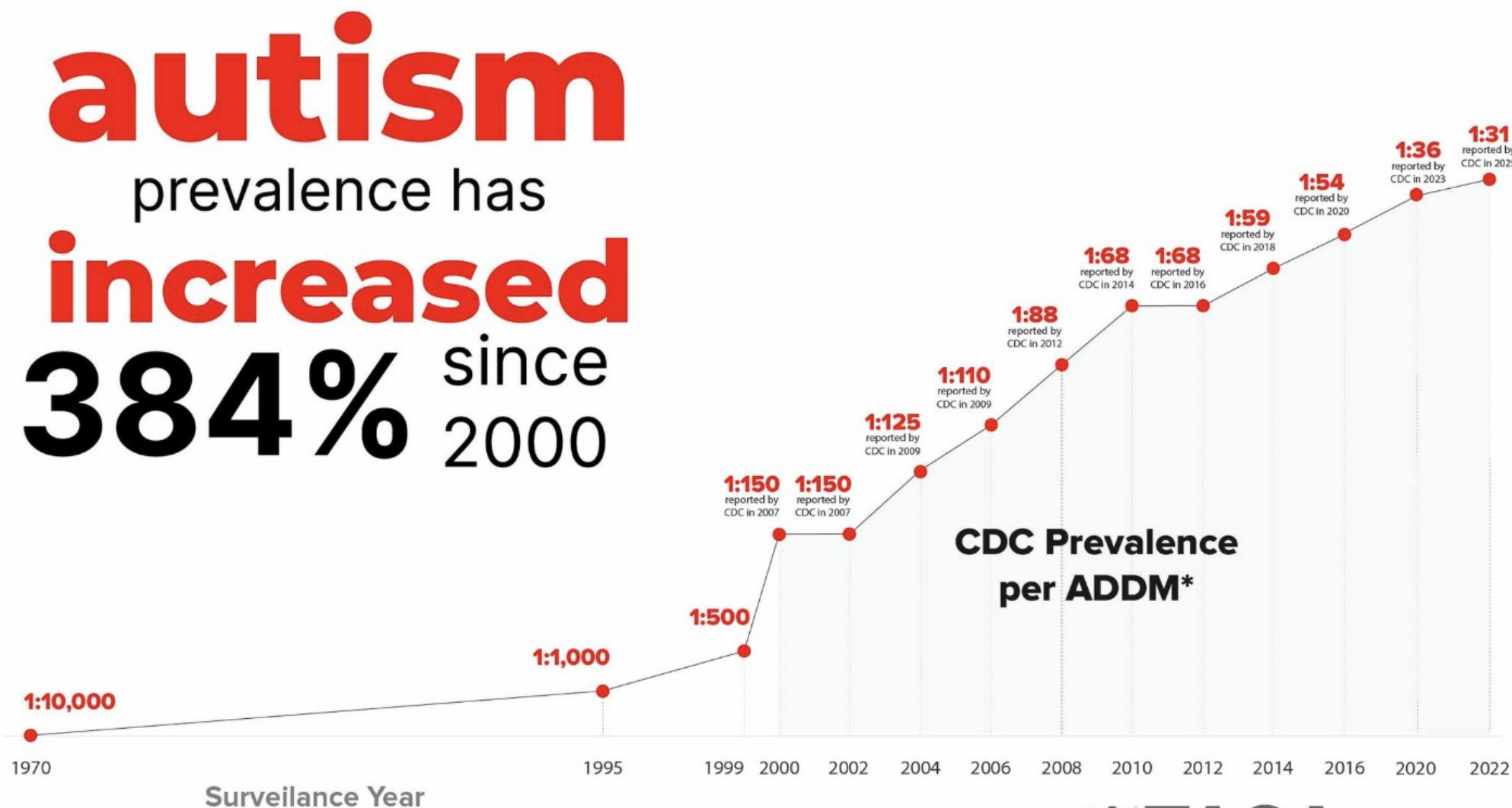


# Current Understanding of Autism Spectrum Disorder

- NIMH definition: Neurological & developmental disorder affecting interaction, communication, learning, behavior
- Persistent deficits in social communication + restricted/repetitive behaviors
- High regressive phenotype rate (88% per Ozonoff et al. 2018)
- Real-world evidence: Normal development followed by sudden behavioral changes + inflammatory signs (fever)
- Key autism researchers now acknowledge the gut-brain axis as a feature in the etiology of ASD

# The Epidemic of Autism (US statistics)

**autism**  
prevalence has  
**increased**  
**384%** since  
2000



\*ADDM (Autism and Development Disabilities Monitoring Network)

# The Epidemic of Autism (US statistics)

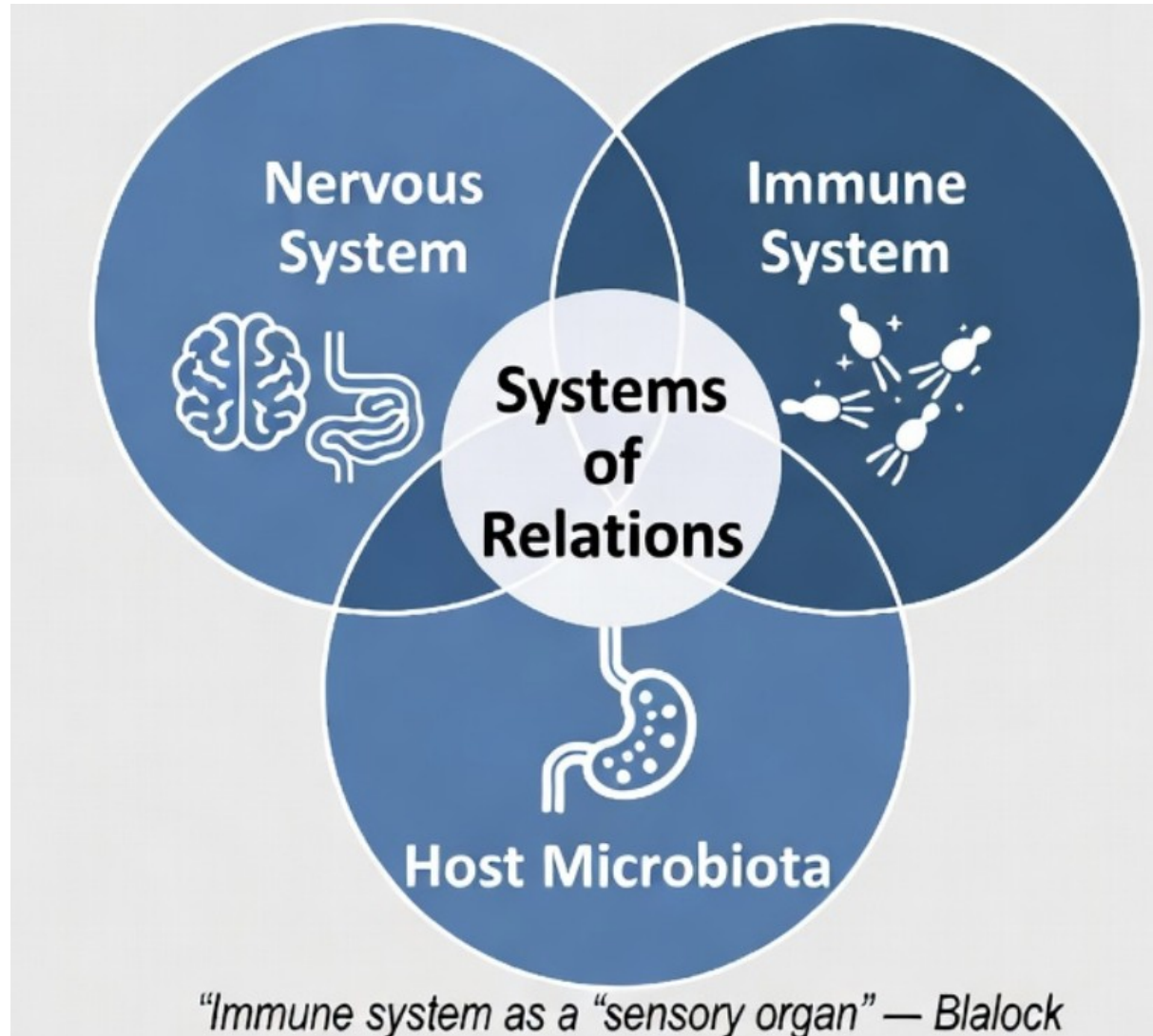
- Strong male bias + comorbidities (GI, metabolic, immune, motor)
- Higher prevalence in blacks – up to 30% of black male children in Los Angeles county have an ASD diagnosis
- Lifetime US cost >\$7 trillion (2019); projected \$11.5 trillion by 2029
- Rising chronic childhood disease epidemic parallels ASD increase
- Profound or low-functioning autism comprises 30-40% of all cases

# Underpinnings: Genetic versus Environmental

- Genetic determinism challenged: Twin studies show stronger shared-environment role (Hallmayer 2011)
- Heritability estimates ~37–52% but no single gene or therapy identified
- Genome Wide Association Studies: Hundreds of common + rare variants; de novo mutations play role but context-dependent
- *There is no single, consistent genetic feature of autism*
- Shift to **epigenetic + gene/environment interplay**

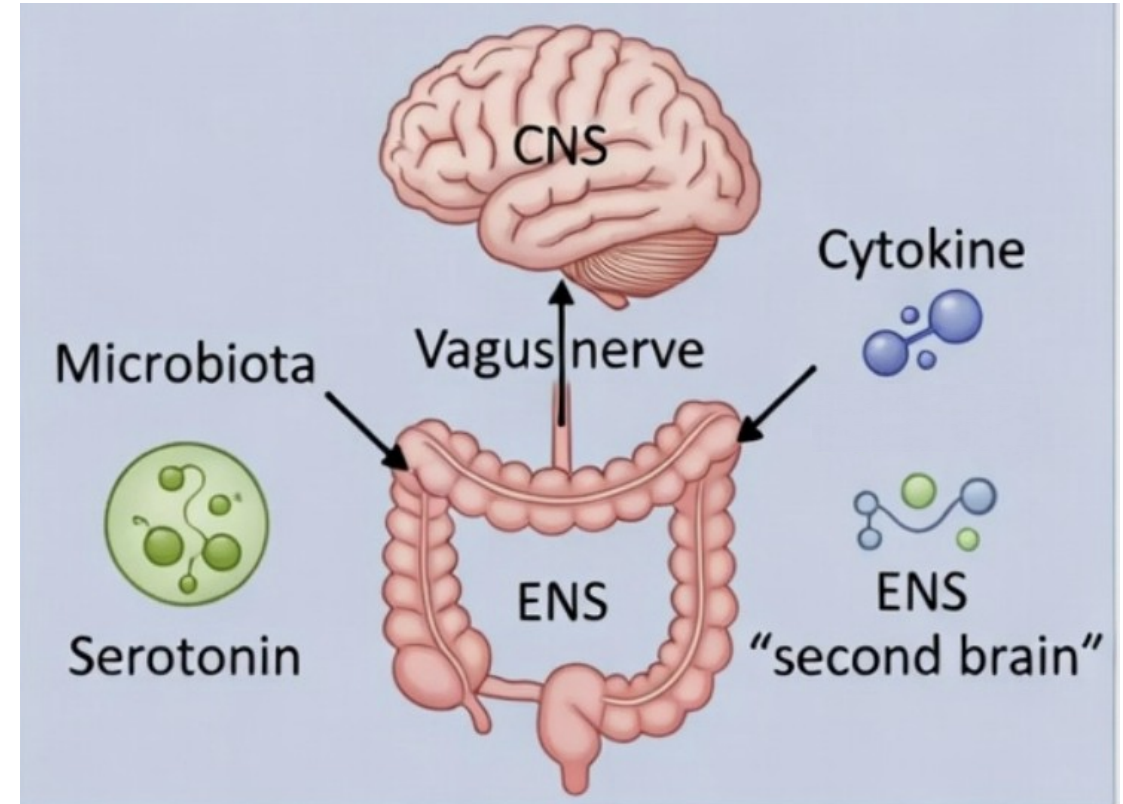
- Heavy metals (Hg, Al, Pb, Cd, As)
- Pesticides & agrochemicals (organophosphates, glyphosate)
- Air, water & soil pollution (e.g., airborne mercury)
- Early life antibiotics (disrupt gut microbiome development)
- Acetaminophen/paracetamol
- Electromagnetic field (EMF) exposure

# Immune System-Nervous System-Microbiota



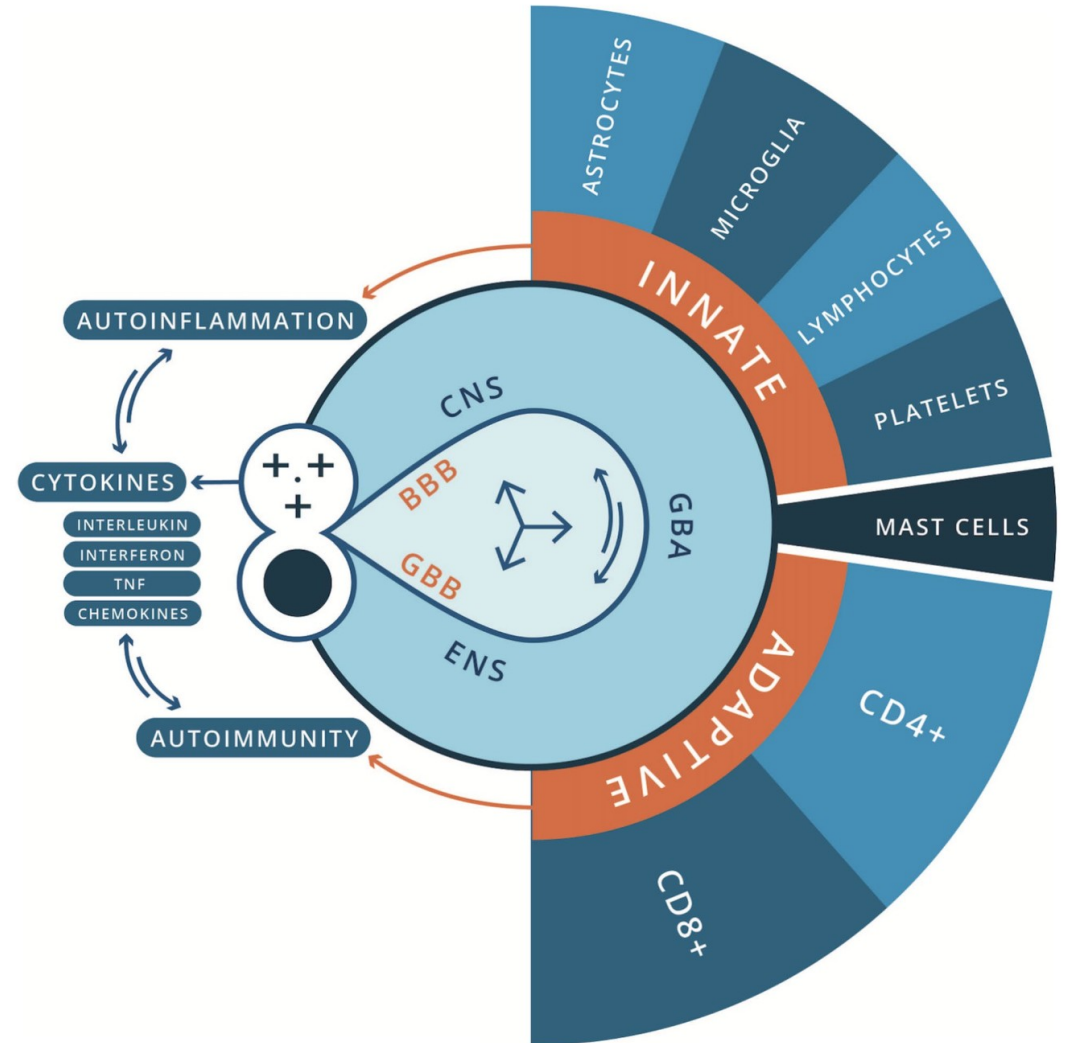
# Interdependence: Gut-Brain Axis

- Bidirectional CNS-ENS-microbiome communication
- 90% of vagus nerve are afferent (gut → brain)
- Gut as the "second brain" (ENS)
- Impaired BBB and gut-blood barrier (GBB) in ASD
- GI function severity correlates with autism severity



# Pathophysiology Overview

- Neuroinflammation (innate) + autoimmune encephalitis (adaptive)
- Oxidative stress, mitochondrial dysfunction, chronic immune dysregulation
- Glial activation, cytokine imbalance, neurotransmitter disruption
- Gut-microbiota influence neurodevelopmental and behavior



## **Central Driver of Autism Pathophysiology**

- Oxidative stress = Imbalance between pro-oxidants and antioxidants → ROS and free radical damage
- PERM hypothesis: Peroxisomes, endoplasmic reticulum, proteasomes and mitochondria as a single “master tuner” in cellular decision making
- Mitochondrial dysfunction in immune cells is central in ASD
- Key ASD findings: elevated lactate/pyruvate ratio, low reduced glutathione and carnitine deficiency

**Links oxidative stress to neuroinflammation and allostatic overload**

- Innate neuroimmune reactions play a major pathogenic role in ASD
- Microglia: "Electricians" of the ENS/CNS; synaptic pruning, E/I balance, BBB integrity
- Astrocytes: Synapse formation, BBB maintenance, gliotransmission
- Oligodendrocytes: Myelinlike (IGF-role)

# Acquired Immune Dysfunction and Autoimmunity

- Th1/Th2/Th17/Treg imbalance; elevated pro-inflammatory cytokines (IL-6, TNF- $\alpha$ , IL-16)
- Autoantibodies, molecular mimicry, epithelial barrier hypothesis
- Overlap with autoimmune diseases; family history common
- Hygiene/Old Friends (coevolved organisms) hypothesis & xenobiotic triggers

# Autoimmune Encephalitis and NMDAR Encephalitis

- Limbic encephalitis → seizures, behavioral changes, memory issues
- Anti-NMDAR antibodies linked to autistic regression
  - Attack the N-methyl-D-aspartate (NMDA) receptors in the brain
- At least 69% of ASD cases may involve encephalitis (Kern et al.)
- Cerebellar pathology (Purkinje cell loss) & epilepsy comorbidity

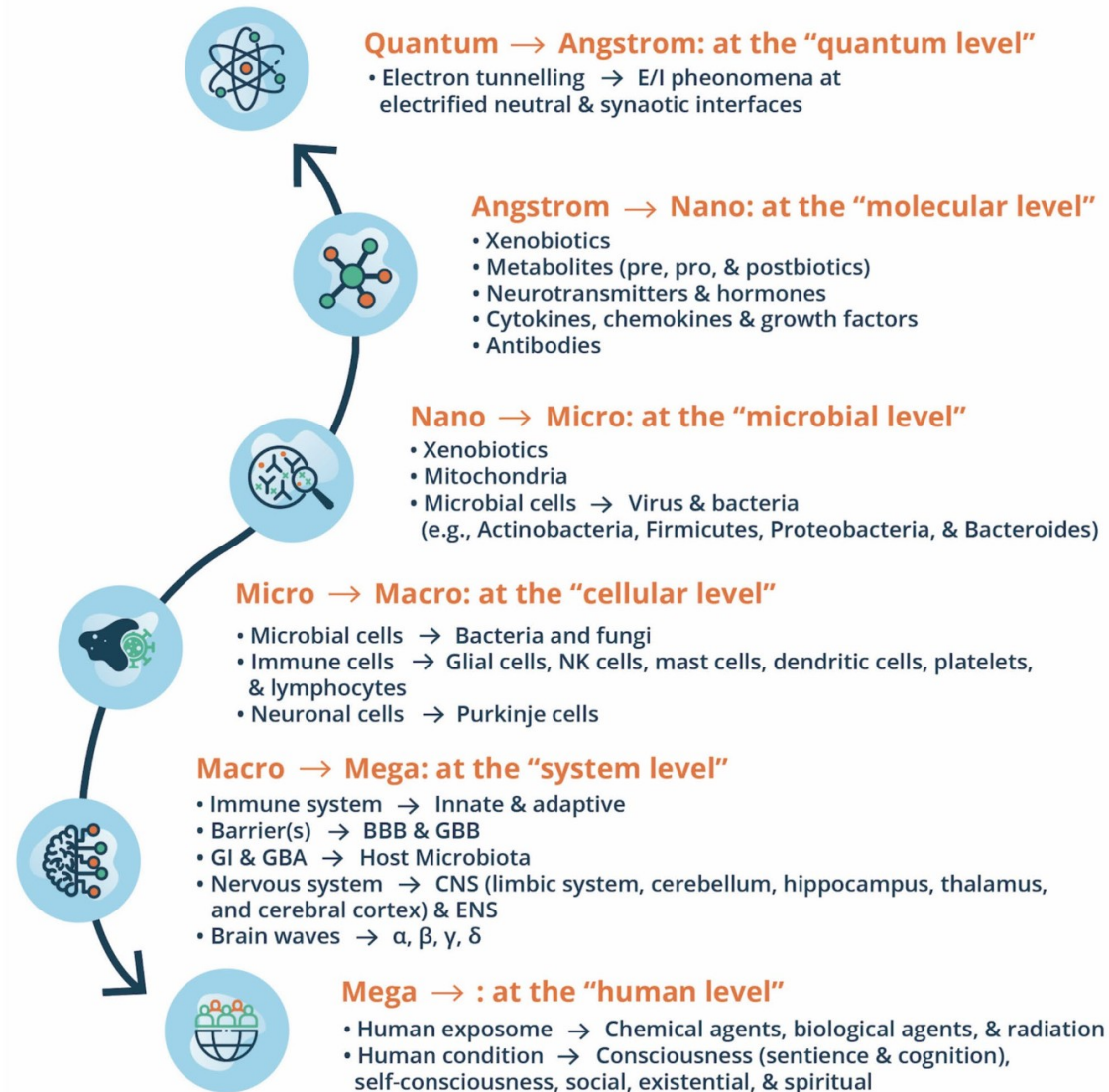
- Gut-associated lymphoid tissue (GALT), Peyer's patches as immune sensors
- Celiac disease comorbidity; gluten/casein opioid excess theory
- Enteric serotonin dysregulation (enterochromaffin cells)
- GFCF diet rationale; inflammation targeting the ganglia of the ENS

- Male bias in ASD vs. female bias in autoimmunity
- Fetal testosterone & microglial masculinization increase vulnerability
- Estrogen protective in females; sex hormones modulate HPA & immune response
- Sex-dimorphic microbiome (girls have more biodiversity in general)

# Higher Level Processing – Cognition, Sentience and Consciousness

- Move beyond neurocentric view to neuroimmunocentric + microbiome framework
- Hierarchical biological resolution
- From quantum/angstrom to mega (human condition) levels
- Immune–microbiome–nervous systems as “systems of relations”

# Higher Level Processing – Cognition, Sentience and Consciousness

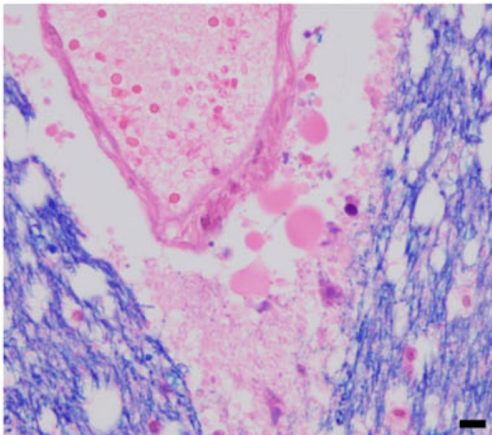
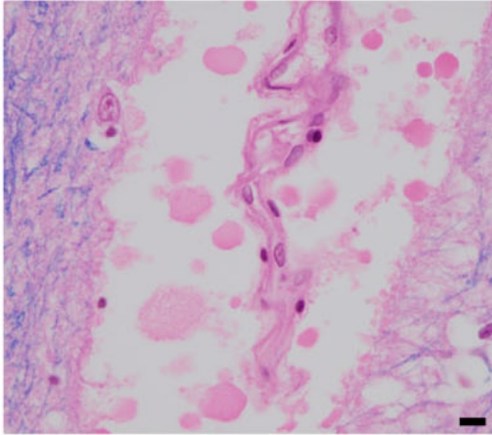


- Sentience (feeling) underpins cognitive consciousness (Pereira)
- Whole-body interoceptive cycles involving immune, gut, heart, CNS
- ASD as disorder of allostatic overload (Singletary)
- GBA & ENS critical for brain plasticity

- Immature brain: enlarged cerebrum (macrocephaly), cerebellar changes, amygdala abnormalities
- White-matter & connectivity differences
- Astrocyte blebbing and reactive astrogliosis in prefrontal cortex (Distasio et al., 2019)
- Not fixed or purely congenital — dynamic, inflammation-driven, and potentially modifiable
- Glial activation links environmental insult to structural changes (Varia et al., 2025)

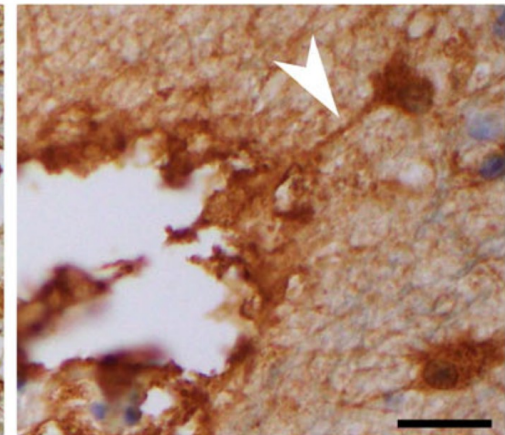
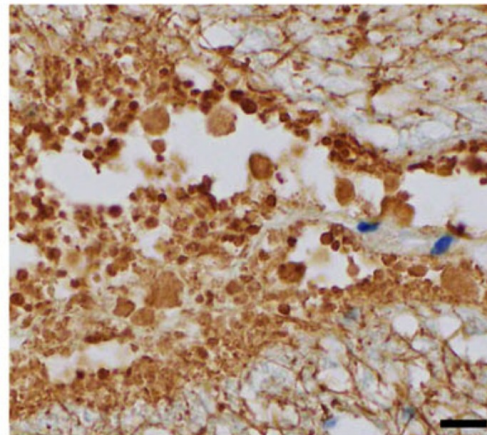
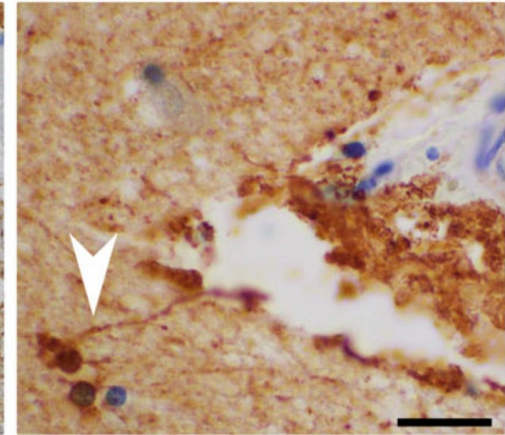
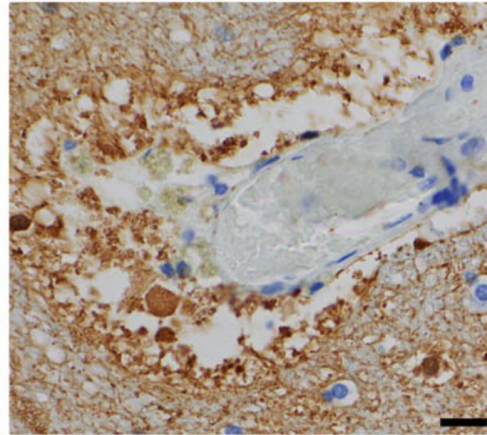
# Neuroanatomical differences

H&E+LFB



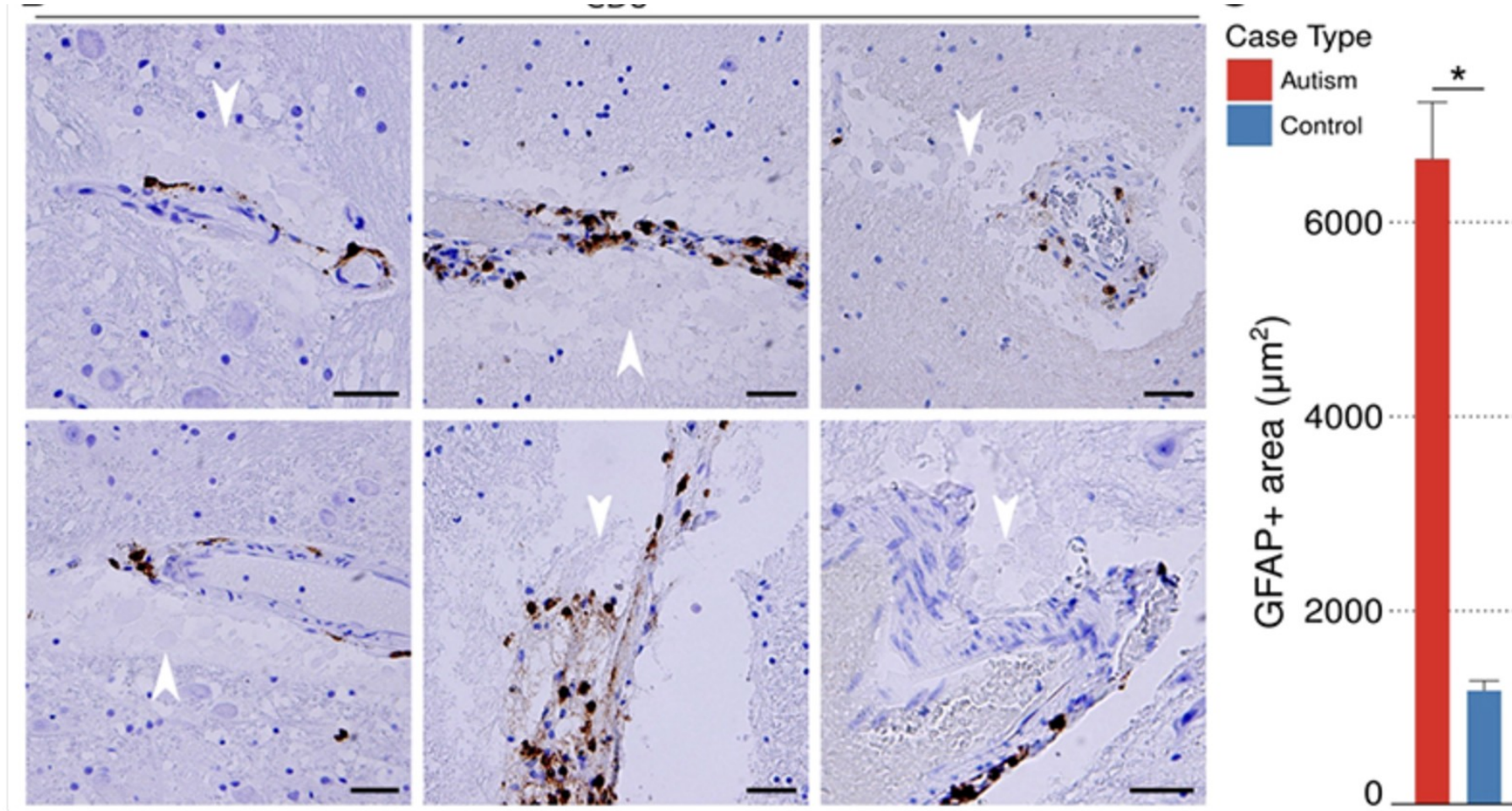
Blebbing

GFAP



Blebs are derived from astrocytes attacked by CD8+ cells

# Neuroanatomical differences



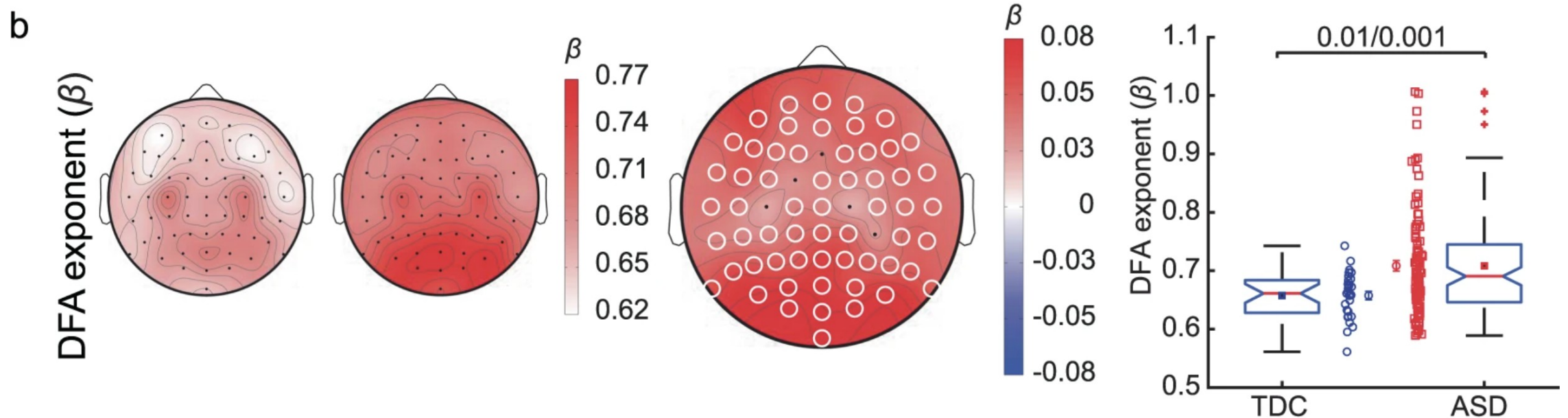
Influx of CD8+ T-cells through brain vasculature

Increase in glial fibrillary acidic protein in autism

- PET/SPECT: Evidence of microglial activation / neuroinflammation in key regions (cerebellum, prefrontal, limbic)
- <sup>1</sup>H-MRS: Reduced GABA (E/I imbalance), N-acetylaspartate (neuronal integrity), & oxidative stress markers (e.g., glutathione)
- Dynamic cellular processes (PERM, redox, immune) link environmental insults to neurodevelopmental pathophysiology

- Gamma & alpha oscillations disrupted → impaired binding, perception, excitation/inhibition balance
- Astrocytic  $\text{Ca}^{2+}$  & glutamate clearance regulate network stability
- EEG as safe, low-cost biomarker; non-epileptiform abnormalities common in ASD

# Alpha Oscillation Variability



Detrended Fluctuation Analysis (DFA) exponent reflects how brain waves behave

- 0.5 – white noise
- 1.0 – pink noise
- >1.0 – too correlated <0.5 – too random

## Rubbish

- *Whole-body dyspraxia*
- *Cell danger response*

### Strong Critique of the Theory of Mind Deficit Model

- Suffers from circular reasoning and lacks robust neuroscientific correlates (Ploog, 2023)
- Many non-speaking autistic individuals demonstrate literacy, symbolic thought, and communicative agency when given appropriate tools (Jaswal et al., 2020)
- Does not account for successful autistic-to-autistic communication

# Whole-body Dyspraxia in Autism (Dana Johnson, PhD)

- Severe motor planning and execution disorder affecting the entire body
- Difficulty initiating and executing purposeful movements
- Common in non-speaking and unreliably speaking autistic patients
- Impaired motor function doesn't equal impaired cognition
- 50-80% of autistic individuals have some form of dyspraxia

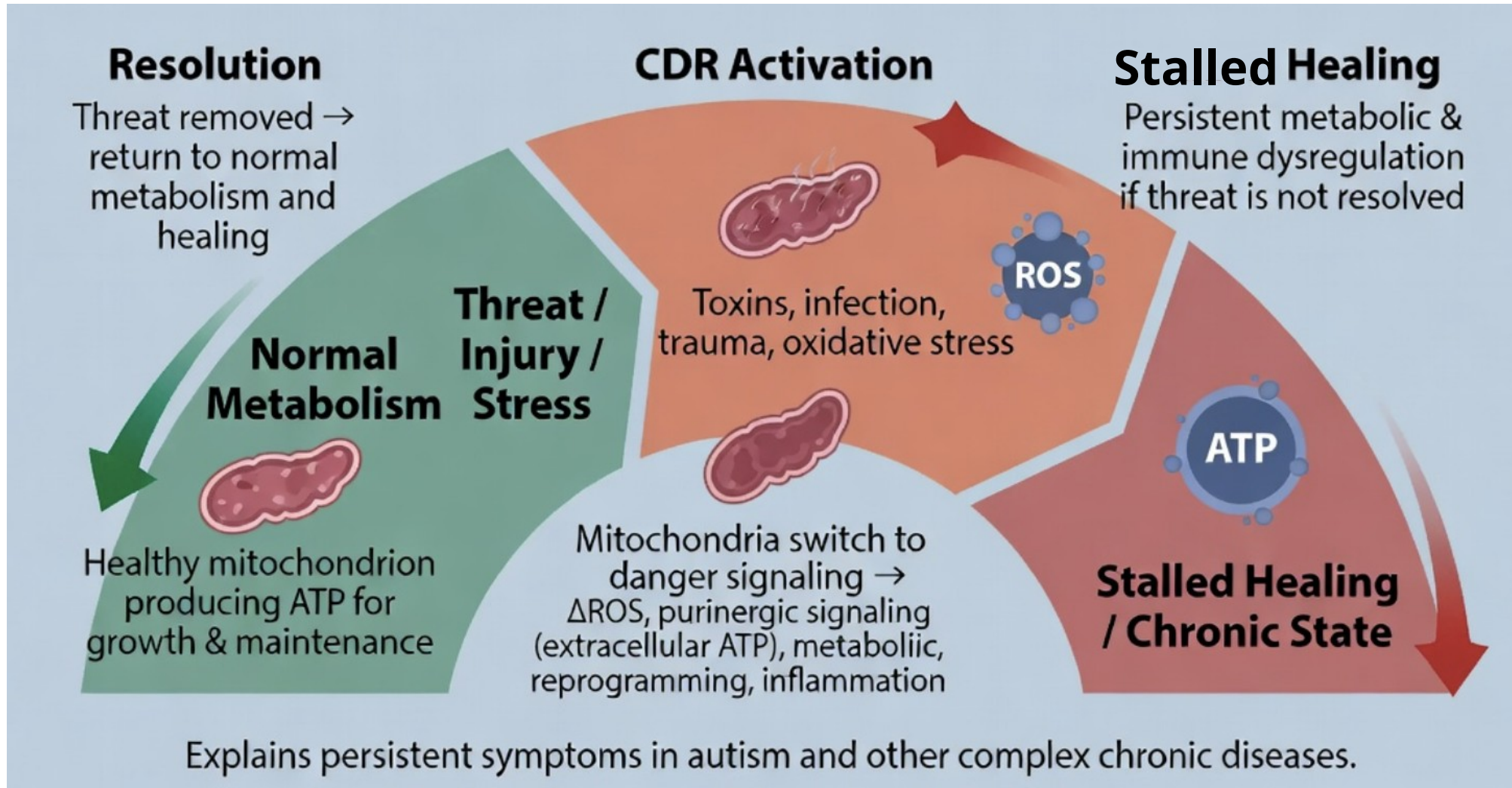
# Whole-body Dyspraxia in Autism (Dana Johnson, PhD)



# The Cell Danger Response in Autism (Robert Naviaux MD PhD)

- Universal, evolutionarily conserved cellular response to threat, injury or stress
- Mitochondria shift from energy production to danger signaling
- Leads to “stalled healing” and persistent metabolic/immune dysregulation
- Hypothesized to underlie chronic symptoms in autism and other complex diseases
- Leads to unique therapeutic targets

# The Cell Danger Response in Autism (Robert Naviaux MD PhD)



# Biomedical Treatment Options

- **Non-pharmacological approaches:** Personalized dietary patterns, microbiome restoration, and fecal microbiota transfer
- **Nutritional & Botanical Strategies:**
  - Omega-3 fatty acids, polyphenols/flavonoids, luteolin, and antioxidants to reduce oxidative stress and microglial activation.
  - Support mitochondrial function and E/I balance via targeted nutrients
- **Mind–Body & Lifestyle:** Exercise, vagus nerve stimulation techniques, mindfulness, and sleep optimization to lower allostatic load and modulate the gut–brain axis.
- **Core Targets:** Immune dysregulation, leaky gut & enteric dysfunction, GBA disruption, oxidative stress, neuroinflammation, and allostatic overload.

# Addressing Gut Microbiota Issues

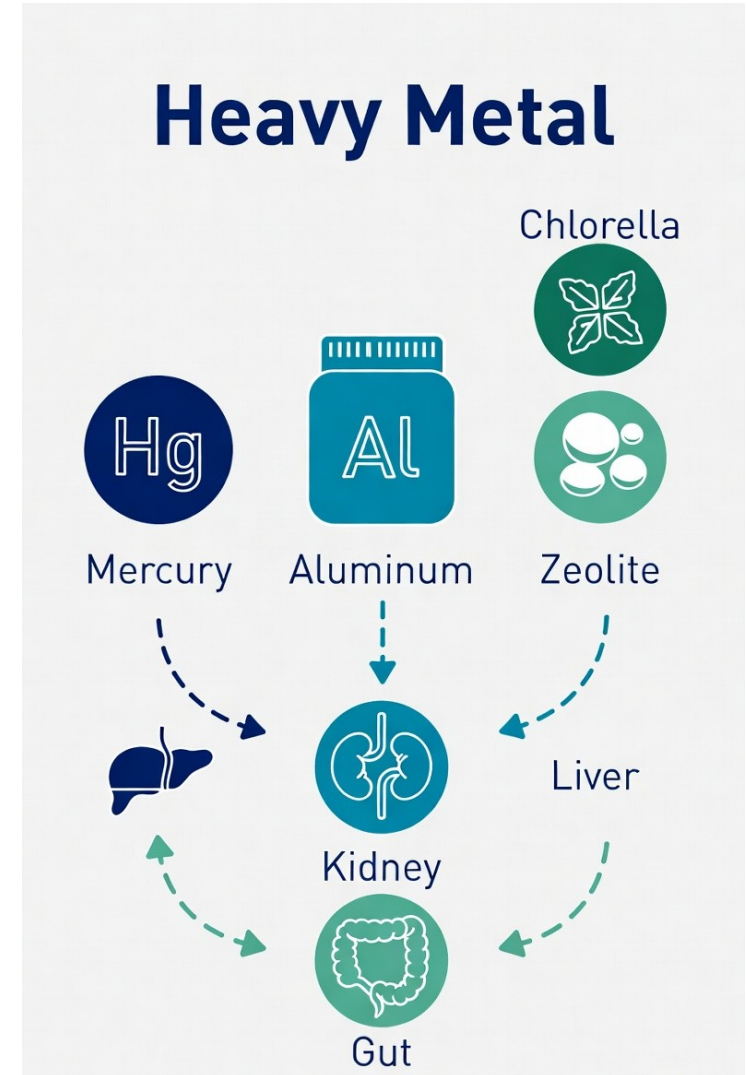
- Probiotics, prebiotics, and postbiotics
- Microbiome-modulating diets, fermented foods
- Targeted antimicrobials (bifidobacterium) / FMT research when indicated
- Restore GBB integrity and reduce systemic inflammation

# Correcting Deficiencies in Sulfation and Detoxification

- Sulfate donors (Epsom salts, STS, NAC)
- Support methylation/sulfation cycle (B-vitamins, methylfolate, folinic acid, zinc, molybdenum)
- Antioxidant & mitochondrial support (CoQ10, carnitine, ALA)
- Addresses PERM hypothesis and redox imbalance

# Metals Detoxification

- Natural binders (modified citrus pectin, chlorella, zeolite, charcoal)
- Targeted chelation protocols (under medical supervision)
- Support Phase I/II/III detox pathways
- Reduce neurotoxic load and protect BBB integrity



# Phase I/II/III Detoxification

- **Phase I:** Balanced CYP450 activity (avoid overload)
- **Phase II:** Glutathione, methylation, sulfation support
- **Phase III:** Transporter function + bile flow + bowel regularity

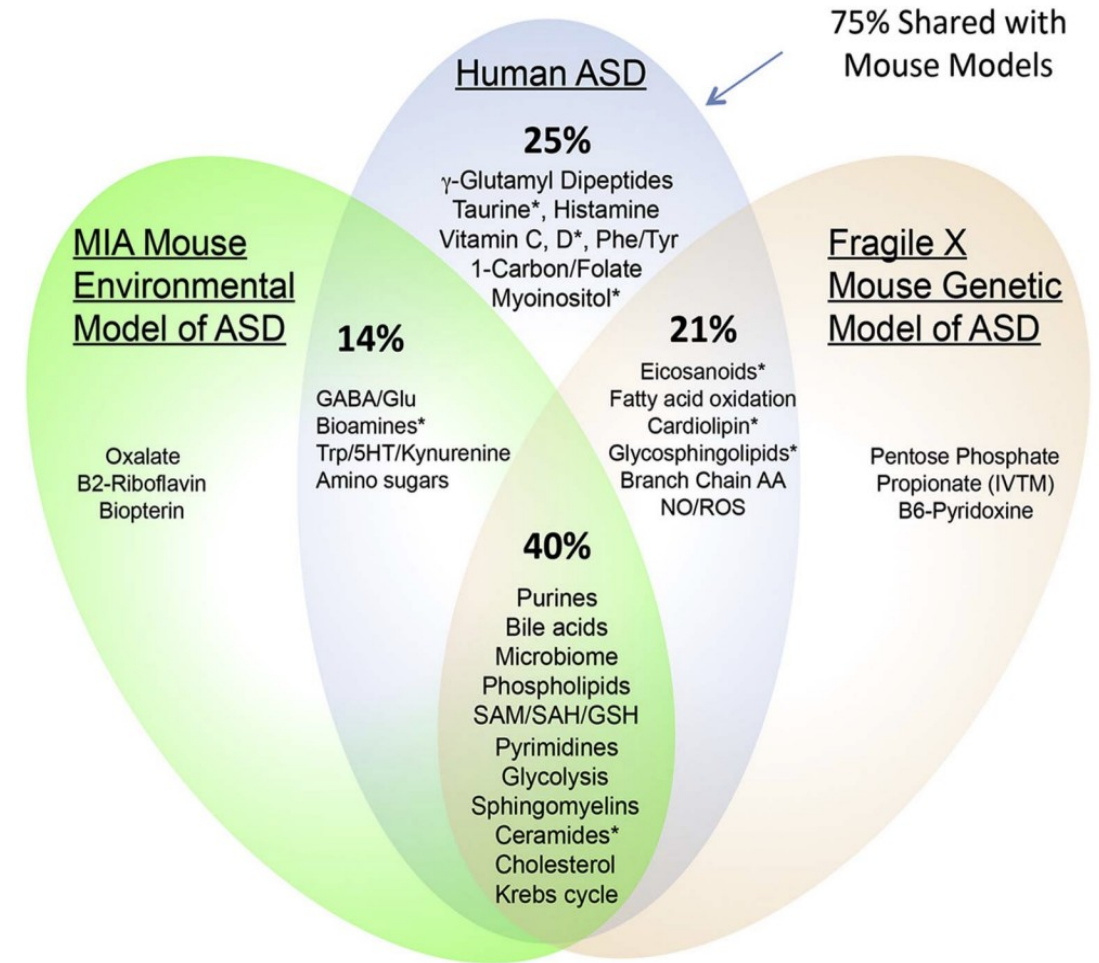


# Leucovorate (Folinic Acid) Therapy

- Bypasses folate cycle blocks better than folic acid
- Especially for anti-folate receptor antibody producers
- Methylfolate may be added or substituted depending on MTHFR mutations
- Improves cerebral folate transport and methylation
- Supports neurotransmitter synthesis and reduces oxidative damage
- Often combined with B12 and other cofactors

# Cell Danger Response and Suramin Therapy

- Naviaux's model of stalled cellular healing
- Mitochondria shift to danger signaling (↑ ROS, purinergic signaling)
- Suramin as investigational purinergic antagonist
- Potential to reset CDR and restore mitochondrial/GBA function



# Naviaux's Suramin Trial – SAT-1, 2017

- **Study Design:** Double-blind, placebo-controlled pilot trial 10 boys with ASD (ages 5–14) Single low-dose IV suramin (20 mg/kg) vs placebo (5 per group)
- **Key Results:**
  - Significant improvement in ADOS-2 core autism symptoms
  - Suramin group: **-1.6 points** (8.6 → 7.0)
  - Placebo group: **No change**
  - Large effect size (Cohen's  $d = 2.9$ ,  $p = 0.0028$ )
- **Improvements Seen In:**
  - Language and social interaction
  - Repetitive/restricted behaviors
- **Safety:** Well-tolerated Only mild, temporary rash in suramin group

# The Neuroimmunology of Autism



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# THANK YOU

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