

# Multifactorial approaches to autism causes, contributors and mechanisms

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# Emerging Science Leading to Major Reconceptualizations of What Autism Is

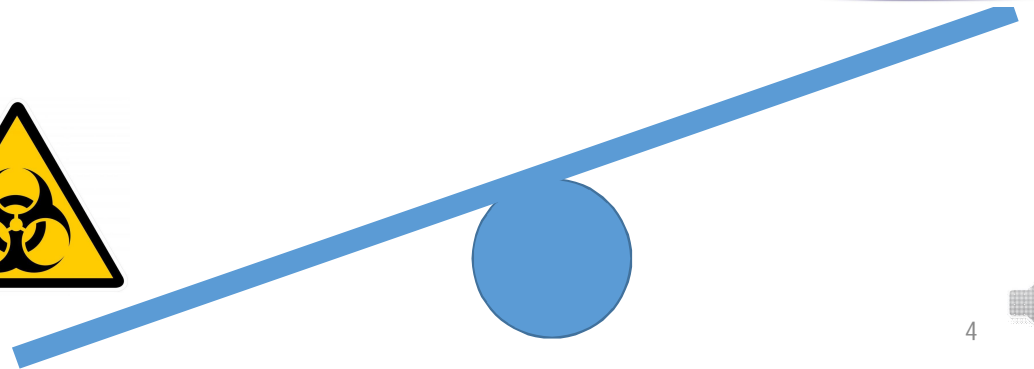
- Not a broken brain
  - Many with autism are highly gifted
  - Issues are often expression and coordination, not capability
    - (more dyspraxia than deficit)
- Not purely genetic
  - Environment plays big role
  - Number actually going up
- Not just brain
  - Whole body, multi-system pathophysiological involvement
    - (brain, gut, immune, endocrine, metabolism, bioenergetics)
- Not life sentence
  - Variable, changeable, treatable, some who lose diagnosis
  - Great potential

CHALLENGES TO THE IDEA THAT  
"AUTISM" IS SPECIFICALLY AND  
UNIQUELY DETERMINED

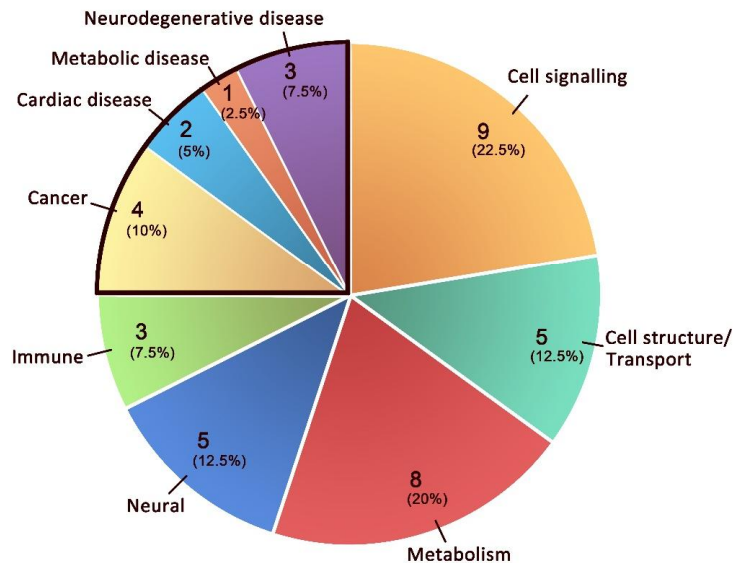
# Where do these problems come from?

## For most of us, probably environment

- We all have genetic vulnerabilities but they are usually not that serious
- Most strongly influential mutations in autism are rare
- Environment brings them to the surface
  - The **heavier the environmental load**, the **less genetic vulnerability you need** to get sick
  - The physiological problems DRIVE the symptoms; the genes and/or environment are INFLUENCES



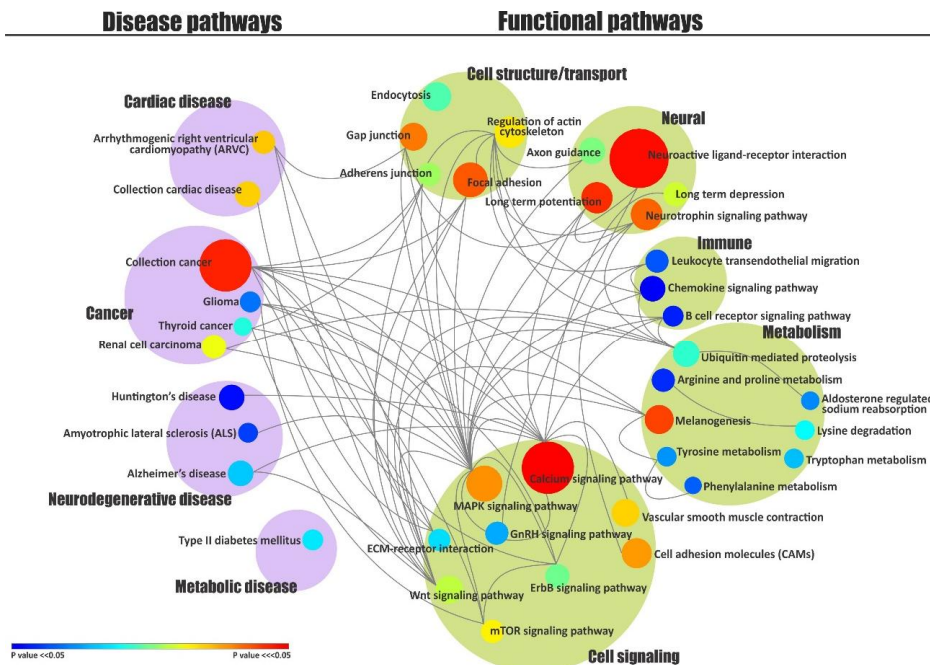
# Genes not specific for Autism: Overlaps with other medical conditions



- Substantial genetic overlap with
  - Cancer
  - Cardiac disease
  - Metabolic Disease
  - Neurodegenerative disease

Wen et al., PLOS ONE, 2016 April

# Genes and Pathways are profoundly interconnected



- A cell is like a city, and pathways are like streets
- Hubs are like major intersections or traffic circles
- Problems with HUBS are like traffic jams in critical places: they can proliferate widely in the system

Wen et al., PLOS ONE, 2016 April

ARE AUTISM BEHAVIORS REALLY  
"SPECIFIC"  
OR ARE THEY THE OUTPUTS OF A  
CHALLENGED BRAIN?

# Model: Autism as emergent property of a challenged brain

- Environmental influences trigger ENVIRONMENTALLY VULNERABLE PHYSIOLOGY.
- The PHYSIOLOGY IMPACTS change HOW the BRAIN FUNCTIONS
- These BRAIN FUNCTIONAL CHANGES are the PROXIMAL CAUSE of Autism
  - -- not by hardwiring the brain, but by changing function MOMENT BY MOMENT EVERY DAY.

**Contributions of the environment and environmentally vulnerable physiology to autism spectrum disorders**

Martha R. Herbert

*Current Opinion in Neurology*, April, 2010

M Herbert chapter on TRANSDUCTION in Valerie Hu's 2014 FRONTIERS IN AUTISM..... book

Available on [www.marthahebert.org](http://www.marthahebert.org)



HOW does the vulnerability of environmentally vulnerable physiology **BECOME VULNERABLE??**

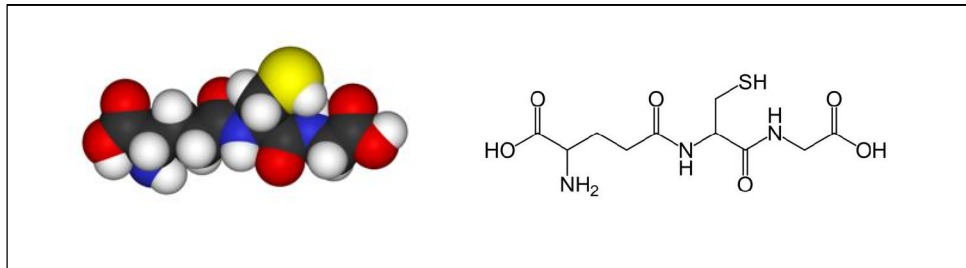
- PARTLY from genetic weak spots
- Partly from early influences on brain development
- To a MAJOR DEGREE from **ongoing environmental INTERFERENCE with OPTIMAL FUNCTION**

# Glutathione as a “Final Common Pathway”

- **GSH is depleted by thousands of toxins, oxidative stress, infection, inflammation, EMF (electromagnetic fields) and nutrient-poor diet**
- **Small exposures of any one thing can still add up to a substantial depletion of antioxidant resilience**
- **Genetic or environmental interference with glutathione synthesis targets a particularly core aspect of protective physiology**
  - “Glutathione: a novel treatment target in psychiatry” – *Trends Pharmacol Sci.* 2008 Jul;29(7):346-51
  - Lee, D. H., D. R. Jacobs, Jr., et al. (2009). "Hypothesis: a unifying mechanism for nutrition and chemicals as lifelong modulators of DNA hypomethylation." *Environ Health Perspect* 117(12): 1799-1802.

# GLUTATHIONE BUILDS RESILIENCE BY PROTECTING CELLS

from environmental and inflammatory stress,  
but is often low in **ASD** (and many other chronic conditions)



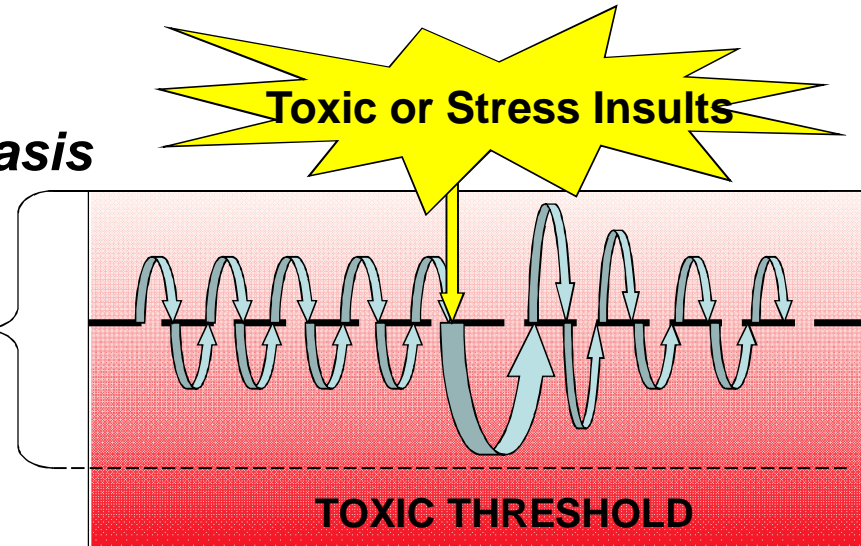
Made in the liver from  
three amino acids:  
**Glutamine + Cysteine +  
Glycine**

- **GLUTATHIONE (GSH) is vital for detoxification**
  - Mops up toxins and free radicals
- The body's most potent anti-oxidant
- **The most abundant antioxidant in the BRAIN**
  - Reduced Glutathione = GSH (active form)
  - Oxidized Glutathione = GSSG (used-up form)

# Vulnerability to Toxics and Stress with low Glutathione (GSH)

**Normal Homeostasis**

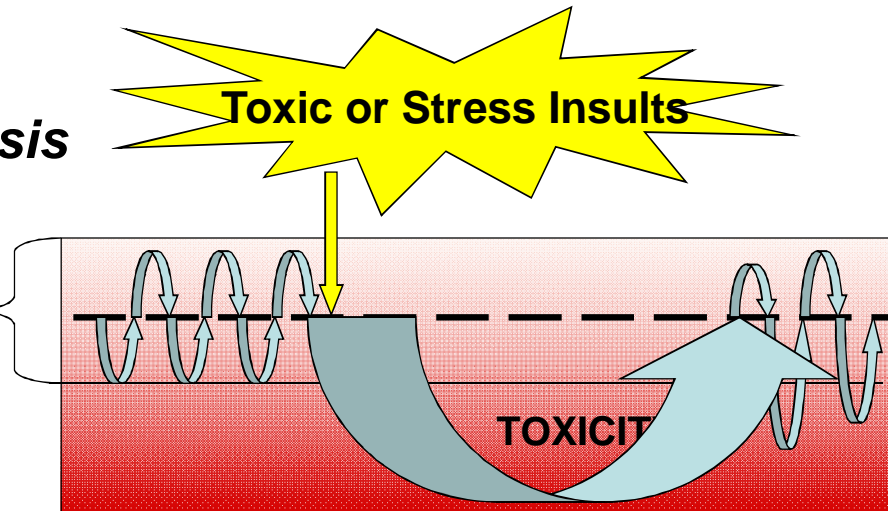
**OK GSH/GSSG**



With enough GSH, you can **BOUNCE BACK**

**Fragile Homeostasis (limited reserve)**

**↓ GSH/GSSG**



If your GSH is **LOW**, Recovery may be difficult

# **Environmentally vulnerable physiology overlaps over many conditions**

- **Still need to understand mechanisms whereby some people get autism, others get asthma, etc.**
- **What specifically about brain structure and function leads to its greater vulnerability in some people?**