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.marthaherbert.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 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

Fragile Homeostasis (limited reserve)

↓ GSH/GSSG

With enough GSH, you can BOUNCE BACK

If your GSH is LOW, Recovery may be difficult

S. Jill James
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?