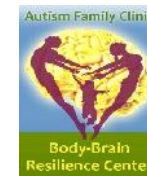


# **TRANSCENDING AUTISM: A Whole-body-brain systems and gene-environment approach**

Martha R Herbert PhD, MD  
Harvard Medical School, Neurology  
Martinos Center for Biomedical Imaging, TRANSCEND Research  
Higher Synthesis Health/Foundation/Works  
[www.bodybrainresilience.com](http://www.bodybrainresilience.com)  
[www.AutismRevolution.org](http://www.AutismRevolution.org)



# Changing Concepts and Findings on Autism

Sir Michael Rutter, JADD, 2012

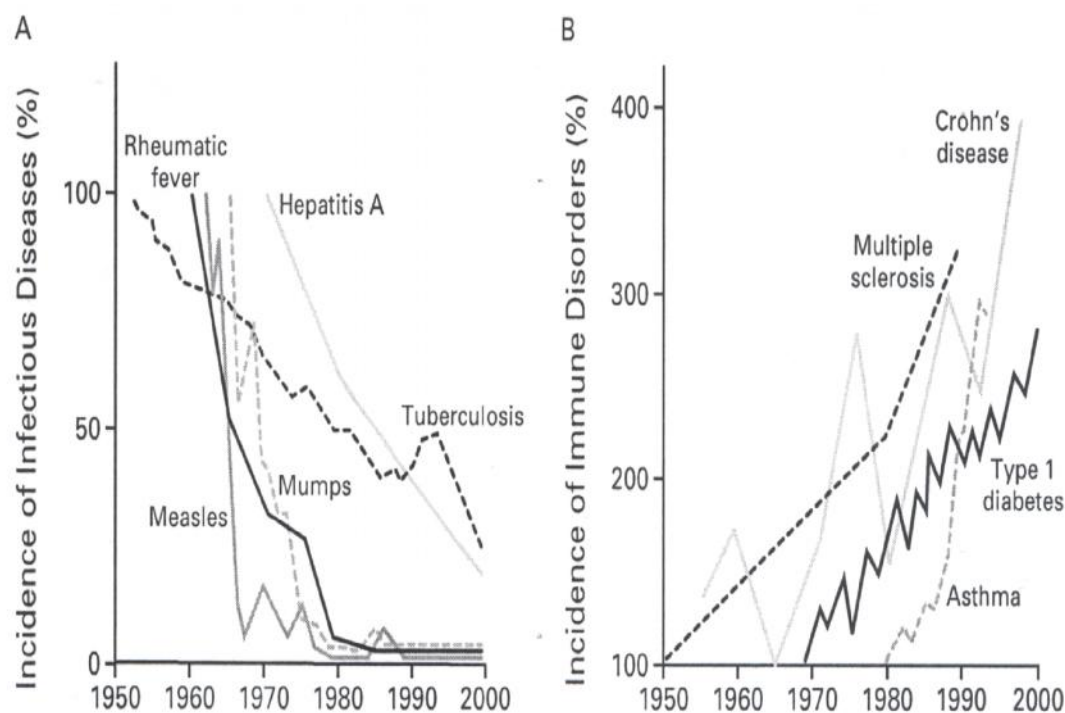
- “New research findings provide major challenges regarding our understanding of the concept of autism. .... It is concluded that, although there have been major research advances.... there is a need for a reconceptualization and an avoidance of claims that go beyond the evidence.”
- In fact, many of the things we have believed about autism have gone beyond the evidence. We were doing the best we could. Now we have a great opportunity to regroup!

# 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

**ALSO, at levels of mechanism  
and of time trends, AUTISM IS  
NOT UNIQUE**

## Drop in Infectious and Rise in Chronic Immune-related disorders

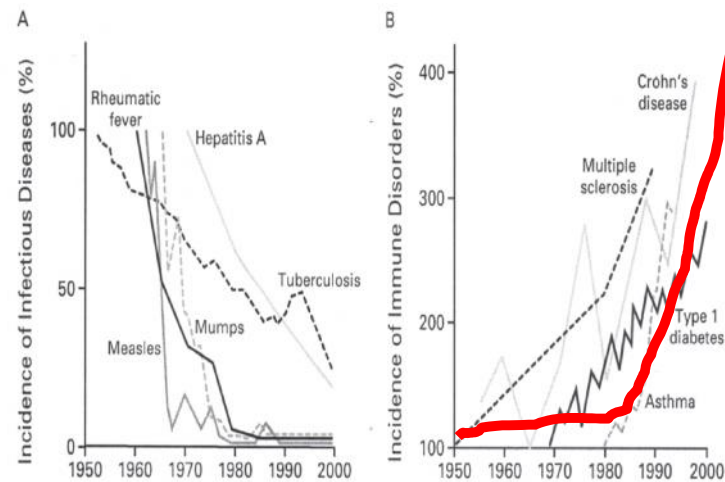


**Figure 1.** Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

In Panel A, data concerning infectious diseases are derived from reports of the Centers for Disease Control and Prevention, except for the data on hepatitis A, which are derived from Joussemet et al.<sup>12</sup> In Panel B, data on immune dis-

# Rise in Autism Prevalence v. Other Major Chronic Conditions in US

Autism



**Figure 1.** Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

In Panel A, data concerning infectious diseases are derived from reports of the Centers for Disease Control and Prevention, except for the data on hepatitis A, which are derived from Joussemet et al.<sup>12</sup> In Panel B, data on immune disorders are derived from Swarbrick et al.,<sup>10</sup> Dubois et al.,<sup>13</sup> Tuomilehto et al.,<sup>14</sup> and Pugliatti et al.<sup>15</sup>

# Many new observations in ASD: Where might they point?

- It is necessary to think really carefully about what we think autism “is” and how autism “works”
- Critical to ask:
  - What is “behavior”?
  - What *generates* behavior?
  - How can we modulate the processes that generate behavior?

**GENES and ENVIRONMENT are not DIRECT  
CAUSES OF BEHAVIOR!**

**There are a lot of in-between steps**

GENES

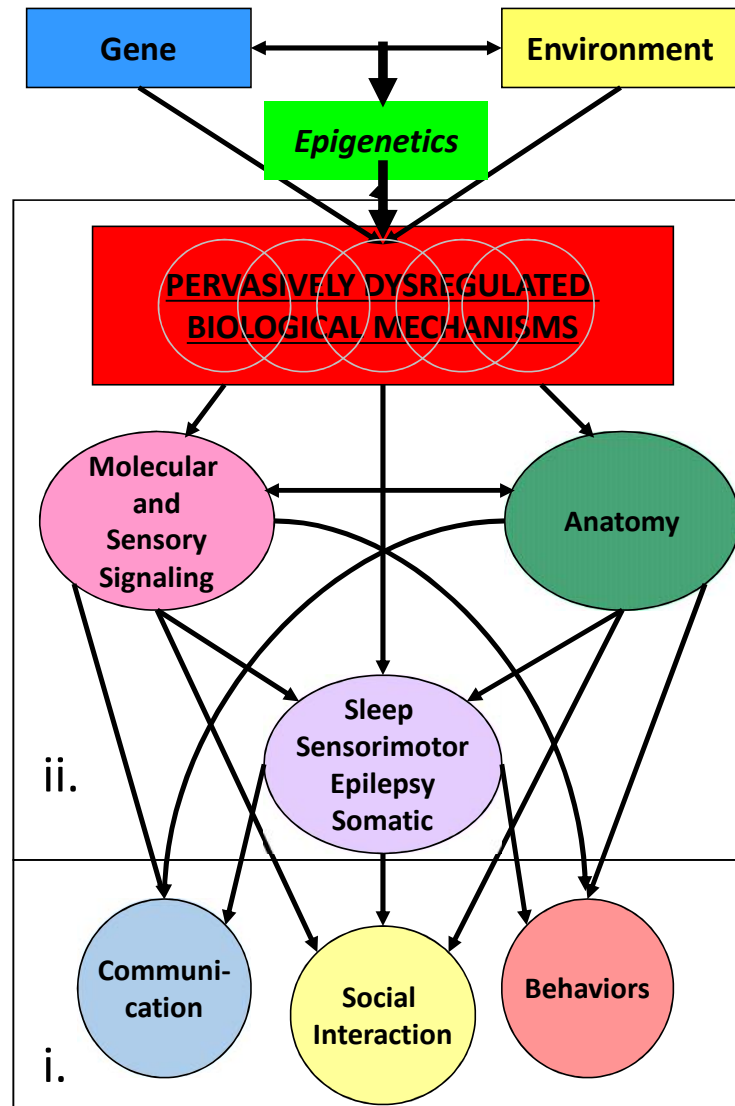
ENVIRONMENT



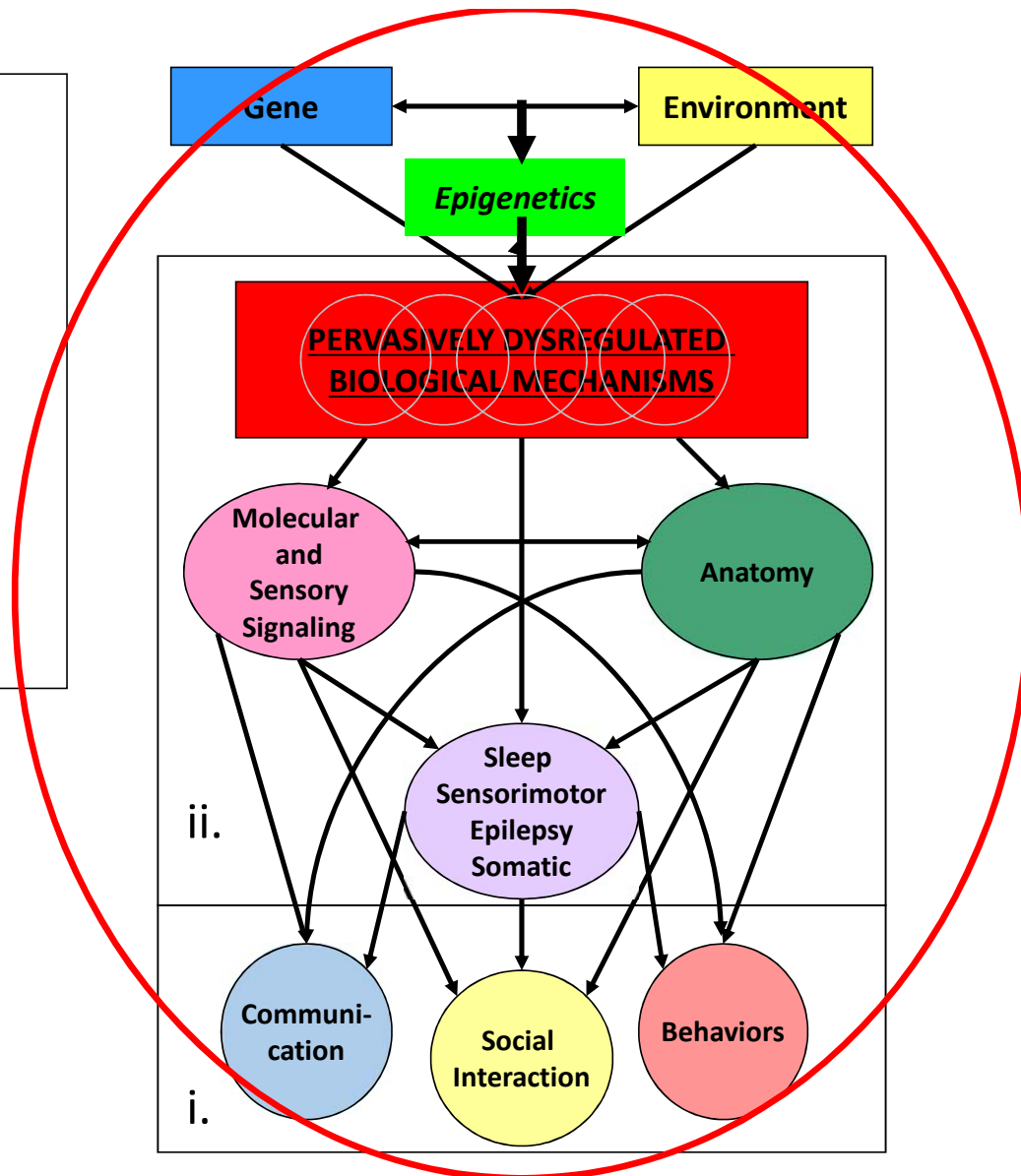
BEHAVIOR



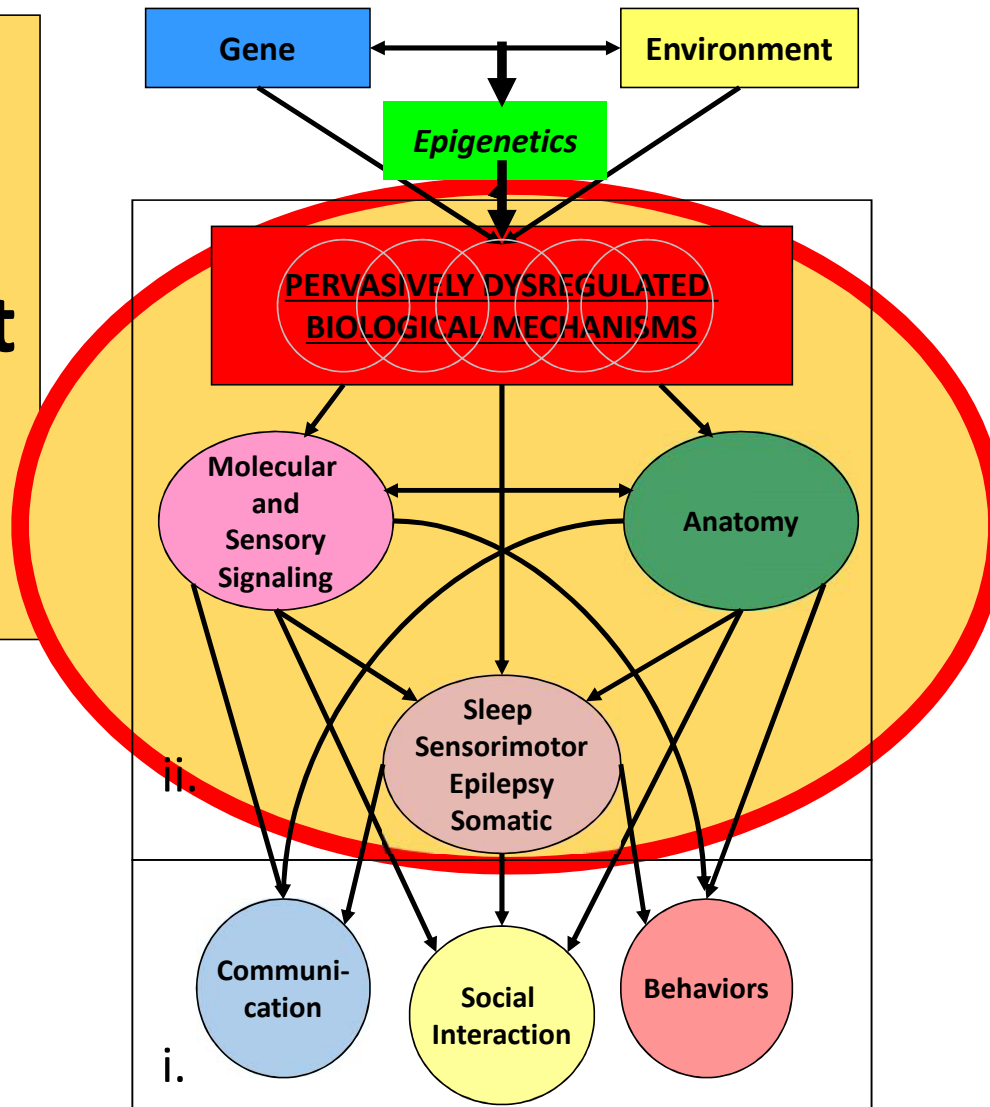
Behaviors are  
**OUTPUTS.**  
What's in the  
**middle** is  
**COMPLEX**  
**SYSTEMS** that  
are inter-  
related



**THIS gives us a  
Whole-Body,  
Whole-Brain,  
Whole-Person  
Understanding  
of Autism**



This “COMPLEX STUFF IN THE MIDDLE” is what is **DRIVING** the autism!

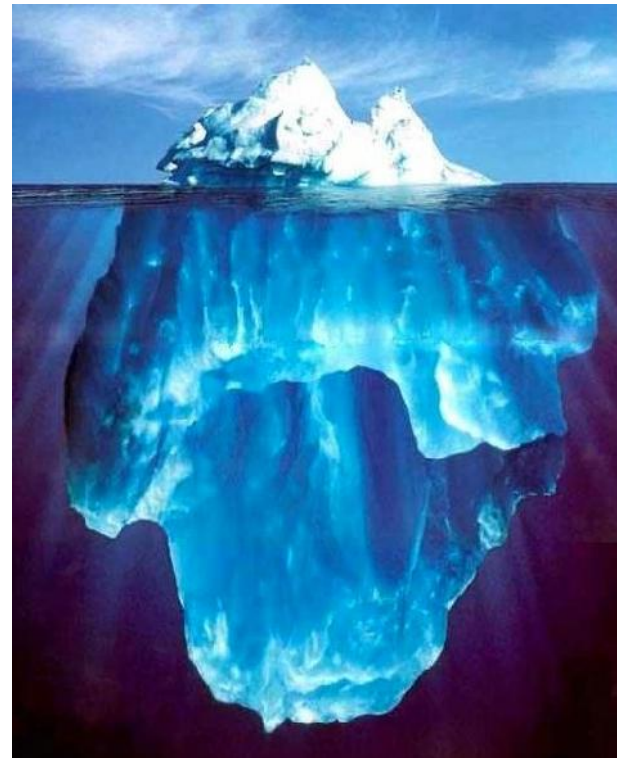


# Whole Body-Brain Systems Model: Symptoms **Emerge** from Problems with **Underlying Functions**

**VISIBLE Social  
& Behavioral  
SYMPTOMS  
are OUTPUT**

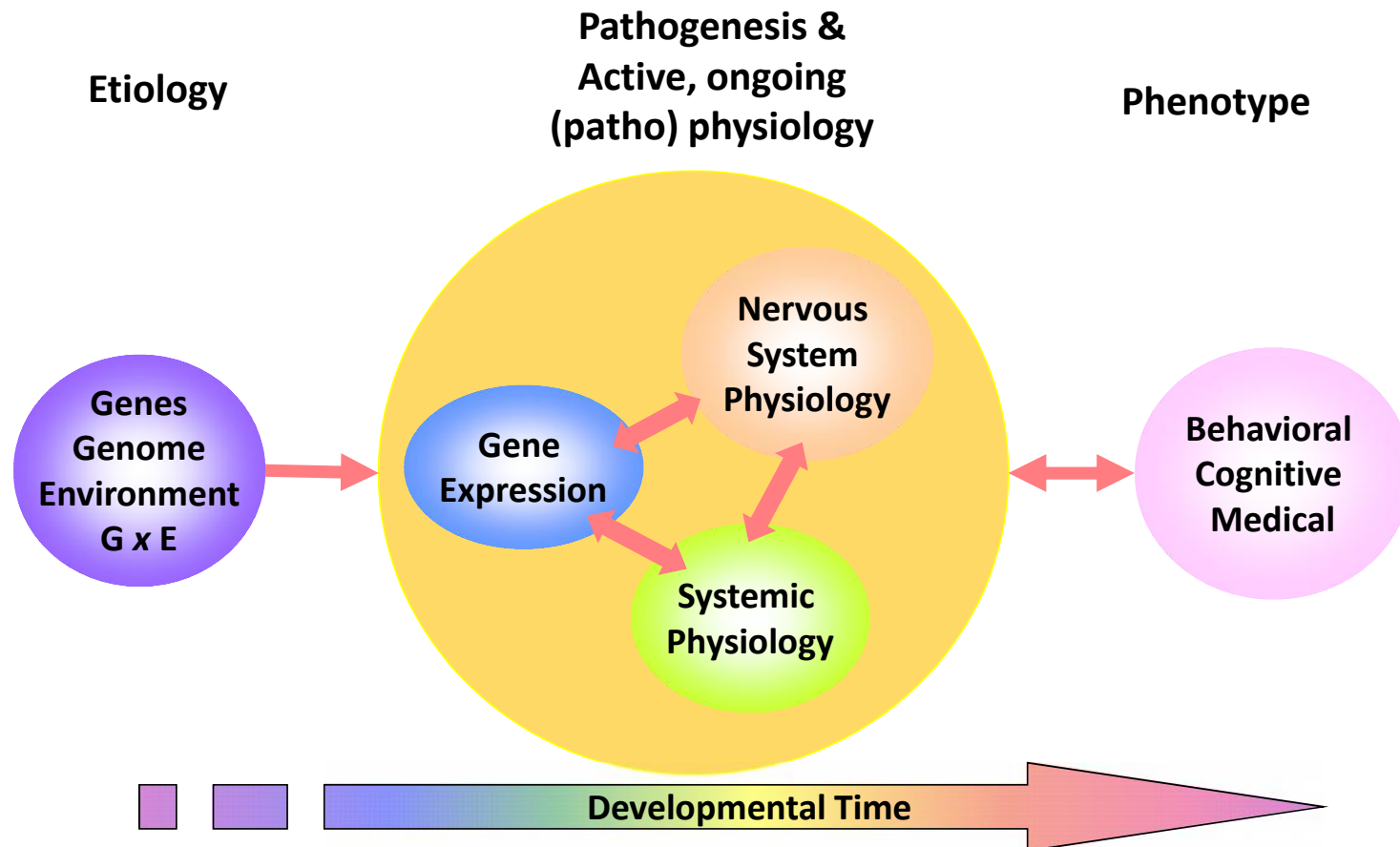


**DISTURBANCE OF  
CORE UNDERLYING  
**BODY and BRAIN  
FUNCTIONS** are  
GENERATORS**



# A Middle-Out Approach to Autism: Multi-Scale, (Patho)Physiology Centered

(see Denis Noble THE MUSIC OF LIFE)



**Environmental influences trigger  
ENVIRONMENTALLY VULNERABLE PHYSIOLOGY.**

**The PHYSIOLOGY changes  
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)

**HARDWIRED brain issues are in most “idiopathic” cases likely **DOWNSTREAM** of chronic physiology problems**

Herbert, M. R. (2014 ).

**Translational Implications of a Whole-Body Approach to Brain Health in Autism:  
How **Transduction** Between Metabolism and Electrophysiology Points to Mechanisms for Neuroplasticity.**

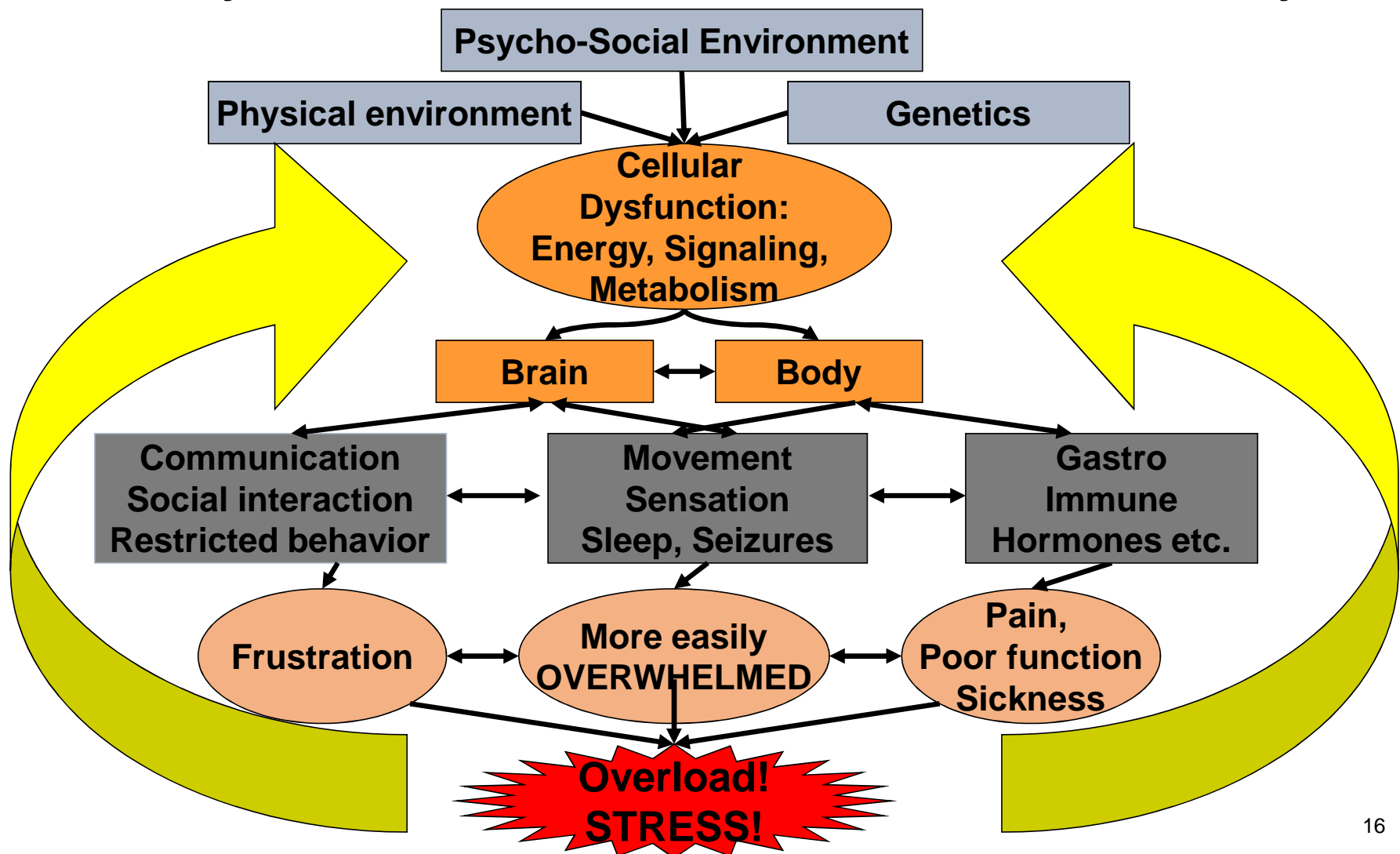
Frontiers in Autism Research: New Horizons for Diagnosis and Treatment.

V. W. Hu. Hackensack, NJ, World scientific.

See also Herbert and Sage, : “Autism and EMF: Plausibility of a Pathophysiological Link”

*Pathophysiology 2013 and Bioinitiative 2012*

# Whole Body-Brain Model: Vicious circles in brain and body





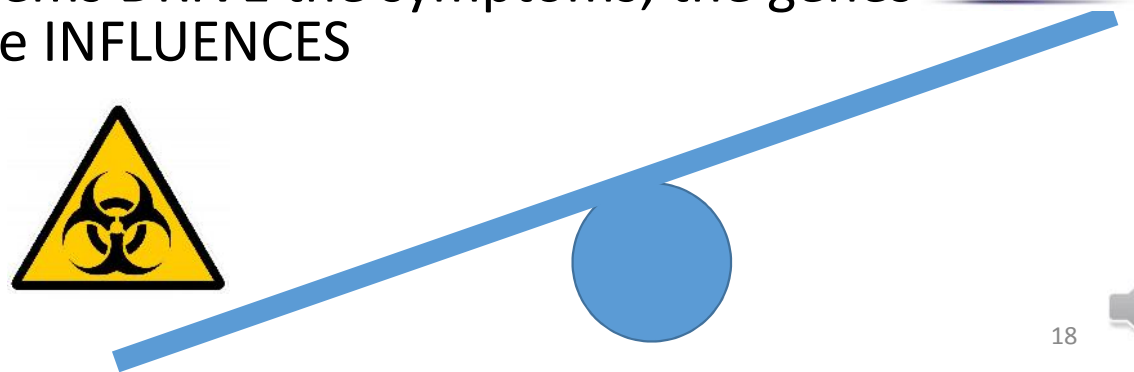
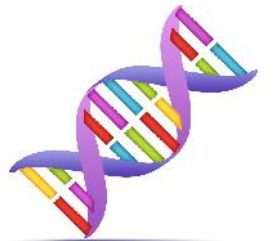
**HOW does environmentally vulnerable physiology **BECOME VULNERABLE??****

- **PARTLY** from genetic weak spots
- To a **MAJOR DEGREE** from **environmental INTERFERENCE with OPTIMAL FUNCTION**

# 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



# Autism comorbidities

Rzhetsky, 2007, PNAS

## Pervasive Developmental Disorders

- PDD, Fragile X

## Neurological disorders

- Attention deficit, epilepsy, cerebral palsy, schizophrenia, bipolar disorder, neurofibromatosis, Parkinson's Disease, Migraine

## Bacterial, viral, protozoan

- Viral infections of CNS, tuberculosis, viral infections of other systems, staphylococcal and *Helicobacter pylori* infections

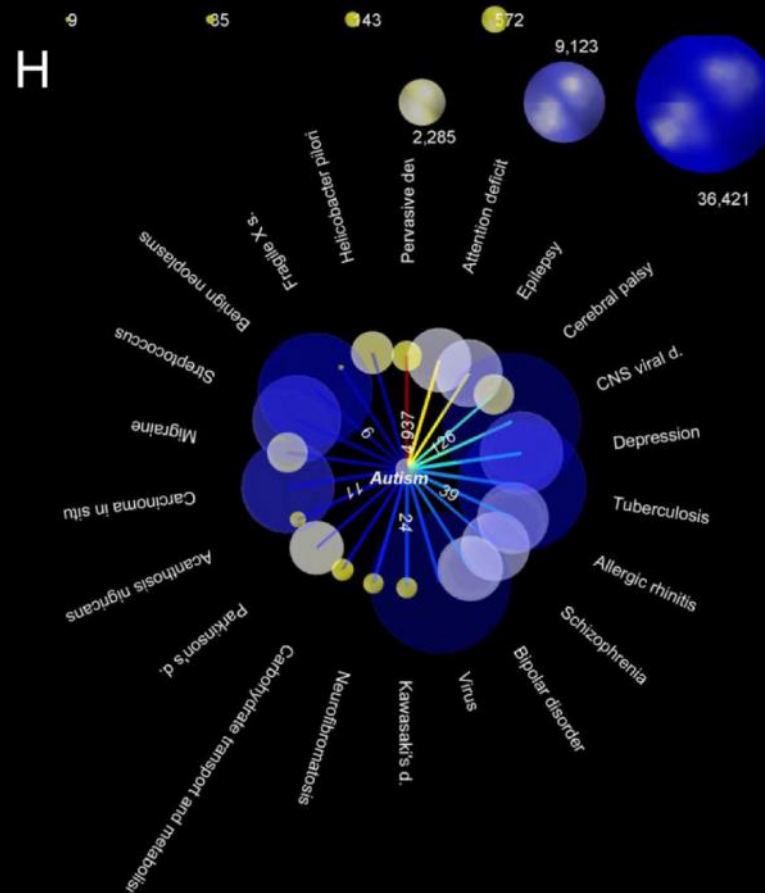
## Allergies, Autoimmune disorders

- Allergic rhinitis, eczema, psoriasis

## Benign and Malignant Neoplasms

## Other

- Kawasaki's disease, acanthosis nigricans, aberrations of carbohydrate metabolism



**Genes that had biggest impact and/or occurred most commonly across 9 comorbid conditions largely had *immune function***

ADHD  
cerebral palsy  
depression  
schizophrenia  
tuberculosis  
allergic rhinitis  
bipolar disorder  
Parkinson's

NR4A2	DRD2
TNF	CD14
IL6	SLC11A1
IL4	GAD1
SLC6A4	HLA-DRB1
DRD4	NOS2A
SLC6A3	IL1B
ACE	IL18
IFNA1	CYP2D6
COMT	MAOA
IL10	LTA
MBL2	TPH1
ADRB2	PTGS2
BDNF	TLR4
APOE	IFNG
HTR2A	HLA-DQB1
IL13	VDR
NOS3	

- Substantial overlap in genes implicated in multiple co-morbid conditions
- Many of the genes highly ranked in multiple conditions have immune relevance

Method: GeneSelectAssist service in CDC's HuGE website

**Scandinavian study:**

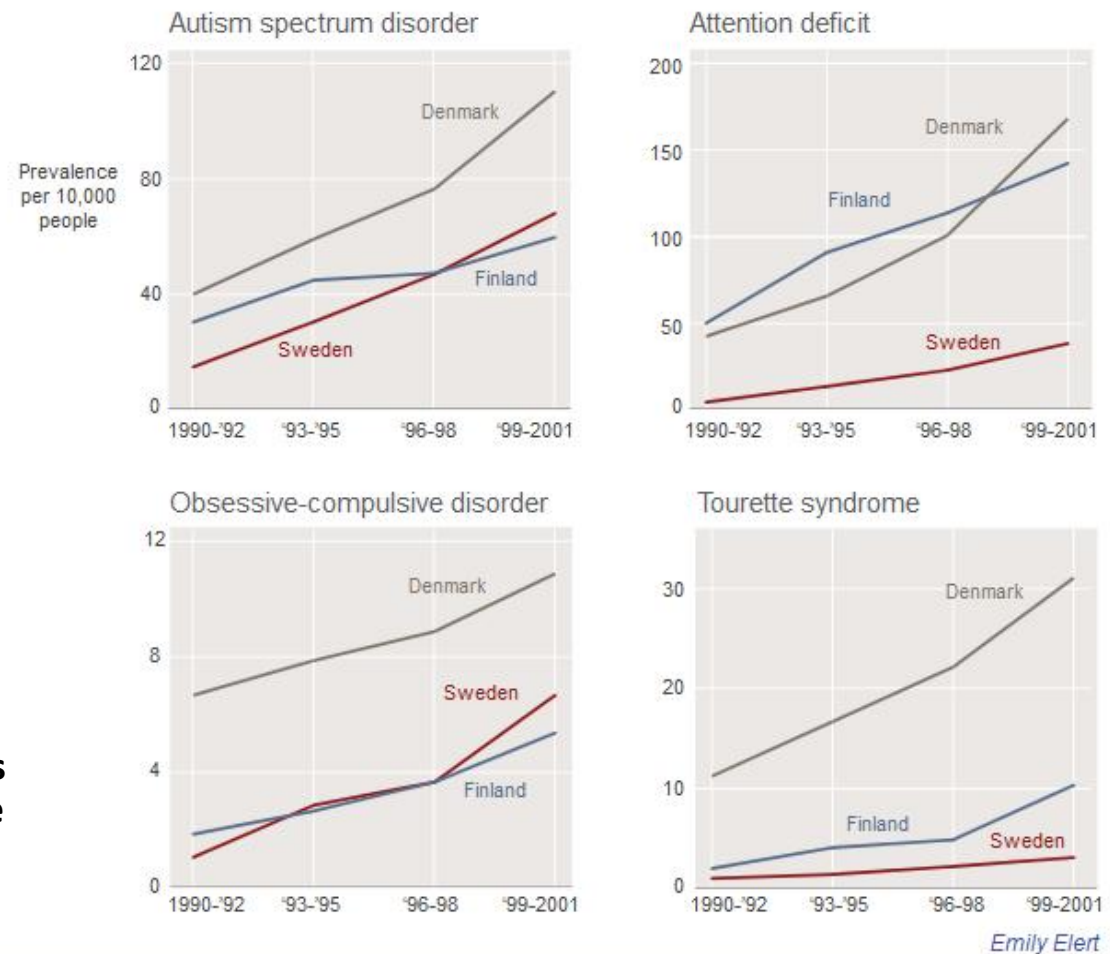
# **ASD, ADD, OCD, TOURETTE'S – ALL GOING UP**

**Can this be dismissed as “due  
to greater awareness” since  
“these are all distinct  
conditions”?**

**The increasing prevalence of reported diagnoses  
of childhood psychiatric disorders : a descriptive  
multinational comparison.**

**Atladottir, European Child & Adolescent  
Psychiatry, 06.05.2014.**

Prevalence of mental disorders at age 10 in four birth cohorts

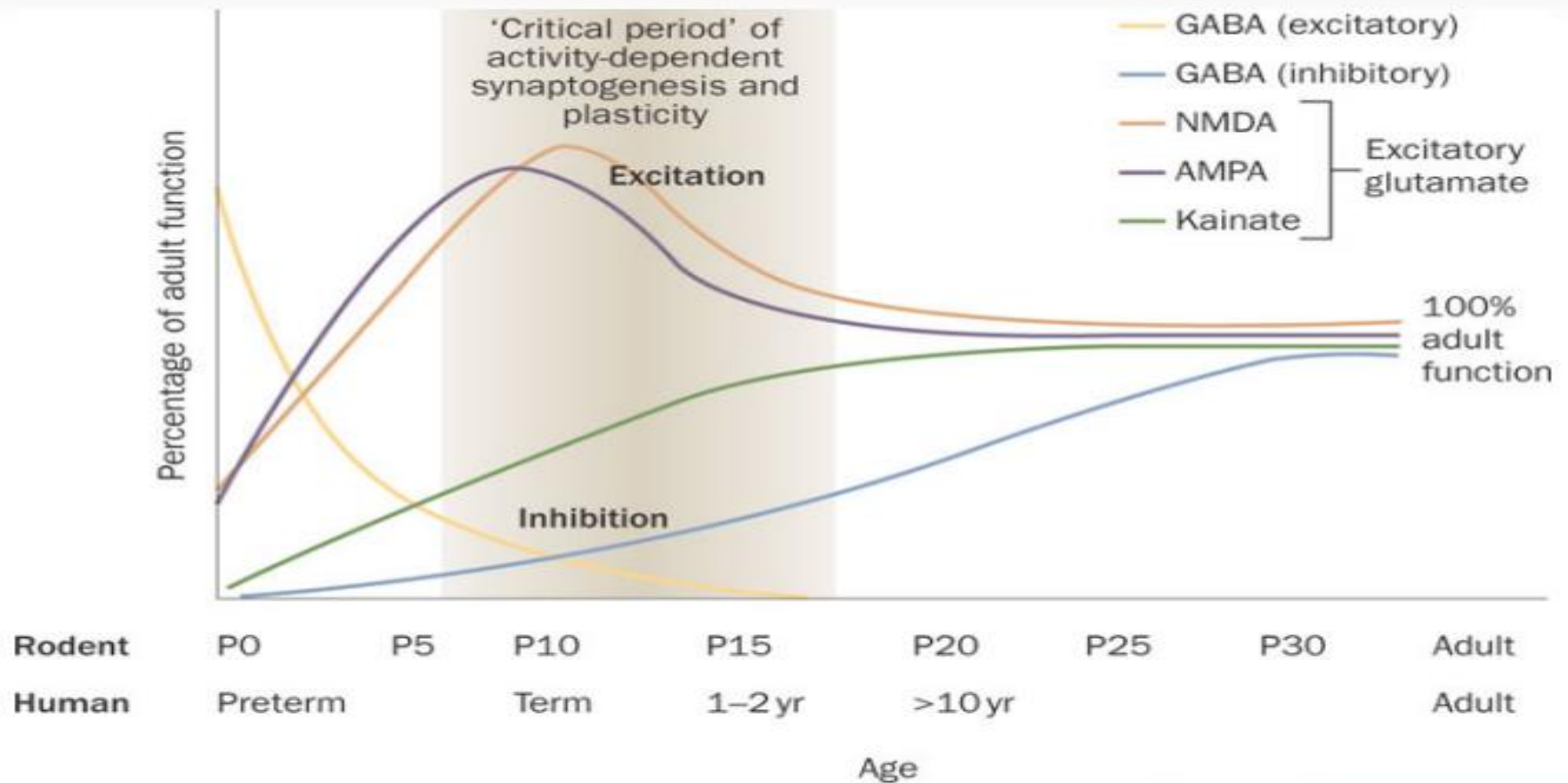


**OKAY, so if the underlying triggers are similar, why isn't everybody autistic?**

**AT LEAST IN PART, BECAUSE OF  
THE TIME OF ONSET**

**Along with the  
severity of vulnerability and genetic weak spots**

## Maturational changes in Glutamate and GABA receptor function in the developing brain



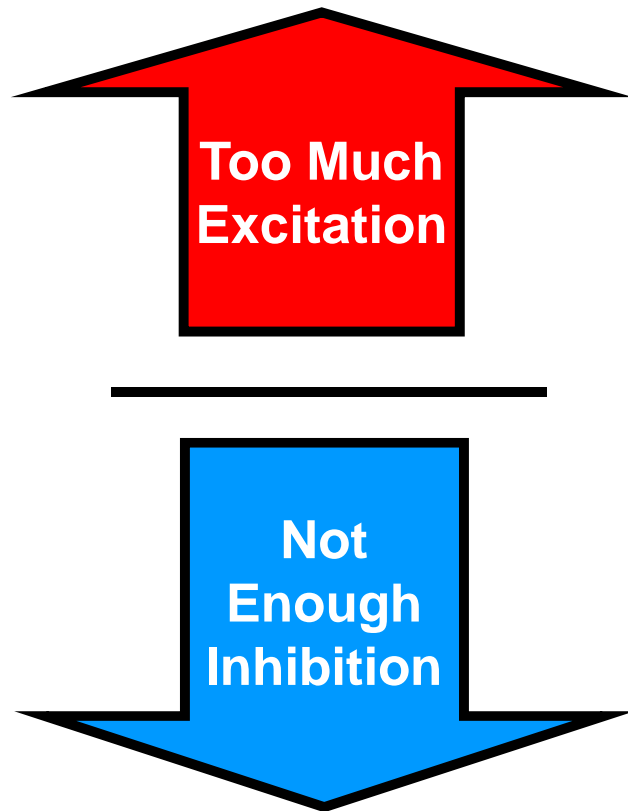
Rakhade, S. N. and Jensen, F. E. (2009), *Nat. Rev. Neurol.*  
 Talos et al *J. Comp Neurol*, 2006; Dzhala V et.al. *Nature Medicine*, 2005

**nature**  
 REVIEWS **NEUROLOGY**

# A FINAL COMMON PATHWAY

Model of autism: Increased ratio of  
excitation / inhibition in key neural systems

Rubenstein & Merzenich, *Genes, Brain and Behavior* (2003) 2: 255-267



*Loss of  
informational  
complexity  
and  
organization*

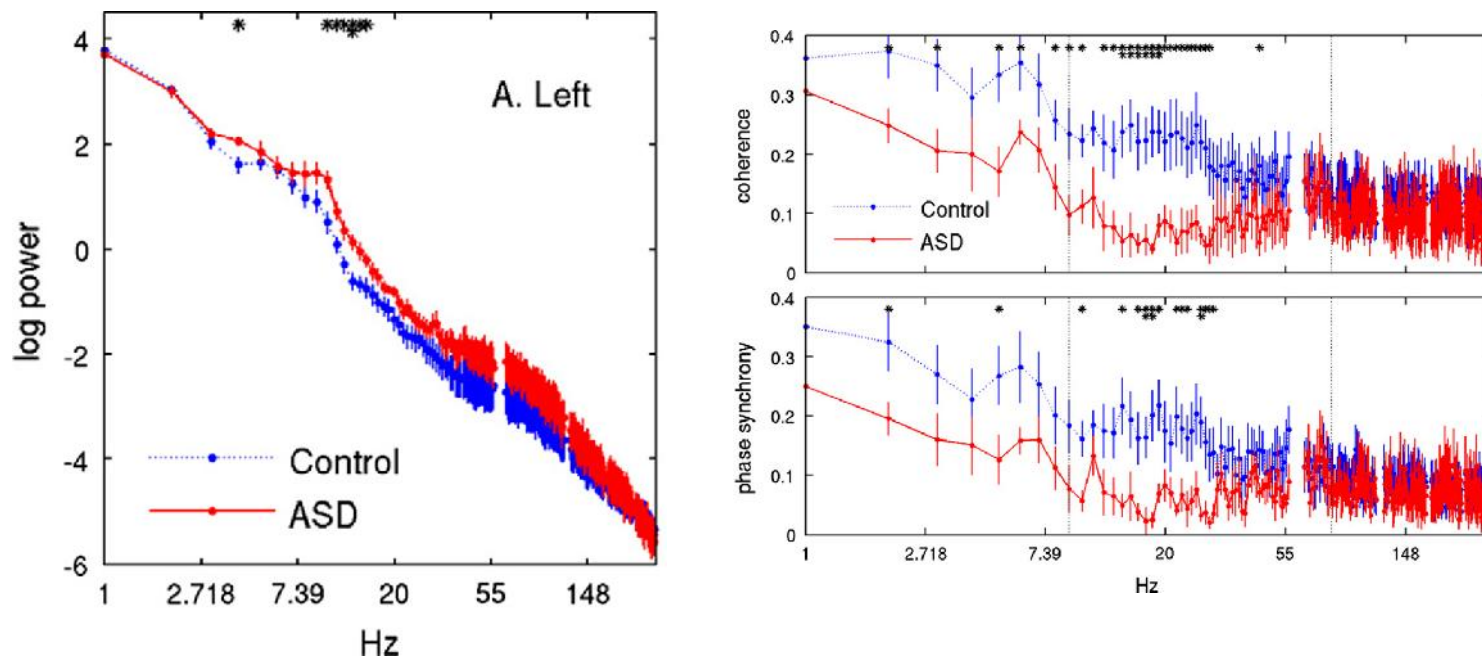
*Reduced  
signal to noise  
ratio*





# “Inefficiency” in brain **signaling** in autism

J.R. Isler, K.M. Martien, P.G. Grieve, R.I. Stark, M.R. Herbert  
Clinical Neurophysiology 121 (2010) 2035–2043



ASD has more power than controls... but less coherence  
**POOR SNR – Sound and Fury, signifying nothing**

**ARE AUTISM BEHAVIORS REALLY  
“SPECIFIC”?**

**OR THEY THE OUTPUTS OF A  
CHALLENGED BRAIN?!?**

# The core defining behaviors all involve a challenge to the brain's ability to coordinate complex information

- In order to speak, communicate, be flexible rather than repetitive, there needs to be a fluidity, an ability to pull in vastly distributed bits of information and coordinate them elegantly in real time
- A brain with inflammation, mitochondrial dysfunction and a shortage of ingredients (nutrients) to drive brain functions **WILL HAVE A HARDER TIME DOING COMPLICATED THINGS.**
- This is not specific, not “caused” by specific genes or brain lesions.

# **Everything I found in brain anatomy of ASD was similar – only milder – in developmental language disorder (DLD)**

- **LARGER**

- Brains
- White matter
- Prefrontal white matter

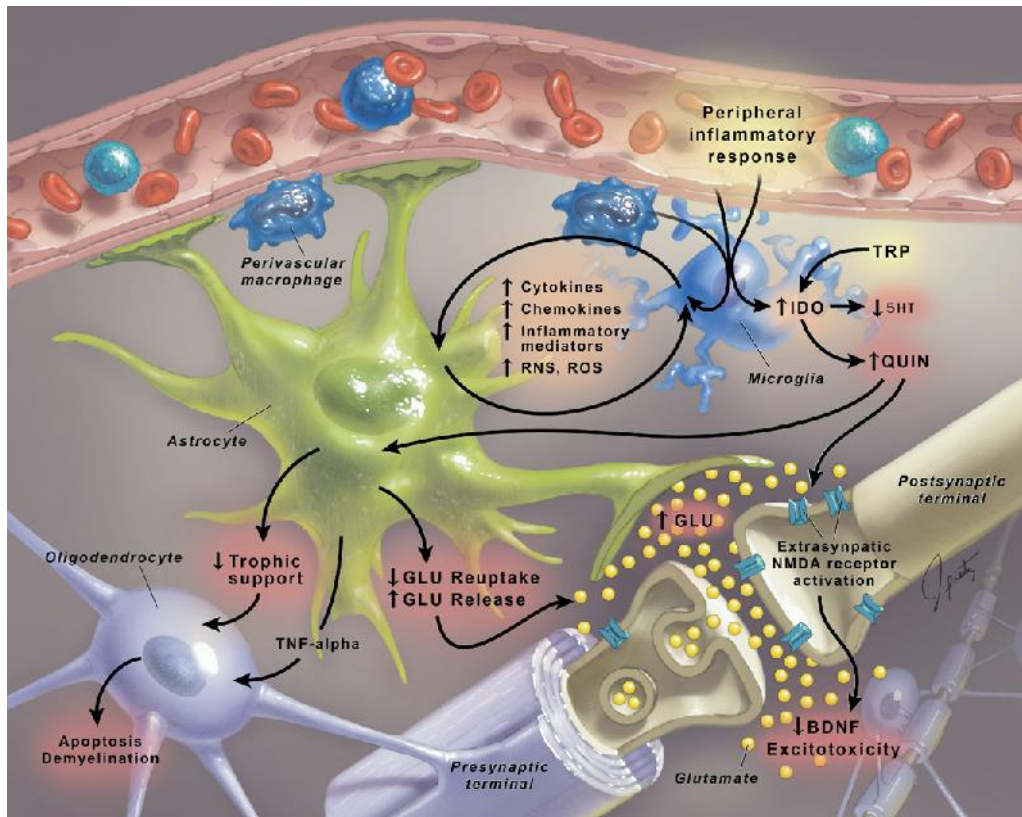
**BUT LESS SO in DLD**

- **GREATER**

- Asymmetries in regions  
associated with complex  
integrative brain function

**BUT LESS SO in DLD**

# Inflammation in the brain creates **cellular noise** that interferes with information processing



- Excitatory chemicals created by activated glial cells
- Normal housekeeping functions of glial cells get neglected
- Chronic inflammation is irritating and promotes excitotoxicity
- Chronic inflammation can cause damage

Inflammation and Its Discontents: The Role of Cytokines in the Pathophysiology of Major Depression.

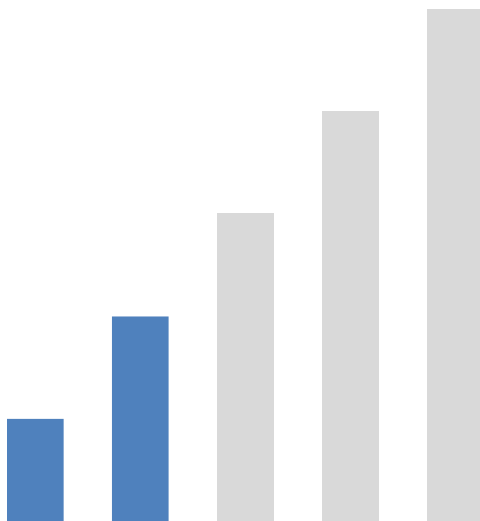
Miller et al., BIOL PSYCHIATRY 2009;65:732–741



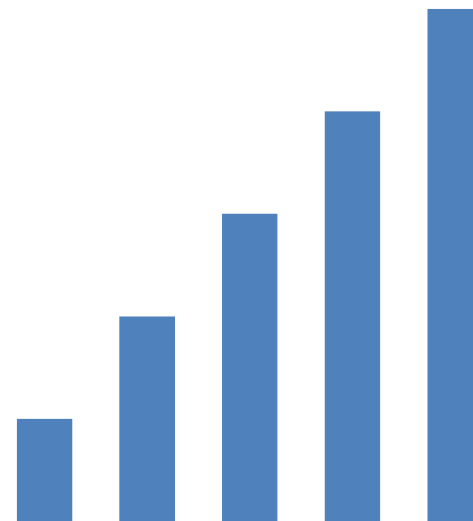
**Tissue pathophysiology creates NOISE that  
REDUCES BRAIN BANDWIDTH**

**→ Too much noise/static; not enough SIGNAL**

**Poor Bandwidth:  
Limited Reception**



**Lots of Bandwidth:  
Good Reception**



**Better Reception Allows Better Discernment of  
Differences and More Spontaneous Learning**

**AUTISM: NOT BORN BUT MADE**

# **Problems that often precede the autism diagnosis (plenty of data on this)**

- Parents with health problems
  - Health issues, particularly Metabolic Syndrome (diabetes, hypertension, etc)
  - Exposures (toxins, EMF/radiation, stress) leading to genotoxicity and metabolic dysfunction
- Pregnancy issues
  - Inadequate nutrition
  - Exposures (toxics, medications, EMF, stress, infections, allergens)
- Infancy issues
  - Infections, antibiotics that injure microbiome
  - Allergens, lack of microbiome support
  - Insufficiency of various nutrients for handling load of stressors



# The ALLOSTATIC LOAD (or Total Load) Theory of Autism

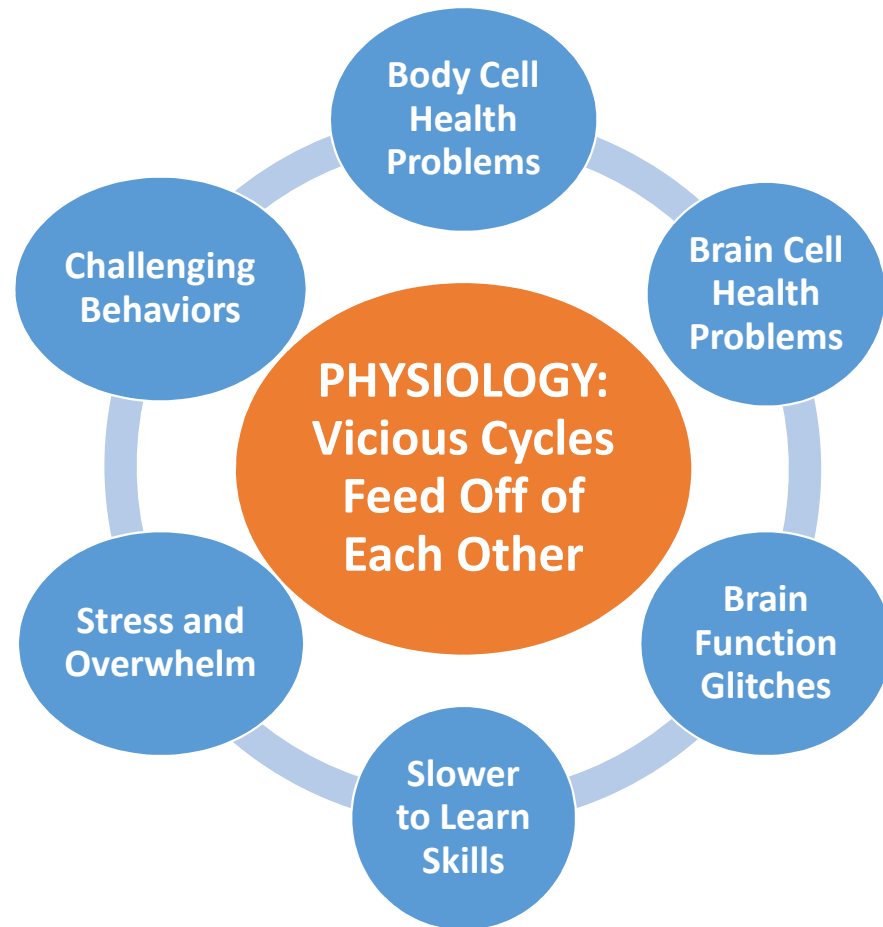
- **TOO MANY NOXIOUS EXPOSURES → INCREASED FRAGILITY**
  - Toxicants, Radiation, Noise
  - Infections
  - Stress
- **POOR DEFENSES → NOT ENOUGH RESILIENCE**
  - Dietary insufficiencies
  - Weak social supports
  - Poor lifestyle
  - Damaged microbiome
  - Genetic weak spots

# Autism REGRESSION as a TIPPING POINT

- The system's ability to regulate itself deteriorates and you see problems with:
  - Sleep, sensory perception, digestion, hormones, coordination
- Depending on how far this deterioration goes, and which systems are more vulnerable, you may get
  - Sensory processing and motor coordination disorders
  - ADHD
  - Allergies, asthma, diabetes
  - Language delays and/or social awkwardness
  - Autism

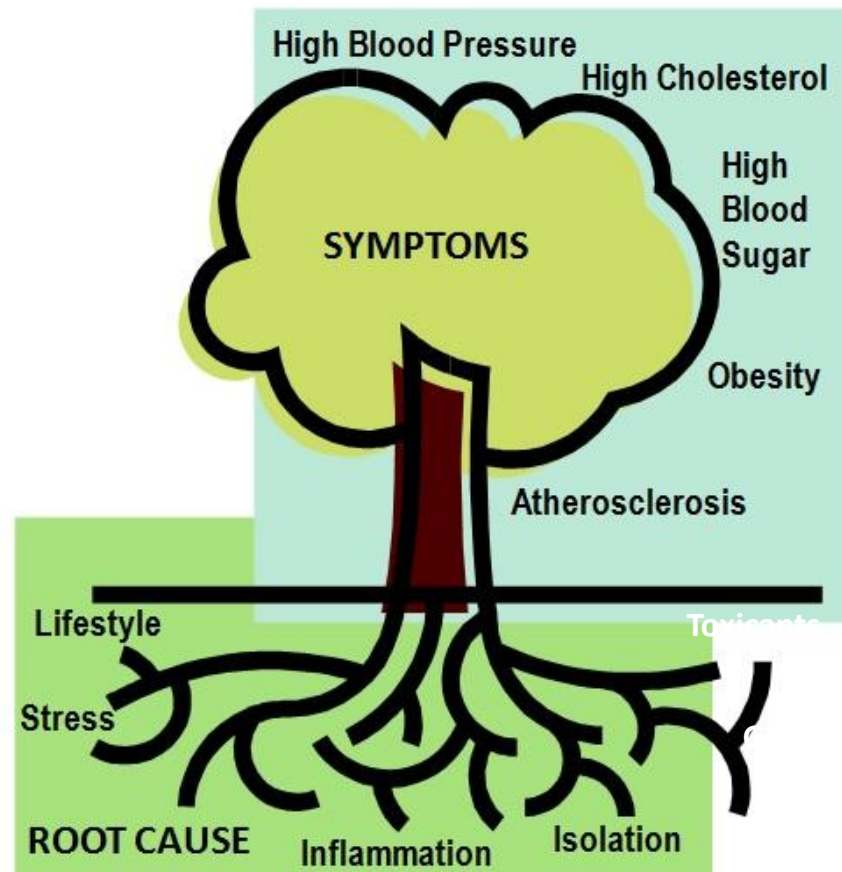
# Problems in each area make trouble for the other areas

**This is  
consistent  
with  
emerging  
SYSTEMS  
BIOLOGY**



**PROPOSITION / ASSERTION:**  
**We know enough now to promote  
health and hunt for and remove  
contributors to harm**

**The most effective treatments will deal with the root causes.**



**WHAT DO WE NEED TO DO?**



# MORE SIGNAL, LESS NOISE

## MORE SIGNAL

- Slow things down
  - Mindful variety
  - Rejoice in your child right now
  - Find ways that your child succeeds and build from there
- 
- Read Anat Baniel's book *KIDS BEYOND LIMITS*

## LESS NOISE

- Remove physiological interference from poor nutrition, inflammation, toxicity
- Minimize sleep deprivation
- Minimize stress

# Build **Resiliency** and Reduce Allostatic or “**Total Load**”

## **RESILIENCY**

- High nutrient density food
- Vigorous Activity
- Skilled individualized teaching
- Enhance BRAIN FUNCTION through SMART, SENSITIVE movement
- Family and social supports

## **“TOTAL LOAD”**

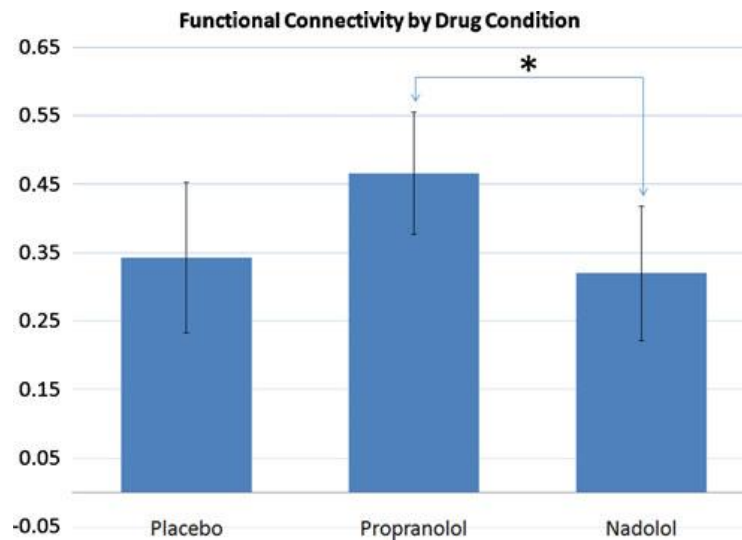
- Avoid unnecessary exposures to chemicals, radiation, infection
- Reduce stress/time management
- Support the body’s immune and detox biochemistry

**Building **RESILIENCY** protects brain  
and body from being degraded by  
**NOXIOUS LOAD.****





# Rapid IMPROVEMENT in brain connectivity access to more parts of brain networks when stress is reduced



**Effect of Propranolol on Functional Connectivity in Autism Spectrum Disorder—A Pilot Study**  
Narayanan et al. (Beverdors lab)  
*Brain Imaging and Behavior*, 2010

- This was interpreted by the authors as an **IMPROVEMENT IN THE SIGNAL TO NOISE RATIO**
- There are many other ways we could do that using everyday epigenetics.

# EVERYDAY EPIGENETICS:

Doing the SMART THINGS we can ALREADY  
do IN OUR DAILY LIVES to help epigenetics  
and support healthy physiology

*North American Journal of Medicine and Science*

**Commentary**

**www.najms.net 2013; 6(3)** 167

## **Everyday Epigenetics: From Molecular Intervention to Public Health and Lifestyle Medicine**

Martha R. Herbert, MD, PhD\*

*Department of Neurology, Massachusetts General Hospital, Charlestown, MA*

Epigenetics, which refers to changes in which genes are turned on or off rather than to the genetic code itself, helps us understand that we have much more power over our health and well-being than we could

# Autism Revolution: Ten Tips

1. *Go for the extraordinary.*
2. *Know what you can't control — and what you can.*
3. *Repair and support cells and cycles.*
4. *Get gut and immune systems on your side.*
5. *Build better brain health.*
6. *Calm brain chaos*
7. *Join your child's world.*
8. *Love, rejoice, and make breakthroughs.*
9. *Lead the revolution!*
10. *Do it for yourself, your next baby, your family, and your world.*

[www.AutismRevolution.org](http://www.AutismRevolution.org)

