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

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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 Joussen et al. In Panel B, data on immune dis-
Rise in Autism Prevalence v. Other Major Chronic Conditions in US

Figure 1: Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1960 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. In Panel B, data on immune disorders are derived from Swarbrick et al., Dubois et al., Tuomilehto et al., and Pugliatti et al.
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?

www.autismWHYandHOW.org
GENES and ENVIRONMENT are not DIRECT CAUSES OF BEHAVIOR!
There are a lot of **in-between steps**
Behaviors are OUTPUTS. What’s in the middle is COMPLEX SYSTEMS that are inter-related.

![Diagram showing complex interactions between gene, environment, and epigenetics leading to behaviors, communication, social interaction, anatomy, molecular and sensory signaling, sleep, sensorimotor, epilepsy, somatic, and gene environment epigenetics interactions.]

i. Communication
ii. Social Interaction

PERVASIVELY DYSREGULATED BIOLOGICAL MECHANISMS

- Molecular and Sensory Signaling
- Anatomy
- Sleep
- Sensorimotor
- Epilepsy
- Somatic
- Behaviors
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 **Emerg**e from Problems with **Underlying Functions**

VISIBLE Social & Behavioral SYMPTOMS are **OUTPUT**

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

Ziggarut model: http://www.texasautism.com/
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.marthaherbert.org
HARDWIRED brain issues are in most “idiopathic” cases likely DOWNSTREAM of chronic physiology problems


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

See also Herbert and Sage, : “Autism and EMF: Plausibility of a Pathophysiologival Link”
Pathophysiology 2013 and Bioinitiative 2012
Whole Body-Brain Model: Vicious circles in brain and body

Psycho-Social Environment

Physical environment
Genetics

Cellular Dysfunction: Energy, Signaling, Metabolism

Brain
Body

Communication
Social interaction
Restricted behavior

Movement
Sensation
Sleep, Seizures

Gastro
Immune
Hormones etc.

Frustration

More easily OVERWHELMED

Pain,
Poor function
Sickness

Overload!
STRESS!
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

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

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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.
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

Talos et al J. Comp Neurol, 2006; Dzhalal V et.al. Nature Medicine, 2005
A FINAL COMMON PATHWAY
Model of autism: Increased ratio of excitation / inhibition in key neural systems

Too Much Excitation

Not Enough Inhibition

More: irritability, hypersensitivity, overload

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

• 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 (diabesity, 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

- 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.

Effect of Propranolol on Functional Connectivity in Autism Spectrum Disorder—A Pilot Study
Narayanan et al. (Beversdorf lab)
*Brain Imaging and Behavior, 2010*
EVERYDAY EPIGENETICS:
Doing the SMART THINGS we can ALREADY do IN OUR DAILY LIVES to help epigenetics and support healthy physiology

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

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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