Taking a Fresh Look At Autism

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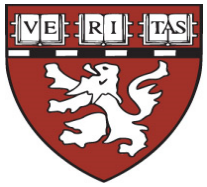


Changing Concepts and Findings on Autism

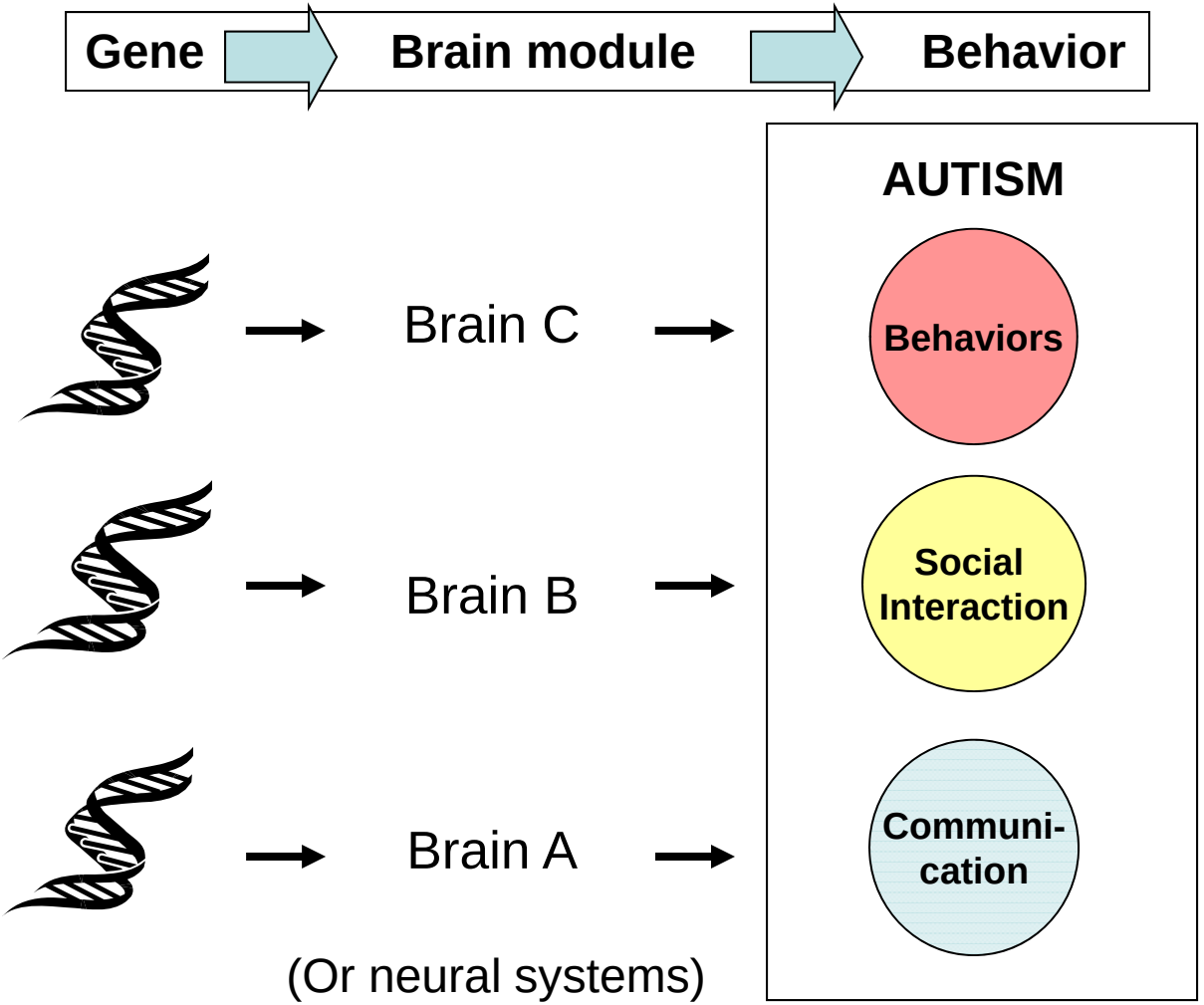
Michael Rutter, JADD, 2012

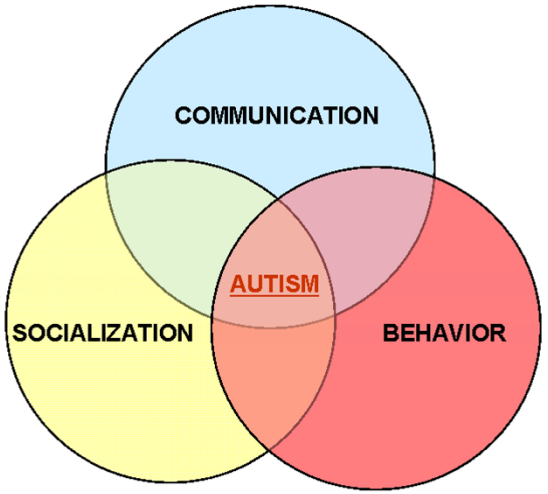
- **"New research findings provide major challenges regarding our understanding of the concept of autism. ….. It is concluded that, although there have been major research advances; there is a need for a reconceptualization and an avoidance of claims that go beyond the evidence."**
- **In fact, many 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!**

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?**

From Definition to Model of Autism: Classic Modular Framework





Assumption: Autism is a "developmental disorder"

This seems obvious.

But it carries a lot of extra baggage.

Assumption: Autism is a "developmental disorder"

What are the IMPLICATIONS of this assumption?

1. **It's all genetic and predetermined**
2. **The damage is done really early, probably before you are born**
3. **The brain is fundamentally and irretrievably differently structured and "broken"**
4. **Brain changes are the cause of ALL the problems**
5. **There is nothing you can do about it**

These assumptions are not supported by evidence.

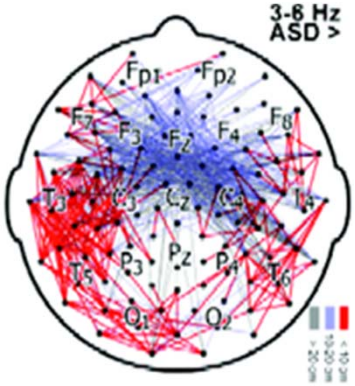
Emerging science contradicts them.

Beyond Genes

- **Not a Static Prevalence**
- **Not Just Genes: Environmental Contributors**
- **Not Just a Few High-Impact Genes: Hundreds of Mostly Lower-Impact Genes**
- **Not Just Inherited Genes: De Novo Mutations (that children have but their parents don't – where do they come from??)**
- **Not Even Mainly Genes: Substantial Environmental Contribution**
- **Not Just Mutations: Epigenetics**

Beyond the Brain

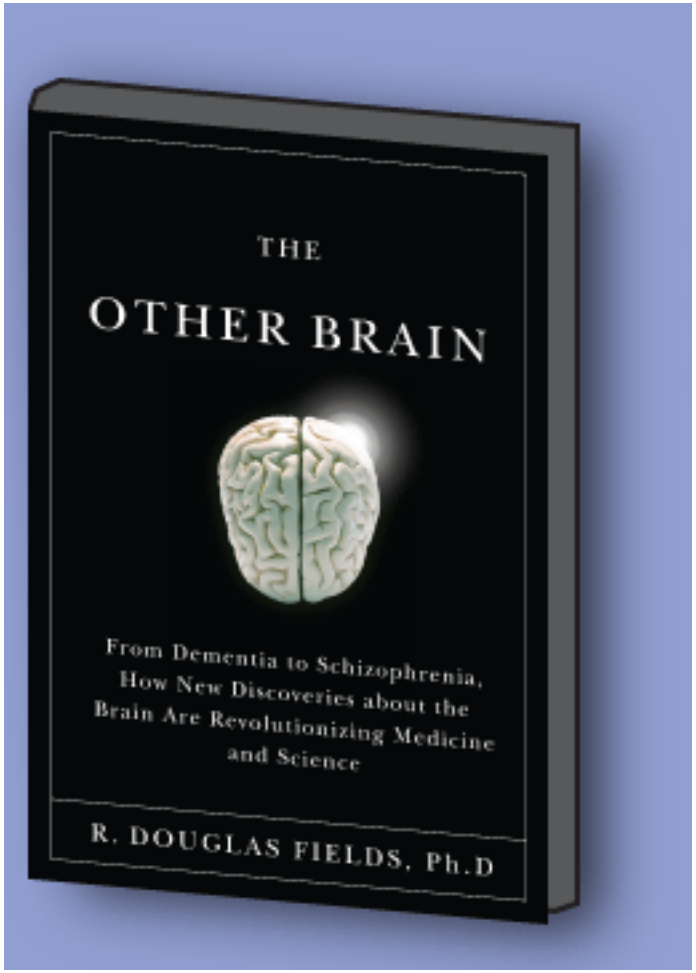
- **Not Just Brain Genes: Also expressed systemically**
- **Not Just Local, Modular Brain Disturbances: Whole Brain Involvement**
- **Not Just Regional Problems: Brain Coordination is Widely Challenged**
- **Not Just Brain Wiring: Active tissue pathophysiology in the brain (inflammation, oxidative stress,)**
- **Not Just the Brain – Whole Body, Whole System Involvement**



Beyond Neurons

- **Not Just Neurons: Glial Cells**
- **Not Just Brain Cells: Blood flow**
- **Not Just Brain Cells: maybe even Extracellular Matrix**

THE OTHER BRAIN
by Douglas Fields, PhD, NIH scientist



ABOUT GLIAL CELLS

www.theotherbrainbook.com

Beyond
"Prenatally Programmed Deficit"

- **Not Just Deficit: Giftedness and High Intelligence.**
- **Not Just Prenatal**
- **Not Necessarily Present at Birth**
- **Not Just Behavior**

Beyond Hopelessness

- **Not a Life Sentence: Evidence of**
  - **Severity that varies, particularly in individuals with autism and mitochondrial disease**
  - **Transient marked reduction of severity in fever**
  - **Remission and loss of diagnosis (currently being studied at the NIMH)**

From Static to Dynamic Encephalopathy

Improvement in core autism behaviors in setting of fever: not consistent with “hard-wired” cause

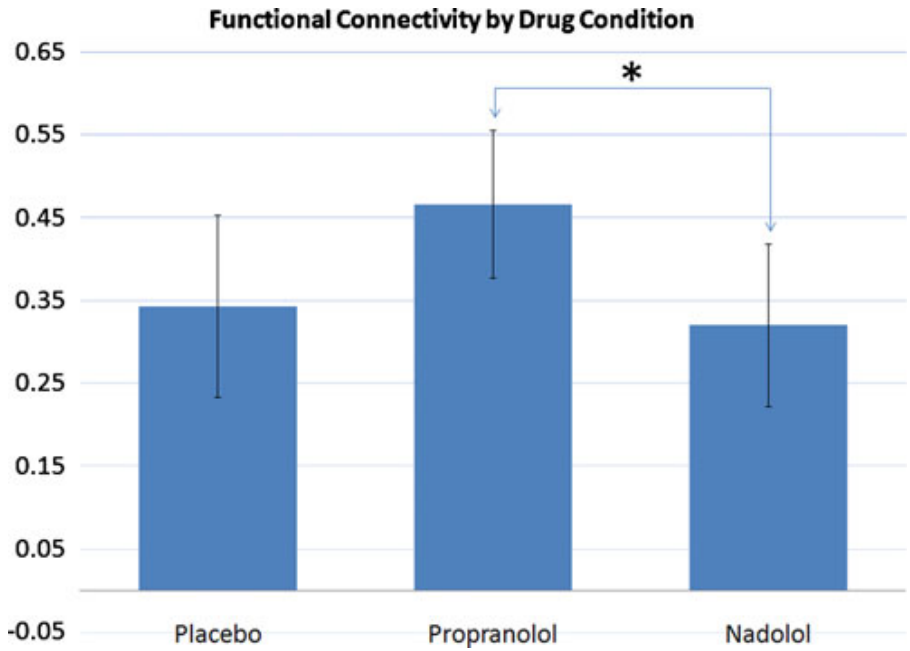
Behaviors Associated with Fever in Children with Autism Spectrum Disorders.
Curran et al, Pediatrics 2007

<u>Challenges posed by this study:</u>

- **This is not consistent with “static encephalopathy”**
- **What mechanisms might be consistent with this?**
  - **Proposed so far: locus ceruleus, environmental impact on glial gap junctions, cytokines, membrane lipids, dysfunctional electrophysiological oscillations**

- **Additional pertinent citations:**
  Helt / Fein et al, Neuropsychology Review, 2007; Herbert in Chauhan et al CRC Press late 2009, Mehler & Purpura 2009

Rapid IMPROVEMENT in brain connectivity suggests "state" not "trait"



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

- **Functional connectivity, assumed to be a fixed trait, changed rapidly with drug that impacts brain stress level (propranolol)**

Reversal in Mouse Models

PNAS

Inhibition of p21-activated kinase rescues symptoms of fragile X syndrome in mice

Mansuo L. Hayashi*†, B. S. Shankaranarayana Rao‡, Jin-Soo Seo§, Han-Saem Choi§, Bridget M. Dolan*, Se-Young Choi§, Sumantra Chattarji¶, and Susumu Tonegawa*‖

*The Picower Institute for Learning and Memory, Howard Hughes Medical Institute, RIKEN–Massachusetts Institute of Technology Neuroscience Research Center, and Departments of Biology and Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139; ‡Department of Neurophysiology, National Institute of Mental Health and Neurosciences, Bangalore 560029, India; §Department of Physiology, College of Dentistry, Seoul National University, Seoul 110-749 Korea; and ¶National Center for Biological Sciences, Tata Institute of Fundamental Research, Bangalore 560065, India

Contributed by Susumu Tonegawa, May 29, 2007 (sent for review May 21, 2007)

Fragile X syndrome (FXS), the most commonly inherited form of mental retardation and autism, is caused by transcriptional silencing of the *fragile X mental retardation 1 (FMR1)* gene and conse-

ticity at glutamatergic synapses, such as long-term potentiation (LTP) in the cortex and long-term depression in the hippocampus, is abnormal in *FMR1* KO mice (11–13).

Reversal of Neurological Defects in a Mouse Model of Rett Syndrome

Jacky Guy,[1] Jian Gan,[2] Jim Selfridge,[1] Stuart Cobb,[2] Adrian Bird[1]*

Rett syndrome is an autism spectrum disorder caused by mosaic expression of mutant copies of the X-linked *MECP2* gene in neurons. However, neurons do not die, which suggests that this is

Reversal of learning deficits in a *Tsc2*$^{+/-}$ mouse model of tuberous sclerosis

Dan Ehninger[1], Sangyeul Han[2], Carrie Shilyansky[1], Yu Zhou[1], Weidong Li[1], David J Kwiatkowski[3], Vijaya Ramesh[2] & Alcino J Silva[1]

"Wild-type microglia arrest pathology in a mouse model of Rett syndrome"

Derecki et al, Nature, 2012

- **Rett features had been attributed to neuronal dysfunction**
- **Astroglial cells now known to contribute**
- **Now microglia shown to contribute as well: bone marrow transplant of wild type microglia**
  - **Increased lifespan, normalized breathing, increased body weight, improved locomotor activity**
  - ***Improvement even without direct change to neurons***
  - **Improvements lost when microglial phagocytic (garbage-collecting) activity inhibited**

GENETIC EXPLANATIONS

Sense and Nonsense

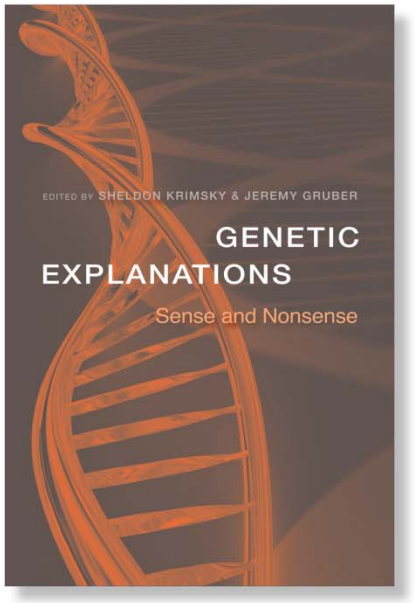
Edited by SHELDON KRIMSKY and JEREMY GRUBER

Can genes determine which fifty-year-old will succumb to Alzheimer's, which citizen will turn out on voting day, and which child will be marked for a life of crime? Yes, according to the Internet, a few scientific studies, and some in the biotechnology industry who should know better. Sheldon Krimsky and Jeremy Gruber gather a team of genetic experts to argue that treating genes as the holy grail of our physical being is a patently unscientific endeavor. ***Genetic Explanations*** urges us to replace our faith in genetic determinism with scientific knowledge about how DNA actually contributes to human development.

The concept of the gene has been steadily revised since Watson and Crick discovered the structure of the DNA molecule in 1953. No longer viewed by scientists as the cell's fixed set of master molecules, genes and DNA are seen as a dynamic script that is ad-libbed at each stage of development. Rather than an autonomous predictor of disease, the DNA we inherit interacts continuously with the environment and functions differently as we age. What our parents hand down to us is just the beginning. Emphasizing relatively new understandings of genetic plasticity and epigenetic inheritance, the authors put into a broad developmental context the role genes are known to play in disease, behavior, evolution, and cognition.

Rather than dismissing genetic reductionism out of hand, Krimsky and Gruber ask why it persists despite opposing scientific evidence, how it influences attitudes about human behavior, and how it figures in the politics of research funding.

Sheldon Krimsky is Professor of Urban & Environmental Policy & Planning in the School of Arts and Sciences and Adjunct Professor of Public Health and Community Medicine in the School of Medicine at Tufts University. **Jeremy Gruber** is President and Executive Director of the Council for Responsible Genetics.



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384 pages • 6⅛ x 9¼ inches • 2 graphs, 4 tables

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New Book with Critiques of Genetic Overexplanation

Harvard U Press 2013

Ch.10 on Autism:

From Static Genetic Brain Defect to Dynamic Gene-Environment-Modulated Pathophysiology

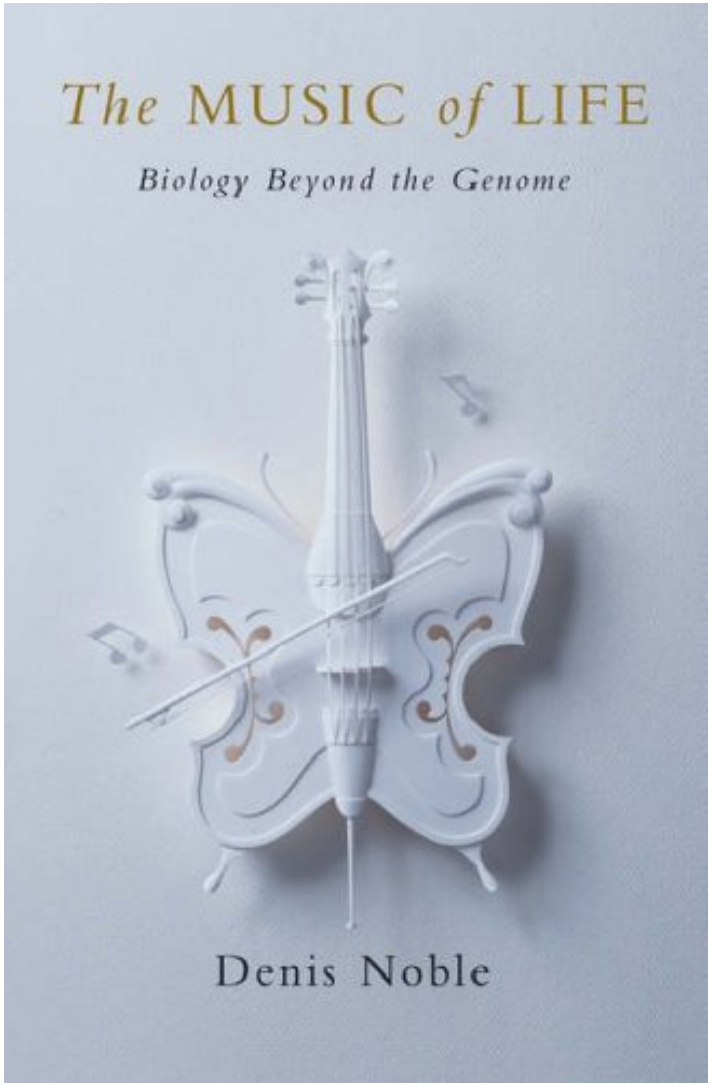
By Martha Herbert

Autism: WHY and HOW ?

www.autismWHYandHOW.org

- **A website reviewing multiple viewpoints and their intersections**
- **A literature repository**
- **A framework for reflective discourse**

The Music of Life: Biology Beyond the Genome

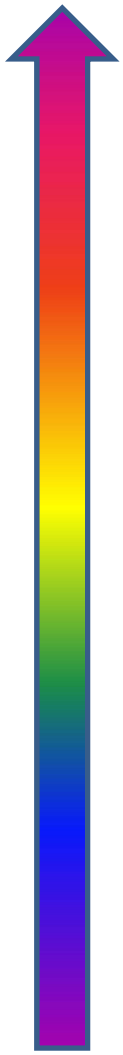


Beautiful readable book

Discusses physiology and the "middle→out" approach

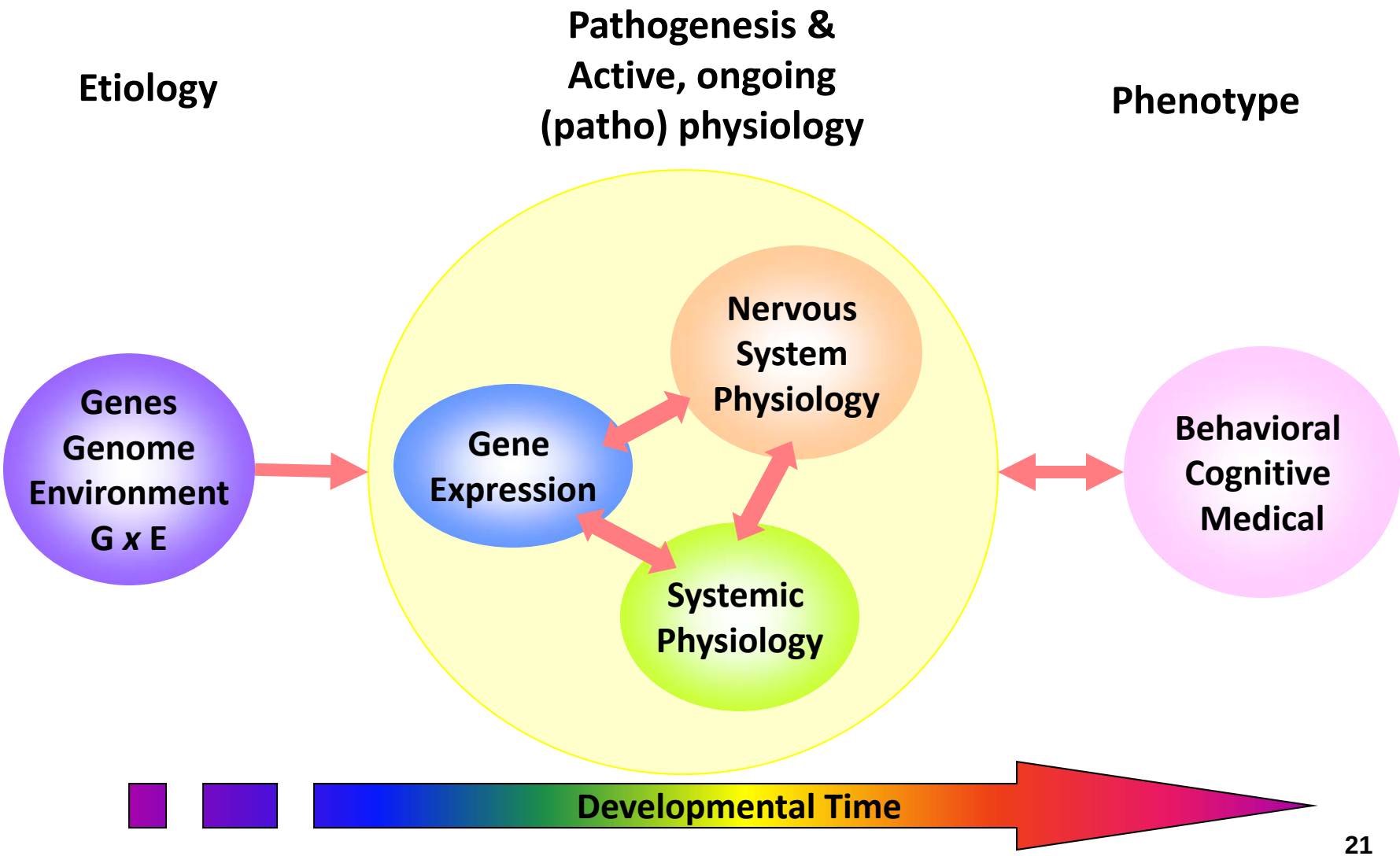
http://www.musicoflife.co.uk/

Zoom through Autism's Multi-Scale Complexity: Levels that are all involved AT THE SAME TIME



Creativity
Social interaction
Learning
Behavior
Brain as information system
Stress System
Brain as wet physical organ
Organs – GI, Immune
Cells
Chemistry
Genes and environment

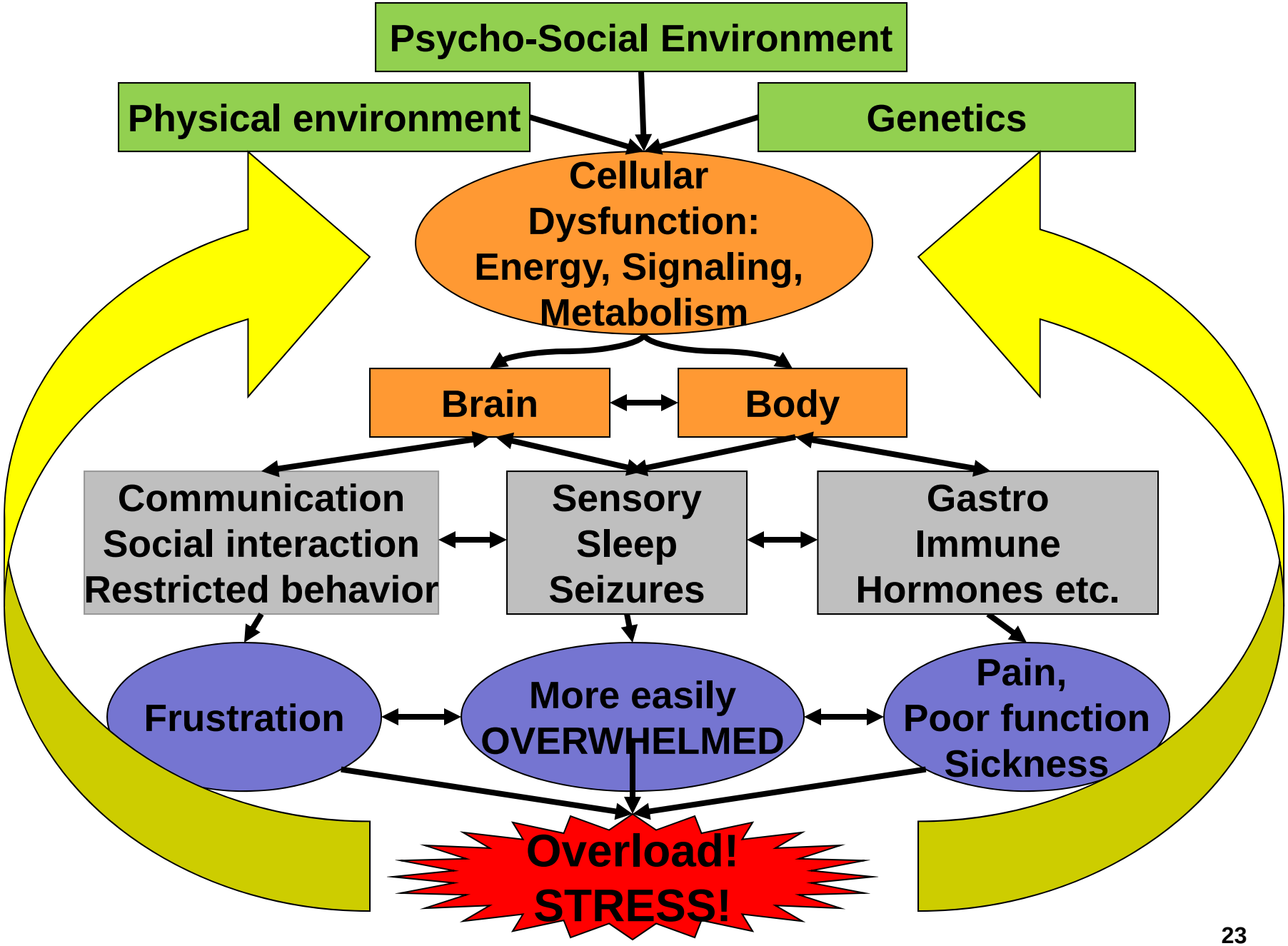
A Middle-Out Approach to Autism: Multi-Scale, (Patho)Physiology Centered



Everything we do relies on our cells.

- Energy
- Moving things around
- Digestion
- Changing one chemical into another
- Taking out the trash
- Communicating
- Holding things together (structure)
- Protection

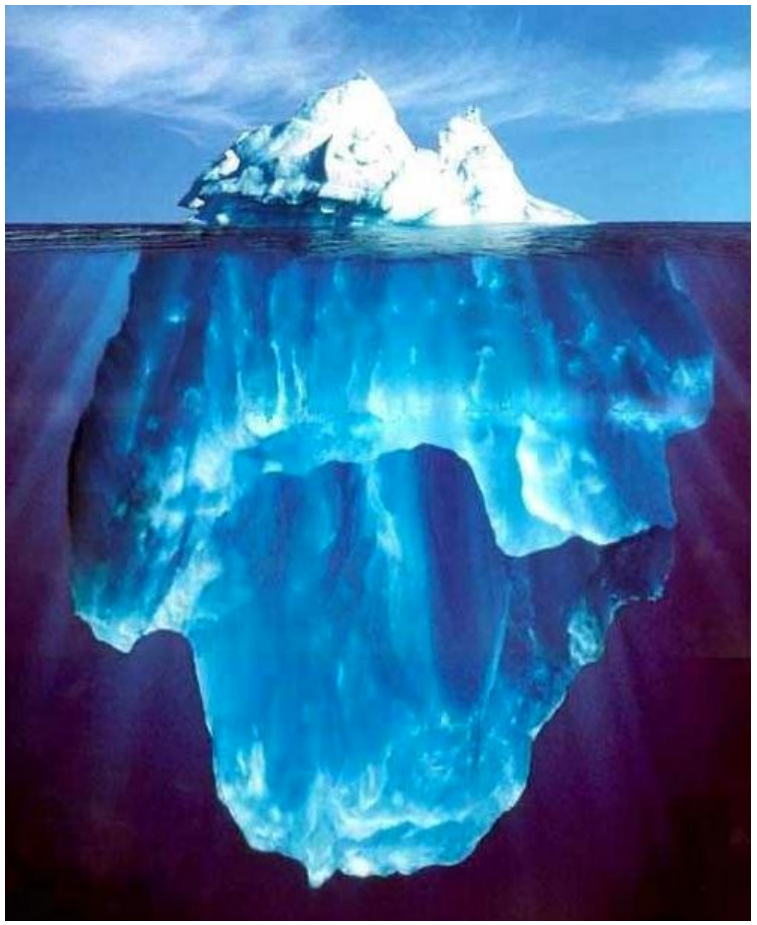
Whole Body Model: Vicious circles in brain and body



Whole Body systems Model: Symptoms Emerge from Problems with Underlying Functions

VISIBLE Social & Behavioral SYMPTOMS →

UNDERLYING SYSTEMIC FUNCTIONAL DISTURBANCES →



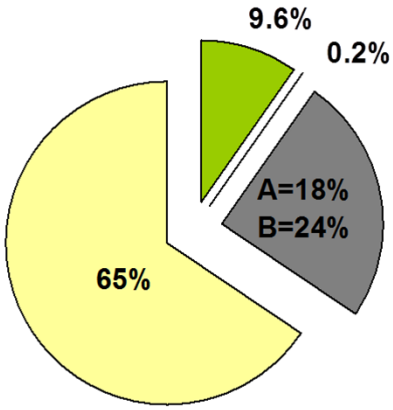
Ziggarut model: http://www.texasautism.com/

Transduction: Critical Question in Multi-Scale Biology

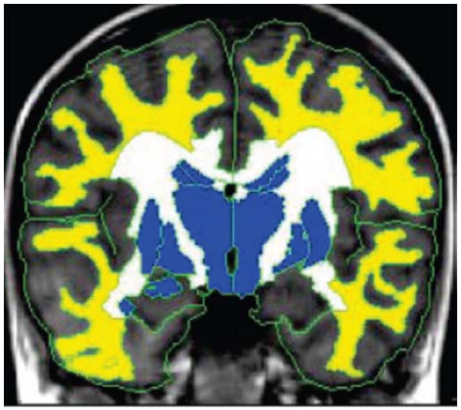
- **How do processes at one level get TRANSDUCED into changes at other levels?**
- **A classical model is sensory transduction**
  - **From light through eyes/brain to vision**
  - **From vibrations through ears/brain to sound**
- **For autism, from a middle-out perspective, the core question is:**

How do we get from tissue pathophysiology to altered brain function?

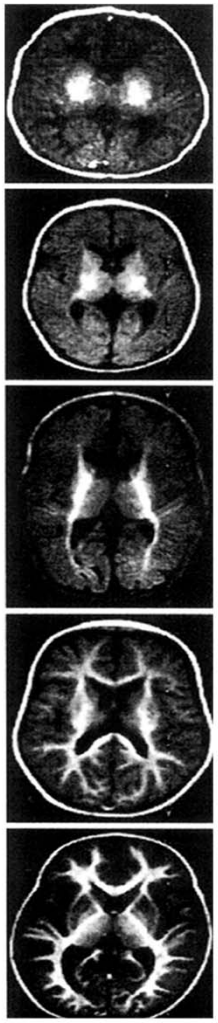
Location of white matter enlargement points to postnatal brain changes



White Matter Contributes Most to Autism Volume Increase



Radiate White Matter Enlargement



I- 1st Month

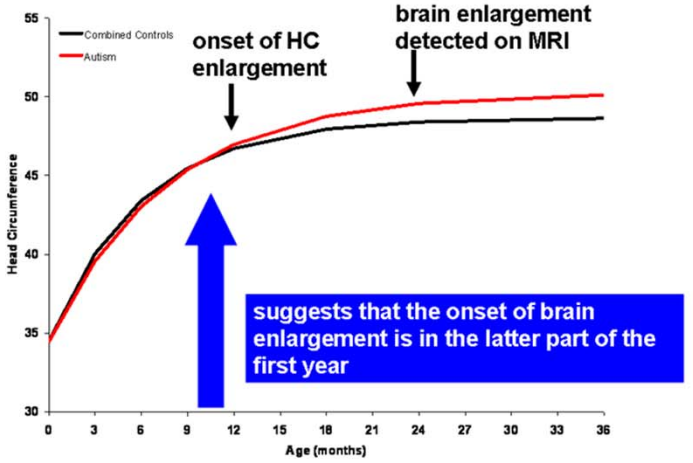
II- 2nd Month

III- 3rd-6th Month

IV- 7th-9th Month

V- > 9th Month

Inversion Recovery MRI Image
(Van der Knaap & Valk)

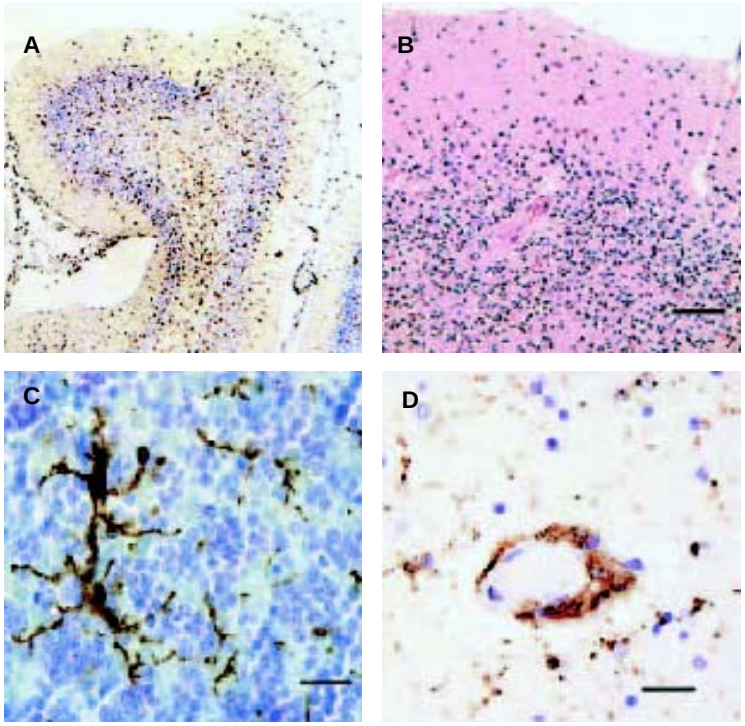


What do we need to learn about the brain and about autism to understand this?

Inflammation and Oxidative Stress in Autism: chronic, ongoing postnatal medical problems, not confined to brain

Neuroglial activation and neuroinflammation in the brain of patients with autism
Vargas et al, 2005, Annals of Neurology

Oxidative stress in brain tissues from autistic patients Increased concentration of isoprostanes
Vargas et al, 2005, Annals of Neurology

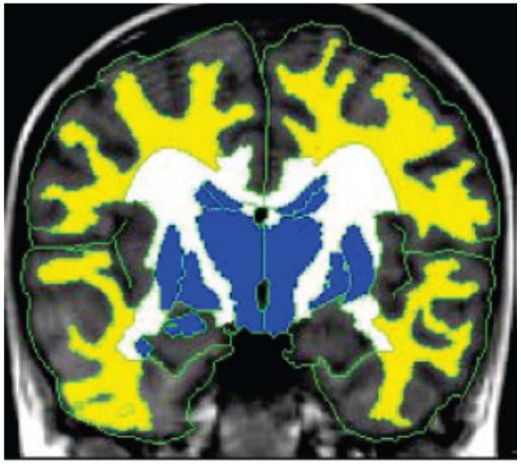


- These changes were found at similar intensities in brain aged 5-44 years
- Greater intensity of inflammation in a 3-year old's brain

Pardo: Astrogliosis in Radiate White Matter

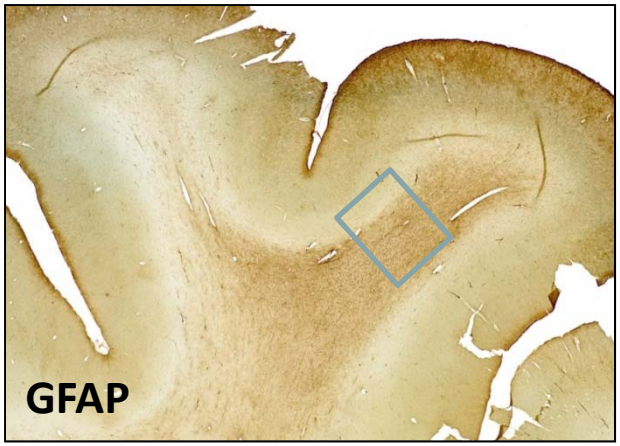
Astrogliosis

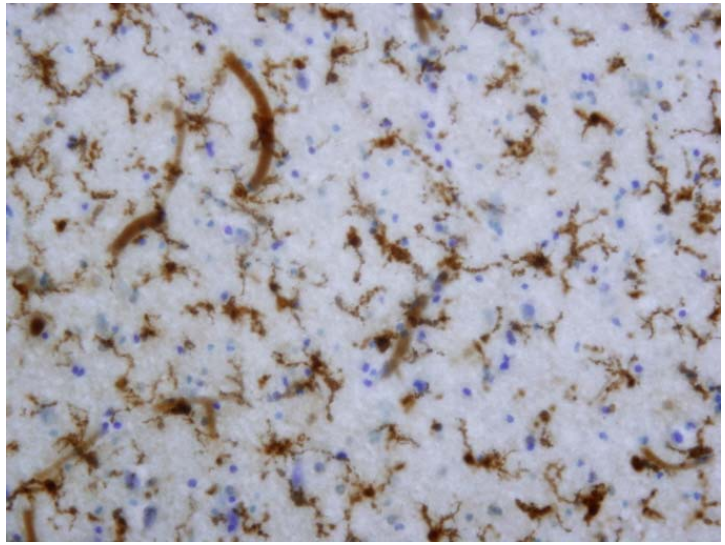
Microgliosis



Herbert:

Radiate White Matter Enlargement





Pardo

Mitochondrial dysfunction and molecular pathways of disease

Exp Mol Pathol. 2007 Jan 17

– "A wide range of seemingly unrelated disorders, such as schizophrenia, bipolar disease, dementia, Alzheimer's disease, epilepsy, migraine headaches, strokes, neuropathic pain, Parkinson's disease, ataxia, transient ischemic attack, cardiomyopathy, coronary artery disease, chronic fatigue syndrome, fibromyalgia, retinitis pigmentosa, diabetes, hepatitis C, and primary biliary cirrhosis, have underlying pathophysiological mechanisms in common, namely reactive oxygen species (ROS) production, the accumulation of mitochondrial DNA (mtDNA) damage, resulting in mitochondrial dysfunction. Antioxidant therapies hold promise for improving mitochondrial performance."

– "diets deficient in micronutrients can accelerate mitochondrial decay and contribute to neurodegeneration"

Metabolic Findings in Parents of Children with Autism

- **86 autism parents differ from 200 controls in the following:**

  – **Higher homocysteine** (Hcy)
  – **Higher SAH (**S-adenosylhomocysteine**)**
  – **Lower GSH** (glutathione)
  – **Increased GSSG** (oxidized glutathione)

  (All markers of oxidative stress and inflammation)

J Autism Dev Disord. 2008 Nov;38(10):1966-75

Genome-wide expression studies in Autism spectrum disorder, Rett syndrome, and Down syndrome

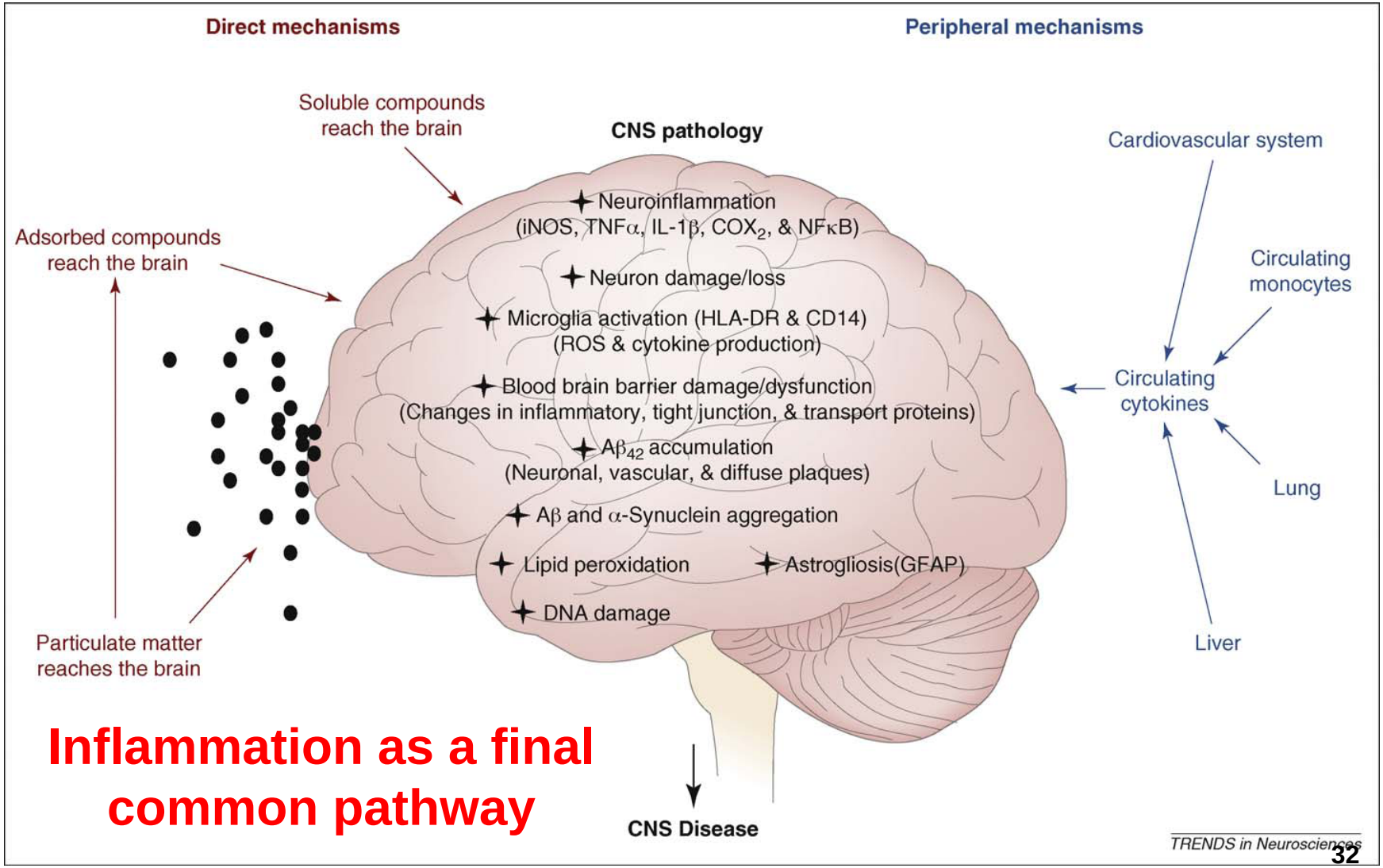
Lintas et al., *Neurobiol Dis,* 2010

…Our results surprisingly converge upon immune, and not neurodevelopmental genes, as the most consistently shared abnormality in genome-wide expression patterns. A dysregulated immune response, accompanied by enhanced oxidative stress and abnormal mitochondrial metabolism seemingly represents the common molecular underpinning of these neurodevelopmental disorders. This conclusion may be important for the definition of pharmacological therapies able to ameliorate clinical symptoms across these disorders.

Air Pollution and Brain Inflammation

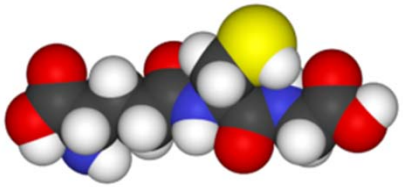
Block and Calderon-Gardicuenas, TNS, 2009

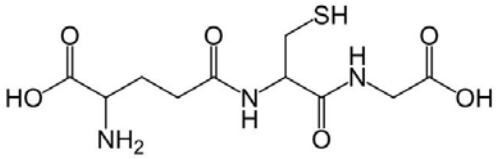
Air pollution already linked to autism (e.g. Palmer 2006; Windham 2006; Volk 2011)



Inflammation as a final common pathway

GLUTATHIONE PROTECTS CELLS from environmental stress, but is often low in ASD (and many other chronic conditions)





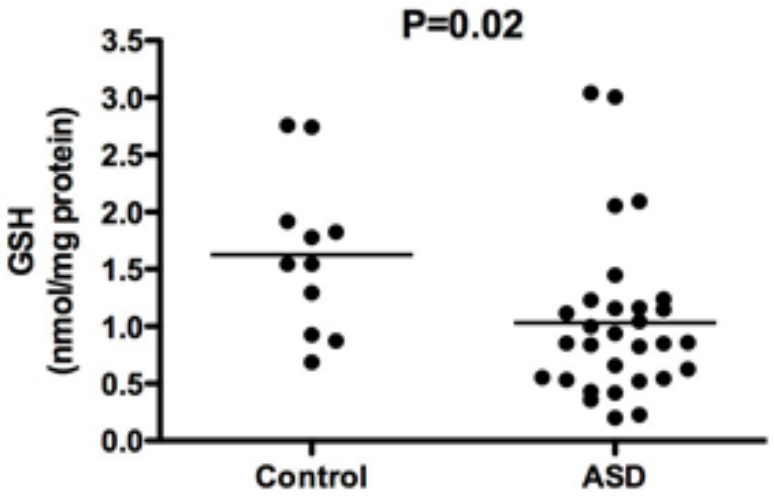
Made in the liver from three amino acids: Glutamate + Cysteine + Glycine

- **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**

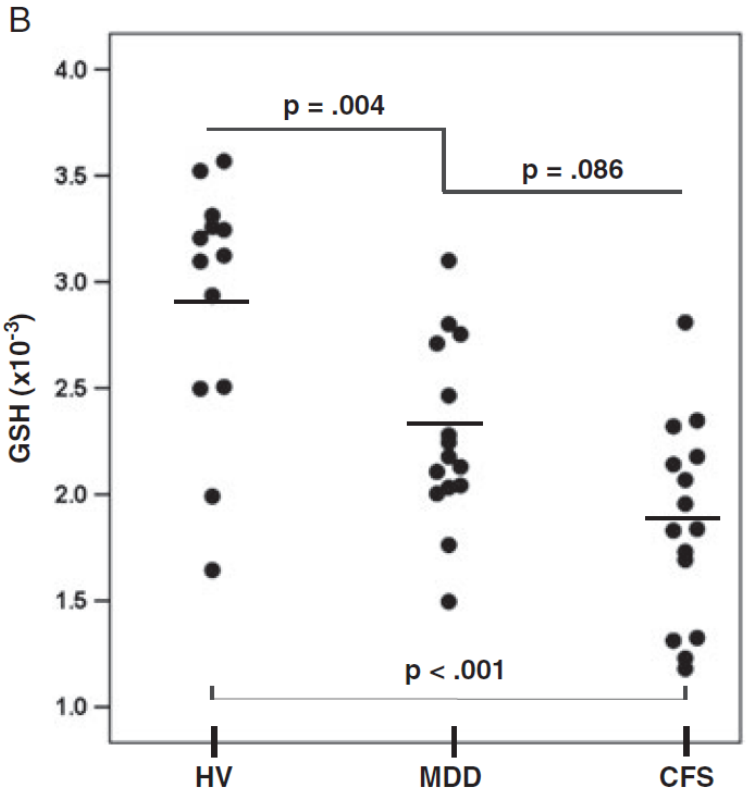
- **Reduced Glutathione = GSH (active form)**
- **Oxidized Glutathione = GSSG (used-up form)**

LOW GLUTATHIONE

Glutathione - critical antioxidant and detox chemical - low levels in brains of depressed patients, lower in brains in Chronic Fatigue Syndrome – And low systemically in Autism



Suh, J., W. Walsh, et al. (2008). American Journal of Biotechnology and Biochemistry **4**(2): 105-113,

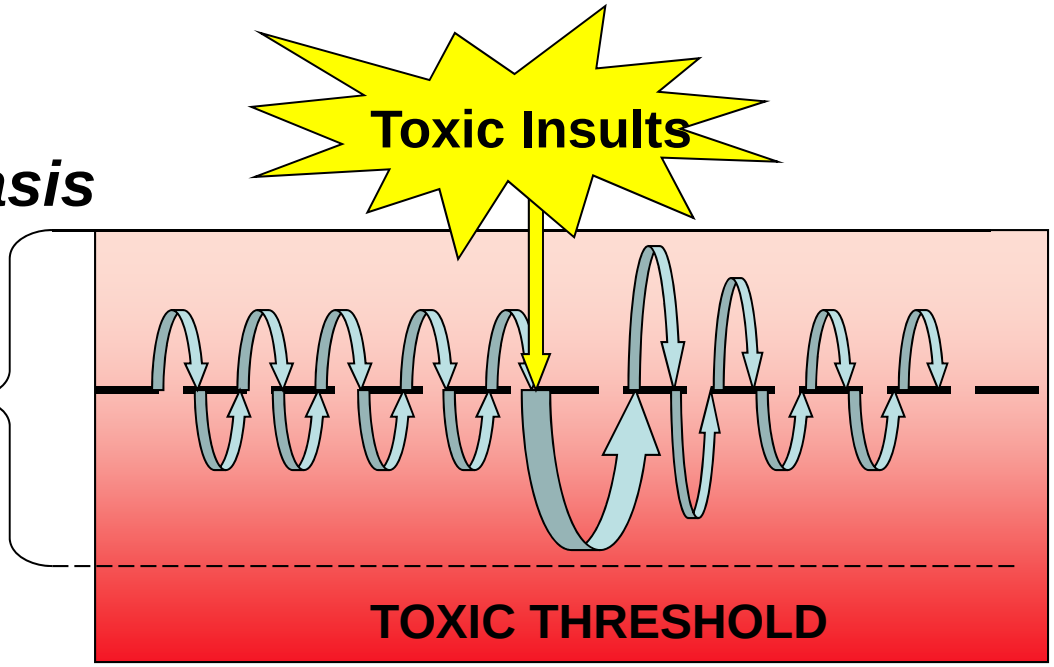


Shungu et al., 2012

Vulnerability with low GSH

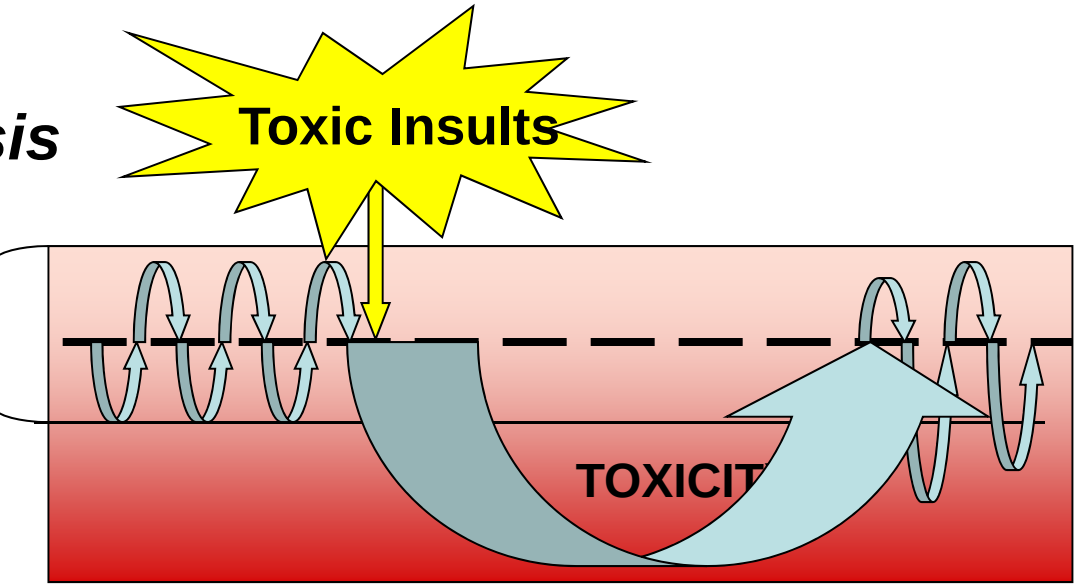
Normal Homeostasis

OK GSH/GSSG



Fragile Homeostasis
(limited reserve)

↓ GSH/GSSG



Glutathione as a "Final Common Pathway"

- **GSH is depleted by thousands of toxins, oxidative stress, infection, inflammation, EMF and nutrient-poor diet**

- **Small exposures of any one thing can still add up to a substantial depletion of antioxidant resilience**

- For reflection: "Glutathione: a novel treatment target in psychiatry" – *Trends Pharmacol Sci. 2008 Jul;29(7):346-51*

A must-read statement of a systems biology approach to complex illness:

From ‘omics’ to complex disease: a systems biology approach to gene-environment interactions in cancer

By Sarah S Knox: http://www.cancerci.com/content/10/1/11

Looks at cancer as accumulated ALLOSTATIC LOAD from diet and environment

Advocates a dynamic *transdisciplinary systems biology approach aimed at reversing multiple levels of dysfunction*.

JUST ABOUT EVERYTHING SHE SAYS

APPLIES TO AUTISM

Oxidative Stress and Psychiatric Disorders

- **A meta-analysis indicates an association of oxidative stress in the majority of DSM-IV psychiatric disorders including: autism, Rett's, ADHD, schizophrenia, anxiety, and mood disorders.** *Full text available at: http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=2330073&blobtype=pdf*

- **"…all these psychiatric disorders might benefit from a change to a whole-food plant-based diet."**

ENVIRONMENTALLY VULNERABLE PHYSIOLOGY

Current Opinion in Neurology, April, 2010

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

Martha R. Herbert

TRANSCEND Research Program, Pediatric Neurology, Massachusetts General Hospital, Charlestown, Massachusetts, USA

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Tel: +1 617 724 5920;
e-mail: mherbert1@partners.org

Current Opinion in Neurology 2010, 23:000–000

Purpose of review

To present a rationale and evidence for contributions of environmental influences and environmentally vulnerable physiology to autism spectrum disorders (ASDs).

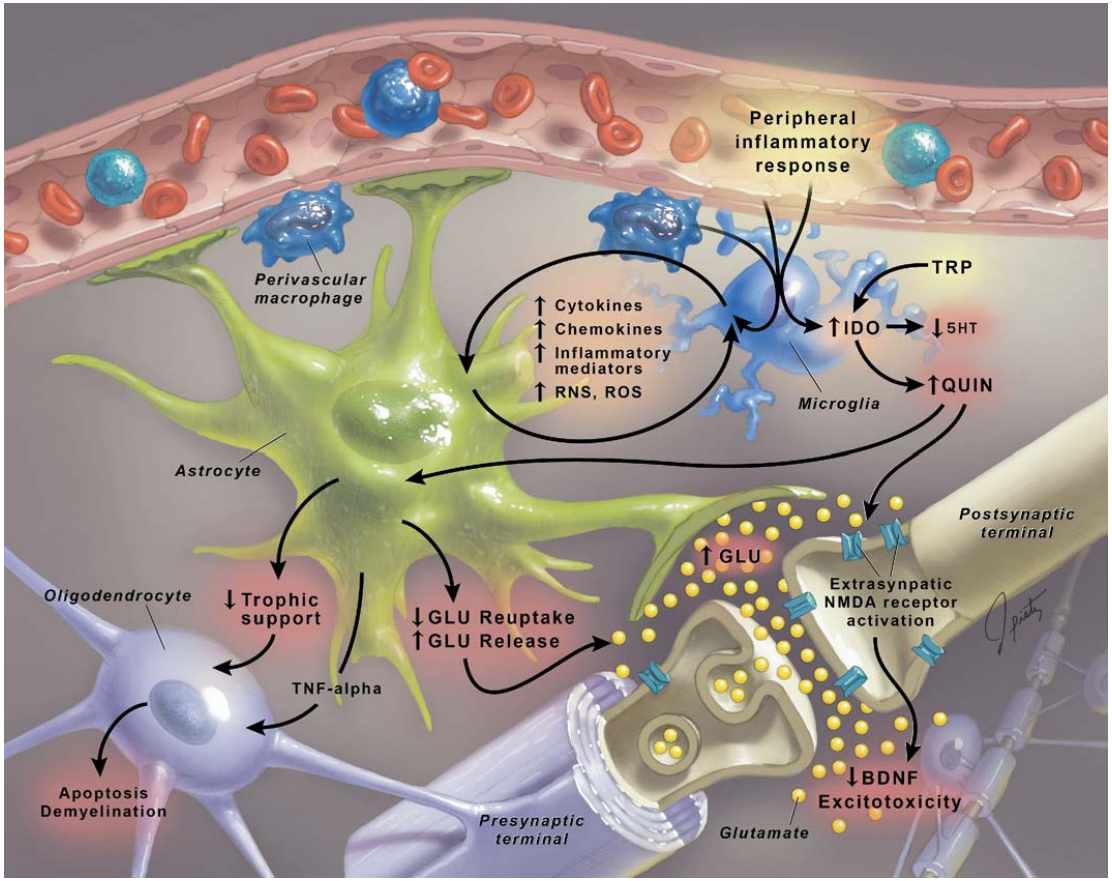
Recent findings

Recent studies suggest a substantial increase in ASD prevalence above earlier Centers for Disease Control figures of one in 150 only partly explicable by data artifacts, underscoring the possibility of environmental contributors to increased prevalence. Some gene variants in ASD confer altered vulnerability to environmental stressors and exposures. De-novo mutations and advanced parental age as a risk factor for ASD also suggest a role for environment. Systemic and central nervous system pathophysiology, including oxidative stress, neuroinflammation, and mitochondrial dysfunction can be consistent with a role for environmental influence (e.g. from air pollution, organophosphates, heavy metals) in ASD, and some of the underlying biochemical disturbances (such as abnormalities in glutathione, a critical antioxidant and detoxifier) can be reversed by targeted nutritional interventions. Dietary factors and food contaminants may contribute risk. Improvement and loss of diagnosis in some with ASD suggest brain circuitry amenable to environmental modulation.

Summary

Prevalence, genetic, exposure, and pathophysiological evidence all suggest a role for environmental factors in the inception and lifelong modulation of ASD. This supports the need for seeking targets for early and ongoing medical prevention and treatment of ASD.

Brain cells in inflammation: What is the FUNCTIONAL IMPACT?



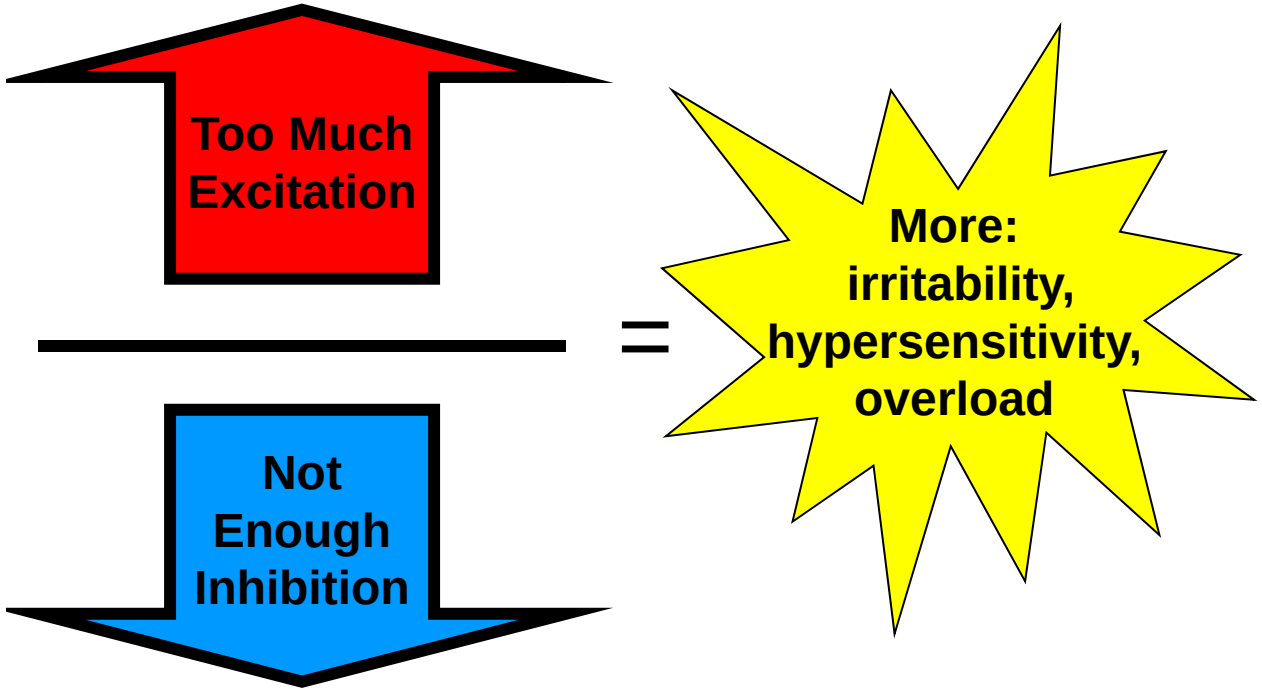
- **Excitatory chemicals created by activated glial cells**
- **Normal housekeeping functions of glial cells get neglected**
- **Chronic inflammation is irritating and promotes excitotoxicity**
- **Chronic inflammation can cause damage**

Inflammation and Its Discontents: The Role of Cytokines in the Pathophysiology of Major Depression. Miller et al., BIOL PSYCHIATRY 2009;65:732–741

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

Mitochondrial Dysfunction and Synapses

- **Neurons impacted by metabolic dysfunction have the energy to stay alive,**
  ➔ *but not always enough to fire electric signals*

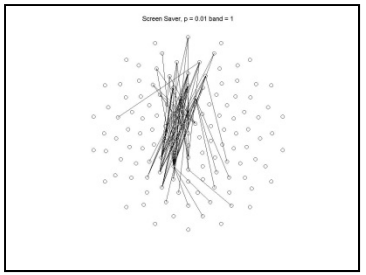
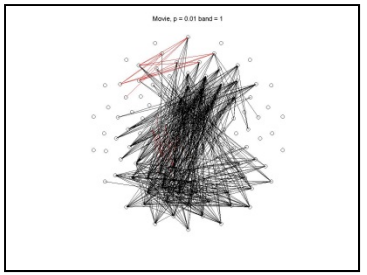
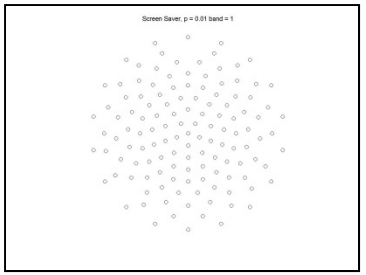
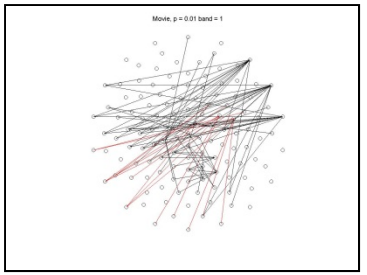
Efrati et al., PLoS One, 2013

EEG of Sensory Responses

- **Sensory stimulation can be overwhelming**

Lines indicate differences between ASD and age-matched controls

- **Much more dysfunction when more stimulation**
- **Looks milder in older kids**

	Screen Saver: **Less Stimulation**	Movie: **More Stimulation**
5-8 years old		
9-11 years old		

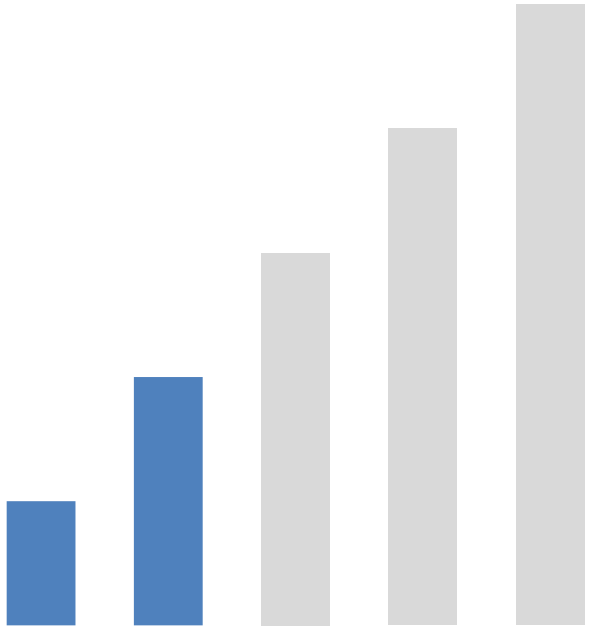
Prediction:
Improved connectivity with effective treatment

Martien et al. 2008

Metaphor: Tissue pathophysiology REDUCES BRAIN BANDWIDTH

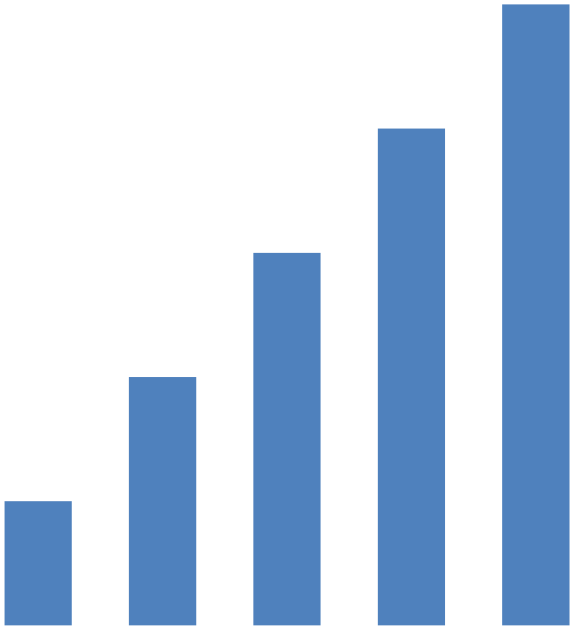
Poor Bandwidth:

Limited Reception



Lots of Bandwidth:

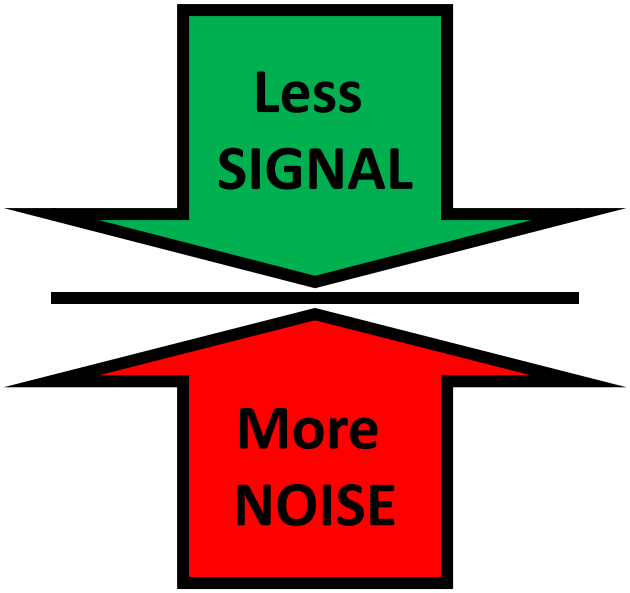
Good Reception



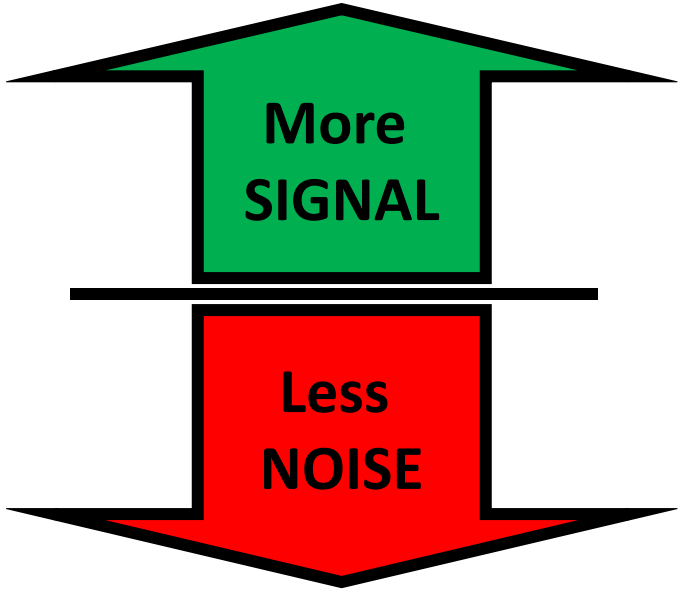
Better Reception Allows Better Discernment of Differences and More Spontaneous Learning

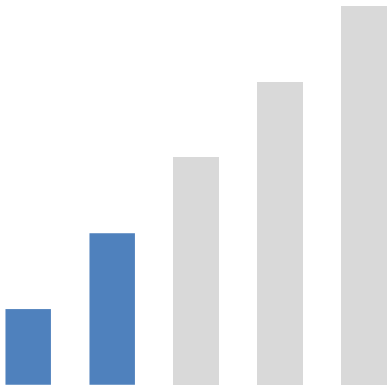
Worse SNR, Less Bandwidth

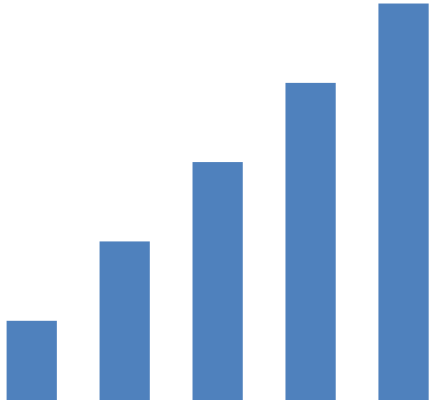
Better SNR, Better Bandwidth



SIGNAL to NOISE ratio (SNR) and BANDWIDTH







Better Reception Allows More Spontaneous Learning

The “Fluid Theory” of Connectivity Alterations in ASD

- **Water, not fiber changes in brain tissue**

  Hendry 2005

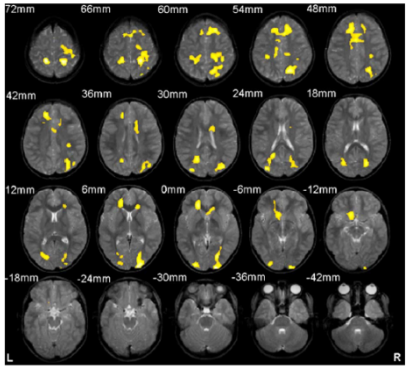
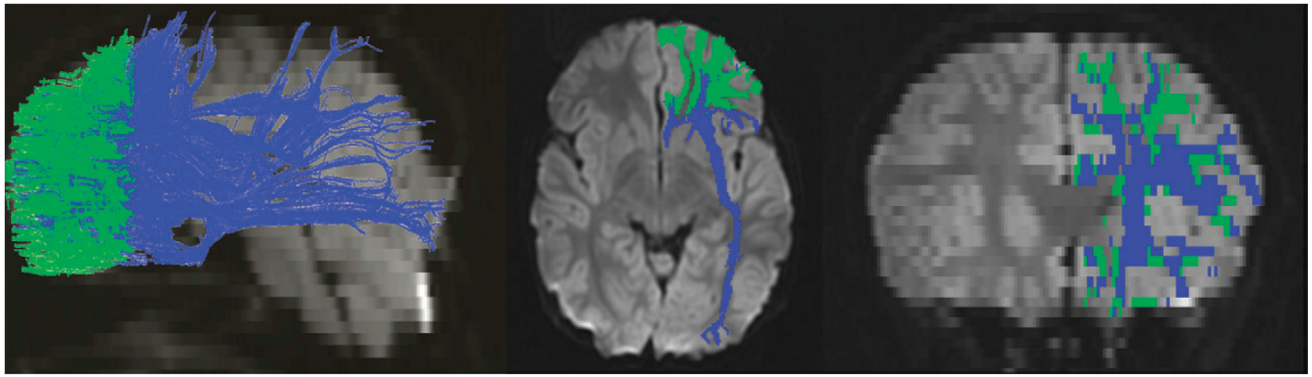


Fig. 2. Axial slices showing regions of increased T2 relaxation time in patients with autism compared to controls.

The idea that brain connectivity abnormalities arise from metabolic, immune and vascular disturbances that affect synaptic function.

- **Less white matter integrity**
- **Less restriction of water flow**
- **More diffusivity**

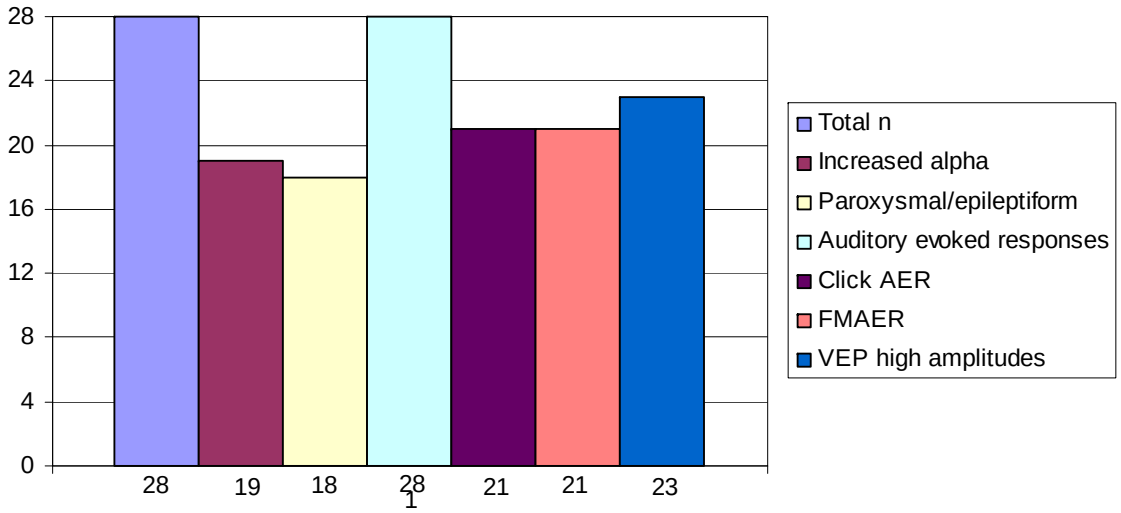


Sundaram 2008

- **Lower perfusion in ASD brains (by many PET or SPECT studies) could impact brain function.**

How might this affect brain electrophysiology?

Autism Electrophysiological Abnormalities something in everyone, much in some



15 of these patients had no seizure history.

Visual Evoked Potential (VEP) amplitude was bigger: standard deviation was 2.42-8.92 SD (average 5.4 SD):

Same stimulus elicits larger response

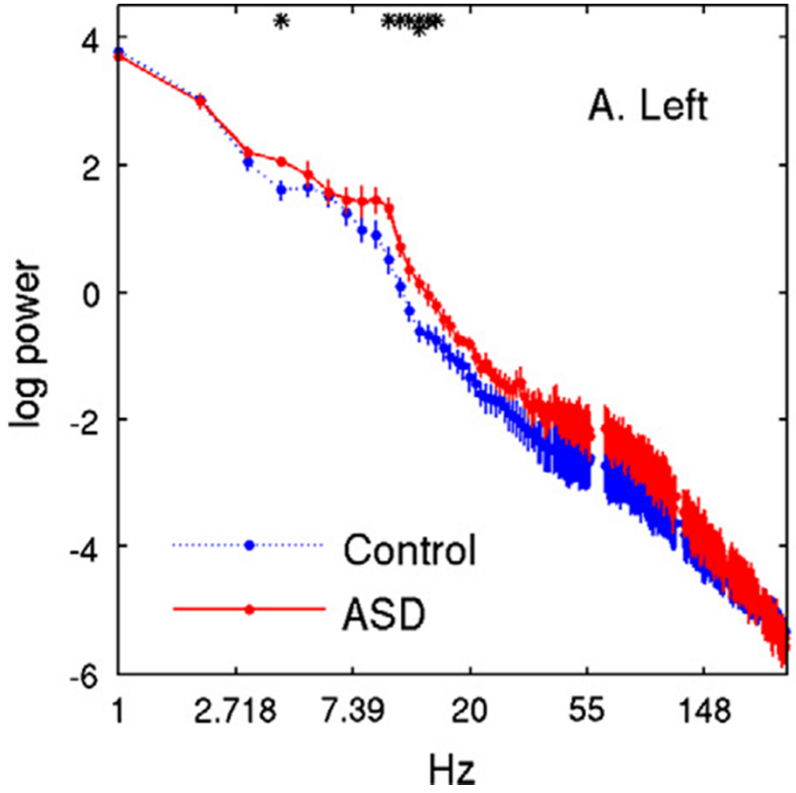
Prediction: Less extreme sensory reactivity with effective treatment

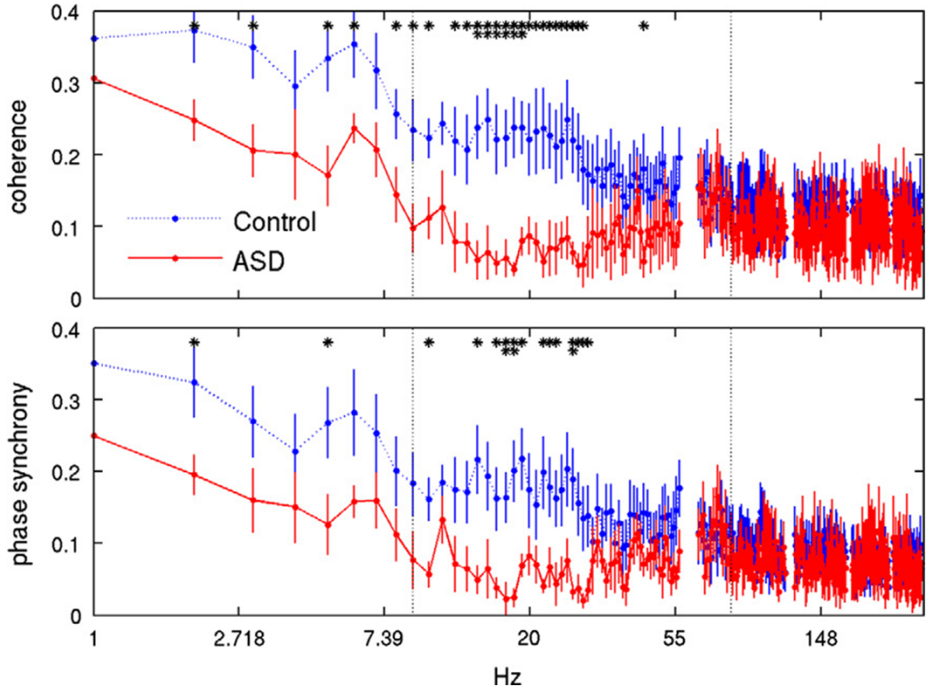
Martien & Duffy

“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 <u>more power</u> than controls… but *<u>less coherence</u>***

<u>POOR SNR – Sound and Fury, signifying nothing</u>

A Different Model of Autism: Autism as an emergent property of a system with altered parameters

- **Autism could be a dynamic, active consequence of *challenges to cellular function throughout the body, including the brain***
- ***These cellular changes may be related to environmental insults***
- **Altered cellular response could be at the root of brain and body problems**
- **This could explain the dynamic features**
- ***Many cellular problems can be treated***

Herbert, 2009 in press,
"Autism: The centrality of pathophysiology and the shift from static to dynamic encephalopathy"
In Chauhan et al, Autism: Oxidative stress, inflammation and immune abnormalities

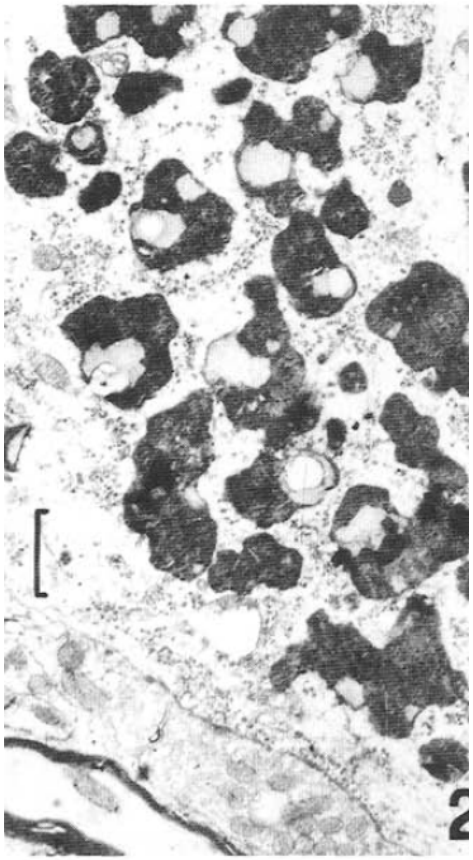
"Wild-type microglia arrest pathology in a mouse model of Rett syndrome"

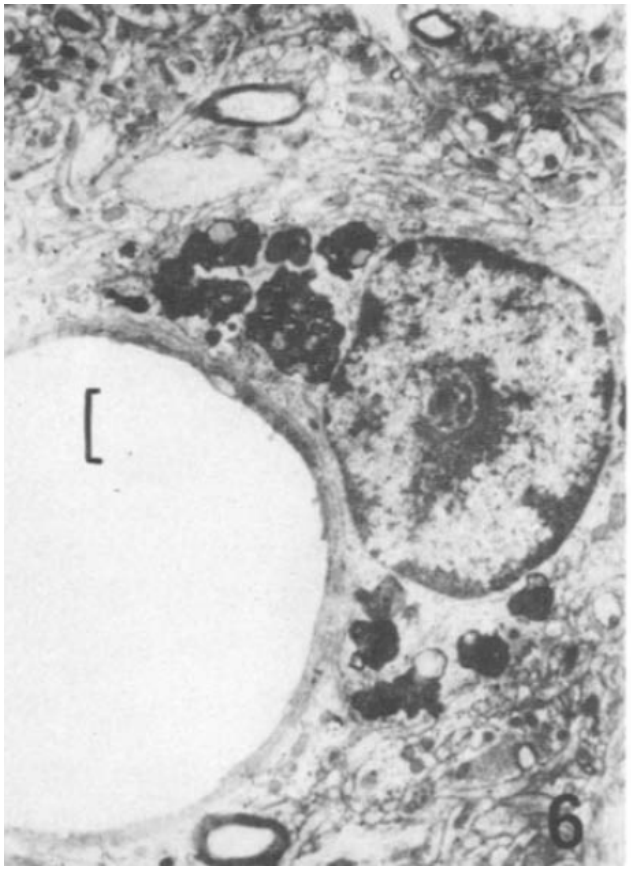
Derecki et al, Nature, 2012

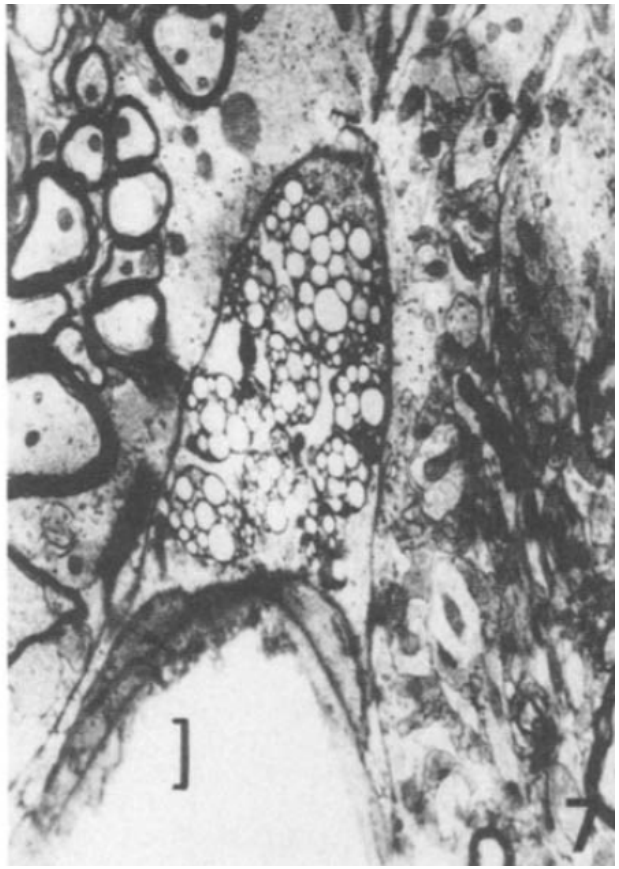
- **Rett features had been attributed to neuronal dysfunction**
- **Astroglial cells now known to contribute**
- **Now microglia shown to contribute as well: bone marrow transplant of wild type microglia**
  - **Increased lifespan, normalized breathing, increased body weight, improved locomotor activity**
  - ***Improvement even without direct change to neurons***
  - **Improvements lost when microglial phagocytic (garbage-collecting) activity inhibited**

Electron microscopy of therapeutically activated glia turning into “brain garbage collectors and transporters”

RIGA, S. et al., *Ann. N.Y. Acad. Sci.* 1067: 383–387 (2006)
RIGA, S. et al., *Arch. Gerontol. Geriatr.* suppl. 4 (1994) 227-234







Why does garbage pile up?

TOO MUCH BAD STUFF

- **Toxicants**
- **Molecular debris from cellular stress and inflammation**

NOT ENOUGH GOOD STUFF

- **Not enough nutrients needed to run clean-up operations**
- **Blood flow that is less than it should be due to sickness or poor nutrition**

The brain needs energy and nutrition supplies

- **Abundant supplies allow the brain to**
  - **work at its best**
  - **protect it from being dragged down by inflammation and other health problems.**
  - **TAKE OUT THE GARBAGE!**
- **Better brain health will help restore the brain's full powers.**
- **We can support brain health through "nutrient flooding" – high nutrient density diet**

Build Resiliency and Reduce Allostatic or "Total Load"

RESILIENCY

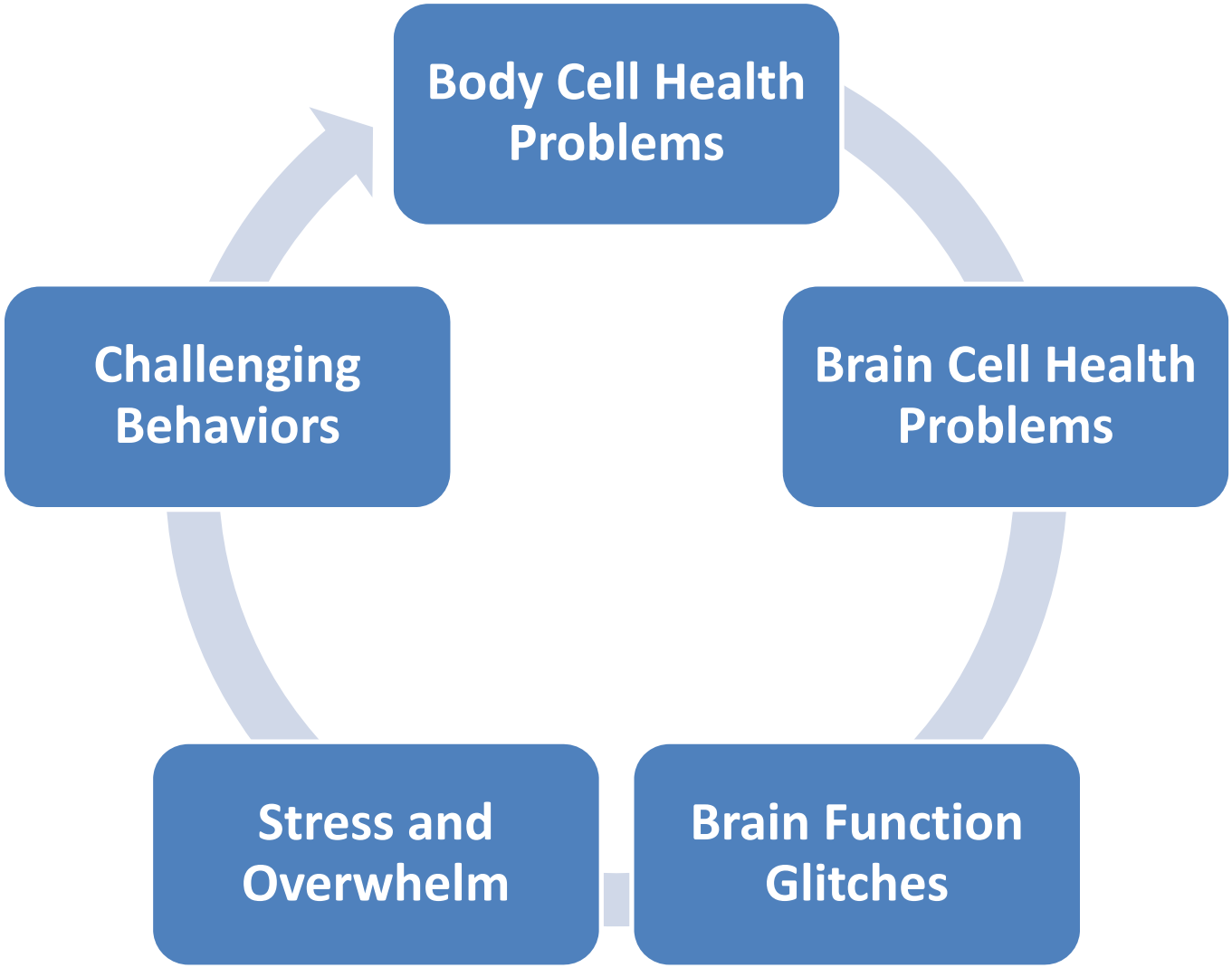
- The TOTAL SET of strengths, adaptations, skills, cell health, nutritional fortitude, exercise, community and more

"TOTAL LOAD"

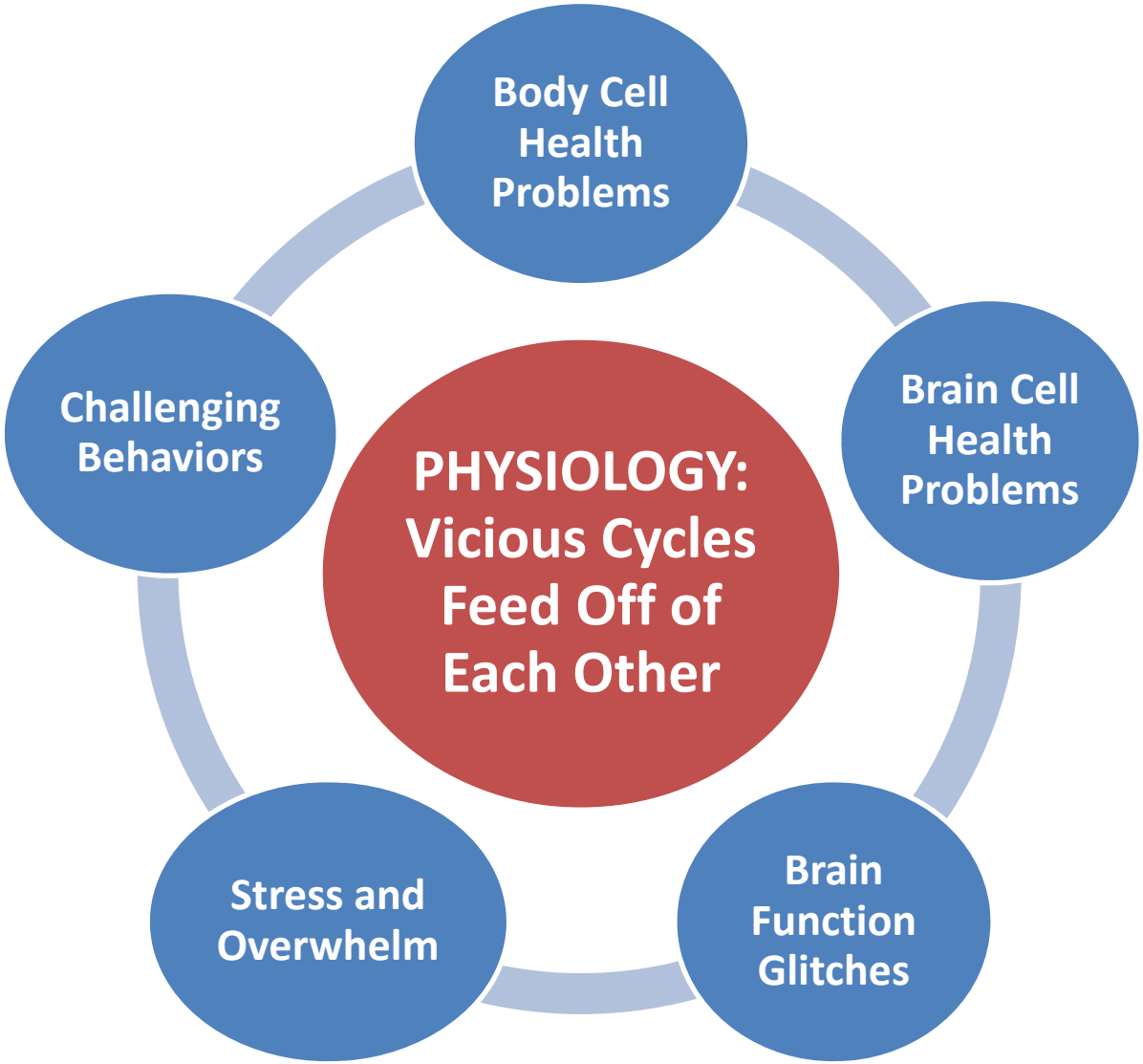
- The TOTAL BUILD-UP of noxious exposures, stressors and deficiencies

Building RESILIENCY protects brain from the debilitating impacts of tissue pathophysiology

Physiology across levels: Interrelated



Problems in each area make trouble for the other areas



Dialing back the problems and Moving Toward Whole Body-Brain Health

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

Toward the Pathophysiology of Autistic Regression

- ***Too much allostatic load plus genetic and environmental weak points.***
- ***Oxidative stress and inflammation***
- ***Cells become hypersensitive and overreactive***
- ***Tipping point is reached.***
- ***Brain glial cells poop out and don't keep up their housekeeping functions.***
- ***Brain energy production gets less efficient.***
- ***Brain networks get weaker***
- ***Weaker brain networks produce weaker interactions with world***
- ***This produces behaviors we call "autistic."***

Spelled out in more detail in Chapter 5 of THE AUTISM REVOLUTION (Herbert 2012)

DoD Funded Study:
A MULTI-SYSTEM ASSESSMENT OF INFANTS AT HIGH RISK FOR AUTISM

Initiating PI: Martha Herbert
Partnering PI: Margaret Bauman

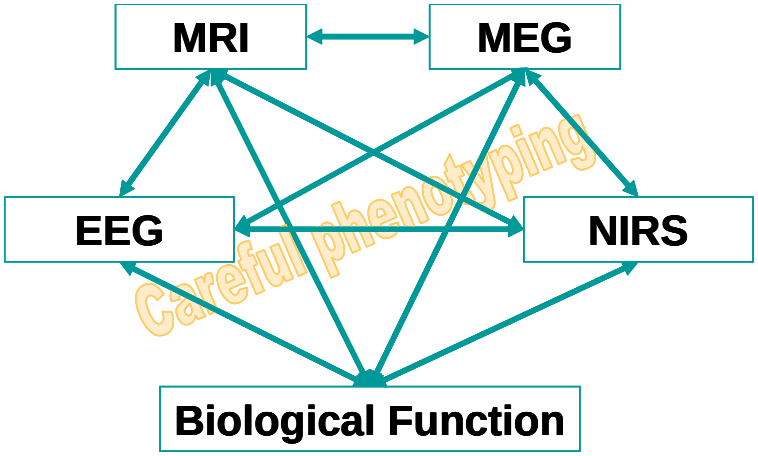
- **Longitudinal Multisystem assessment**
  - **Metabolism, Immune, Toxics, Endocrine**
  - **Brain (EEG), Autonomics**
  - **Medical Comorbidities**
  - **Developmental/Behavioral Phenotyping**

Infant EEG

Photos used with permission

TRANSCEND Research Program

Treatment
Research
And
Neuro
SCience
Evaluation of
Neurodevelopmental
Disorders



Integrative multimodal measurement platform
Optimization of measures that can detect change
In development, in regression, in improvement

www.transcendresearch.org
transcend@partners.org

Autism Revolution: Ten Tips

1. ***Go for the extraordinary.***
2. ***Know what you can't control (genes) — and what you can (gene expression and environment).***
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.***

From THE AUTISM REVOLUTION (Random House/Harvard Health Publications, 2012)

www.AutismRevolution.org