Toxicity and Cell Danger Response

treatautism.ca

BIOMEDICAL TREATMENT
CHANGING CHILDREN'S LIVES

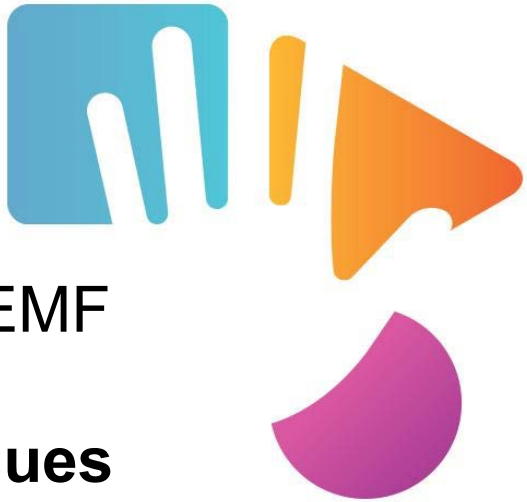
The Perfect Storm

Causes – Multi-factorial

1. **Genetic predisposition**
   - 15% show de novo alterations in genes

2. **Subclinical metabolic problems such as:**
   - suboptimal handling of adenosine or homocysteine
   - Folate and B12 chemistry – “Folate traps”
   - MTR and CBS enzyme dysfunction
   - Glutathione transferase or GSH oxidation-reduction problems
   - Reduced activity of detox enzymes / processes
   - Mitochondrial impairments

Stressors



- **Environmental Toxins**
  - Heavy Metals, Chemical, Xenobiotics, EMF
- **Nutrient Deficiencies or conversion issues**
  - Zinc, folate
- **Viruses or viral overload**
  - CMV, measles, paramyxoviruses, mumps
- **Bacterial**
  - Clostridia, Strep
- **Endocrine**
  - thyroid function and adrenals

HARVARDgazette

SCIENCE & HEALTH > HEALTH & MEDICINE

Toxic chemicals linked to brain disorders in children

Harvard study finds six newly recognized chemicals to add to list

February 14, 2014 |

Harvard Study - Lead

- Lead is of the most extensively researched compounds in terms of neurodevelopment
- There is no safe level of exposure
- Low IQ, behavioral problems, attention problems, hearing problems, kidney damage, delayed physical growth, aggressive behavior, difficulty sleeping, headaches, irritability, and loss of acquired developmental skills, low appetite and energy, as well as reduced sensations
- Dr. Needleman recommended all 2 years olds be tested for lead - **UBIQUITOUS**

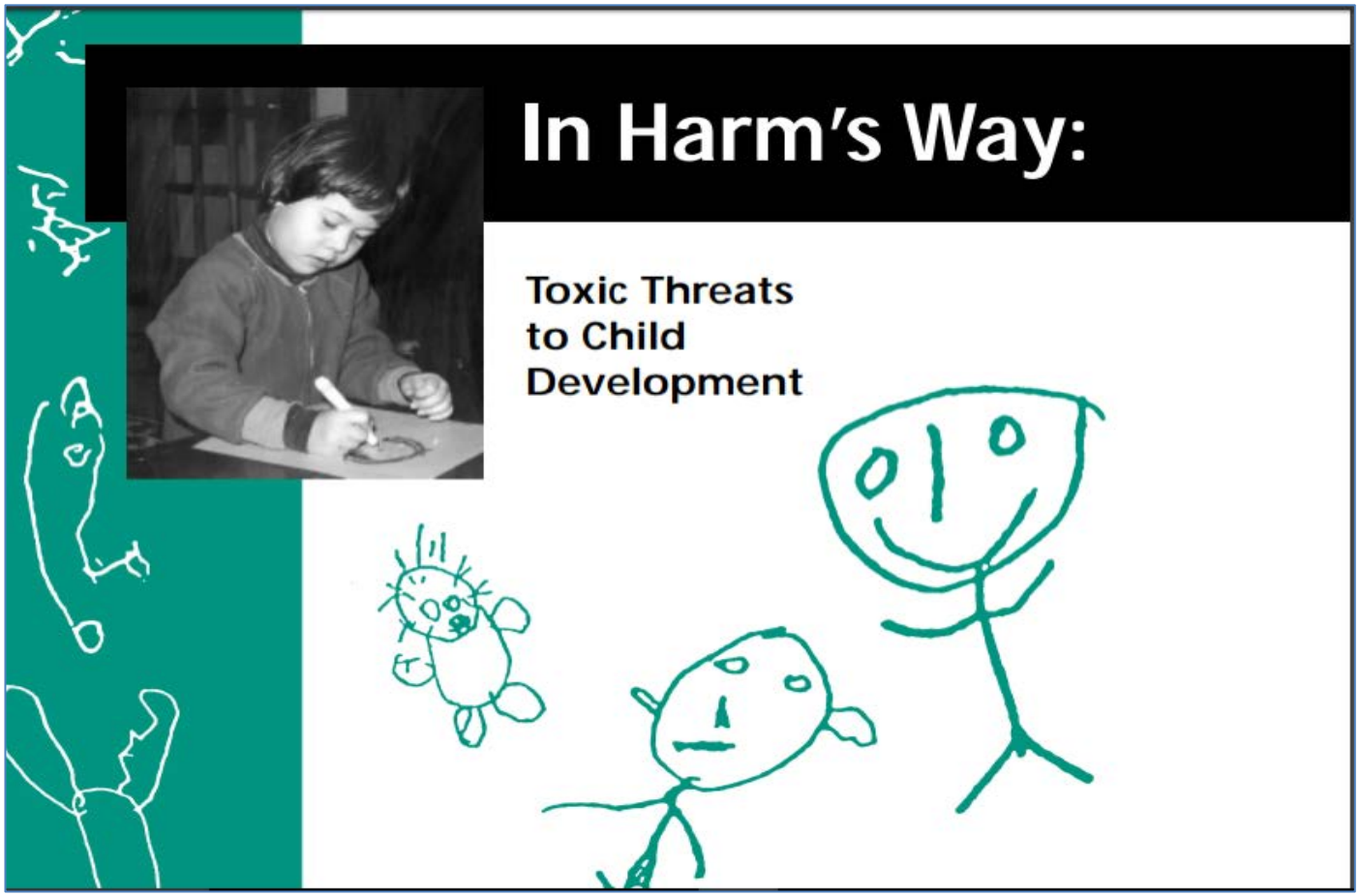
Mercury

- Methylmercury affects the neurological development of the fetus

- Exposure often comes from maternal intake of fish containing high levels of mercury ~ 1.46 million women of childbearing age eat enough to cause fetal damage

- Less than 2 cans of tuna per week = above EPA safety levels *(In Harm's Way – GBPSR)*

Greater Boston Physicians for Social Responsibility



Pesticides

- 5.5 billion lbs/yr
- 1.2 billion lbs/yr in US
- PCBs studies show altered neurons (longer, more complicated)
- Bioaccumulation: fish, peanuts, eggs

Is organic too expensive?

The average family with a child on the spectrum spends $15, 000 / year on therapies

Format: Abstract Send to

Int J Toxicol. 2003 Jul-Aug;22(4):277-85.

Reduced levels of mercury in first baby haircuts of autistic children.

Holmes AS[1], Blaxill MF, Haley BE.

Author information

Abstract

Reported rates of autism have increased sharply in the United States and the United Kingdom. One possible factor underlying these increases is increased exposure to mercury through thimerosal-containing vaccines, but vaccine exposures need to be evaluated in the context of cumulative exposures during gestation and early infancy. Differential rates of postnatal mercury elimination may explain why similar gestational and infant exposures produce variable neurological effects. First baby haircut samples were obtained from 94 children diagnosed with autism using Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM IV) criteria and 45 age- and gender-matched controls. Information on diet, dental amalgam fillings, vaccine history, Rho D immunoglobulin administration, and autism symptom severity was collected through a maternal survey questionnaire and clinical observation. Hair mercury levels in the autistic group were 0.47 ppm versus 3.63 ppm in controls, a significant difference. The mothers in the autistic group had significantly higher levels of mercury exposure through Rho D immunoglobulin injections and amalgam fillings than control mothers. Within the autistic group, hair mercury levels varied significantly across mildly, moderately, and severely autistic children, with mean group levels of 0.79, 0.46, and 0.21 ppm, respectively. Hair mercury levels among controls were significantly correlated with the number of the mothers' amalgam fillings and their fish consumption as well as exposure to mercury through childhood vaccines, correlations that were absent in the autistic group. Ha control. These data cast doubt on the efficacy of traditional ha In light of the biological plausibility of mercury's role in neurodev e mechanism by which early mercury exposures could increase the

PMID: 12933322 DOI: 10.1080/10915810305120

Hair excretion patterns among autistic infants were significantly reduced relative to control

Format: Abstract

Send to

Environ Health Perspect. 2012 Jul;120(7):1003-9. doi: 10.1289/ehp.1104833. Epub 2012 Apr 25.

PCB-95 modulates the calcium-dependent signaling pathway responsible for activity-dependent dendritic growth.

Wayman GA[1], Bose DD, Yang D, Lesiak A, Bruun D, Impey S, Ledoux V, Pessah IN, Lein PJ.

Author information

Abstract

BACKGROUND: Non-dioxin-like (NDL) polychlorinated biphenyls (PCBs) promote dendritic growth in hippocampal neurons via ryanodine receptor (RyR)-dependent mechanisms; however, downstream signaling events that link enhanced RyR activity to dendritic growth are unknown. Activity-dependent dendritic growth, which is a critical determinant of neuronal connectivity in the developing brain, is mediated by calcium ion (Ca(2+))-dependent activation of Ca(2+)/calmodulin kinase-I (CaMKI), which triggers cAMP response element binding protein (CREB)-dependent Wnt2 transcription. RyRs regulate

modulation of this signaling pathwa

OBJECTIVE: We tested the hypoth

arborization.

METHODS AND RESULTS: Ca(2+

pentachlorobiphenyl; a potent RyR

ryanodine. As determined by West

Blocking CaMKK, CaMKIα/γ, MEK

(GABA) receptors with bicuculline

knockdown of RyR blocked BIC-in

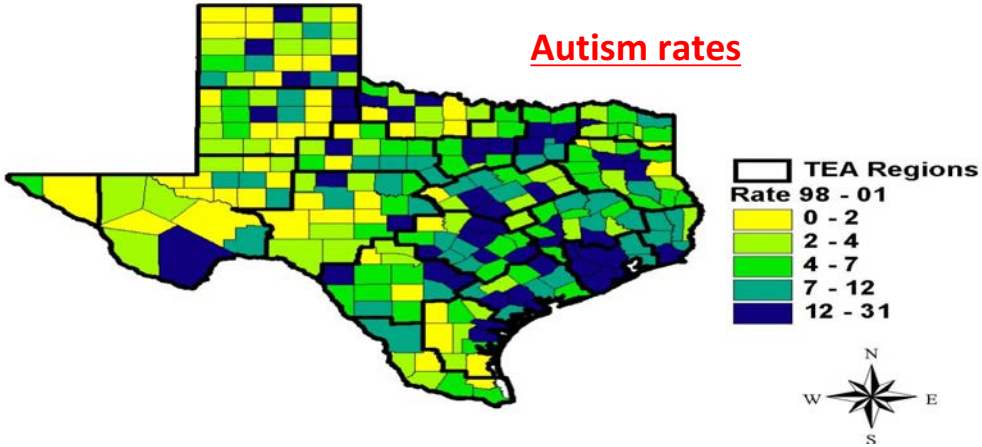
t2.

Our findings identify PCBs as candidate environmental risk factors for neurodevelopmental disorders, especially in children with heritable deficits in calcium signaling associated with autism

Why is ASD on the rise?

- **6 trillion** tons of over 85, 000 chemicals produced annually
- PCBs, fire retardants, phthalates, Bisphenol A, metals… the list is too long… and depressing
- 80% or more – **NOT TESTED**
- Chemical manufacturers are not required to prove safety

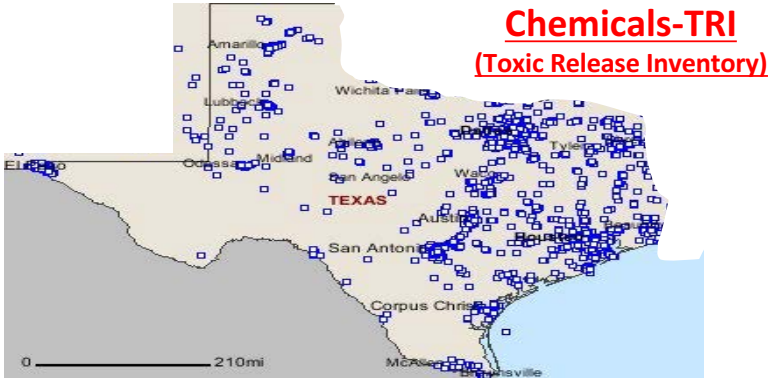
Oberved Rate of Autism 1998 - 2000 By County of Texas
Aggregated from School Districts
With Texas Education Agency Districts



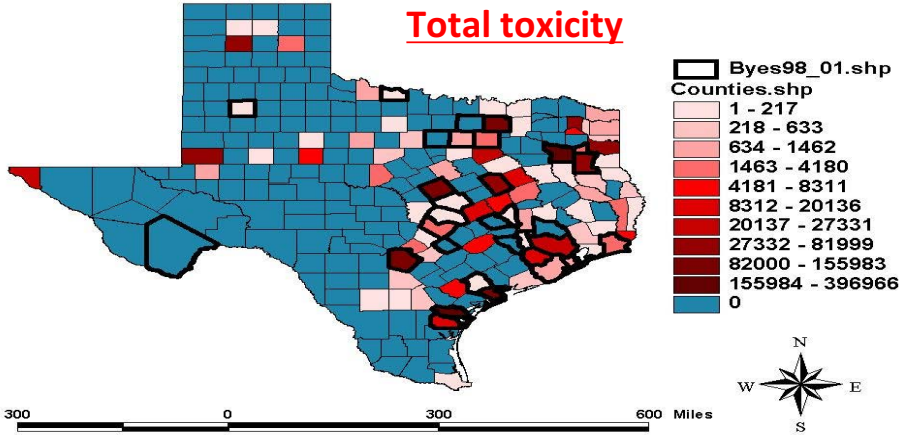
On average, for each 1000 lb of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism.

Palmer et al. Health & Place 12 (2006) 203–209

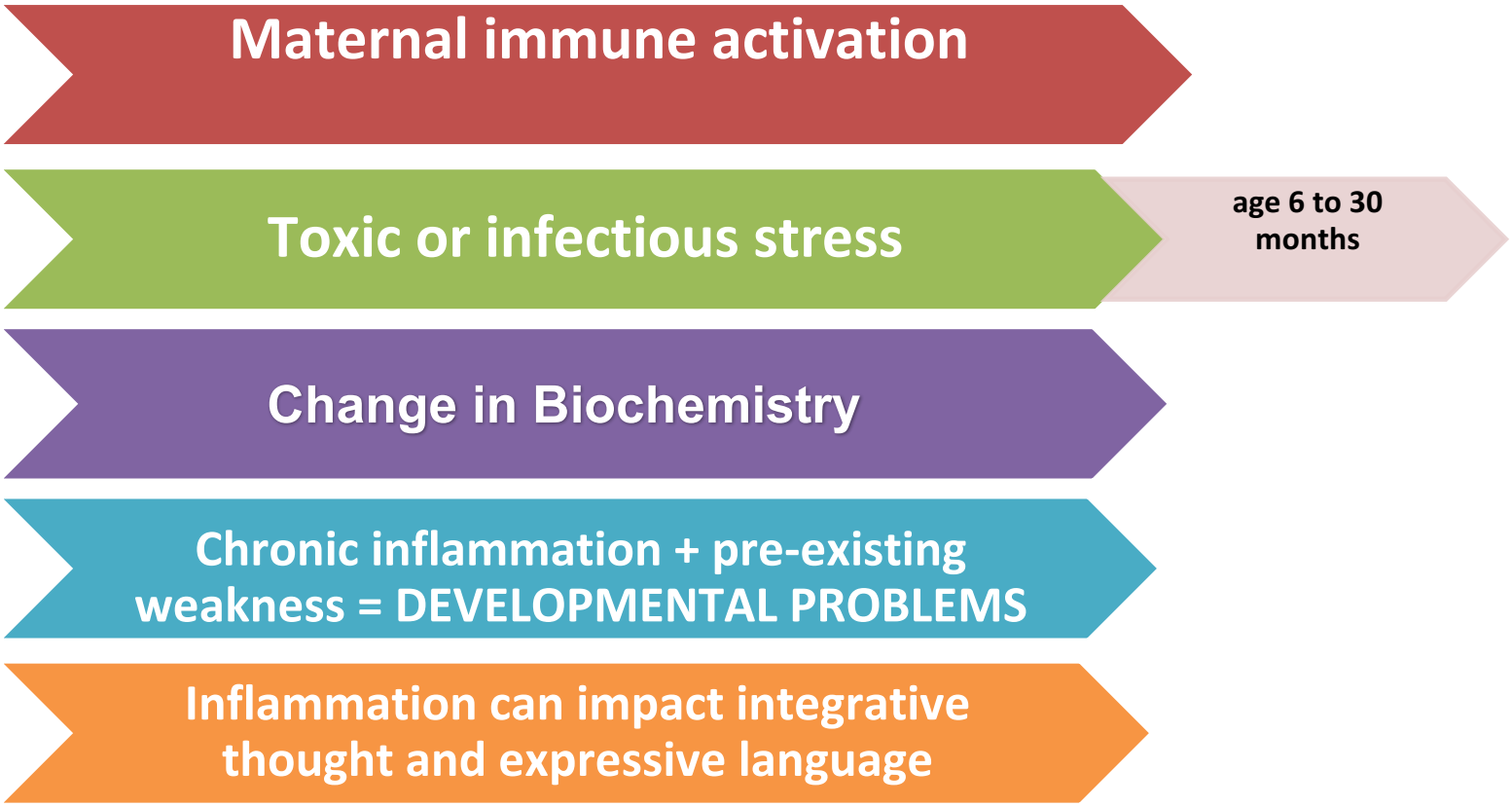
All Reporting Facilities, All Chemicals TRI-(1987-2002)
Map shows **3,683** of **48,205** facilities reporting nationwide



Draft (21204) Levels of Total Toxicity by County for 2001
with Top Two Deciles of Bayesian Autism Rates (98 - 01)
Texas



The impact of stressors



The impact of stressors

Impact on cell function

- Altered BBB
- Impaired glial function
- Sequestering / retaining of toxins and infectious agents
- Dysfunctional **detox** capacity
- Altered insulin response – need sugar to digest
- Excess glutamate
- Serotonin and dopamine dysregulation
- Immune dysregulation / autoimmunity
- Altered enzyme function – MTR and CBS
- **Persistent inflammation = brain allergy (TNF, IL-6, IL-1)**

Front Psychiatry. 2012; 3: 118.
Published online 2013 Jan 18. doi: 10.3389/fpsyt.2012.00118
PMCID: PMC3548163

Environmental Factors in Autism

Andreas M. Grabrucker[1,*]

Author information ► Article notes ► Copyright and License information ►

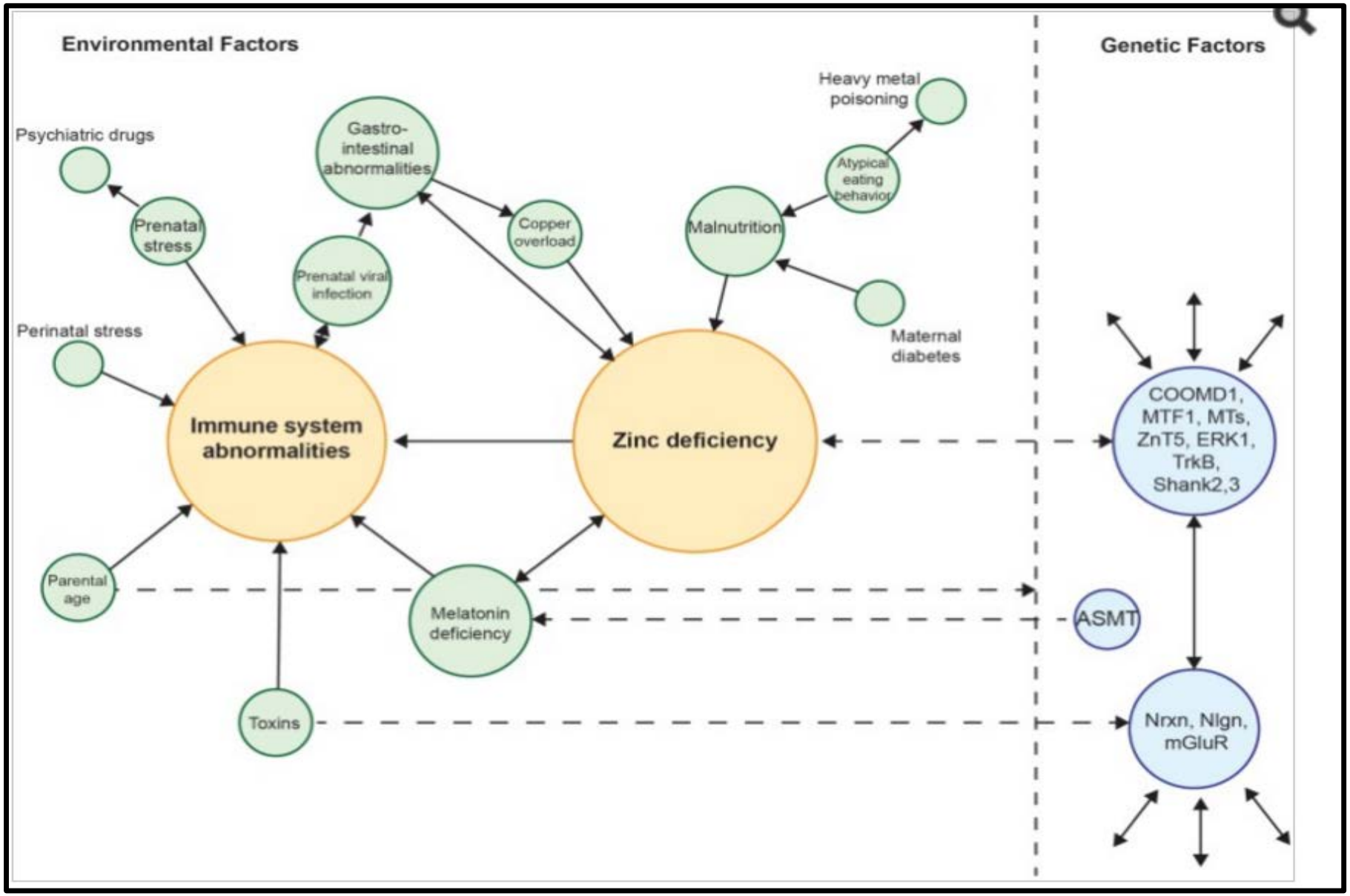
This article has been cited by other articles in PMC.

Abstract

Go to:

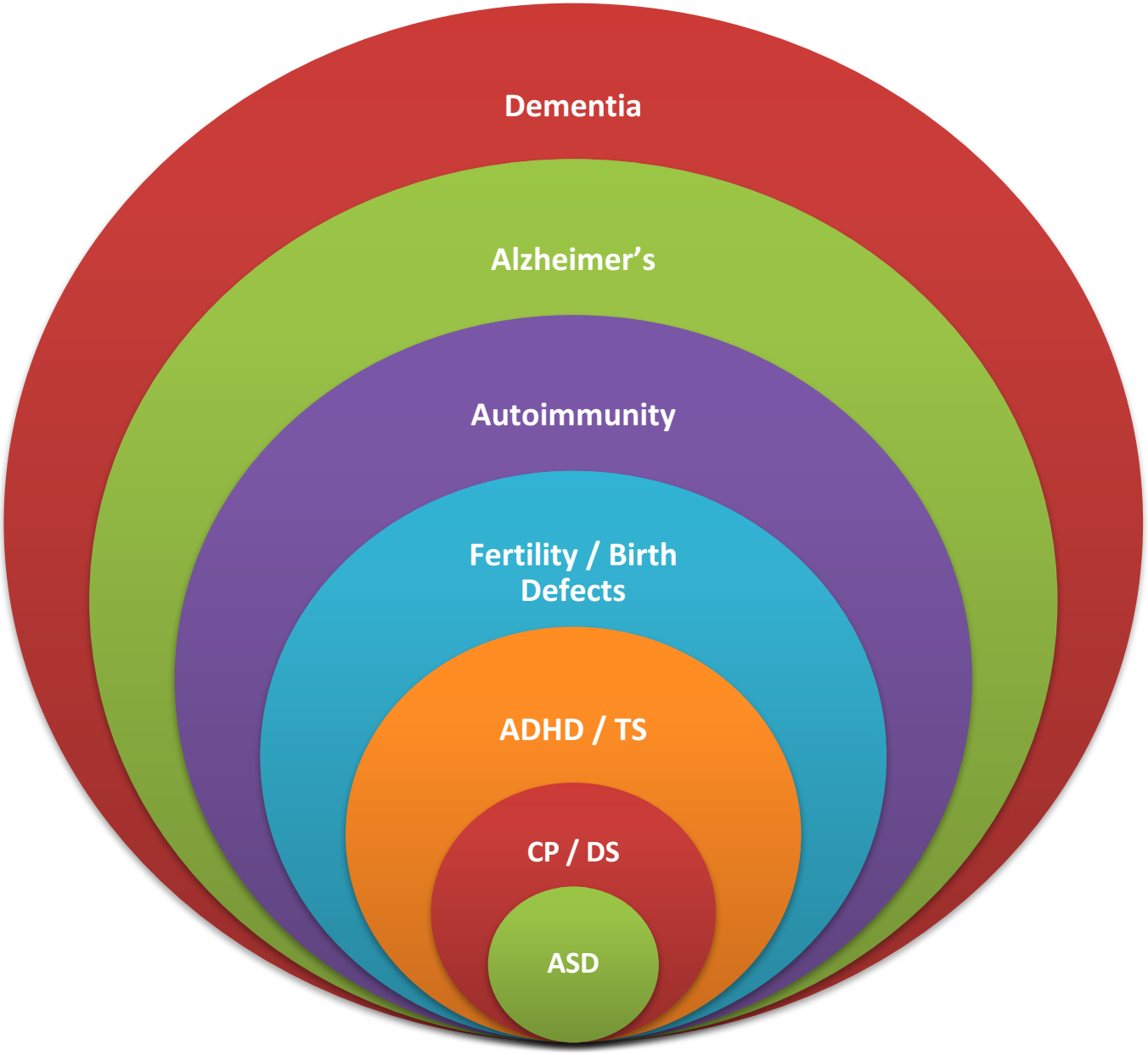
Autism is a neurodevelopmental disorders characterized by impa ts in communication and social behavior, and by repetitive behaviors. Although genetic f ight be largely responsible for the occurrence of autism the ly that in addition to a certain combination of autis al factors might act as risk factors triggering the development o environmental factors in autism is an important area of research and rece ssed in this review. Interestingly, the results show that many enviro interrelated and their identification and comparison might unveil a com eme of a s on a contextual as well as molecular level. For example, b disruption in the im e system and in zinc homeostasis may affect synaptic transmission in autism. Thus, here, a model is proposed that interconnects the most important and scientifically recognized environmental factors. Moreover, similarities in how these risk factors impact synapse function are discussed and a

Great Literature Review


Environmental Factors
Genetic Factors
Psychiatric drugs
Prenatal stress
Gastro-intestinal abnormalities
Heavy metal poisoning
Atypical eating behavior
Copper overload
Malnutrition
Prenatal viral infection
Perinatal stress
Maternal diabetes
Immune system abnormalities
Zinc deficiency
COOMD1, MTF1, MTs, ZnT5, ERK1, TrkB, Shank2,3
Parental age
Melatonin deficiency
ASMT
Toxins
Nrxn, Nlgn, mGluR

AUTISM is the key

- Language, social, cognitive
- Mood
- Behaviour
- Autoimmunity
- Decreasing impact of environment toxins
- Repairing methylation
- Fertility
- Neurodegenerative
- …..


Dementia
Alzheimer's
Autoimmunity
Fertility / Birth Defects
ADHD / TS
CP / DS
ASD

What causes oxidative stress and microglial activation?

- Maternal infection – priming of microglia
- Maternal exposure to toxins – BPA
- Weak mitochondria
- Methylation and detoxification impairments
- Gut microbes
- Impaired immune function
- Autoimmunity
- Exposure to toxic substances

Altern Ther Health Med. 2008 Nov-Dec;14(6):46-53.

A possible central mechanism in autism spectrum disorders, part 1.

Blaylock RL[1].

Author information

Abstract

The autism spectrum disorders (ASD) are a group of related neurodevelopmental disorders have been increasing in incidence since the 1980s. Despite a considerable amount of data collected from cases, a central mechanism has not been offered. A careful review of ASD c discloses a number of events that adhere to an immunoexcitotoxic mechanism. This mecha explains the link between excessive vaccination, use of aluminum and ethylmercury as vac

IMMUNOEXCITOTOXICITY

Curr Opin Neurol. 2010 Apr;23(2):103-10. doi: 10.1097/WCO.0b013e328336a01f.

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

Herbert MR[1].

Author information

Abstract

PURPOSE OF REVIEW: This review presents a rationale and evidence for contributions of environmental influences and environmentally vulnerable physiology to autism spectrum dis (ASDs).

RECENT FINDINGS: Recent studies suggest a substantial increase in ASD prevalence abo

SCIENCE & HEALTH > HEALTH & MEDICINE

Toxic chemicals linked to brain disorders in children

Harvard study finds six newly recognized chemicals to add to list

Free Radic Biol Med. 2014 Nov;76:25-33. doi: 10.1016/j.freeradbiomed.2014.07.030. Epub 2014 Aug 4.

Bisphenol A induces oxidative stress and mitochondrial dysfunction lymphoblasts from children with autism and unaffected siblings.

Kaur K[1], Chauhan V[2], Gu F[2], Chauhan A[3].

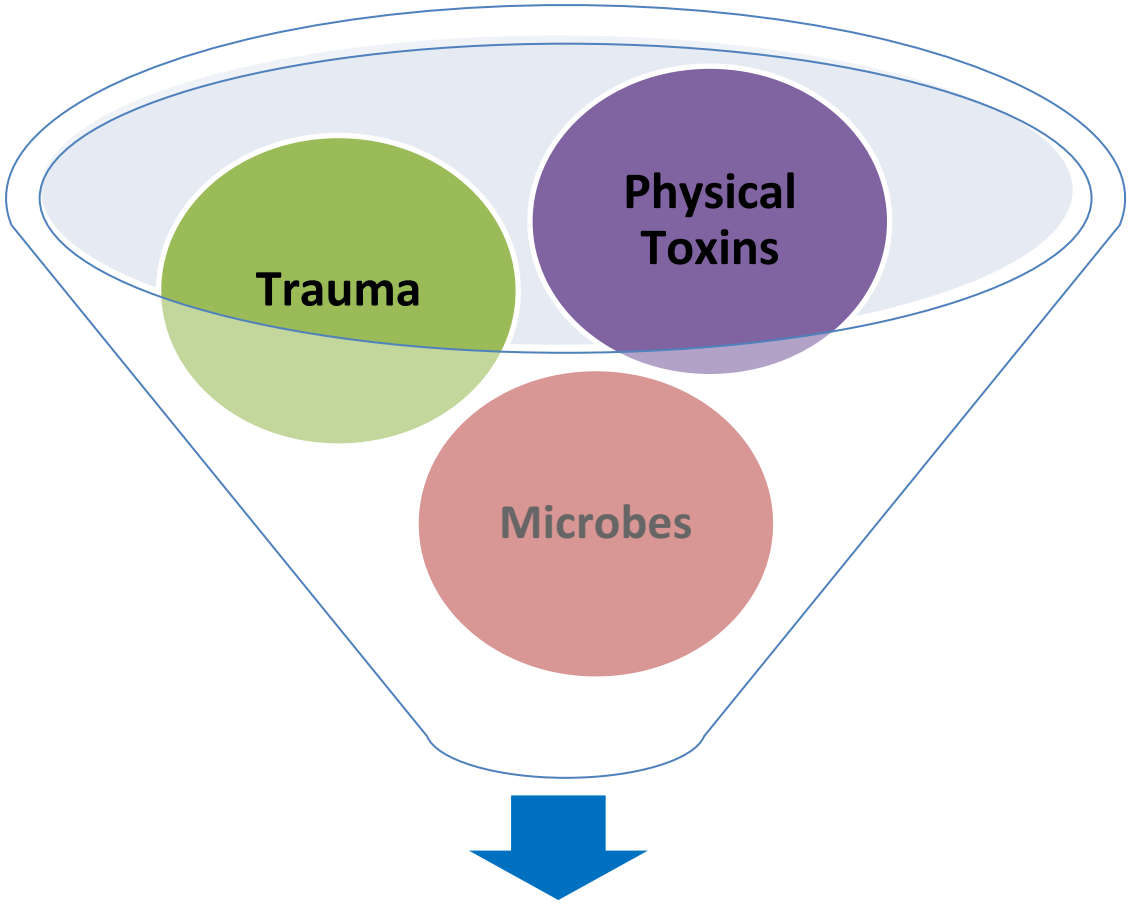
Author information

Abstract

Autism is a behaviorally defined neurodevelopmental disorder. Although there is no single identifiable cause for autism, roles for genetic and environmental factors have been implicat autism. Extensive evidence suggests increased oxidative stress and mitochondrial dysfunct autism. In this study, we examined whether bisphenol A (BPA) is an environmental risk facto autism by studying its effects on oxidative stress and mitochondrial function in the lymphobl

How do toxins cause damage?

- Oxidative stress
- Gut damage
- Immunotoxic
- Damage mitochondria
- Cause inflammation
- Deplete glutathione
- Increase glutamate
- Epigenetic damage
- TRANSGENERATIONAL BIOACCUMULATION



CELL DANGER RESPONSE

ELSEVIER

Mitochondrion

Volume 16, May 2014, Pages 7–17

Metabolic features of the cell danger response

Robert K. Naviaux

Show more

http://dx.doi.org/10.1016/j.mito.2013.08.006

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- The Cell Danger Response (CDR) is defined in terms of an ancient metabolic response to threat
- The CDR encompasses inflammation, innate immunity, oxidative stress, and the ER stress response
- The CDR is maintained by extracellular nucleotide (purinergic) signaling
- Abnormal persistence of the CDR lies at the heart of many chronic diseases
- Antipurinergic therapy (APT) has proven effective in many chronic disorders in animal models.

Cell Danger Response

- **SLOWS DOWN METHYLATION!**
- Stiffens cell membranes
- Creates **REACTIVE OXYGEN SPECIES**
- Pathways are immature in newborns and children leading not only to inflammatory and immune changes but also negatively impacting neurodevelopment

Cell Danger Response

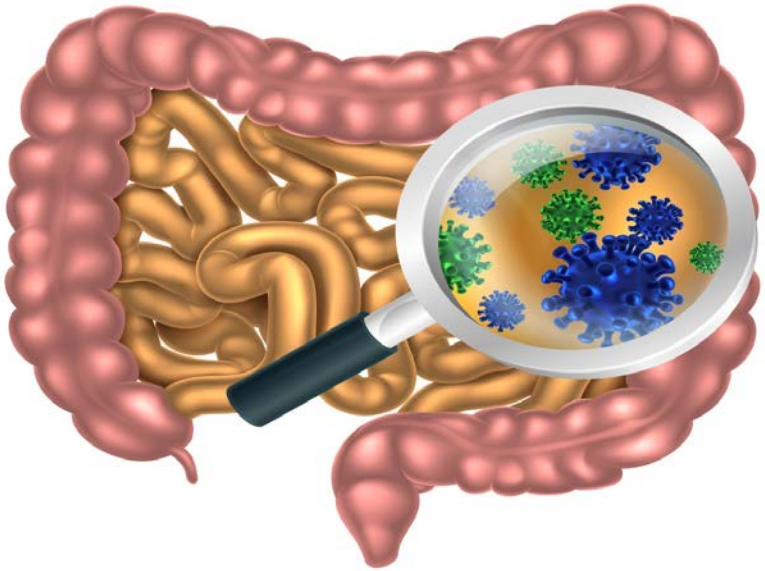
- Rapid metabolism of MITO (and ability to monitor electron flow and sulfur oxidation) = **ideal to act as generalized cell "danger alarms**”
- Trace heavy metals trigger a MITO response that is similar to a **viral infection**
- Synthesized molecules (dyes, pesticides, drugs, and industrial chemicals) are highly **electrophilic** and will cause **"electron steal"** that will activate a **CDR**

Cell Danger Response

- If CDR persists = altered metabolis
- Slows down metabolism to preserve O2 and create ROS = oxidative stress
- Reduction in thyroid function
- **Slows methylation**, microglial activation, excess glutamate…

…IMMUNOEXCITOTOXICITY

Cell Danger Response



- **SAMDC**
  – upregulated by CDR

- Shifts methyl donors
  to product POLYAMINES
  which are immunosuppressive

- Supporting methylation, supports microbes (both helpful and unhelpful)

Mitochondria

- Require digestive system to breakdown carbs and fat
- Meta analysis – majority of studies in kids dx with ASD have MITO dysfn
- Subtle weakness = significant impact on development
- MITO dysfunction is involved in Autism, Down Syndrome, asthma, cerebral palsy, dyspraxia / apraxia, speech delay, elements of ADHD, delayed fine and gross motor skills, low tone and many rare genetic disorders

Heavy Metal Tests

- Pre test
- Post with DMSA 30mg/kg
- For the post test, collect all urine for 6 hours and then one sample for that amount

POTENTIALLY TOXIC METALS

METALS	RESULT µg/g CREAT	REFERENCE RANGE	WITHIN REFERENCE RANGE	ELEVATED	VERY ELEVATED
Aluminum	< dl	< 25			
Antimony	0.3	< 0.6			
Arsenic	140	< 120			
Beryllium	< dl	< 0.5			
Bismuth	< dl	< 10			
Cadmium	1.1	< 2			
Lead	430	< 5			
Mercury	7.1	< 3			
Nickel	12	< 10			
Platinum	< dl	< 1			
Thallium	0.3	< 0.7			
Thorium	< dl	< 0.3			
Tin	8.5	< 9			
Tungsten	0.2	< 0.7			
Uranium	< dl	< 0.1			