Las preocupaciones del cerebro en ASD son más que el intestino - conexión del cerebro: Neurotransmisores y ediciones de Neuroimmune en desordenes del espectro del autismo

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Biomarkers

- La causa el autismo puede ser definida.
- Después de que se haya definido puede ser tratado.

¿Cuál es la causa más probable del autismo en niños?

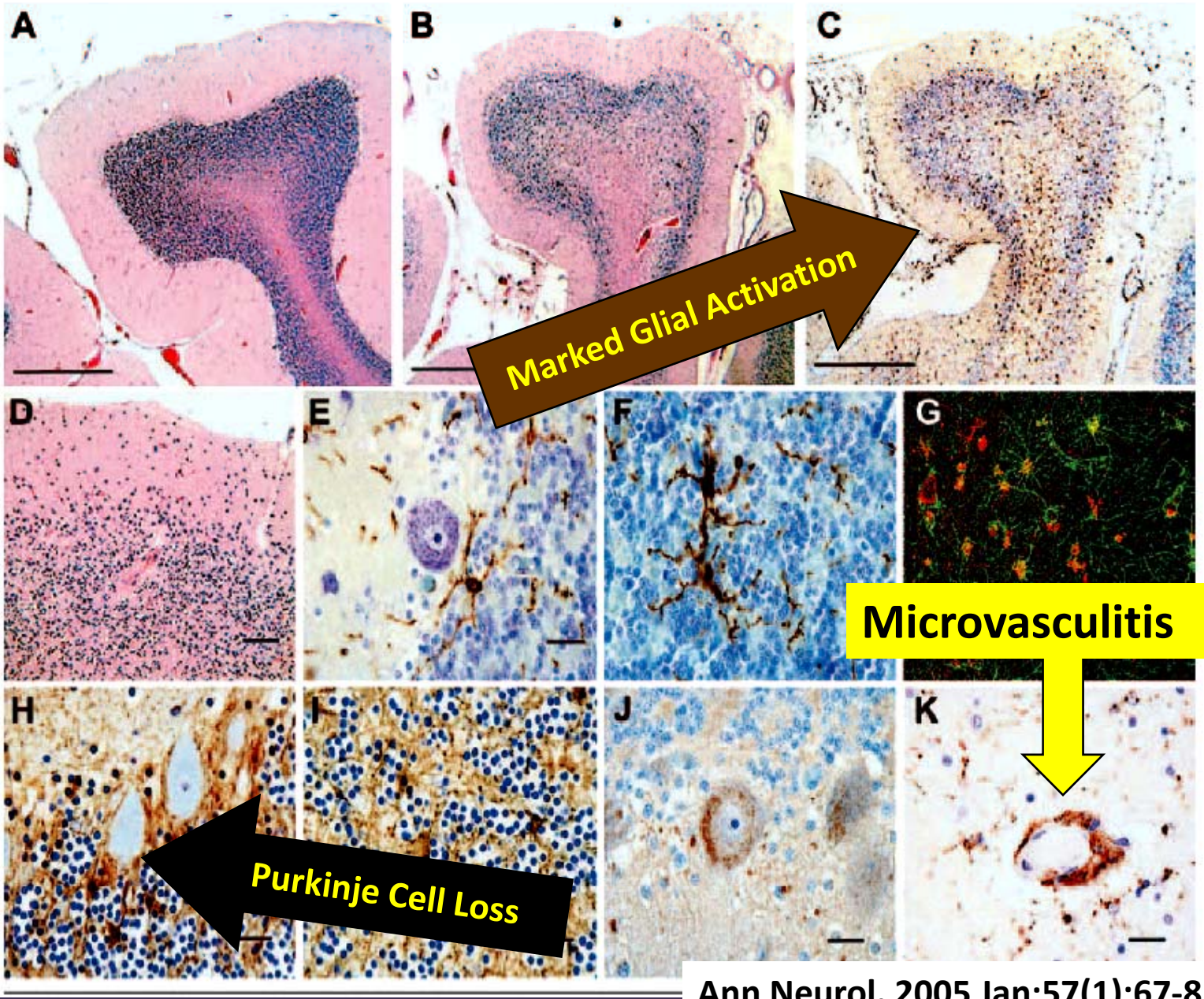
El autismo es causado por la inflamación del cerebro y de los intestinos.

Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism

Diana L. Vargas, MD,[1,2] Caterina Nascimbene, MD,[1–3] Chitra Krishnan, MHS[1]
Andrew W. Zimmerman, MD,[1,4] and Carlos A. Pardo, MD[1,2,5]

Autism is a neurodevelopmental disorder characterized by impaired communication and social interaction and may be accompanied by mental retardation and epilepsy. Its cause remains unknown, despite evidence that genetic, environmental, and immunological factors may play a role in its pathogenesis. To investigate whether immune-mediated mechanisms are involved in the pathogenesis of autism, we used immunocytochemistry, cytokine protein arrays, and enzyme-linked immunosorbent assays to study brain tissues and cerebrospinal fluid (CSF) from autistic patients and determined the magnitude of neuroglial and inflammatory reactions and their cytokine expression profiles. Brain tissues from cerebellum, midfrontal, and cingulate gyrus obtained at autopsy from 11 patients with autism were used for morphological studies. Fresh-frozen tissues available from seven patients and CSF from six living autistic patients were used for cytokine protein profiling. We demonstrate an active neuroinflammatory process in the cerebral cortex, white matter, and notably in cerebellum of autistic patients. Immunocytochemical studies showed marked activation of microglia and astroglia, and cytokine profiling indicated that macrophage chemoattractant protein (MCP)–1 and tumor growth factor–β1, derived from neuroglia, were the most prevalent cytokines in brain tissues. CSF showed a unique proinflammatory profile of cytokines, including a marked increase in MCP-1. Our findings indicate that innate neuroimmune reactions play a pathogenic role in an undefined proportion of autistic patients, suggesting that future therapies might involve modifying neuroglial responses in the brain.

Ann Neurol. 2005 Jan;57(1):67-81



Ann Neurol. 2005 Jan;57(1):67-81

Serum autoantibodies to brain in Landau-Kleffner variant, autism, and other neurologic disorders

Anne M. Connolly, MD, Michael G. Chez, MD, Alan Pestronk, MD, Susan T. Arnold, MD, Shobhna Mehta, BSc, and Ruthmary K. Deuel, MD

(J Pediatr 1999;134:607-13)

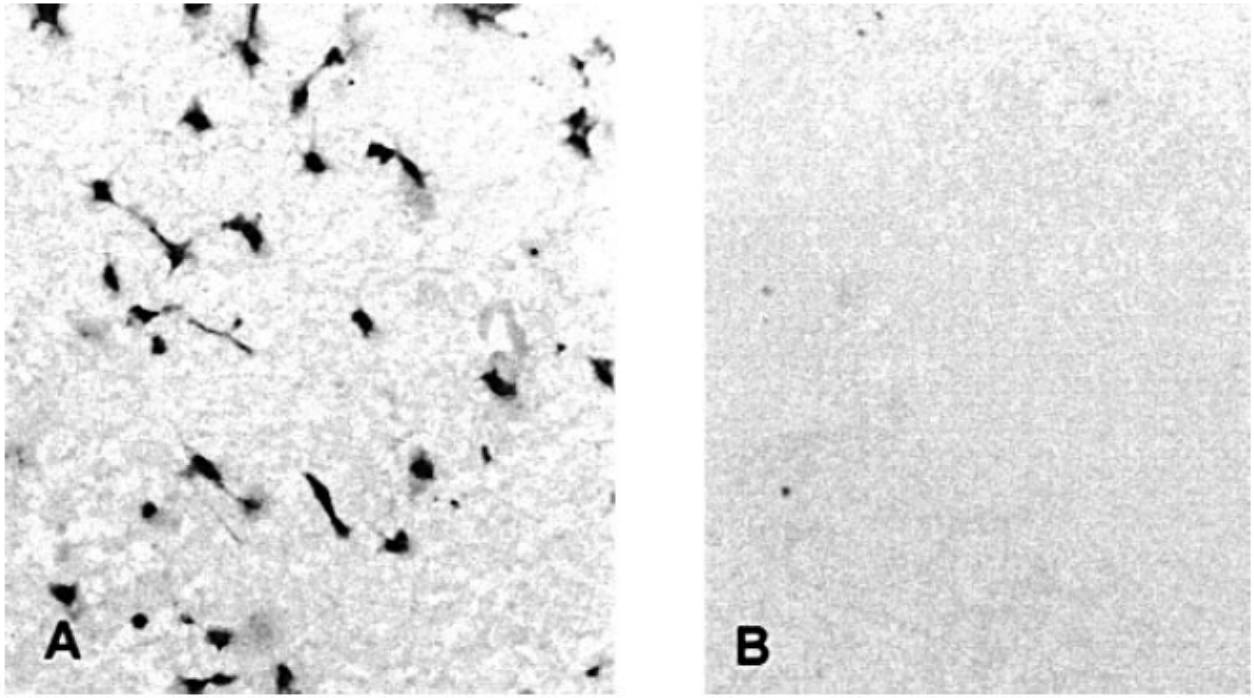
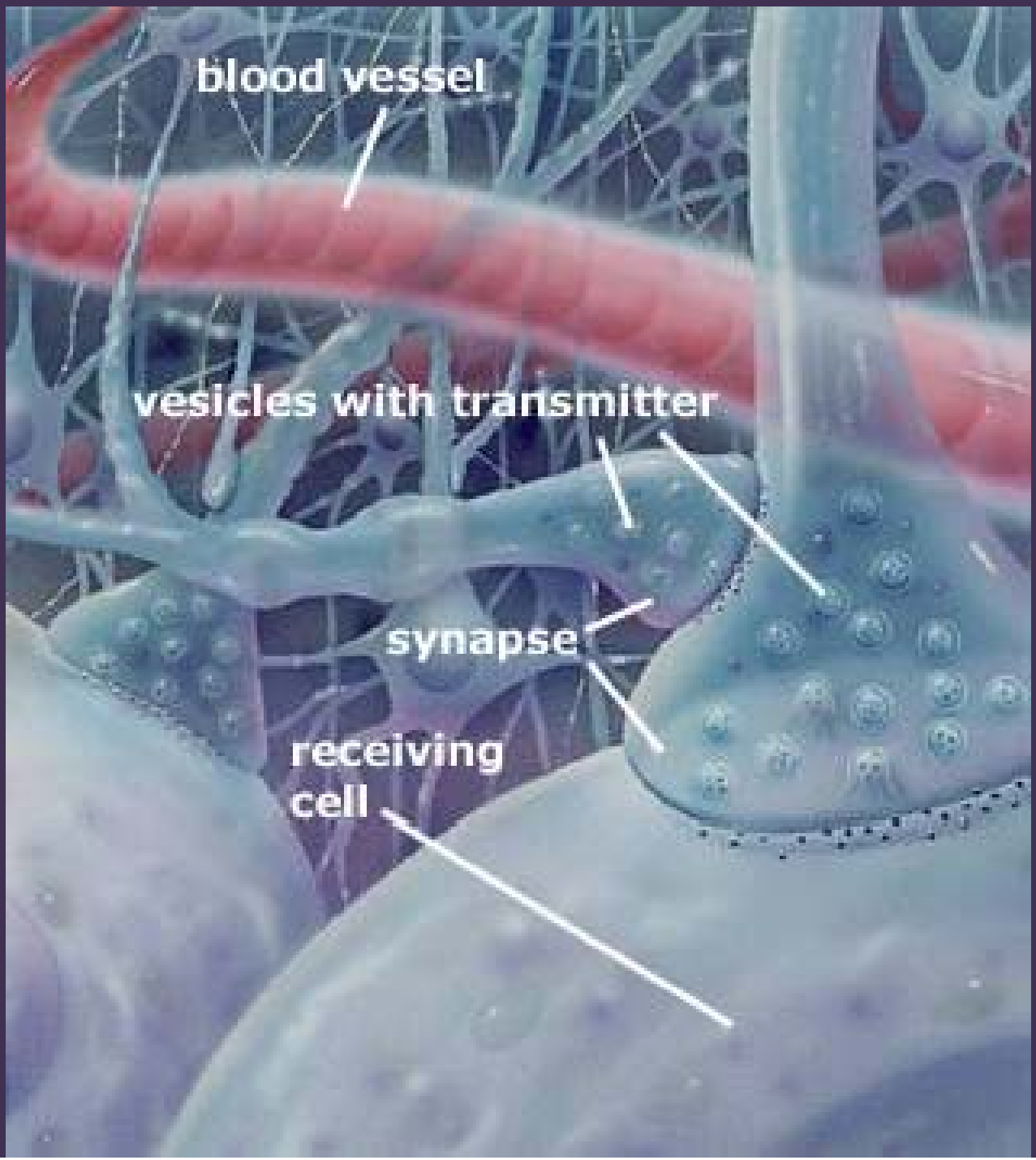


Fig 1. **A,** IgG antibodies from a child with LKSV binding to small blood vessels in human temporal lobe cortex (original magnification ×80). Immunostaining (1:100) demonstrates distinct capillary staining. **B,** Control serum shows no specific labeling.


blood vessel
vesicles with transmitter
synapse
receiving
cell

Urinary levels of neopterin and biopterin in autism

S. Messahel[a,b], A.E. Pheasant[a,*], H. Pall[b], J. Ahmed-Choudhury[a], R.S. Sungum-Paliwal[c], P. Vostanis[c]

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[b]Department of Neurology, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK
[c]Department of Child Psychiatry, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK

Neuroscience Letters 241 (1998) 17–20

Table 1

Urinary neopterin and biopterin levels in autistic children, their siblings and control children

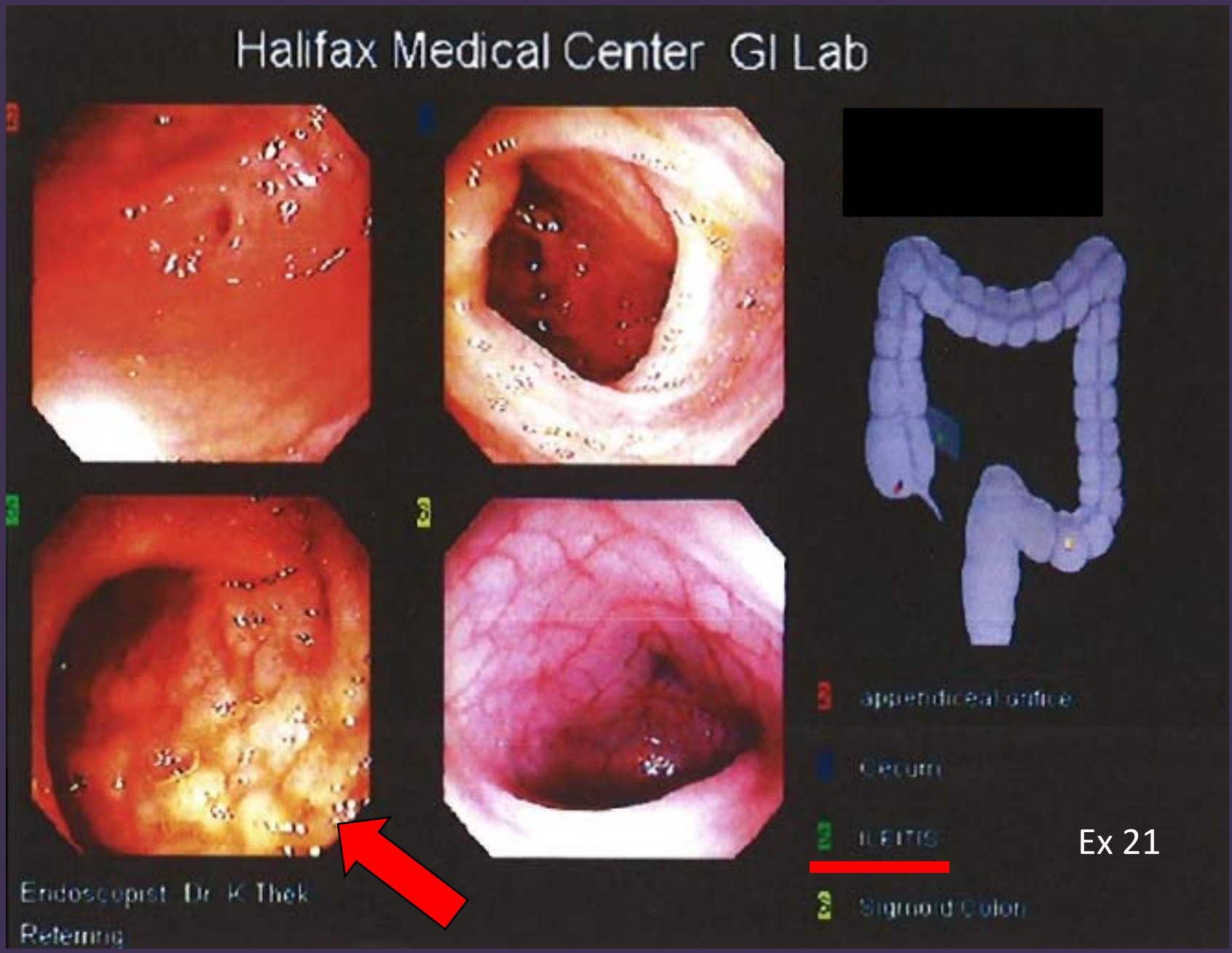
	Neopterin (μmol/mol creatinine)	Biopterin (μmol/mol creatinine)
Autistic children ($n = 14$)	3116 ± 686*	3691 ± 882**
Siblings ($n = 21$)	1490 ± 346	2923 ± 626**
Control children ($n = 16$)	908 ± 201	359 ± 80

Data are the mean ± SEM. Significantly different from controls: *$P < 0.01$; **$P < 0.001$.

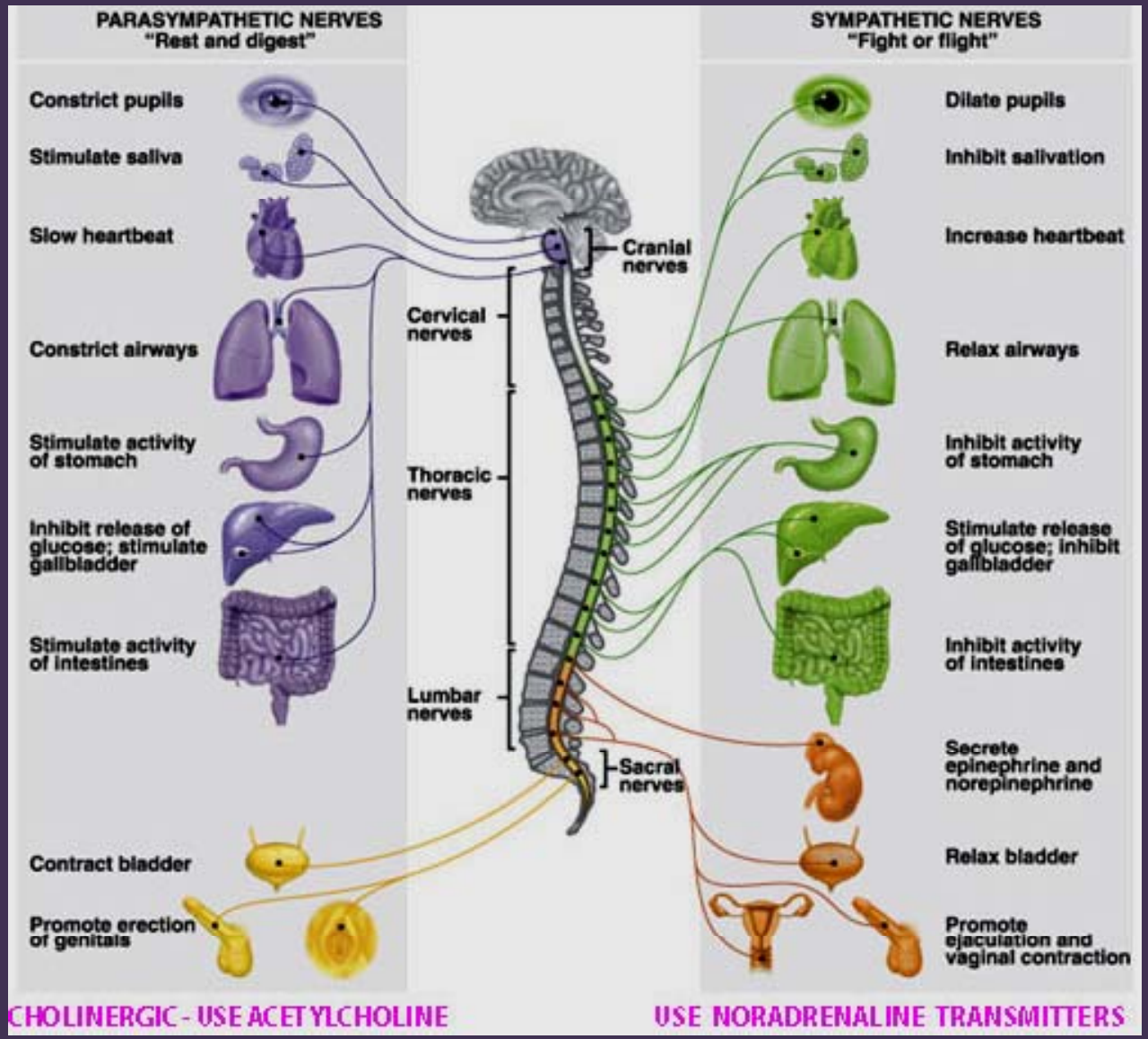
"The observed increase in urinary native **neopterin** in autism agrees with our previous observations and indicates activation of cellular immunity in these children thus supporting the possible involvement of **autoimmunity** in the pathogenesis* of autism."

Messahel et al, Neuroscience Letters 241 (1998) 17–20

*Pathogenesis = the cause of disease


Halifax Medical Center GI Lab
Endoscopist Dr K Thek
Retiming
Ex 21

THE GUT- BRAIN Connection – Autonomic Nervous System (Vagus Nerve)



Acetyl Choline (Nicotine) effect

Noradrenaline effect

Reduced cardiac parasympathetic activity in children with autism.

Brain Dev. 2005 Oct;27(7):509-16
Ming X, et al

Department of Neuroscience, New Jersey Medical School, UMDNJ, Newark, 90 Bergen Street, DOC 8100, NJ 07103, USA.
mingxu@umdnj.edu

Many of the clinical symptoms of autism suggest autonomic dysfunction. **results suggest that there is low baseline cardiac parasympathetic activity with evidence of elevated sympathetic tone in children with autism whether or not they have symptoms or signs of autonomic abnormalities.**

Subclinical effects of prenatal methylmercury exposure on cardiac autonomic function in Japanese children.

Int Arch Occup Environ Health. 2006 May;79(5):379-86. Epub 2005 Dec 20.

Murata K, Sakamoto M, Nakai K, Dakeishi M, Iwata T, Liu XJ, Satoh H

Department of Environmental Health Sciences, Akita University School of Medicine, 010-8543, Akita, Japan, winestem@med.akita-u.ac.jp.

Conclusions: Despite the potential limitations involved in the retrospective study, **these findings suggest that prenatal methylmercury exposure (median of estimated maternal hair mercury at parturition, 2.24 mug/g) may be associated with reduced parasympathetic activity and/or sympathovagal shift**.

IN OVERVIEW

The Cholinergic Anti-inflammatory Pathway: A Missing Link in Neuroimmunomodulation

VALENTIN A PAVLOV,[1] HONG WANG,[1] CHRISTOPHER J CZURA,[1] STEVEN G FRIEDMAN,[1,2] AND KEVIN J TRACEY[1]

This review outlines the mechanisms underlying the interaction between the nervous and immune systems of the host in response to an immune challenge. The main focus is the cholinergic anti-inflammatory pathway, which we recently described as a novel function of the efferent vagus nerve. This pathway plays a critical role in controlling the inflammatory response through interaction with peripheral $\alpha 7$ subunit–containing nicotinic acetylcholine receptors expressed on macrophages. We describe the modulation of systemic and local inflammation by the cholinergic anti-inflammatory pathway and its function as an interface between the brain and the immune system. The clinical implications of this novel mechanism also are discussed.

Sin la ventaja del efecto colinérgico, la inflamación aumenta del cerebro y de los intestinos.

Without the benefit of the cholinergic effect, inflammation increases in the brain and intestines.

CNS Anti-inflammatories

- Things active in the gut may not cross into the brain, ie: 5-ASA (sulfasalazine) type meds.
- Nonsteroidals (Ibuprofen) may work but at the risk of further worsening esophagitis and gastritis.
- Steroids may be effective but long term problems limit use.
- IVIG often effective but expensive and insurance coverage limited.
- Novel Agents; Pioglitazone (Actos), **Spironolactone**, Minocycline and others.


PETA
got autism?
Studies have shown a link
between cow's milk and autism.
find out more at GoVeg.com

Evaluation of an association between gastrointestinal symptoms and cytokine production against common dietary proteins in children with autism spectrum disorders

Jyonouchi H, Geng L, Ruby A, Reddy C, Zimmerman-Bier B.

Journal of Pediatrics, 2005 May;146(5):605-10

FINDINGS: ASD children produced more tumor necrosis factor-alpha (TNF-alpha)/interleukin-12 (IL-12) than those obtained from control subjects with cow's milk protein, beta-lactoglobulin, and alpha-lactoalbumin, irrespective of objective GI symptoms. They also produced more TNF-alpha with gliadin, which was more frequently observed in the group with loose stools.

American Journal of Medical Genetics Part B (Neuropsychiatric Genetics) 141B:1–10 (2006)

Letter to the Editor

Metabolic Endophenotype and Related Genotypes are Associated With Oxidative Stress in Children With Autism

S. Jill James,[1]* Stepan Melnyk,[1] Stefanie Jernigan,[1] Mario A. Cleves,[1] Charles H. Halsted,[2] Donna H. Wong,[2] Paul Cutler,[3] Kenneth Bock,[4] Marvin Boris,[5] J. Jeffrey Bradstreet[Q1 5,6], Sidney M. Baker,[7] and David W. Gaylor[8]

[1] Department[Q2] of Pediatrics, University of Arkansas for Medical Sciences, Arkansas Children's Hospital Research Institute, Little Rock, Arkansas
[2] Genome and Biomedical Sciences Facility, West Health Science Drive, University of California Davis, Davis California
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[5] Froelich Farm Blvd., Woodbury, New York, New York
[6] International Child Development Resource Center, Hibiscus Blvd, Melbourne, Florida
[7] Sag Harbor, New York, New York
[8] Department of Biostatistics, Arkansas Children's Hospital Research Institute, Little Rock, Arkansas

TABLE II. Transmethylation and Transsulfuration Metabolites in Autistic Cases and Controls

	Control[a] (n = 73)	Autistic[a] (n = 80)	*P*-value
Methionine (μmol/L)	28.0 ± 6.5	20.6 ± 5.2	<0.0001
SAM (nmol/L)	93.8 ± 18	84.3 ± 11	<0.0001
SAH (nmol/L)	18.8 ± 4.5	23.3 ± 7.9	<0.0001
SAM/SAH ratio	5.5 ± 2.8	4.0 ± 1.7	<0.0001
Adenosine (μmol/L)	0.19 ± 0.13	0.28 ± .13	0.001
Homocysteine (μmol/L)	6.0 ± 1.3	5.7 ± 1.2	0.03v
Cystathionine (μmol/L)	0.19 ± 0.1	0.24 ± 0.1	<0.0001
Cysteine (μmol/L)	207 ± 22	165 ± 14	<0.0001
Cysteinylglycine (μmol/L)	39.4 ± 7.3	38.9 ± 11	0.78
Total GSH (μmol/L)	7.53 ± 1.7	5.1 ± 1.2	<0.0001
Free GSH (μmol/L)	2.2 ± 0.9	1.4 ± 0.5	<0.0001
GSSG (μmol/L)	0.24 ± 0.1	0.40 ± 0.2	<0.0001
Total GSH/GSSG ratio	28.2 ± 7.0	14.7 ± 6.2	<0.0001
Free GSH/GSSG ratio	7.9 ± 3.5	4.9 ± 2.2	<0.0001

SAM, S-adenosylmethionine; SAH, S-adenosylhomocysteine; GSH, glutathione; GSSG, glutathione disulfide.
[a]Means ± SD.

Environmental Health Perspectives • VOLUME 115 | NUMBER 2 | February 2007

Succimer Chelation Improves Learning, Attention, and Arousal Regulation in Lead-Exposed Rats but Produces Lasting Cognitive Impairment in the Absence of Lead Exposure

Diane E. Stangle,[1] Donald R. Smith,[2] Stephane A. Beaudin,[3] Myla S. Strawderman,[3] David A. Levitsky,[1,3] and Barbara J. Strupp[1,3]

[1]Department of Psychology, Cornell University, Ithaca, New York, USA; [2]Department of Environmental Toxicology, University of California, Santa Cruz, California, USA; [3]Division of Nutritional Sciences, Cornell University, Ithaca, New York, USA

BACKGROUND: There is growing pressure for clinicians to prescribe chelation therapy at only slightly elevated blood lead levels. However, very few studies have evaluated whether chelation improves cognitive outcomes in Pb-exposed children, or whether these agents have adverse effects that may affect brain development in the absence of Pb exposure.

OBJECTIVES: The present study was designed to answer these questions, using a rodent model of early childhood Pb exposure and treatment with succimer, a widely used chelating agent for the treatment of Pb poisoning.

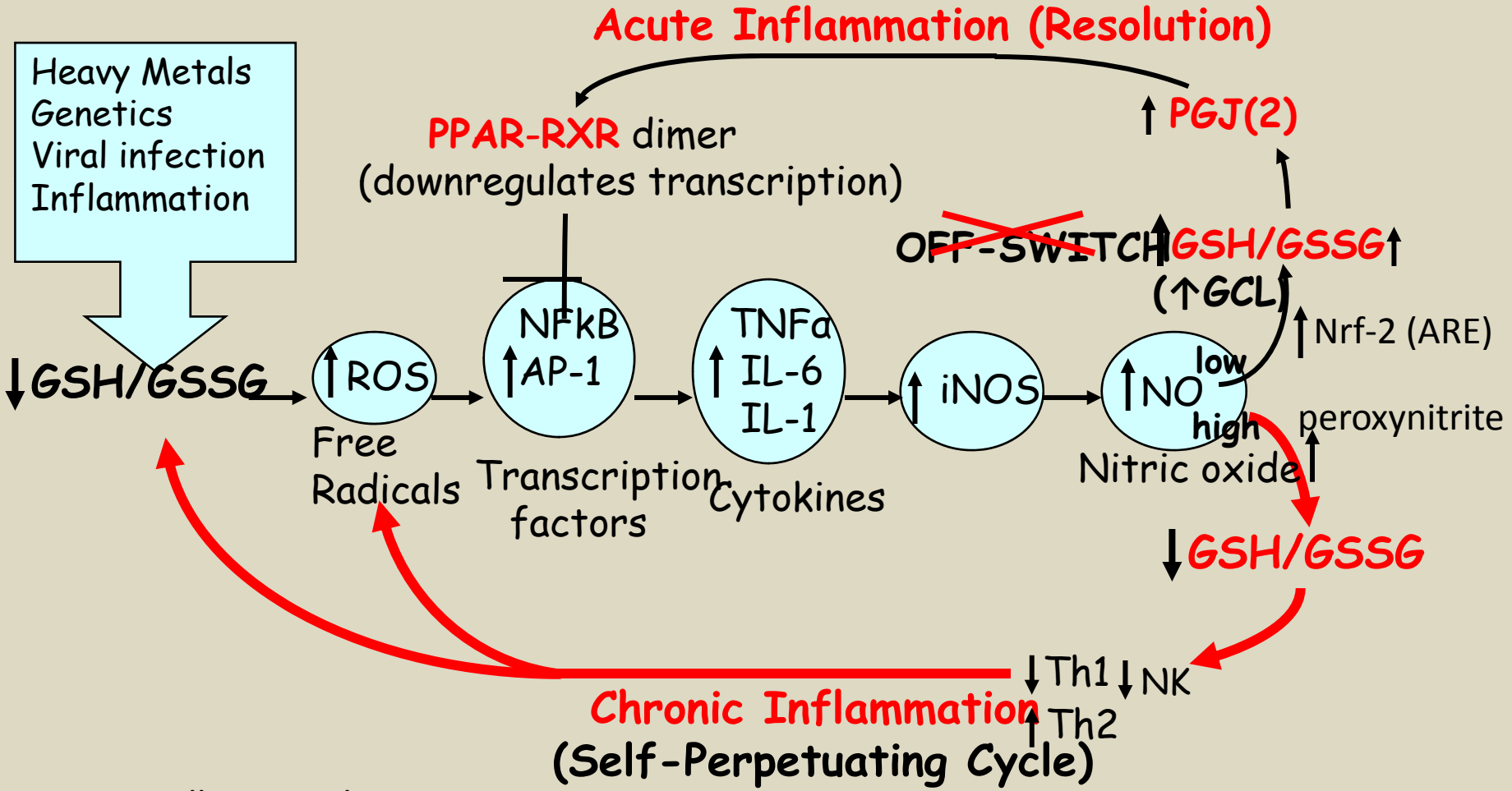
RESULTS: Pb exposure produced lasting impairments in learning, attention, inhibitory control, and arousal regulation, paralleling the areas of dysfunction seen in Pb-exposed children. Succimer treatment of the Pb-exposed rats significantly improved learning, attention, and arousal regulation, although the efficacy of the treatment varied as a function of the Pb exposure level and the specific functional deficit. In contrast, succimer treatment of rats not previously exposed to Pb produced lasting and pervasive cognitive and affective dysfunction comparable in magnitude to that produced by the higher Pb exposure regimen.

CONCLUSIONS: These are the first data, to our knowledge, to show that treatment with any chelating agent can alleviate cognitive deficits due to Pb exposure. These findings suggest that it may be possible to identify a succimer treatment protocol that improves cognitive outcomes in Pb-exposed children. However, they also suggest that succimer treatment should be strongly discouraged for children who do not have elevated tissue levels of Pb or other heavy metals.

A Possible Model For Autism: DMSA Induced Cysteine Deficiency During Development

- DMSA binds 2 cysteine molecules when it does not bind a metal.
- 90% or more of DMSA is bound to cysteine when excreted in the urine even when mercury or lead are present.
- As demonstrated by Stangle et al (EHP 2007) in animals without lead exposure DMSA induces a lasting cognitive and affective dysfunction.
- It is reasonable to assume the difference is secondary to serious hypocysteinemia: a condition well documented in ASD.

The failure to maintain GSH/GSSG redox balance and to resolve acute inflammatory stress promotes a self-perpetuating cycle of chronic inflammation



Courtesy Jill James PhD

Journal of Autism and Developmental Disorders, Vol. 26, No. 4, 1996

Brief Reports

Brief Report: Dysregulated Immune System in Children with Autism: Beneficial Effects of Intravenous Immune Globulin on Autistic Characteristics[1]

Sudhir Gupta,[2] Sudeepta Aggarwal, and Cathy Heads
Division of Basic and Clinical Immunology, University of California, Irvine

Journal of Nutritional & Environmental Medicine
December 2005; 15(4): 169–176

Taylor & Francis
Taylor & Francis Group

CLINICAL RESEARCH

Improvement in children with autism treated with intravenous gamma globulin

MARVIN BORIS, MD[1], ALLAN GOLDBLATT, PA-C[2] &
STEPHEN M. EDELSON, PhD[3]

[1]*New York University School of Medicine, New York, USA,* [2]*Truro College, New York, USA, and* [3]*Autism Research Institute, 4182 Adams Ave, San Diego, CA 92116, USA*

Medical Hypotheses (2007) 68, 979–987

ELSEVIER

medical hypotheses

http://intl.elsevierhealth.com/journals/mehy

Spironolactone might be a desirable immunologic and hormonal intervention in autism spectrum disorders

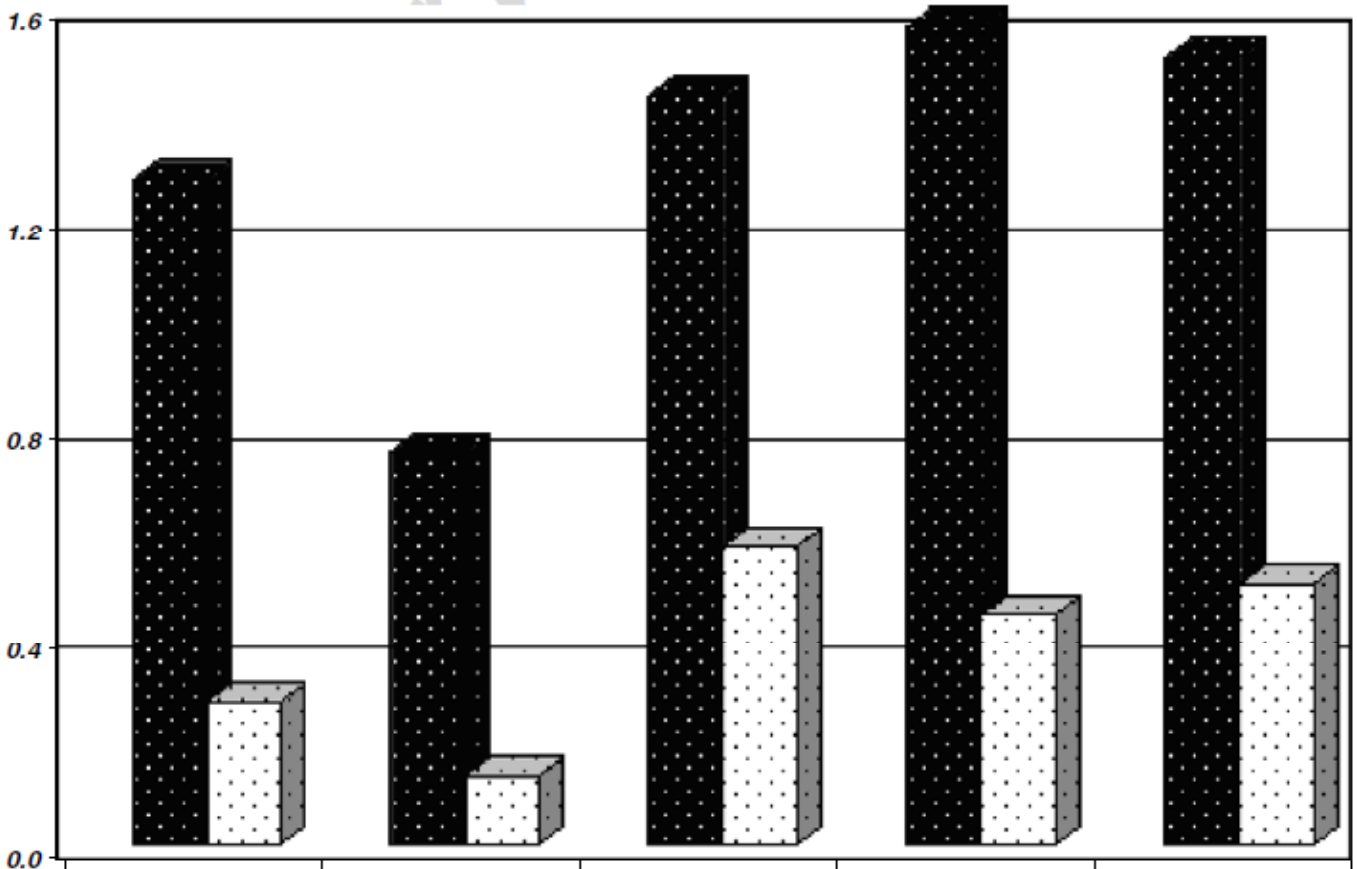
James Jeffrey Bradstreet [a,*], Scott Smith [a], Doreen Granpeesheh [b], Jane M. El-Dahr [c], Daniel Rossignol [d]

[a] *International Child Development Resource Center, Melbourne and Florida Hospital, Celebration, 1688 West Hibiscus Boulevard, Melbourne, FL 32901, United States*
[b] *Center for Autism Related Disorders, Tarzana, CA, United States*
[c] *Tulane University Health Sciences Center, Departments of Pediatrics and Medicine, Section of Pediatric Allergy, Immunology and Rheumatology, New Orleans, LA, United States*
[d] *University of Virginia, Department of Family Medicine, P.O. Box 800729, Charlottesville, VA, United States*

Table 2 Summary of the proposed effects of spironolactone on autism findings

Clinical finding	Autism finding	Effect of spironolactone
Interferon gamma	↑ [19]	↓ [55]
TNF-α	↑ [24,25]	↓ [54,55]
MCP-1	↑ [34]	↓ [54,56]
Inflammation	↑ [27,34]	↓ [53,55]
Oxidative stress	↑ [57]	↓ [62]
Testosterone effects	↑[a] [5–7]	↓ [59]

[a] Elevated in a subset of autistic individuals.



	Irritability	Lethargy	Stereotypy	Hyperactivity	Inappropriate Speech
Pre Spironolactone	1.27	0.75	1.43	1.56	1.50
Post Spironolactone	0.27	0.13	0.57	0.44	0.5

Figure 1 Changes in the ABC subset scores pre- and post-spironolactone at a dose of 2 mg/kg daily for 4 weeks.

Developmental Regression and Mitochondrial Dysfunction in a Child With Autism

ABSTRACT

Autistic spectrum disorders can be associated with mitochondrial dysfunction. We present a singleton case of developmental regression and oxidative phosphorylation disorder in a 19-month-old girl. Subtle abnormalities in the serum creatine kinase level, aspartate aminotransferase, and serum bicarbonate led us to perform a muscle biopsy, which showed type I myofiber atrophy, increased lipid content, and reduced cytochrome *c* oxidase activity. There were marked reductions in enzymatic activities for complex I and III. Complex IV (cytochrome *c* oxidase) activity was near the 5% confidence level. To determine the frequency of routine lab-

Poling JS, Frye RE, Shoffner J, Zimmerman AW.
Developmental regression and mitochondrial dysfunction in a child with autism.
J Child Neurol. 2006 Feb;21(2):170-2

American Journal of Biochemistry and Biotechnology 4 (2): 208-217, 2008
ISSN 1553-3468

Evidence of Mitochondrial Dysfunction in Autism and Implications for Treatment

Daniel A. Rossignol, J. Jeffrey Bradstreet
International Child Development Resource Center, 3800 W. Eau Gallie Blvd., Suite 105,
Melbourne, FL 32934

Abstract: Classical mitochondrial diseases occur in a subset of individuals with autism and are usually caused by genetic anomalies or mitochondrial respiratory pathway deficits. However, in many cases of autism, there is evidence of mitochondrial dysfunction (MtD) without the classic features associated with mitochondrial disease. MtD appears to be more common in autism and presents with less severe signs and symptoms. It is not associated with discernable mitochondrial pathology in muscle biopsy specimens despite objective evidence of lowered mitochondrial functioning. Exposure to environmental toxins is the likely etiology for MtD in autism. This dysfunction then contributes to a number of diagnostic symptoms and comorbidities observed in autism including: cognitive impairment, language deficits, abnormal energy metabolism, chronic gastrointestinal problems, abnormalities in fatty acid oxidation, and increased oxidative stress. MtD and oxidative stress may also explain the high male to female ratio found in autism due to increased male vulnerability to these dysfunctions. Biomarkers for mitochondrial dysfunction have been identified, but seem widely under-utilized despite available therapeutic interventions. Nutritional supplementation to decrease oxidative stress along with factors to improve reduced glutathione, as well as hyperbaric oxygen therapy (HBOT) represent supported and rationale approaches. The underlying pathophysiology and autistic symptoms of affected individuals would be expected to either improve or cease worsening once effective treatment for MtD is implemented.

Medscape Medical News

Mitochondrial Dysfunction May Play a Role in Autism Spectrum Disorders Etiology

Caroline Cassels

April 15, 2008 (Chicago, IL) — New research suggests mitochondrial dysfunction may play a role in the etiology of autism spectrum disorders (ASD) in a subset of this patient population.

Here at the American Academy of Neurology 60th Annual Meeting, a retrospective analysis of 41 children with ASD who were being evaluated for suspected mitochondrial disease showed that 32 (78%) had defects in skeletal muscle oxidative phosphorylation (OXPHOS) enzyme function and 29 of 39 (74%) harbored abnormalities in the OXPHOS proteins.

"We're very excited by these findings, and, based on these results, we will continue to pursue this [mitochondrial dysfunction] as a potential cause in a segment of the autistic population," principal investigator John Shoffner, MD, owner of Medical Neurogenetics, in Atlanta, Georgia, told *Medscape Neurology & Neurosurgery*.

Utilizando bio-marcadores podemos determinar que esta mal en el niño.
Utilizo laboratorios especiales para medir problemas comunes: oxidación, inflamación, y toxicidad

3 year old boy with autism

Muchacho de 3 años con autismo

Oxidative Mitochondrial Dysfunction Biomarkers and Treatment

- Isoprostane = oxidized fatty acid membranes
- 8 OHG = oxidized RNA
- Biopterin = oxidation due to inflammation
- Neopterin = immune activation which will lead to oxidation
- Porphyrins = coproporphyrin may rise from oxidation not just metal related events.
- Ammonia & lactic acid link to mito dysfunction
- Carnitine Profile = fuel for mitochondria
- Dysbiosis markers may reflect on these issues

Increased excretion of a lipid peroxidation biomarker in autism.

Ming X, Stein TP, Brimacombe M, Johnson WG, Lambert GH, Wagner GC.
Department of Neurosciences, UMDNJ-New Jersey Medical School, Newark, 07103, USA.

Prostaglandins Leukot Essent Fatty Acids. 2005 Nov;73(5):379-84.

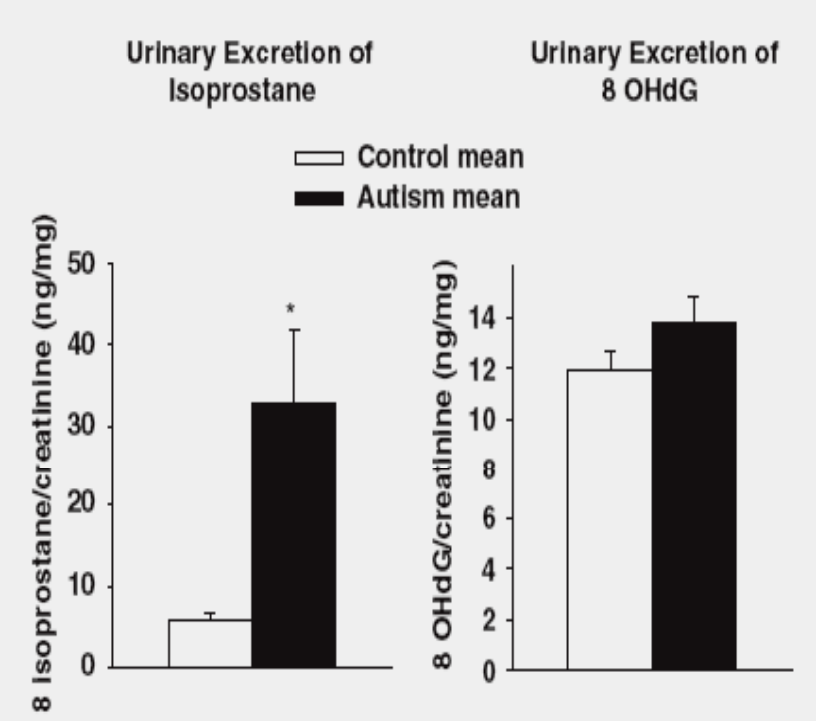


Fig. 1. Urinary excretion of isoprostane and 8-OHdG in children with autism and controls. *$P < 0.05$, Student's t-test.

Immune/Gut Case male age 3

Membrane Oxidative Damage

Urinary IsoprostaneF2-alpha

LC/MS-MS-immunoaffinity cartrige extraction -deuterated standard

8-iso-PGF2 alpa	**618** ng/gCr	80-160

Increased oxidative stress damage

Immune/Gut Case male age 3

02/01/2008

DNA Oxidative Stress

		reference range
8OHdG	**26** nmole/gCr	12-25

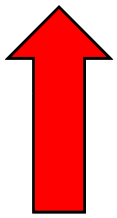
urinary 8-hydroxy deoxyguanosine

Moderate elevated urinary 8OHdG, reflecting mildly increased DNA oxidative damage

In Children 3-9 years old, urinary 8OHdG is 25% higher than in adults (Bogdanov et al, Free Radical Biol. Med 27, 647-686, 1999)

RNA Oxidative Stress

8 OHG	**123** nmole/gCr	20-40



urinary 8-hydroxy guanosine

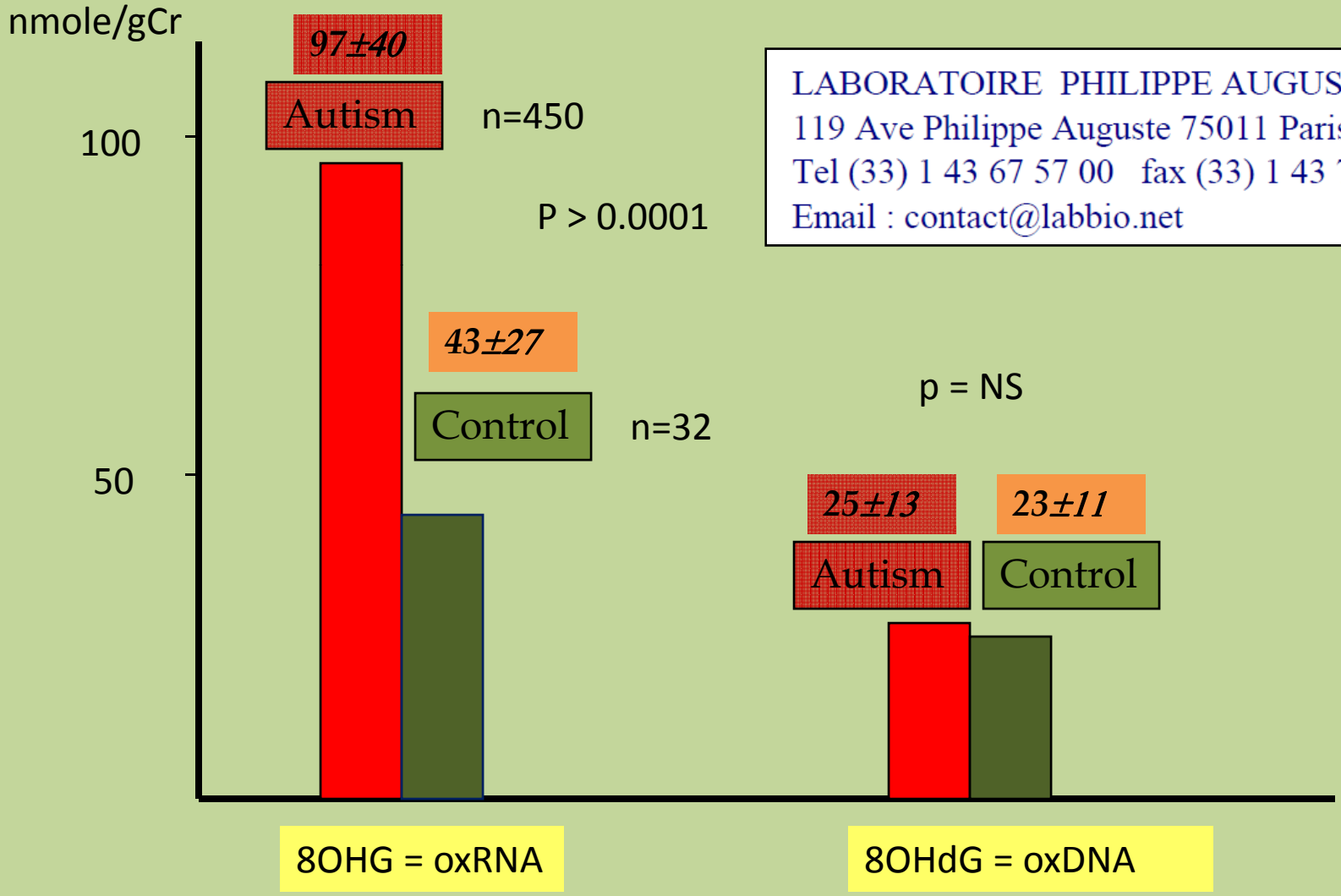
strongly increased urinary 8OG, reflecting high RNA oxidative damage

RNA/DNA

8OHG/8OHdG	**4,7**	<2

urinary creatinin **955** mg/l

DNA and RNA Oxidative Markers preliminary results in 110 Children w/Autism (age = 2-11 years old)



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Email : contact@labbio.net

Antioxidant Effect per 1 gram of whole food

Muscadine Grape Seed**	559
Acai*	387
Goji Berry*	253
Noni*	151
Pomegranates*	105
Raspberries*	82
Blueberries*	77
Red Grapes*	74
Prunes*	57
Cherries*	67
Strawberries*	36

*Antioxidant Capacities of Foods. J. Agric. Food Chem., Vol. 52, No. 12, 2004 4027

*Wu X, Beecher GR, Holden JM, Haytowitz DB, Gebhardt SE, Prior RL, J Agric Food Chem. "Lipophilic and hydrophilic antioxidant capacities of common foods in the United States." 2004 Jun 16;52(12):4026-37

Gastrointestinal Microflora Studies in Late-Onset Autism

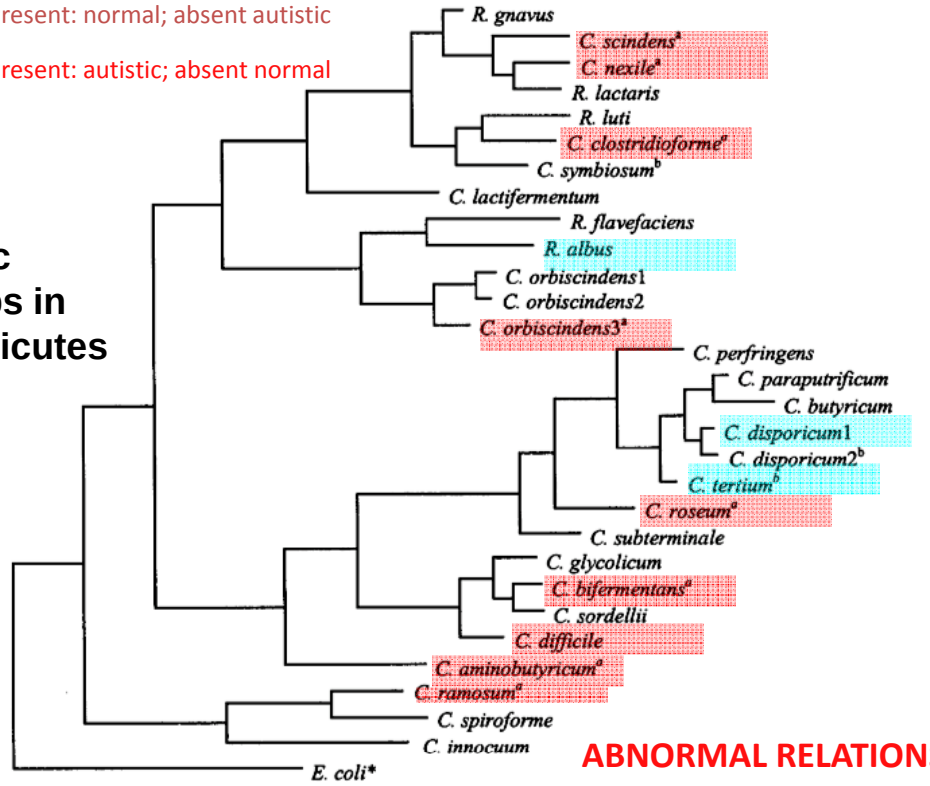
Clinical Infectious Diseases 2002;35(Suppl 1):S6–16

Sydney M. Finegold,[1,4,5] Denise Molitoris,[2] Yuli Song,[2] Chengxu Liu,[2] Marja-Liisa Vaisanen,[2] Ellen Bolte,[6] Maureen McTeague,[3] Richard Sandler,[6] Hannah Wexler,[2,5] Elizabeth M. Marlowe,[2,5] Matthew D. Collins,[10] Paul A. Lawson,[10] Paula Summanen,[2] Mehmet Baysallar,[2] Thomas J. Tomzynski,[2] Erik Read,[2] Eric Johnson,[7] Rial Rolfe,[8] Palwasha Nasir,[11] Haroun Shah,[11] David A. Haake,[1,5] Patricia Manning,[9] and Ajay Kaul[9]

Present: normal; absent autistic

Present: autistic; absent normal

Phylogenetic Relationships in the Gut Firmicutes



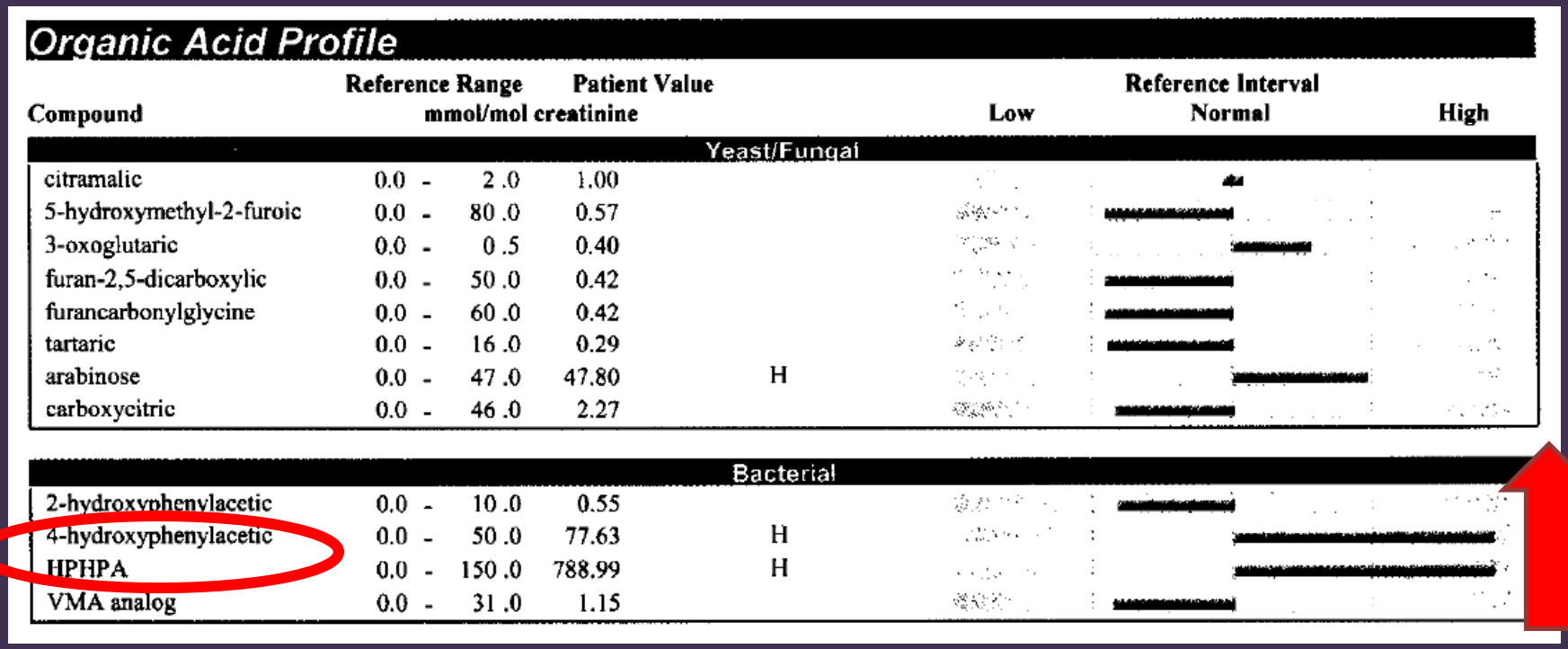
Possible pathways for bacteria-related autism.

Immune-mediated
Toxin
Toxic metabolic product(s)
p-cresol and phenols
Casomorphin, gliadomorphin, and endorphins
Products required for sulfation (e.g., glycosaminoglycans and sulfotransferases) or interfering with sulfation (sulfatase and sulfate-reductase)
Indole derivatives, including serotonin and indolylacryloyl glycine
Naphthalene derivatives
Naphtha derivatives
Mercury (especially methyl mercury) or other metallic ions
Interferons and cytokines

ABNORMAL RELATIONSHIPS IN FIRMICUTES IN AUTISM!

Figure 1. Dendrogram showing the interrelationships within the *Clostridium* and *Ruminococcus* species isolated from autistic and control children's stool specimens. The bar denotes 1% sequence divergence. The asterisk (*) denotes the outgroup standard. [a]*Clostridium* species isolated only from the stool specimens of children with autism. *Clostridium cocleatum* is not shown in this figure because the sequence data are not available. [b]*Clostridium* species isolated only from the stool specimens of control children

Clostridia and Bacteria



Organic Acid Profile

Compound	Reference Range mmol/mol creatinine	Patient Value		Reference Interval Low / Normal / High
Yeast/Fungal				
citramalic	0.0 - 2.0	1.00		
5-hydroxymethyl-2-furoic	0.0 - 80.0	0.57		
3-oxoglutaric	0.0 - 0.5	0.40		
furan-2,5-dicarboxylic	0.0 - 50.0	0.42		
furancarbonylglycine	0.0 - 60.0	0.42		
tartaric	0.0 - 16.0	0.29		
arabinose	0.0 - 47.0	47.80	H	
carboxycitric	0.0 - 46.0	2.27		
Bacterial				
2-hydroxyphenylacetic	0.0 - 10.0	0.55		
4-hydroxyphenylacetic	0.0 - 50.0	77.63	H	
HPHPA	0.0 - 150.0	788.99	H	
VMA analog	0.0 - 31.0	1.15		

Clostridia and Bacteria: male age 3

Metabolites indicator of gut bacterial proliferation

Paracresol	0,2	<6,3
Benzoate	727,9	<5,5
3,4-diOH benzoate	6,8	<2,4
4-OH benzoate	12,8	<7,3
Hippurate	261	30-160
4OHPhenylacetate	89	30-60
3, 4OH PHENYL PROPENOATE	23,21	<10
2OH PHENYLPROPIONATE	0,05	<1
3,4 OH PHENYLPROPIONATE	1,0	<0,12
Indole-3-propionate	0,2	<2
Tricarballylate	5,2	<1
Glycerate	38,4	<10

Immune/Gut Case male age 3

Immune system Methode : HPLC

	patient µmole / mole Cr	reference	result
urinary Neopterine (NEO)	1147	110-180	increased cellular immunity activation
Urinary Biopterin	434		
Biopeterin / Neopterin	0,4	>1,5	very low ratio

Gut Immunology

Analyte	Result	Reference Range
3. Eosinophil Protein X	4.0	<= 7.0 mcg/g
4. Calprotectin	122	<= 50 mcg/g

Yeast Biomarkers: male age 3

Fungal Dysbiosis Markers

Tartarate	21,1	<20
Citramalate	12,8	<10
beta Ketoglutarate	3,5	<11,2
Arabinose	0,25	<1,3
Arabinitol	0,89	<0,5

Energy Production Impairment – Altered Citric Acid (Kreb's) Cycle: Male age 3

Tricarboxylic cycle energy production metabolites

citrate	79	250-750
isocitrate	190	<110
cis aconitate	110	<75
alpha ketoglutarate	3,3	<10
succinate	***64***	<10
fumarate	0,4	0,2-1,2
malate	3,8	
lactate	332,8	<50
pyruvate	1,9	<5

Maladaptive NT Compensation

06/10/2008

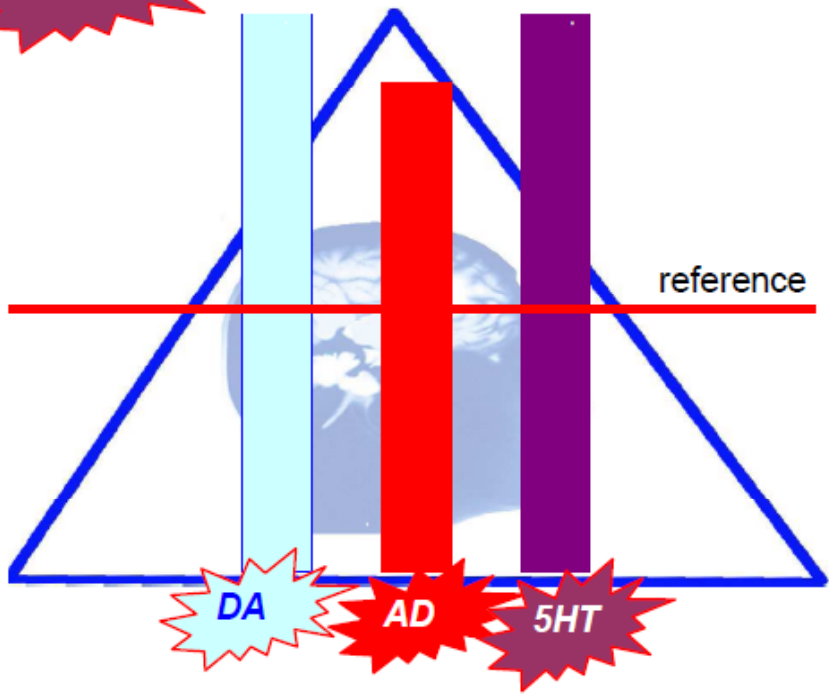
Neurotransmitter metabolism

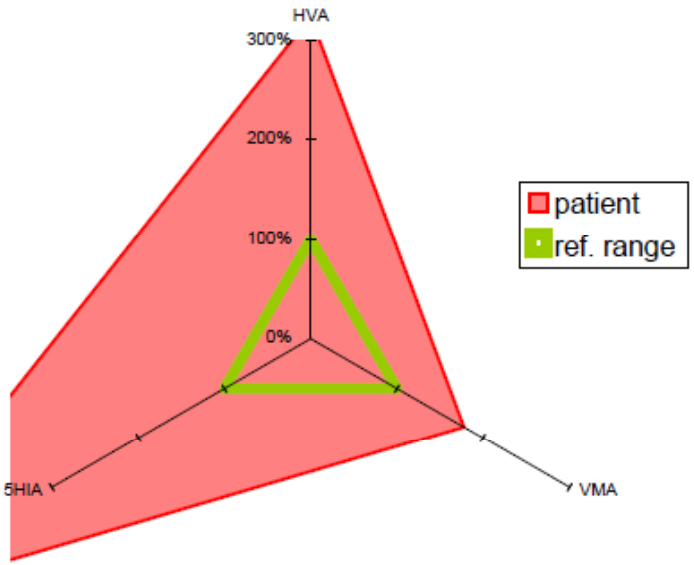
catabolites	patient	reference	Intrepretation
hva	9,68	2,5-3,5	Sharply increased Dopaminergic activity
vma	5,3	2,5-3,5	Sharply increased Adrenergic activity
5hia	20,5	3,0-4,5	Sharply increased Serotoninergic activity

DA

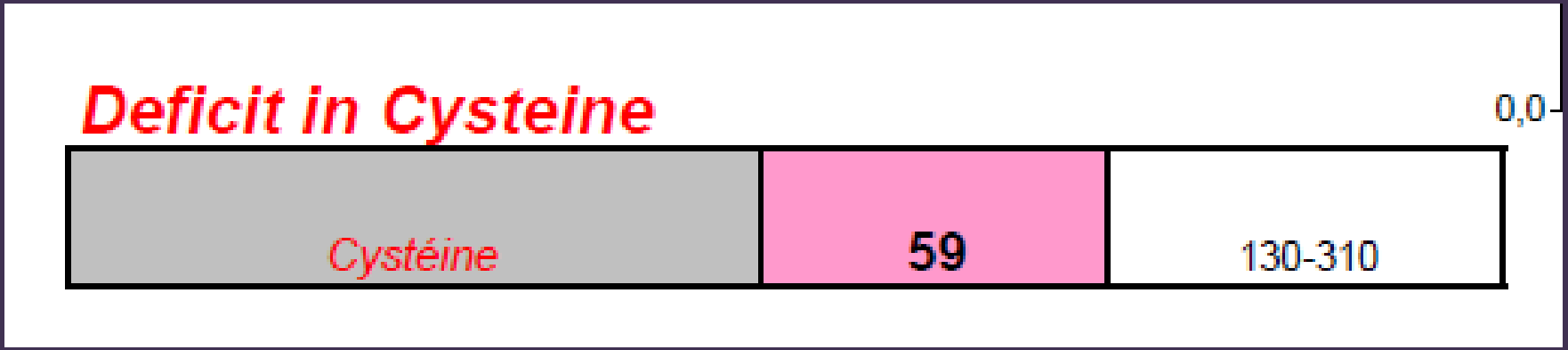
AD

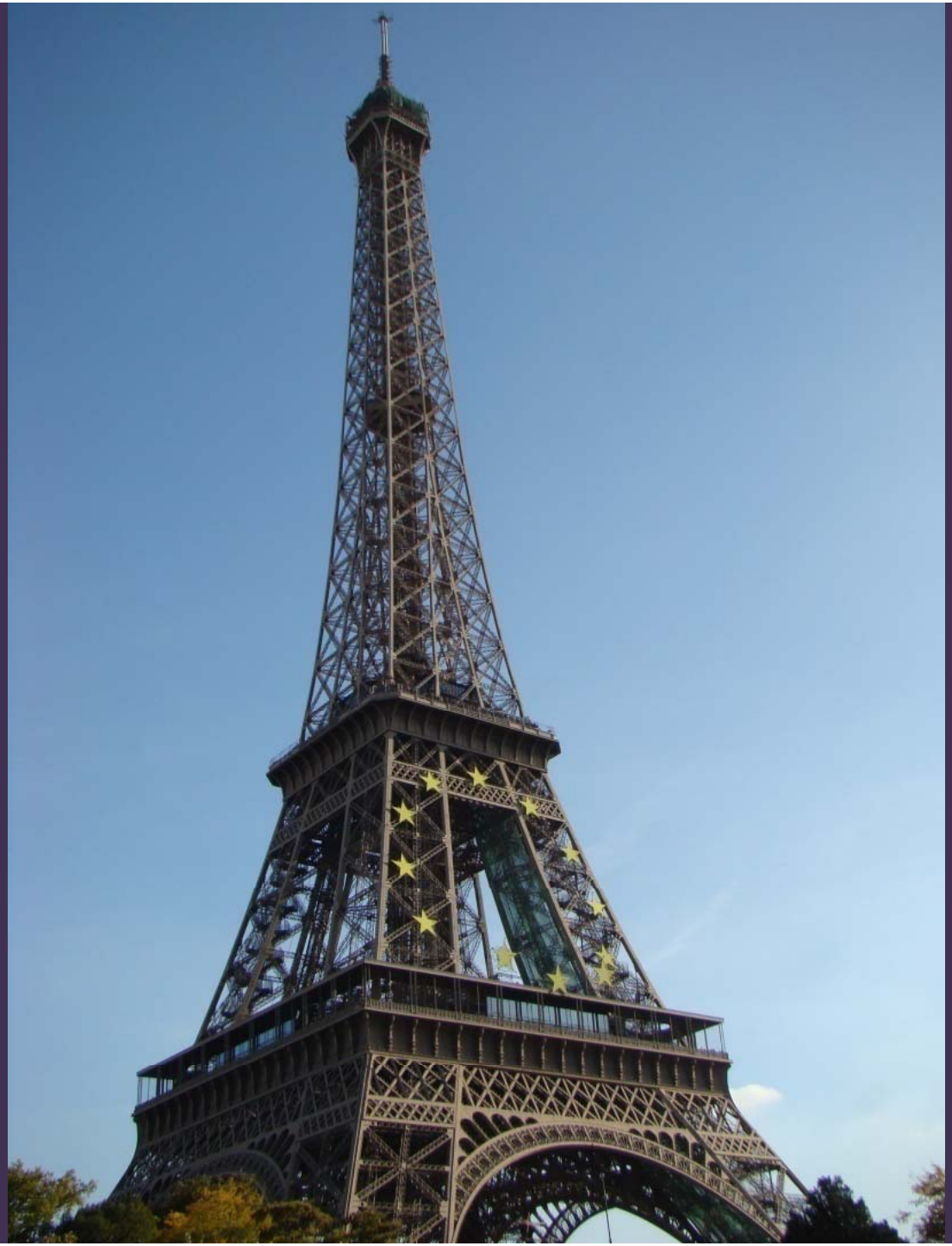
5HIA





Cysteine Deficiency : male age 3



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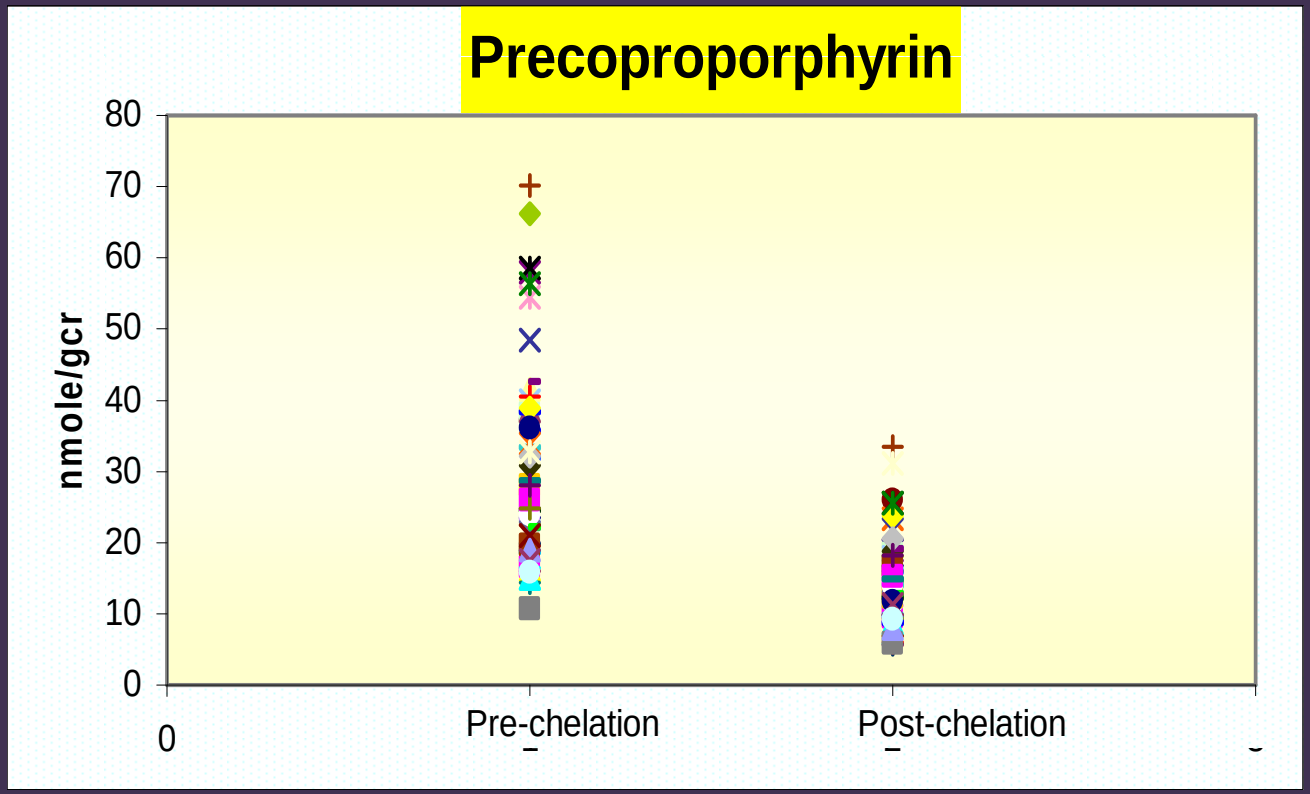
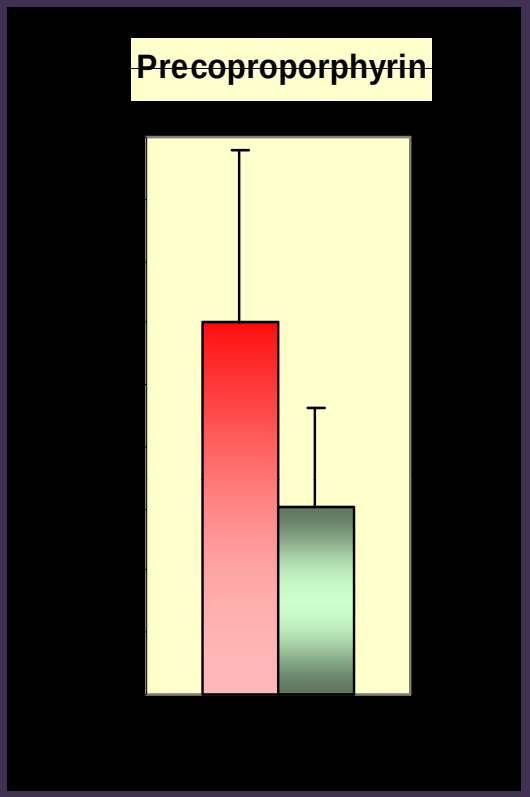
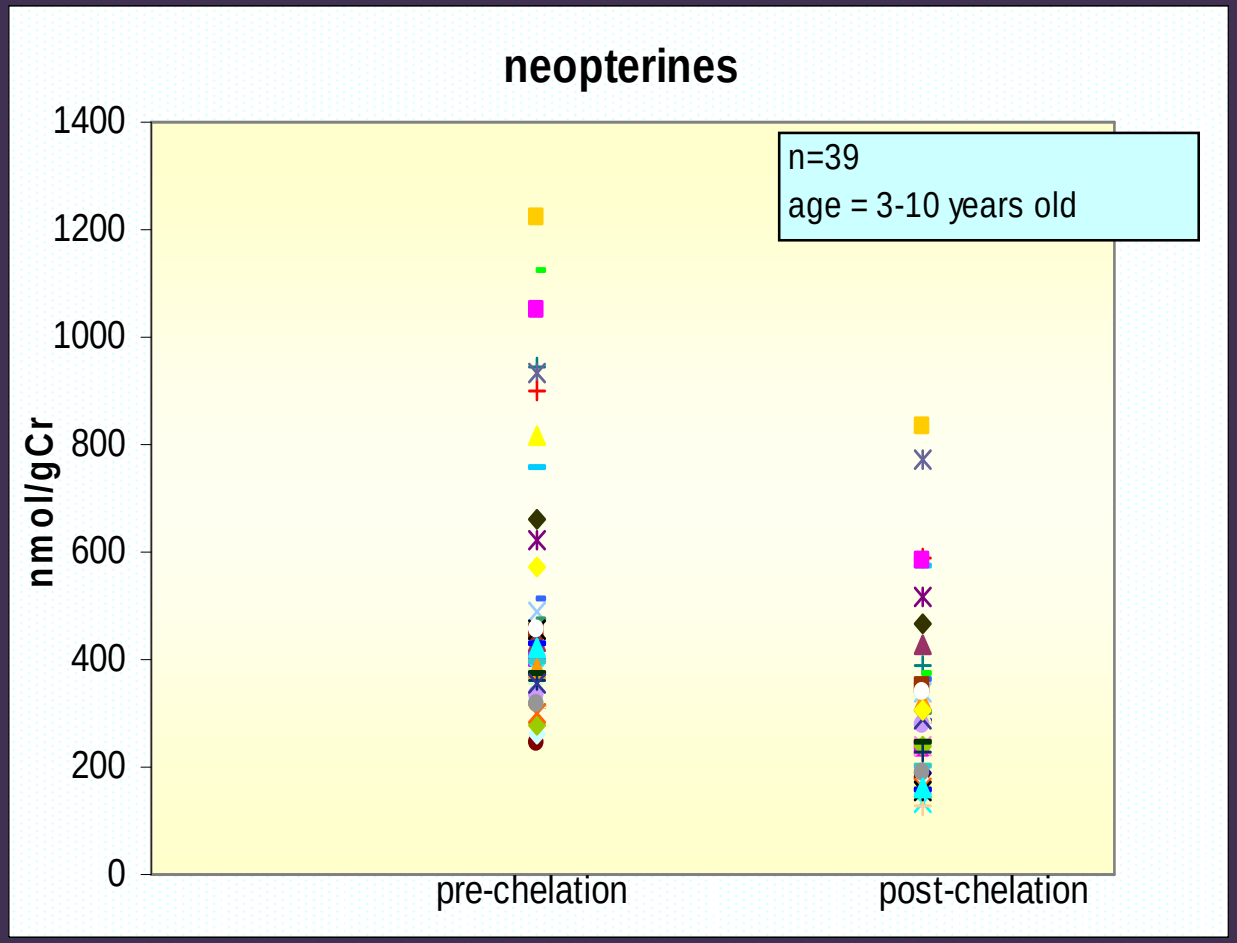
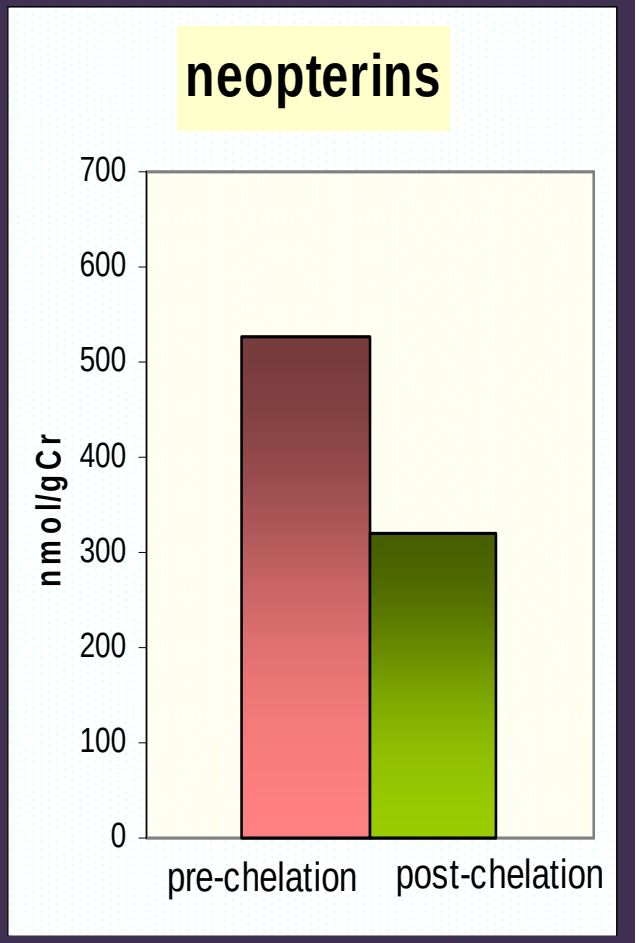




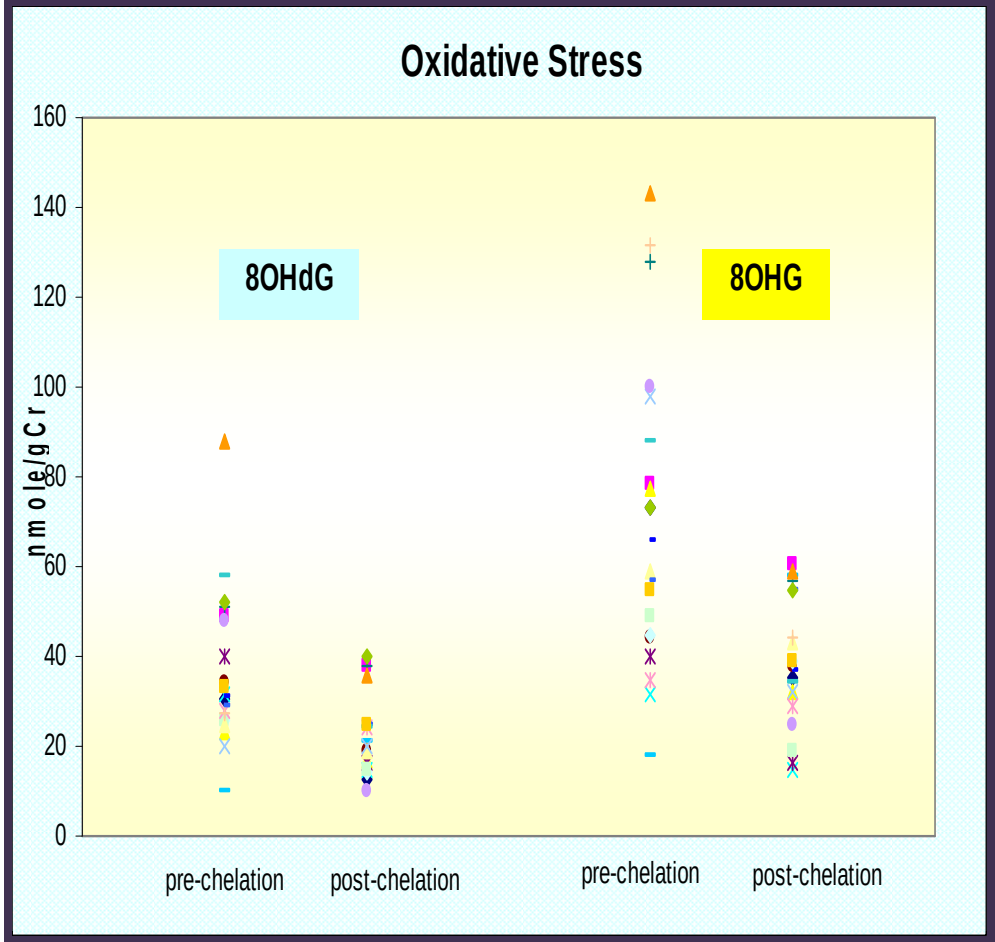
n=190
age = 1-12 years old

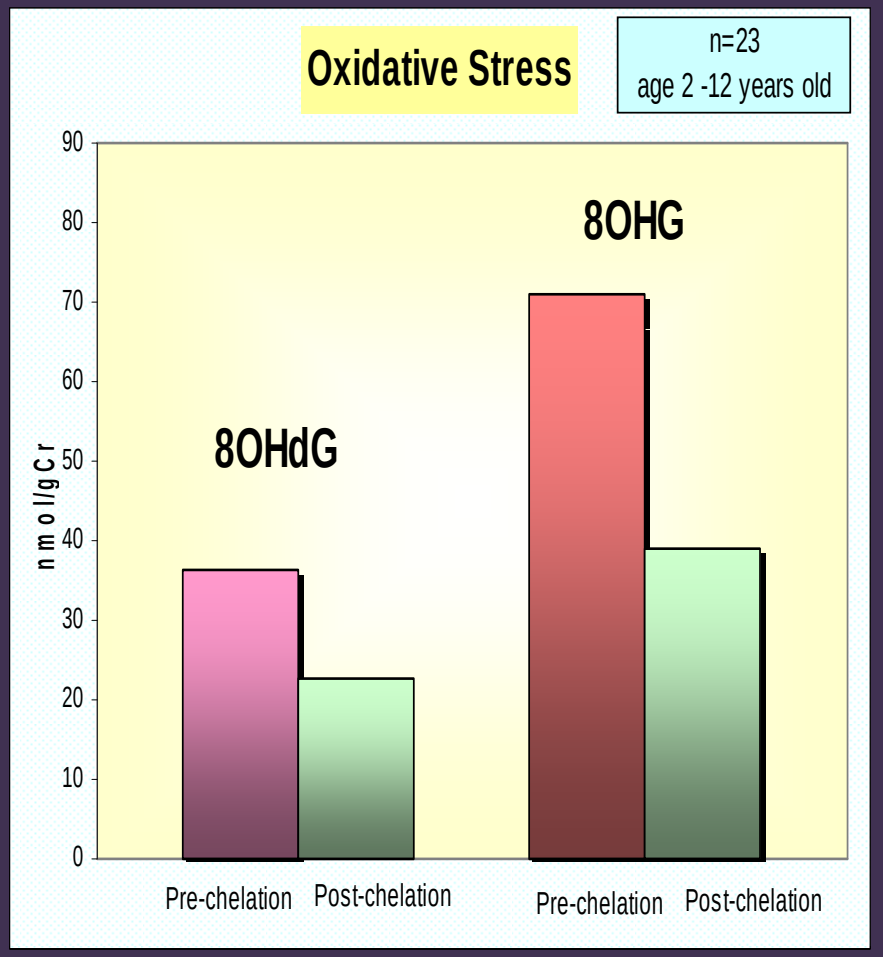
At the same time, associated with Porphyrins reduction, decrease inflammation, as shown by reduction in macrophage activation issued Neopterins.

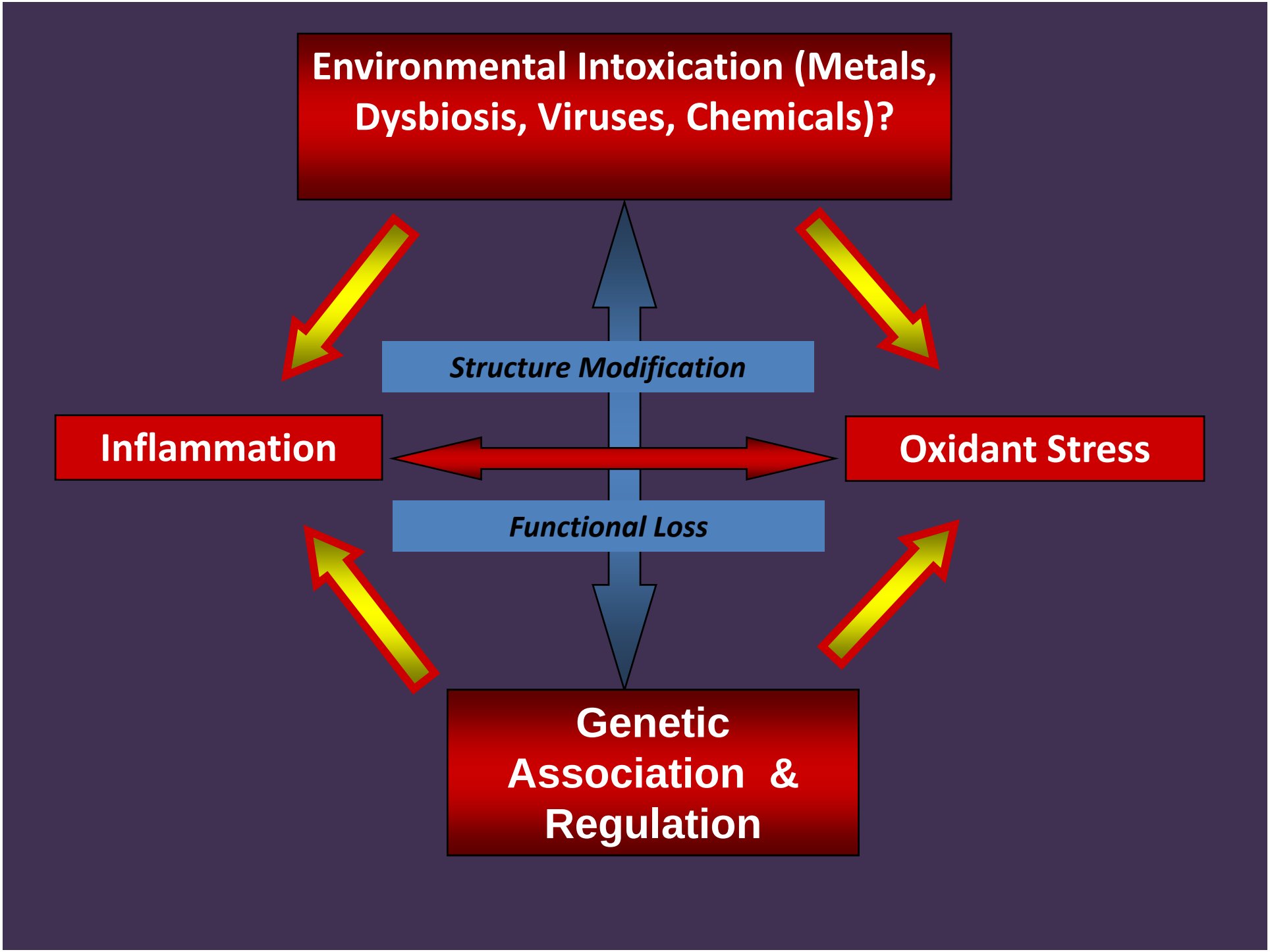




And decrease oxidative stress , inside cell nucleus and through cytosol, as shown by 8-oxo-Deoxyguanosine (8OHdG) and 8-oxo-Guanosine(8OHG) reduction.

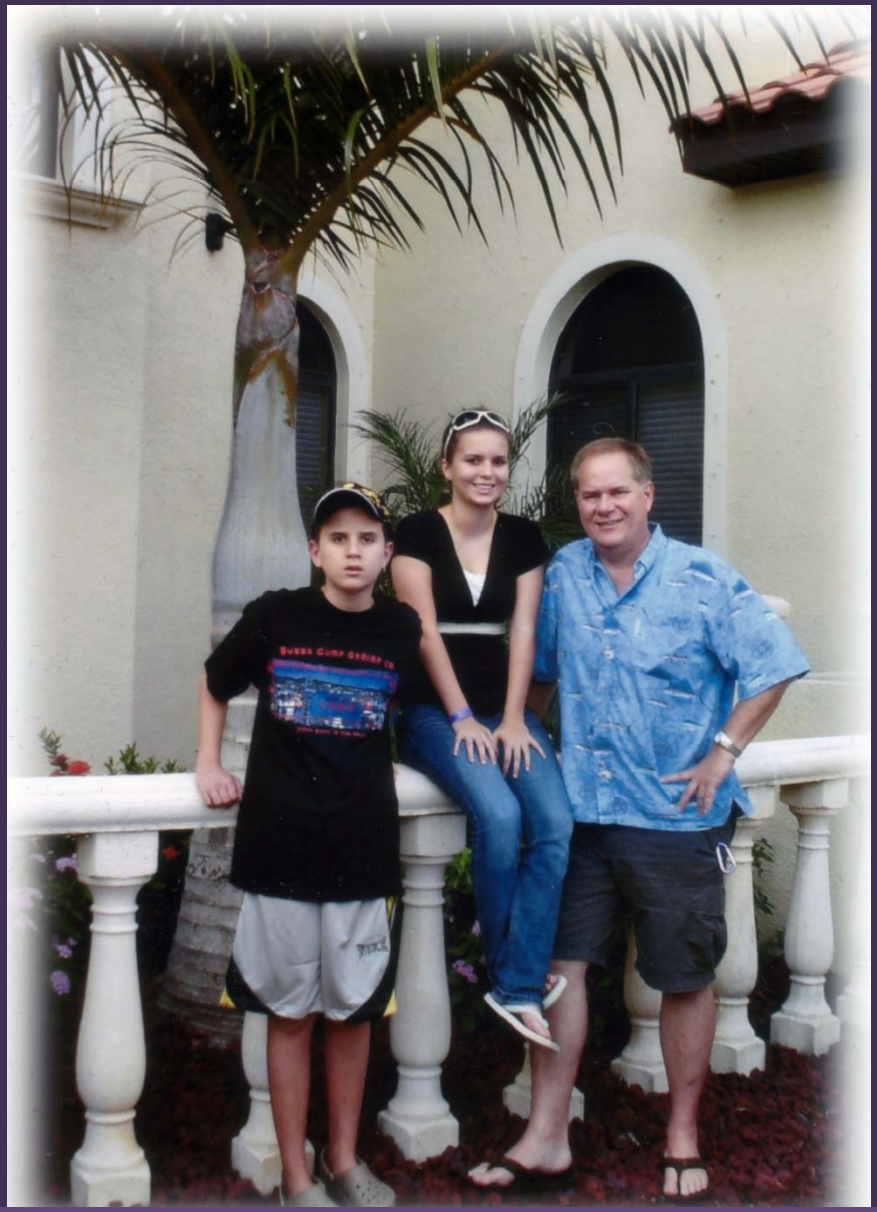





Environmental Intoxication (Metals, Dysbiosis, Viruses, Chemicals)?
Structure Modification
Inflammation
Oxidant Stress
Functional Loss
Genetic Association & Regulation

El autismo puede ser tratado. Hay esperanza. Muchos niños se están recuperando.

Trate la inflamación, la tensión oxidativa, y quite la candida y los clostridiums (bacterias malas) de los intestinos.



Ruego a Dios bendigo le y a sus niños.
Mucho gracias.