ADVANCED NUTRIENT THERAPIES FOR BEHAVIOR DISORDERS, ADHD, AND AUTISM

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Walsh Research Institute

- Nonprofit organization
- Expertise in behavior disorders, ADHD, autism, depression, schizophrenia, bipolar disorder, and Alzheimer's
- International physician training
- Research
Origins of Behavior Research

- Volunteer at Stateville Prison in Illinois
- Coordinated 125 volunteers,
- Prisoner visitation,
- Aid to abused prisoners,
- Chess league,
- Prison Art Shows,
- Ex-Offender program.
Nature or Nurture?

- The ex-offender program involved close contact with families that had produced a criminal,

- Many criminals had been raised in homes with siblings who became law-abiding, productive citizens.

- Many parents reported their future criminal was alarmingly “different” from birth – oppositional, defiant, behavior explosions, cruel to animals, fascination with fire, obsession with weapons.
1975 Question: What is the Cause of a Severe Behavior Disorder?

- Tabula rasa (blank slate) theory: dominance of life experiences,

- Adoption & twin studies indicate inborn predisposition for schizophrenia, bipolar disorder, clinical depression, autism,

- New focus on neurotransmitters, receptors, chemical imbalances for mental disorders.
Metal-Metabolism Abnormalities

- Chemistry studies of convicted felons initiated at Argonne National Laboratory.

- Study of death row residents & other violent offenders revealed unusual levels of Cu, Zn, Pb, Cd, Mn, Na, K, Li, Co in hair tissues.

- Similar chemical imbalances found in behavior disordered children.
Argonne Sibling Experiment

**Test Group**
24 violent males
Age range: 8-18 years
Multiple violent incidents

**Controls**
24 brothers, living in same domicile
Age range: 8-18 years
No violence or delinquency
Results of Sibling Experiment

- Most controls exhibited expected levels of metals;

- Most violent subjects had abnormal levels of Cu, Zn, Mn, Pb, Cd, Na, K, Ca.

- Two distinctive patterns in violent subjects:
  - Type A: Elevated Cu, Cd, Pb
    Depressed Zn, Na, K, Li, Co
  - Type B: Elevated Na, K, Cd, Pb, Mn
    Depressed Cu, Zn, Li, Co
Type A Subjects: Episodic violence, genuine remorse, high incidence of ADHD, LD, and academic underachievement.

Type B Subjects: Oppositional, defiant, cruel, assaultive, high pain threshold, fascination with fire, obsession with weapons.
Double-Blind, Controlled Field Test (n=192)

**Test Group:** 96 extremely violent prison residents, ex-convicts, and assaultive children.

**Controls:** 96 non-violent males, matched for age and socioeconomic level in childhood.
Field Test Results

- Results of sibling experiment confirmed
- Type A & B patterns predominate in violent cohort; Most controls exhibit expected trace metal levels.
- $P < 0.001$

Conclusion:

Most violent persons exhibit abnormal metal metabolism.
Early experiments led to clinical treatments for BD and ADHD

- Carl Pfeiffer and Walsh developed test protocols and early nutrient therapies for ex-convicts and violent children.

- Hundreds of reports of improved behaviors and academics.

- More than 10,000 BD patients and 5,000 ADHD patients treated under this system.
Massive Chemistry Database for Behavior Disorders and ADHD

- More than 1.5 million blood/urine/tissue test results for persons diagnosed with behavior disorders and/or ADHD.

- Striking chemistry differences between these populations and the rest of society.
High-Incidence Imbalances in ADHD and Behavior Disorders

- Overmethylation
- Undermethylation
- Zinc Deficiency
- Copper Overload
- Folate Deficiency or Overload
- Pyrrole Disorder
- Toxics
- Glucose Dyscontrol
- Malabsorption
Forensics Cases

- James Oliver Huberty
- Charles Manson
- Richard Speck
- Henry Lee Lucas
- Patrick Ryan
- Patrick Sherrill
- Ludvig van Beethoven
- Twenty other notable cases
Examples of Forensics Findings

- James Huberty: Cd poisoning; mild Type B
- Charles Manson: Severe Type B chemistry
- Richard Speck: Type A chemistry
- Henry Lee Lucas: Severe Type B chemistry
- Patrick Ryan: No abnormalities detected
- Patrick Sherrill: Pb poisoning, Type A
- Beethoven: Severe Pb poisoning.
LEAD LEVELS IN BEETHOVEN SAMPLES

X-ray fluorescence intensity of Pb in LVB bone sample and control

X-ray Fluorescence Intensity of Pb in LVB hair sample and control
Biochemical Individuality

- Humans exhibit great diversity in blood and brain chemistry.

- Because of genetics and epigenetics, most people are deficient in several nutrients and overloaded in others.
Nutrient Deficiencies that Impair Brain Function

- Zinc
- Methionine
- Folic Acid
- Vitamins B-6 and B-12
- Niacin/Niacinamide
- DHA, EPA, AA (essential fatty acids)
- Antioxidants: Se, GSH, Vitamins C & E, etc.
- Chromium
Nutrient Overloads that Impair Brain Function

- Copper
- Folic Acid
- Iron
- Methionine, SAMe
- Toxics: Lead, Mercury, Cadmium, etc.

**NOTE:** Multiple vitamin-mineral supplements are usually ineffective for BD, ADHD, and can cause harm.
Individualized Nutrient Therapy

- Medical history and review of symptoms,
- Special blood/urine lab tests,
- Diagnosis of chemical imbalances,
- Prescribed nutrient program aimed at normalizing brain chemistry.
Frequently Asked Questions

1. How can vitamins, minerals, or amino acids significantly help an ADHD or behavior-disordered child?

2. Don’t you really need a powerful drug to get the job done?
The Power of Nutrients

1. Neurotransmitter synthesis
2. Epigenetic regulation of gene expression
3. Reuptake processes at synapses
4. Antioxidant Protection
The Brain Is a Chemical Factory

- Serotonin, dopamine, and other NT’s are synthesized in the brain.

- The raw materials for NT synthesis are nutrients: vitamins, minerals, and amino acids.

- A genetic or epigenetic imbalance in a nutrient needed for NT synthesis or regulation can result in serious mental problems.
Serotonin Synthesis

5-Hydroxytryptophan → Serotonin

L-Amino Acid Decarboxylase
PLP (Vitamin B-6)

+ CO₂
Norepinephrine Synthesis

DOPAMINE

\[
\text{CH}_2 - \text{CH}_2 - \text{NH}_2
\]

Dopamine β-Hydroxylase

\[
\text{Cu}^{++}, \text{ Vitamin C, O}_2
\]

NOREPINEPHRINE

\[
\text{CH} - \text{CH}_2 - \text{NH}_2
\]
Dopamine Synthesis

L-DOPA → DOPAMINE

L-Amino Acid Decarboxylase
PLP (Vitamin B-6)

+ CO₂
Pyrrole Disorder

- Double deficiency of B-6 and Zinc
- Reduced Serotonin, Dopamine, GABA
- Depletion of GSH, MT, Cys, SOD, Catalase
- Supplements of B-6 and zinc can normalize pyrrole levels, often resulting in elimination of symptoms and the need for psychiatric medication.
Methylation and Mental Health

- Methyl is a dominant factor in epigenetic processes,

- Methyl has a powerful impact on neurotransmitter activity at synapses,

- More than 50% of ADHD and BD persons exhibit a serious methylation disorder,
Epigenetics

- >20,000 genes in every cell’s DNA, each capable of producing a specific protein,
- Liver, skin, brain, and other tissues require a unique combination of proteins,
- During pregnancy, chemical “bookmarks” attach to DNA to enhance or inhibit gene expression in each tissue,
- Environmental insults at any age can alter gene bookmarks and produce mental disorders and other disease conditions.
Histones – Support Structures for the Fragile DNA

- Composed of 8 linear proteins twisted together like a ball of yarn,

- Originally believed to serve only as structural support for DNA packaging,

- Later found to inhibit or promote gene expression, depending on chemical reactions at histone tails.
The Two Main Components of the Epigenetic Code

(1) DNA Methylation

(2) Histone Modification

Methyl, acetyl and other chemical factors can react with histone tails and either promote or silence gene expression.
Methyl-Acetyl Competition

- Competition between acetyl and methyl groups often determines whether genes are expressed or silenced,

- Acetyl bookmarks promote gene expression,

- Methyl bookmarks inhibit expression,

- Nutrient therapy can change methyl/acetyl ratios and adjust production of enzymes that control serotonin and dopamine neurotransmission rates.
Gene Expression Requires Uncoiling of DNA

- Gene expression involves direct interaction of RNA polymerase and transcription factors with DNA. These large molecules cannot gain access to DNA/Histone regions that are densely compacted,

- The gentle attachment of DNA to histones involves electrostatic attraction – DNA is a weak acid and histones are mild bases (pH above 7.0),

- Acetylation decreases histone pH, causing uncoiling of DNA; methylation increases histone pH, increasing DNA/Histone compaction.
Low methylation promotes gene expression.

Acetyl

CH₃

DNA

Histone tails

Open chromatin
HIGH METHYLATION INHIBITS GENE EXPRESSION

DNA

Acetyl

CH₃

CLOSED CHROMATIN
Reuptake Transport Proteins

- Primary determinant of neurotransmitter activity at serotonin & dopamine receptors – concentrations of serotonin and dopamine are less important,

- Transmembrane proteins that remove neurotransmitters from the synapse (reuptake) like a vacuum cleaner inhaling dust particles,

- Formed by gene expression: amount present depends on methyl/acetyl competition at specific DNA regions.
Enzymes Dominate the Methyl-Acetyl Competition

- Acetylases, deacetylases, methylases and demethylases dominate attachment or removal of acetyl or methyl groups.
- Acetyl-Coenzyme A and SAMe are the donors of acetyl and methyl, respectively – but their concentrations in brain cells are relatively unimportant.
- Epigenetic nutrient therapy for adjustment of serotonin or dopamine activity concentrates on the enzymes.
- Example: B-3 inhibits a major deacetylase inhibitor, thus increasing expression of SERT, DAT transporters and reducing serotonin and dopamine neurotransmission.
Epigenetic Insights Into Nutrient Therapy

- Niacin & niacinamide act as dopamine reuptake promoters,
- Methionine and SAMe are serotonin reuptake inhibitors,
- Folates reduce synaptic activity at serotonin, dopamine, and norepinephrine receptors,
- Zinc and glutathione increase NMDA activity,
- Many nutrients influence neurotransmitter activity and brain function.
Folates Considerations

- Folic Acid, folinic acid, and/or L-methylfolate elevate SAMe/SAH in undermethylated persons.

- However, folates also increase gene expression of SERT transport proteins, resulting in reduced serotonin neurotransmission.

- Most undermethylated patients with a serious low-serotonin condition are intolerant to folates.
A Clue From Cancer Research

Severe oxidative stress can alter established epigenetic bookmarks,

Deviant marks can turn on a cancer gene or silence a cancer-protective gene, initiating a cancer condition,

Antisocial personality disorder, autism, paraphilias, and OCD appear to be epigenetic in nature.
Said a scientist once feeling frisky
I know altering genes can be risky
but I want to learn how
to develop a cow…. 
That will stop giving milk and give whiskey.
Behavior Chemistry

- **Antisocial-Personality Disorder**: Depressed Zn, undermethylation, elevated pyrroles, hypoglycemia, toxic metal overload

- **Intermittent Explosive Disorder**: High Cu/Zn ratio

- **Conduct Disorder**: Severely-elevated pyrroles

- **Oppositional/Defiant Disorder**: Undermethylation, low-normal Cu, low Ca & Mg
Nutrient Therapy Examples

**Undermethylation:** SAMe, methionine, zinc, calcium, inositol, serine, magnesium, vitamins A, B-6, C, D, and E.

**Excess Dopamine Activity:** Folic acid, B-12, niacinamide, zinc, manganese, DMAE, vitamins A, C, and E.

**Copper Overload:** Zinc, molybdenum, vitamins B-6, C and E, MT-Promotion formulation.

**Pyrrole Disorder:** Vitamin B-6, zinc, biotin
Treating Outcomes:
Compliant Assaultive Subjects

- Symptom-Free: 58%
- Partial Improvement: 33%
- No Change: 8%
- Worse: 1%

0% 10% 20% 30% 40% 50% 60% 70%
Symptom-Free Partial Improvement No Change Worse
Case History: Mike

- Father in prison; mother a recovering alcoholic.
- At age 12: oppositional, defiant, cruel to animals, truant, and assaultive.
- Dx: ODD, Antisocial Personality disorder.
- Head of youth gang -- major thefts.
- After 3 months therapy, he became well-behaved and a straight-A student.
- Family moved to Kansas to give Mike a fresh start.
Case History: Brian

- Adopted son of dedicated & capable parents,
- At age 16: violent, destructive, truant, failing academically,
- Severe pyrrole disorder (Zn/B-6 deficiency),
- After normalizing plasma Zn, he became calm, ceased truancy, became an honor student & joined football team.
- Became a college student instead of a high school dropout.
High-Incidence Chemical Imbalances in ADHD

- Elevated Cu (68%)
- Insufficient ceruloplasmin (92%)
- Zinc depletion (96%)
- Methylation disorder (55%)
- Pyrrole Disorder (30%)
- Malabsorption (11%)
ADHD Case History: Danny

- Son of prominent scientist (physicist),

- At age 8, diagnosed with LD/ADD: Special Education and Ritalin recommended,

- Disability disappeared within 2 months of nutrient therapy,

- Danny became superior student and entered graduate school at age 19.
Massive Autism Database

- 6,500 ASD Patients,
- More than 1.5 million chemical assays of blood and urine,
- Striking biochemical differences between ASD children and non-affected children.
Autism Database Highlights

- Autism imbalances more severe than in violent behavior and mental illness,

- Discovery of undermethylation in more than 95% of ASD patients (1999),

- Clear evidence of oxidative stress and metallothionein depletion (2000).
Pervasive Biochemical Abnormalities in Autism

- Undermethylation (>95%)
- Depressed Glutathione & Cysteine
- Elevated toxic metals
- Copper/Ceruloplasmin dysregulation
- Depleted Zinc & Metallothionein
- Elevated Pyrroles
- Low B-6, C, and Selenium
- Elevated Urine Isoprostanes

Note: Each of these imbalances is associated with elevated OXIDATIVE STRESS.
Some Consequences of Excess Oxidative Stress

1. Hypersensitivity to Hg & other toxic metals,
2. Hypersensitivity to casein, and gluten,
3. Poor immune function,
4. Inflammation of the brain & G.I. tract,
5. Depletion of glutathione & metallothioneinein.
Consequences of Oxidative Overload in the G.I. Tract

- Destroys digestive enzymes needed to break down casein & gluten,
- Increases candida/yeast levels,
- Diminishes Zn levels and production of stomach acid,
- Produces inflammation,
- Results in a “leaky intestinal barrier, allowing toxics to enter the bloodstream.”
Many Popular Autism Therapies Have Antioxidant Properties

- Methyl B-12
- Metallothionein Promotion
- Transdermal or Injected Glutathione
- Zn, Se, CoQ-10, Vitamins A,C,D,E
- Chelation with DMSA, DMPS, EDTA.
- Alpha Lipoic Acid
- Risperdal
Pervasive Features of Autism

UNDERMETHYLATION

SEVERE OXIDATIVE STRESS
The Three Musketeers of Antioxidant Protection

Glutathione: First line of defense,

Metallothionein: Nature’s back-up system,

Selenium: Speeds up the process.

Note: All three are depleted in ASD
Undermethylation is a distinctive feature of autism,

Undermethylation results in reduced synthesis of glutathione and cysteine – and weakened ability to cope with toxic metals and other sources of oxidative stress,

An undermethylation environment during pregnancy may alter gene regulation of antioxidant protectors.
Regressive Autism

- About 80% of autism cases involve regression: normal development followed by sudden onset around age 20 months.

- Severe oxidative stress can alter established epigenetic bookmarks,

- The regressive autism event may arise from severe oxidative stress that permanently alters gene regulation.
An Epigenetic Model of Autism

- In-utero undermethylation from genetic SNPs and/or folate deficiency results in life-long vulnerability to oxidative stresses,

- Environmental insults overwhelm antioxidant protectors and produce deviant epigenetic bookmarks…. resulting in autism,

- Since deviant marks survive cell divisions, the autism condition can persist a lifetime.
Mounting Evidence that Autism is an Epigenetic Disorder


Autism Brains Are Different

- Narrowed minicolumns in brain cortex,
- Incomplete maturation in cerebellum, amygdala, pineal gland and hippocampus,
- Poverty of brain dendrites and synapses,
- Brain inflammation and increased head size,
- Damaged fats in autism brains,
- Abnormal levels of calcium and iron,
- Reduced structural connectivity between brain regions.
Low Metallothionein Levels in Autism

p < 0.0092
Why is Metallothionein Important?

- Required for brain cell development,

- Prevents Hg, and other metal toxics from passing intestinal and blood/brain barriers,

- Can safely bind to Hg that enters the brain.

Note: MT functioning can be disabled by severe oxidative stress.
Brain Tissue Studies

Very limited amount of autism brain tissue available for research,

Conventional chemical analysis for zinc, copper, mercury, lead, calcium, etc requires significant sample size,

Until now, little or no data for levels of most elements in ASD brains.
Welcome to the Advanced Photon Source
Advanced Photon Source

1.4 billion dollar facility at Argonne National Laboratory in Illinois,

The APS produces photon beams 100 times brighter than at the surface of the sun,

World’s greatest capability for accurate elemental analysis of tiny samples.
Photon Beam Nanoanalysis of Autism Brain Tissues

- Double blind, controlled study of 176 brain tissues from U. of Maryland’s Autism Brain Bank,

- Elemental analysis for Hg, Pb, Cu, Zn, Ca, and other elements using high-brilliance photons,

- More than 35,000 individual assays obtained for autism & control brain tissues.
Bill Walsh PhD, Principal Investigator
Aditi Gulibani MD, Research Associate
Woody McGinnis MD, Consultant
Stephon Vogt PhD, Argonne Scientist
Barry Lai PhD, Argonne Scientist
Test Subjects

Five autistics: Age range 5-9; 3/2 M/F ratio; All children exposed to Thimerosal,

Five controls: Age range 5-11, 2/3 M/F ratio.

Brain tissues samples prepared at Johns Hopkins
Brain Regions Studied

- Cerebellum
- Superior Cortex
- Deep Cortex
- White Matter

Note: 20 autistic & 20 control tissue samples from each brain region.
Autism/Control Tissue Array
Experimental Procedure

- Samples prepared using special plastic substrate,
- Simultaneous assays for 10-14 elements,
- High-brilliance beam of 0.3 mm diameter,
- Typical protocol: Automated raster scanning using 1 sec. pulses,
- 15 micron thick tissues,
- Non-destructive analysis: Tissue samples available for future experiments.
Modified Gaussian’s fitted to elemental peaks,

NITS/NBS standards 1832 and 1833 used,

Control ppb levels exhibited close agreement with published elemental levels, including expected variations between brain regions.

Conclusion: Assay results appear highly reliable.
Results of Brain Tissue Study

1. Testing of 153 intact samples,

2. Abnormal levels of specific elements found throughout autism brains and not in the controls,

3. Major chemical differences between male and female ASD brains, suggesting that male and female autism may represent distinctly different conditions.
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*p values calculated using two-tailed test.*
Mean Zn Concentration, ppm

- Autistic Males
- Autistic Females
- Control Males
- Control Females
What About Mercury?

- All ASD brain tissues tested were from children exposed to Thimerosal,

- Strong evidence that mercury insults can initiate autism,

- Are brain mercury levels high in ASD brains several years after exposure to Thimerosal?
“Normal” Hg Levels in Brain

- Hg present in brains of all humans,

- Some Hg enters and departs the brain daily,

- Hg concentrations of 5 to 25 ppb considered typical for healthy persons,

- Hg levels exceeding 75 ppb considered a serious health risk.
Mercury Results

- Mercury not detected in any of the autism or control samples, in any brain region,

- Detection limit in this experiment believed to be 40-50 ppb.
Study Limitation

- Small number of autism subjects (five),

- Testing of additional subjects needed to determine if the chemical imbalances and gender differences reported in this study are characteristic features of autism.
1. World’s first extensive measurements of metal levels in autism brains (35,000 assays compared to dozens previously),

2. Abnormal metal levels and gender differences found in autism brains,

3. Testing of additional ASD subjects needed to verify results.
Promise of Epigenetic Therapies

- Deviant epigenetic marks appear to be reversible.

- Future epigenetic therapies may represent the best therapies for children and adults with behavior, learning, or autism disorders.

- Early epigenetic testing and treatment may enable prevention of these disorders.
Summary

- Biochemical imbalances are exhibited by most persons with autism, ADHD or a behavior disorder.

- These imbalances can adversely impact brain function including NT synthesis & regulation.

- Most families report improvement, following nutrient therapy to normalize chemistry.

- The emerging science of epigenetics will lead to vastly improved natural therapies.
“For every drug that benefits a patient, there are natural substances that can produce the same effect”.

Carl C. Pfeiffer, MD, PhD
NUTRIENT POWER
HEAL YOUR BIOCHEMISTRY
AND HEAL YOUR BRAIN

WILLIAM J. WALSH, PhD

Over his impressive career, Dr. Walsh has worked with 30,000 patients with conditions ranging from autism to schizophrenia to Alzheimer’s. His book is an essential tool for anyone who would prefer to heal the brain with nutrients rather than drugs.

Teri Arranga, editor-in-chief, Autism Science Digest