ADVANCED NUTRIENT THERAPIES FOR BIPOLAR DISORDER

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Walsh Research Institute

- Nonprofit organization
- Expertise in schizophrenia, depression, anxiety, bipolar disorder, ADHD, autism, behavior disorders, and Alzheimers
- International physician training
- Experimental Research
Clinical Experience

- 10,000 Behavior & ADHD
- 3,500 Schizophrenia
- 3,200 Depression
- 1,500 Bipolar Disorder
Database Findings

Striking blood/urine chemistry differences between mental illness populations and the rest of society.
High-Incidence Imbalances in Bipolar Disorder Patients

- Overmethylation
- Undermethylation
- Zinc Deficiency
- Copper Overload
- Folate Deficiency or Overload
- Pyrrole Disorder (Low B-6, zinc)
- Heavy-Metal Overload
- Fatty-Acid Abnormalities
Bipolar Phenotypes

- Our chemistry database (250,000 assays) indicates that bipolar patients fit into four major biochemical classifications,

- Each bipolar “biotype” is associated with distinctive symptoms and traits,

- Bipolar disorder appears to be an umbrella term used for different mental disorders, each requiring a different treatment approach.
Bipolar Disorder Phenotypes (preliminary)

- Undermethylation
- Overmethylation
- Copper/Zinc Imbalance
- Severe Oxidative Stress
Frequently Asked Questions

1. How can vitamins, minerals, or amino acids significantly help a patient with a bipolar disorder?

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 (DAT and SERT transport proteins)

4. Antioxidant Protection at NMDA, GABA
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.
Norepinephrine Synthesis

DOPAMINE

Dopamine β-Hydroxylase

Cu++, Vitamin C, O₂

NOREPINEPHRINE
Serotonin Synthesis

5-HYDROXYTRYPTOPHAN → SEROTONIN

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

+ CO₂
Dopamine Synthesis

L-DOPA → DOPAMINE

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

+ CO₂
GABA Synthesis

GLUTAMIC ACID $\xrightleftharpoons{\text{L-Glutamic Acid Decarboxylase}}^{\text{Pyridoxal Phosphate (B-6)}}$ GABA $+\text{CO}_2$
Pyrrole Disorder

- Double deficiency of B-6 and Zinc
- Reduced Serotonin, NMDA, GABA activity
- Severe oxidative overload
- 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,
- About 70% of bipolar patients exhibit a serious methylation disorder,
Methylation Cycle Enzymes

- Methionine
  - THF
  - Mg ATP
  - SAMe

- Homocysteine
  - TMG
  - BHMT
  - SAHH
  - SAH

- Cystathionine
  - CBS
  - Serine B6

- Cysteine
  - Glutathione
  - ADA
  - AK

- Adenosine
  - CH₃
Creatine Synthesis

Arginine + Glycine

Guanidino Acetate + Ornithine

SAMe

SAH

CREATINE

AGAT

GAMT
Enzyme Mutations and Methylation

A Methylation Tug of War

Under Methylation

Over Methylation

Normalcy
Many familial mental disorders appear to be epigenetic, rather than genetic:

-- Schizoaffective disorder
-- Antisocial personality disorder
-- Paranoid schizophrenia
-- Obsessive compulsive disorder
-- Autism
-- Bipolar 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,
- For each tissue, in-utero chemical environment can determine which genes will be expressed throughout life (bookmarking),
- Environmental insults can alter gene marks and produce mental disorders and disease conditions.
Histones

- 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/promote gene expression depending on chemical reactions at histone tails.
The Two Main Components of the Epigenetic Code

1. DNA Methylation
2. Histone Modification

Histone Tails

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,

- Acetylation tends to promote gene expression; Methylation generally inhibits expression,

- Nutrient therapy can change methyl/acetyl ratios and adjust neurotransmitter activity.
LOW METHYLATION PROMOTES GENE EXPRESSION

Acetyl

DNA

Histone Tails

CH₃

OPEN CHROMATIN
HIGH METHYLATION INHIBITS GENE EXPRESSION

DNA

Acetyl

CH₃

CLOSED CHROMATIN
Nutrients and Regulation of Neurotransmitter Activity

Reuptake at synapses through transporter protein “passageways” is the dominant factor in NT activity.

Gene expression of transporters regulated by epigenetic processes.

Methyl, folate, niacin, and other nutrients have a powerful epigenetic impact on gene production of transporters and NT activity.
Epigenetic Insights Into Nutrient Therapy

- Niacin & niacinamide act as dopamine reuptake promoters,
- SAMe is a serotonin reuptake inhibitor,
- Folates reduce synaptic activity at serotonin, dopamine, and norepinephrine receptors,
- Undermethylated bipolar patients are intolerant to folic acid,
- Many nutrients influence neurotransmitter activity and brain function.
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.
Nutrient Therapy & Bipolar

-- Separate nutrient therapies developed for each bipolar phenotype,

-- Open-label outcome studies reveal 74% of patients report treatment effectiveness & ability to reduce or eliminate medication,

-- Double-blind, controlled studies needed to accurately measure treatment effectiveness.
Bipolar Treatment Approach

1. Continuation of psychiatric medication while starting nutrient therapy.

2. After 3-6 months of both treatments together, cautious reductions in medication to identify optimum dosage.
Collaboration between W. Walsh and R. DeVito

Investigation of possible causes of mania

a. Weak mitochondrial production of ATP resulting in reduced neuron membrane voltages

b. Abnormal glial-cell regulation of neuron voltages
PRACTITIONER TRAINING

- USA – February 24-28, 2014
- AUSTRALIA – April 5-13, 2014
- IRELAND (to be announced)
- NORWAY (to be announced)
Pfeiffer’s Law

“For every drug that benefits a patient, there are natural substances that can produce the same effect”.

Carl C. Pfeiffer, MD, PhD
THANK YOU!

Bill Walsh, PhD
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