CHEMICAL BIOTYPES OF DEPRESSION AND INDIVIDUALIZED NUTRIENT THERAPY

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Financial Disclosure Statement

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I have no relevant financial relationships with any commercial interests to disclose.

Main Learning Objectives

- Recognize the five biotypes of clinical depression.
- Learn the role of nutrients in NT synthesis, gene regulation, and antioxidant protection.
- Understand the epigenetic impact of nutrients on serotonin and dopamine reuptake processes
- Learn nutrient protocols tailored for each biotype.

Walsh Research Institute
Naperville, Illinois

- 501c3 Public Charity
- Expertise in behavior disorders, ADHD, autism, depression, schizophrenia, bipolar disorder, and Alzheimers
- International physician training
- Research

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.

Large Depression Database

- Evaluation of 2,800 patients diagnosed with clinical depression,
- More than 230,000 blood/urine chemical assays
- Approximately 320,000 medical history factors

Database Summary

Striking blood/urine chemistry differences between depression patients and the rest of society.

Walsh WJ (2012). *Nutrient Power.* Skyhorse Publishing, New York, NY.

Crayton JW, Walsh WJ (2007). J Trace Elements Med Biol.21:17-21.

Depression Database

High incidence of abnormal concentrations of nutrients that impact neurotransmitter synthesis and regulation.

High-Incidence Imbalances in Depression

- Methylation Disorders
- Zinc Deficiency
- Copper Overload
- Folate Deficiency or Overload
- Oxidative Stress Overload
- Pyrrole Disorder
- Toxic-Metal Overload
- EPA, DHA, and/or AA Deficiency

These factors have a powerful impact on synthesis of neurotransmitters and regulation of NT activity.

The Power of Nutrients

1. Neurotransmitter synthesis
2. Epigenetic regulation of gene expression
3. Influence NT reuptake processes
4. Protection against oxidative stress

Mainstream Psychiatry Misconception

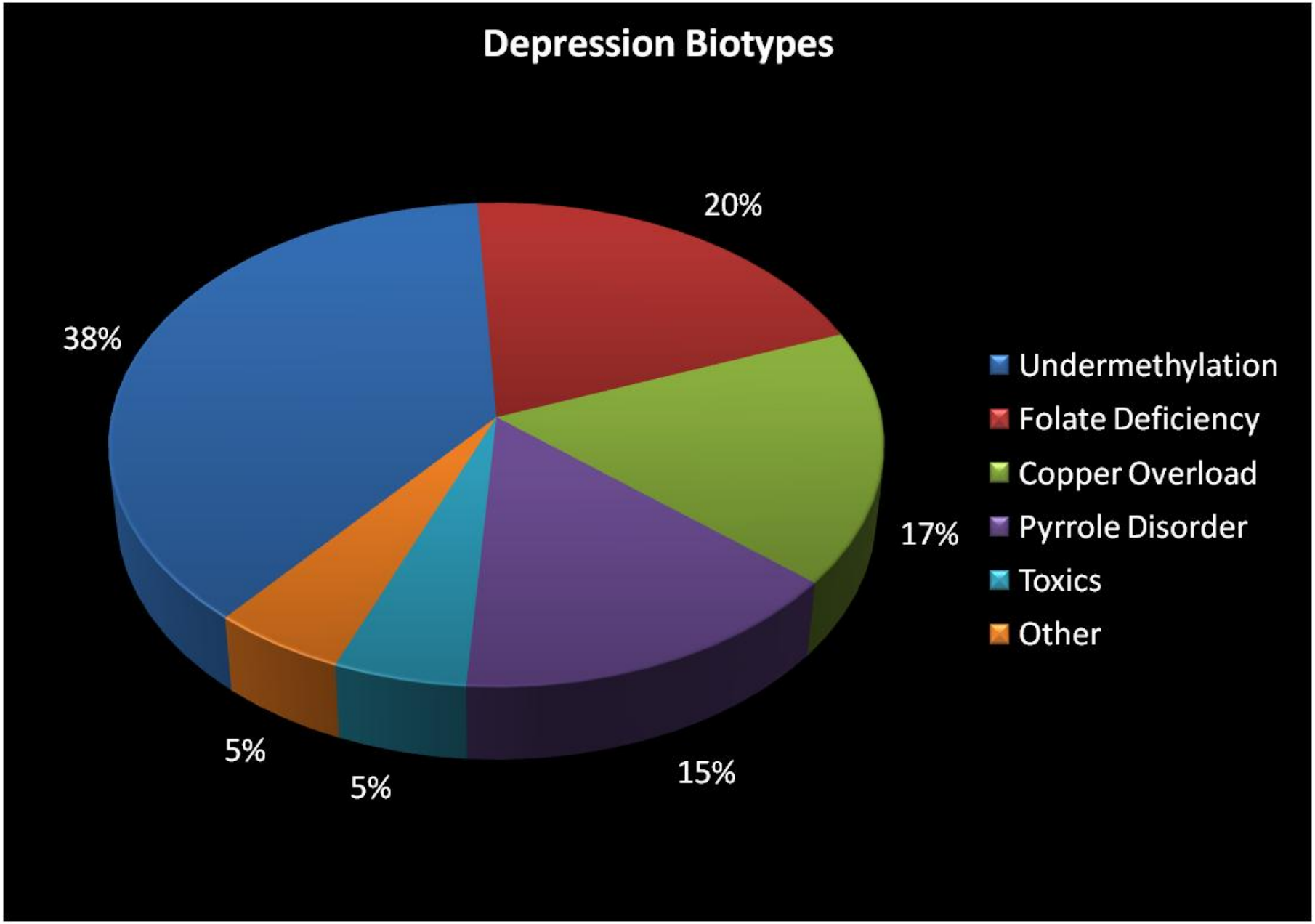
- **Depression** regarded as a single entity with variations along a central theme.
- **Central Belief** -- Low activity at serotonin receptors.
- **Treatment of choice** -- SSRI antidepressants to elevate serotonin activity at synapses.

Chemical Classification of Depression

1. Our database studies have identified five high-incidence depression biotypes,

2. The biotypes appear to be distinctly different disorders, each with unique neurotransmitter imbalances and symptoms,

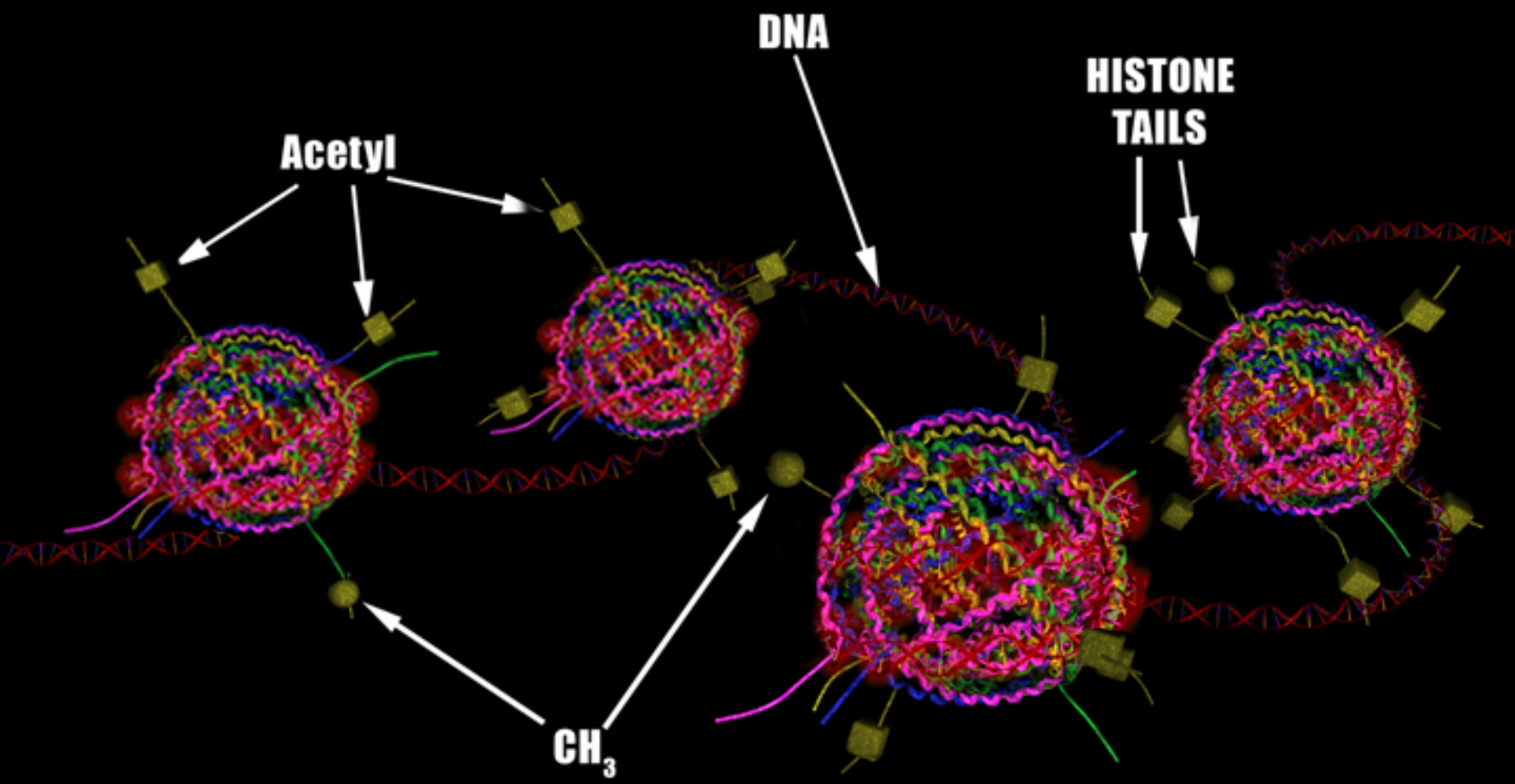
3. A separate treatment approach is needed for each biotype.


Depression Biotypes
20%
38%
17%
5%
5%
15%
Undermethylation
Folate Deficiency
Copper Overload
Pyrrole Disorder
Toxics
Other

Biotype #1
Undermethylated Depression

- 38% of our depression population
- Elevated histamine and low SAMe/SAH ratio in blood; High incidence of MTHFR SNPs
- Excessive gene expression of SERT reuptake proteins (transporters)
- Low activity at serotonin receptors

LOW METHYLATION PROMOTES GENE EXPRESSION



OPEN CHROMATIN

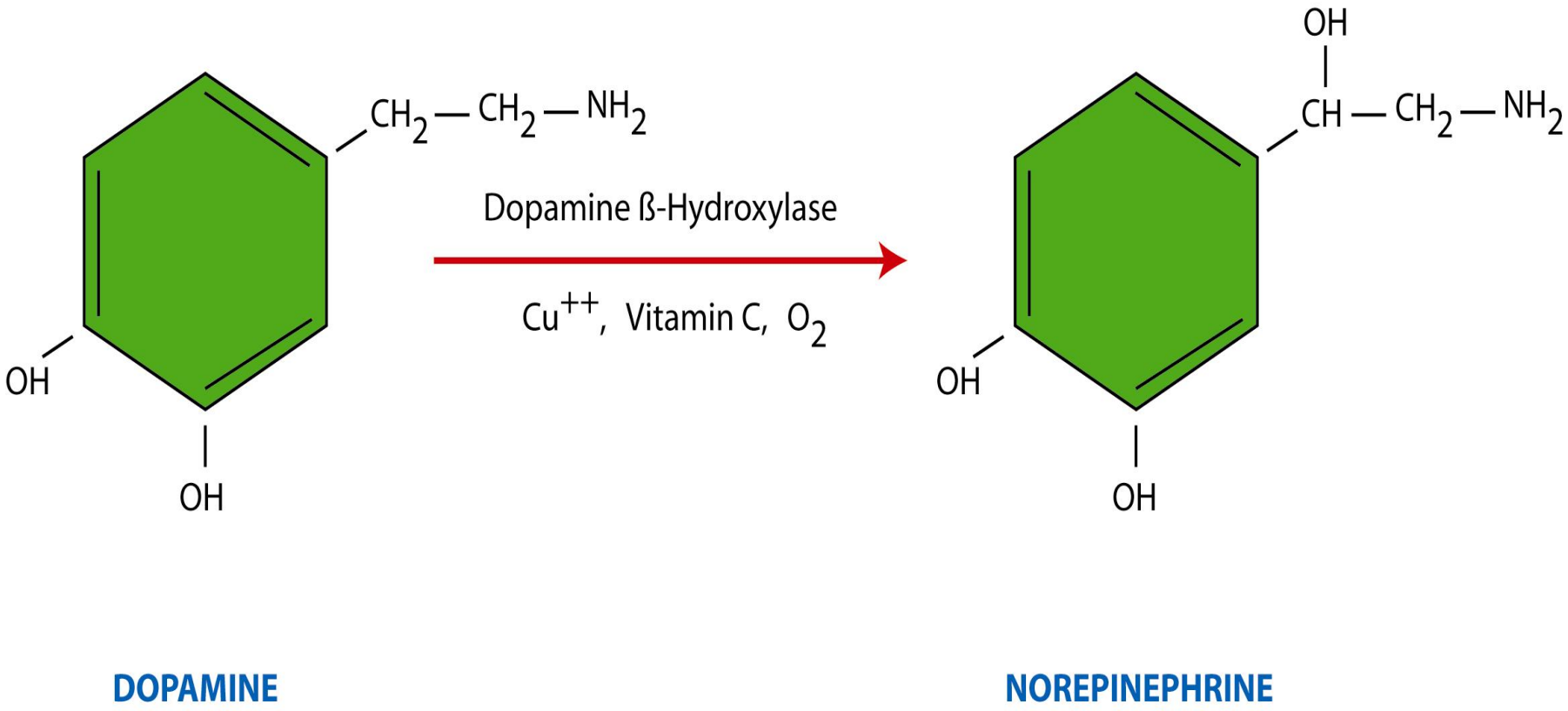
Symptoms & Traits Undermethylated Depression

- Strong will
- OCD tendencies
- High accomplishment
- Calm exterior, but high inner tension
- Competitive & perfectionistic
- Addictive tendency
- Seasonal allergies (75%)
- High libido
- Intolerance to folates
- SSRIs generally beneficial

Biotype #2
High-Copper Depression

- 17% of our depression population
- Elevated norepinephrine, reduced dopamine
- More than 95% are female
- High anxiety, tendency for panic
- Onset during hormonal event
- High incidence of post-partum depression
- Estrogen intolerance
- Tinnitis (ringing in the ears)
- Sensitive skin, intolerance to cheap metals.
- SSRI antidepressants generally reported to be ineffective.

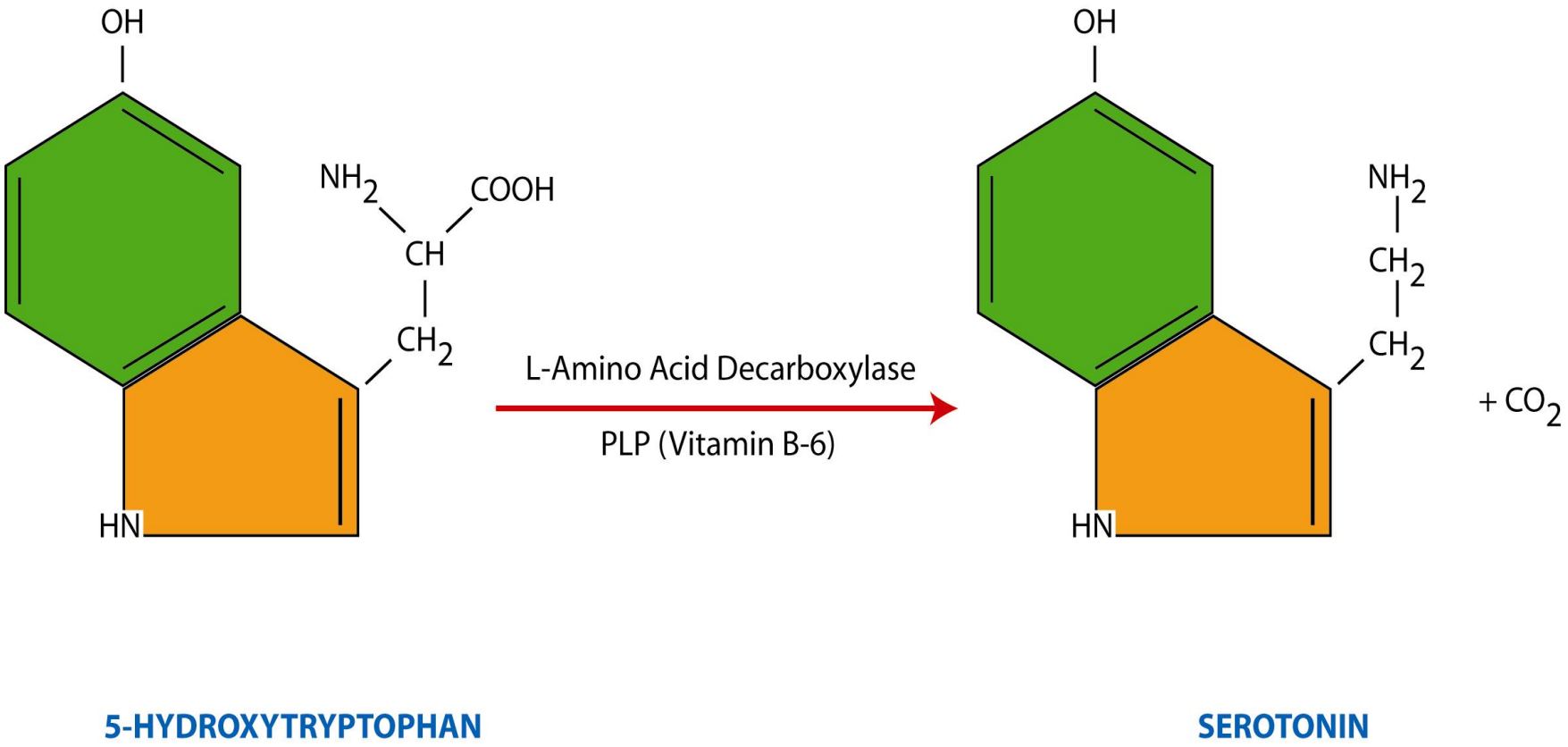
Norepinephrine Synthesis



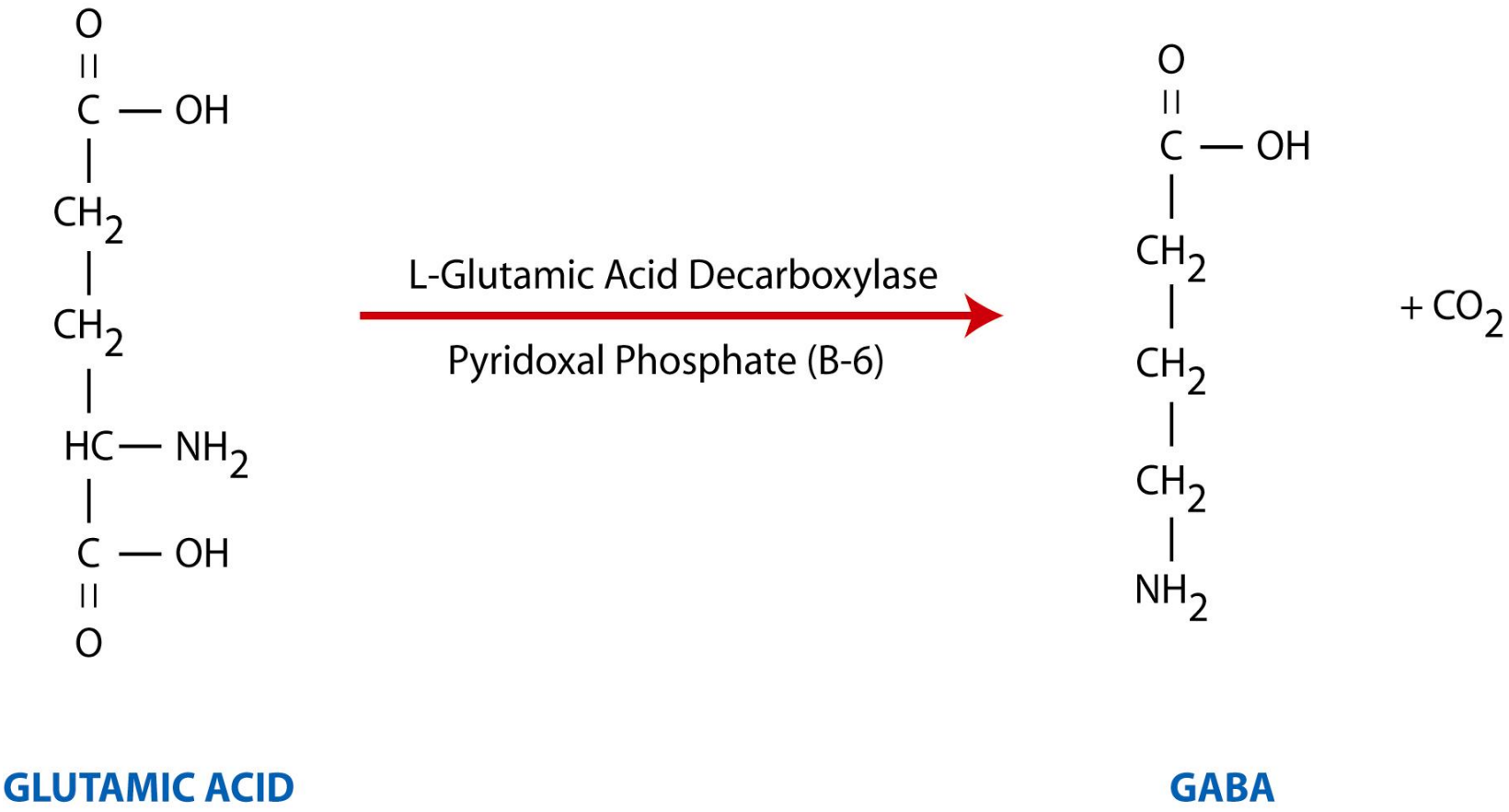
Biotype #3
Pyrrole Depression

- 15% of our depression population
- Double deficiency of B-6 and Zinc
- Reduced synthesis of 5-HT, DA, GABA
- High oxidative stress
- Severe mood swings; explosive anger
- Extreme anxiety, fears
- Poor short-term memory; reading disorder
- Little or no dream recall
- Sensitivity to light, noise
- Abnormal fat distribution,
- Most patients report benefits from SSRIs.

Serotonin Synthesis



GABA Synthesis



Biotype #4
Toxic Metal Depression

- 5% of our depression population
- Severe oxidative stress
- Impaired NMDA function
- Absence of trauma or emotional triggers
- Unrelenting depression
- Abdominal distress
- Metallic taste in mouth, bad breath
- Irritability, anger
- Food sensitivities
- SSRIs usually reported as ineffective

Biotype #5
Low-Folate Depression

- 20% of our depression population
- High anxiety/panic tendency
- Non-competitive in sports or games
- Absence of inhalant allergies
- Food/chemical sensitivities
- High musical or artistic ability
- Underachievement
- Sleep disorder
- Low libido
- Most patients report adverse reaction to SSRIs

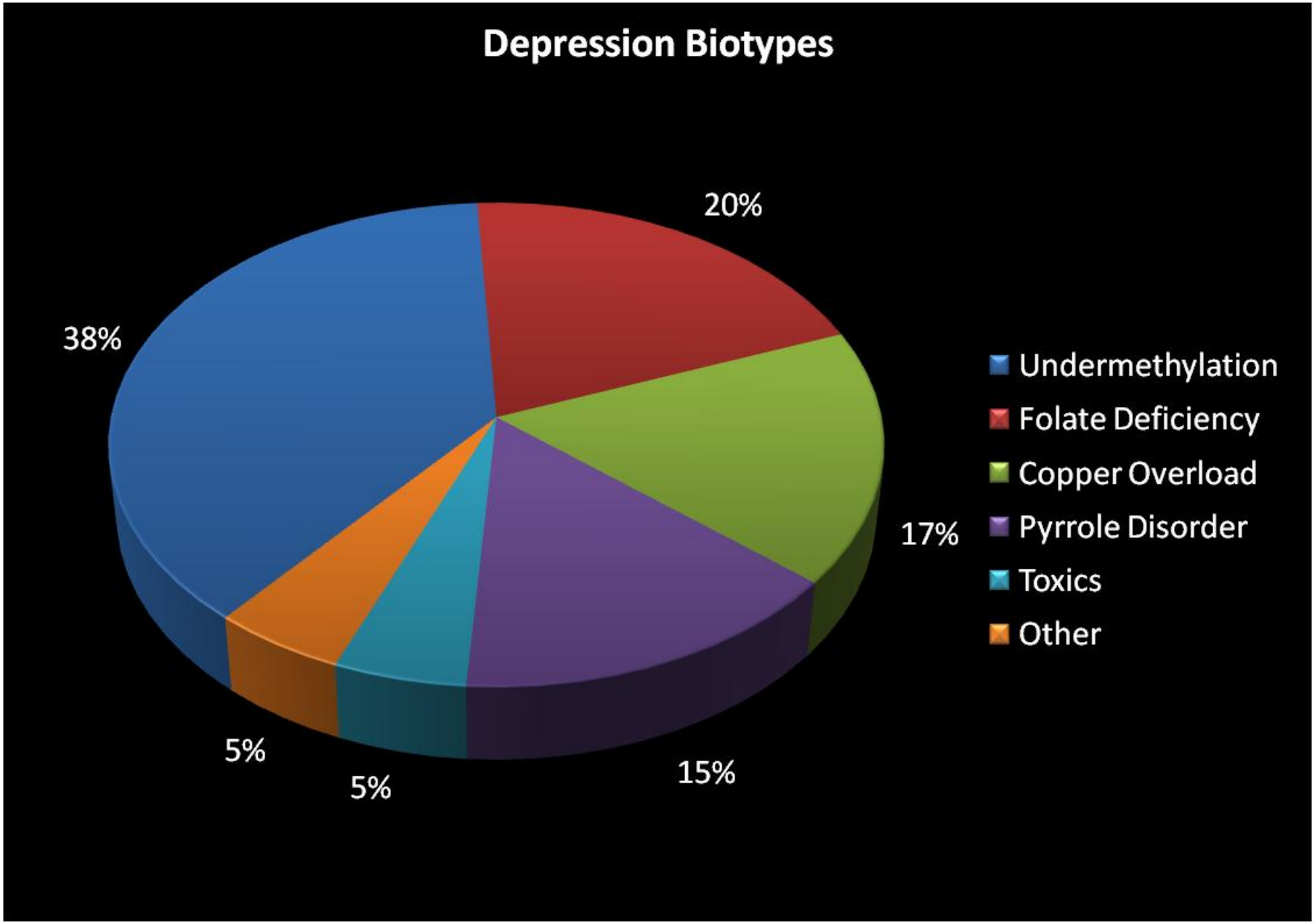
SSRI Antidepressants

- Generally effective for undermethylated and pyrrole-disorder depressives,
- Generally ineffective for copper overload and toxic-metal depressives,
- May cause suicidal & homicidal ideation in certain low-folate patients, especially young males,
- Inexpensive blood tests can identify promising and unpromising candidates for SSRIs, SNRIs, benzodiazapines, etc.

Blood Testing and Medical History Can Identify Depression Biotype

Useful Laboratory Tests

- SAMe/SAH ratio in plasma
- Whole-blood histamine
- Serum folate
- Serum Copper
- Plasma Zinc
- Urine Pyrroles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Methylation and Depression

- Methylation status has been determined for 3,200 depression patients over a 30 year period,
- Most persons diagnosed with depression exhibit a serious methylation imbalance,
- Accurate diagnosis of methylation status is essential to effective treatment.

Reuptake Transport Proteins (SERT, DAT, NET)

- Primary determinant of neurotransmitter activity at serotonin, dopamine and norepinephrine receptors – brain 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.

Undermethylated Depression Nutrient Therapy Approach

- Enhance methylation and suppress acetylation of DNA histones,
- SAMe and methionine act as serotonin reuptake inhibitors by reducing gene expression of SERT,
- Avoidance of folate supplements,
- Augmenting nutrients – zinc, serine, inositol, TMG, Cal/Mag, Vitamins A, B-6, C, D, E.

Low-Folate Depression
Nutrient Therapy Approach

- Support acetylation of DNA histones with folic acid and niacinamide (powerful deacetylase inhibitors).
- Augmenting nutrients DMAE, chromium, Vitamins B-6, B-12, C, D, E.
- Zinc and other antioxidants.

Note: Most low-folate depressives report effectiveness of benzodiazapines.

Folates Reduce Serotonin Activity

- Folic Acid, folinic acid, and L-methylfolate are effective methylating agents.
- However, folates also increase gene expression of SERT transport proteins, resulting in reduced serotonin neurotransmission.
- Most undermethylated depressives with low-serotonin activity are intolerant to folates.

Metal Metabolism Disorders

- Zinc Depletion
- Copper Overload
- Deficiencies of magnesium, calcium, manganese, selenium, iron, etc.
- Overload of lead, mercury, cadmium, and other toxic metals.

Pyroluric Depression Nutrient Therapy Approach

- Emphasis: Normalze B-6 and zinc,
- Antioxidants to enhance NMDA function,
- Augmenting nutrients – Biotin, Primrose Oil.

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.

Summary

- Five distinct biotypes of depression have been identified.
- Inexpensive blood testing can assist in diagnosis and treatment design.
- Nutrient therapy represents an effective weapon in the arsenal of a mental health practitioner.

THANK YOU!

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Walsh Research Institute

www.walshinstitute.org

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*

NUTRIENT POWER

HEAL YOUR BIOCHEMISTRY AND HEAL YOUR BRAIN

WILLIAM J. WALSH, PhD