

Advanced Nutrient Therapies for Mental Disorders

London, England
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Walsh Research Institute

Naperville, Illinois

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

Clinical Experience

William J. Walsh, Ph.D.

- 10,000 Behavior
- 5,600 ADHD
- 3,500 Schizophrenia & Bipolar
- 3,200 Depression
- 6,500 Autism

Massive Chemistry Database

- Laboratory testing of **30,000** mental health patients and controls.
- More than **3 million lab chemistries** for patients diagnosed with a behavior disorder, ADHD, autism, depression, bipolar disorder or schizophrenia.
- More than **2 million medical history factors** for these populations.

Database Findings

Striking blood/urine
chemistry differences
between mental illness
populations 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.

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Nutrient Imbalances & Mental Disorders

- There are more than 300 important nutrients in human biochemistry.
- Some of these nutrients have a powerful impact on activity at serotonin, dopamine, norepinephrine, GABA, and NMDA receptors.
- Our nutrient therapies focus on normalizing blood and brain levels of these nutrients.

High-Incidence Imbalances in Mental Disorders

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

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

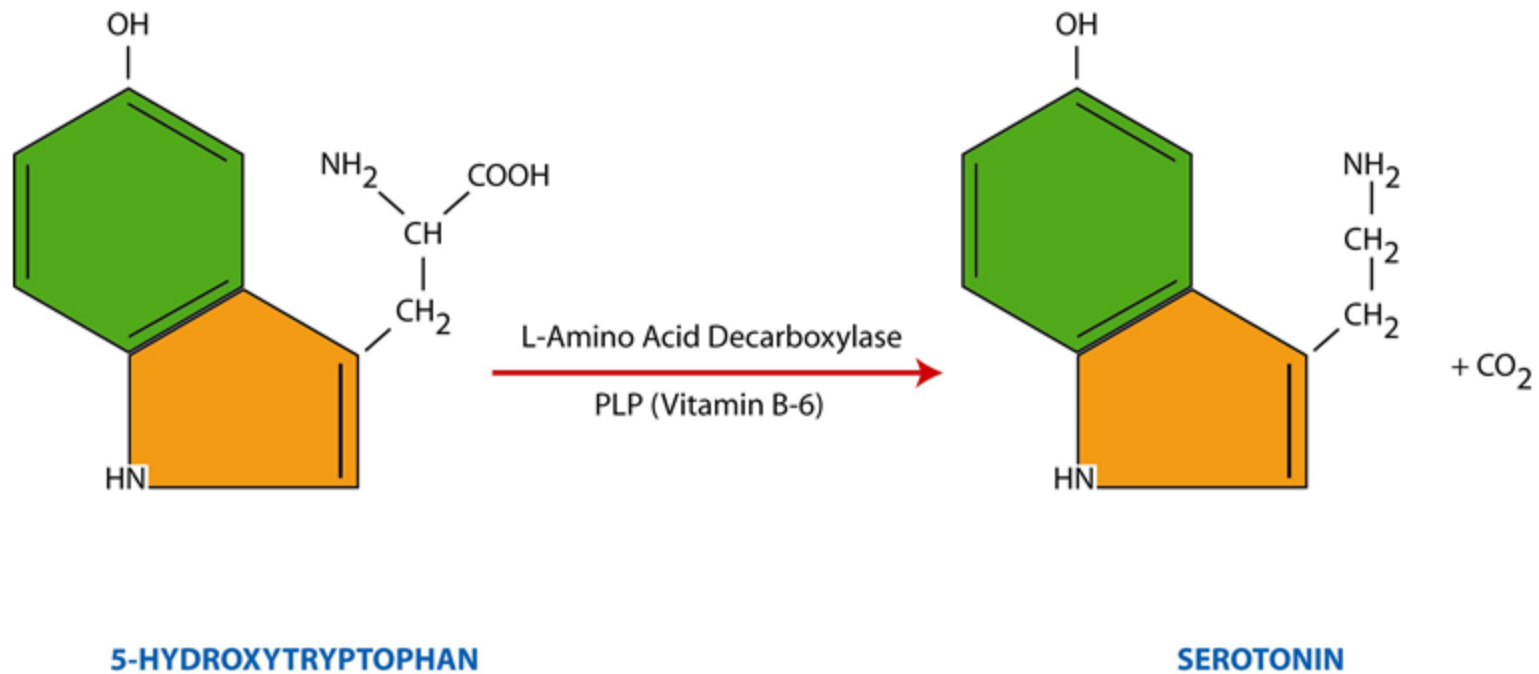
Frequently Asked Questions

1. How can vitamins, minerals, or amino acids significantly help a person with a serious mental illness?
2. Don't you really need a powerful drug to get the job done?

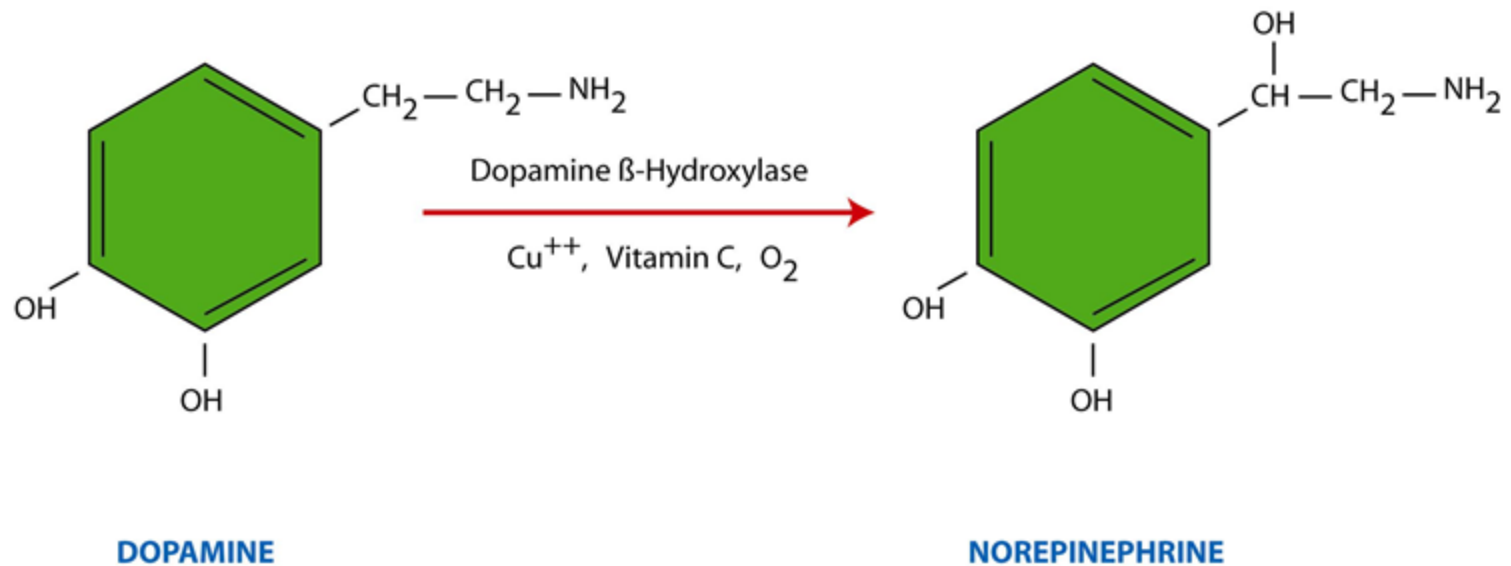
The Power of Nutrients

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

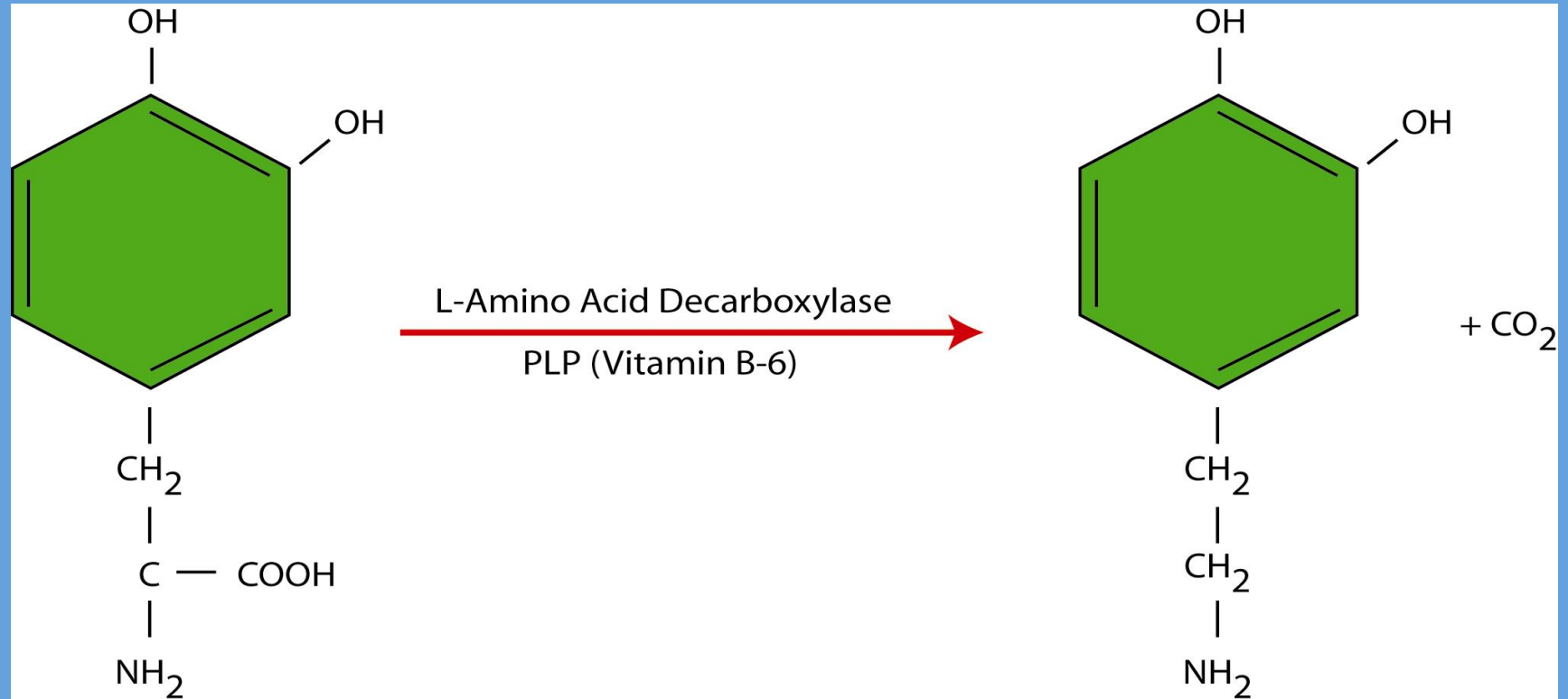
Serotonin Synthesis



Norepinephrine Synthesis



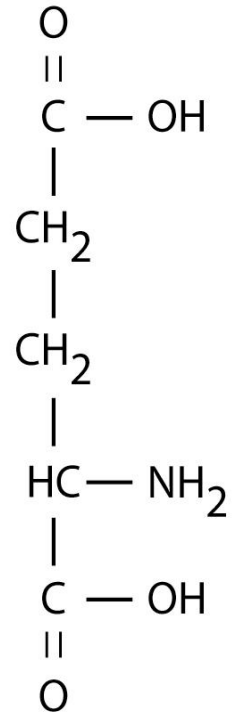
Dopamine Synthesis



L-DOPA

DOPAMINE

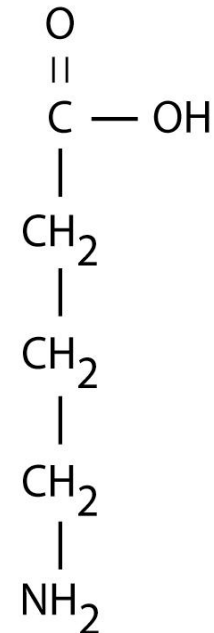
GABA Synthesis



GLUTAMIC ACID

L-Glutamic Acid Decarboxylase

Pyridoxal Phosphate (B-6)



GABA

+ CO₂

Metal Metabolism Disorders

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

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.

Oxidative Stress

What Can Go Wrong?

- Some persons are born with low levels of natural antioxidants glutathione, MT, etc.
- Illnesses, injuries, and emotional trauma can increase oxidative stress.
- Exposure to toxic metals, pesticides, and industrial pollutants increases oxidative stress.

The Three Musketeers of Antioxidant Protection in the Brain

Glutathione: First line of defense.

Metallothionein: Nature's back-up system.

Selenium: Speeds up the process.

Brain Disorders and Oxidative Stress

- Clinical tests include plasma Zn, serum Cu, serum ceruloplasmin, and urine pyrroles.
- Oxidative overload present in 95% of patients diagnosed with a behavior, learning, mood, or psychosis disorder.
- Useful supplements include Vitamins C and E, zinc, selenium, alpha lipoic acid, NAC, and GSH.

Methylation and Brain Disorders

- Methylation status has been determined for 30,000 patients over a 30-year period.
- Most persons diagnosed with mental disorders exhibit a serious methylation imbalance.
- Accurate diagnosis of methylation status is essential to effective treatment.

Recent Advances

in Understanding of Brain Disorders

- Methylation Processes
- Epigenetics

New Capability in Nutrient Therapy

- Regulation of enzyme gene expression
- Control of serotonin & dopamine reuptake
- Improved antioxidant protection in the brain

***“I did then what I knew how to do.
Now that I know better, I do better.”***

Maya Angelou

Methylation and Mental Health

- Methylation is a dominant factor in epigenetic processes that regulate NT activity at serotonin and dopamine receptors.
- The methyl/folate ratio has a powerful impact on gene expression of reuptake transport proteins.
- More than 60% of anxiety, depression and psychosis patients exhibit a serious methylation imbalance.

Methylation Disorders – Two Types

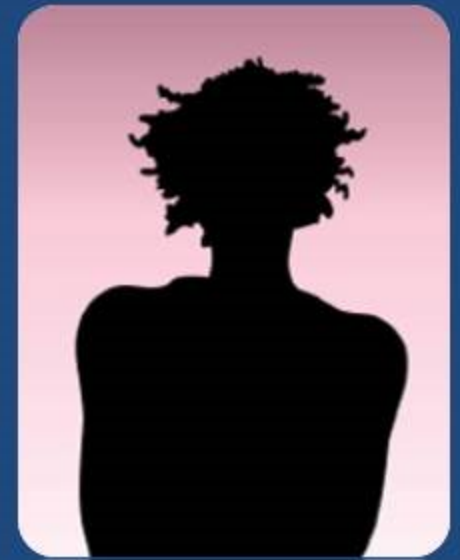
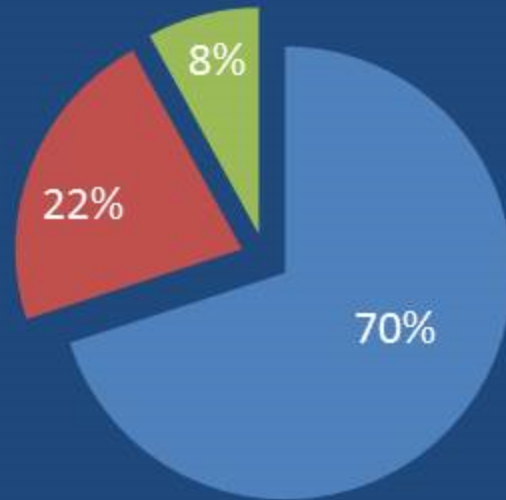
UNDERmethylation



OVERmethylation



Incidence of Methylation Disorders in the General Population



Normal Methylation = 70%

Under Methylation = 22%

Over Methylation = 8%

Incidence of UNDERmethylation

| | |
|--|------------|
| Autism-Spectrum | 98% |
| Antisocial Personality Disorder | 95% |
| Schizoaffective Disorder | 90% |
| Oppositional-Defiance | 85% |
| Anorexia | 82% |
| Depression | 38% |

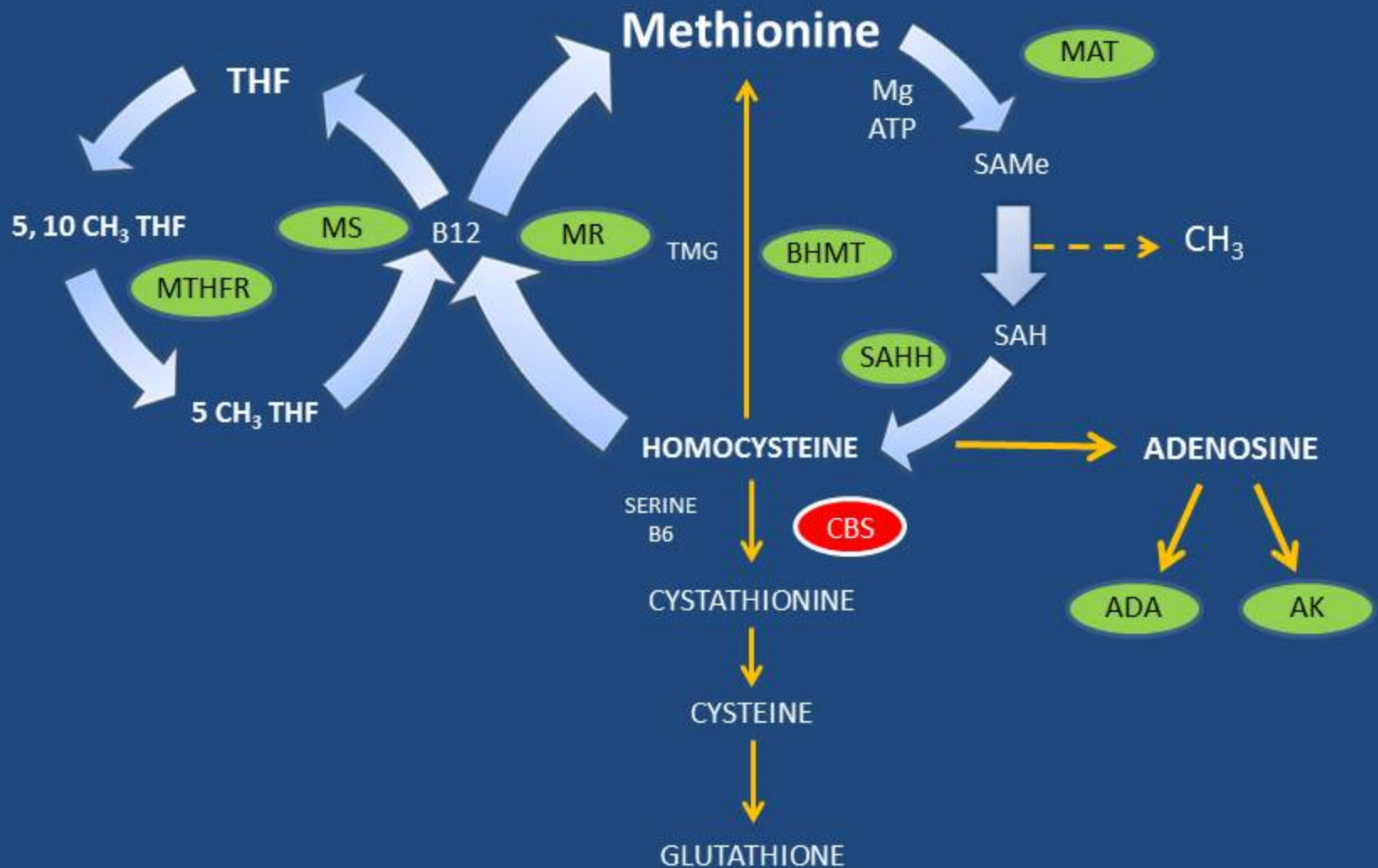
Incidence of OVERmethylation

| | |
|-------------------------------|------------|
| Panic/Anxiety Attacks | 64% |
| Paranoid Schizophrenia | 52% |
| ADHD | 28% |
| Behavior Disorders | 23% |
| Depression | 18% |

Primary Causes of UNDERmethylation

1. Enzyme Mutations (SNPs) in Methylation Cycle
MTHFR, MS, BHMT, MAT, SAHH, etc...
2. Histamine Overload
3. Protein Deficiency or Malabsorption

Methylation Cycle Enzymes



SAMe Synthesis

Methionine

Mg
ATP



SAMe

MAT

Methyl Donation

SAMe

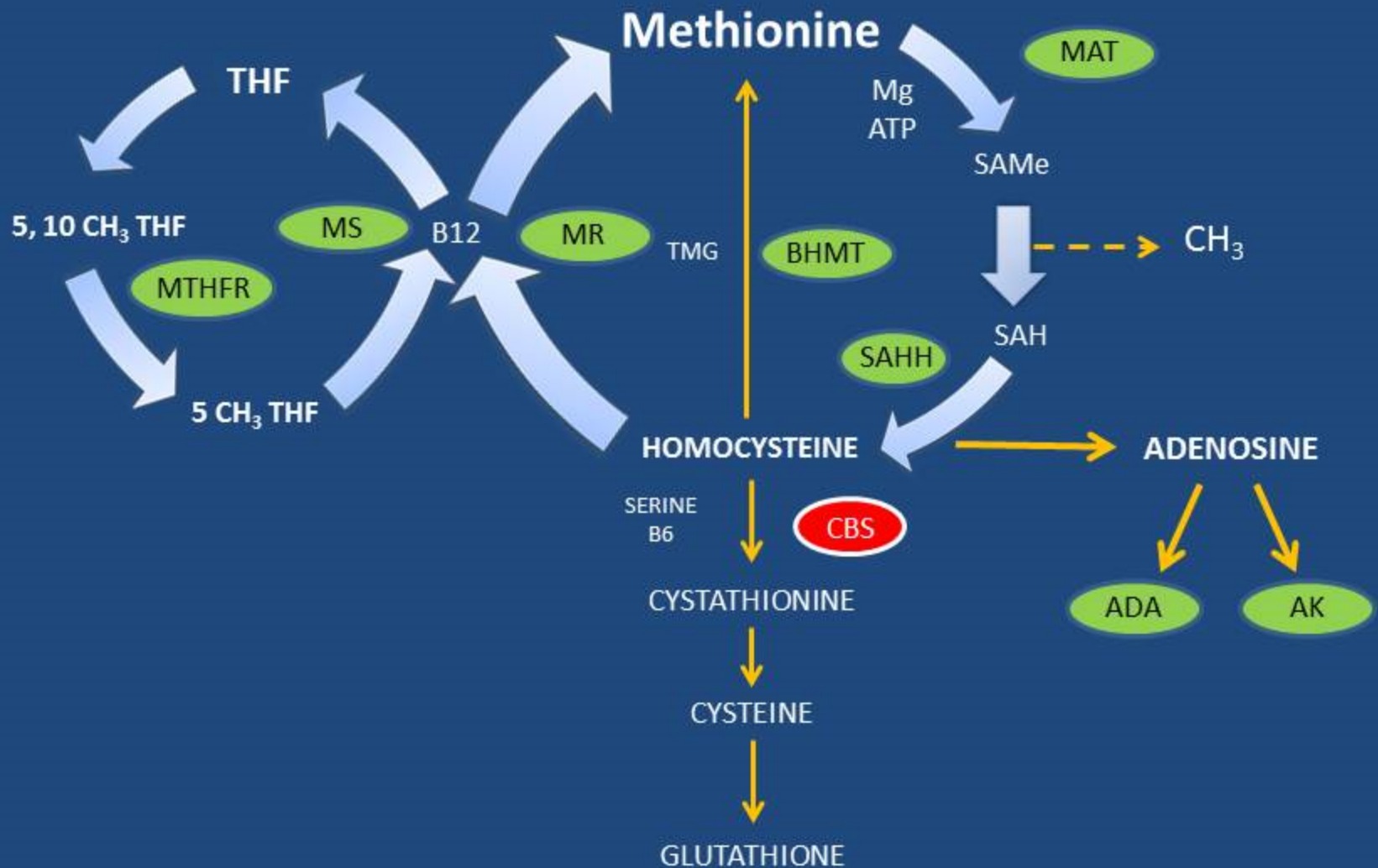


SAH



CH₃

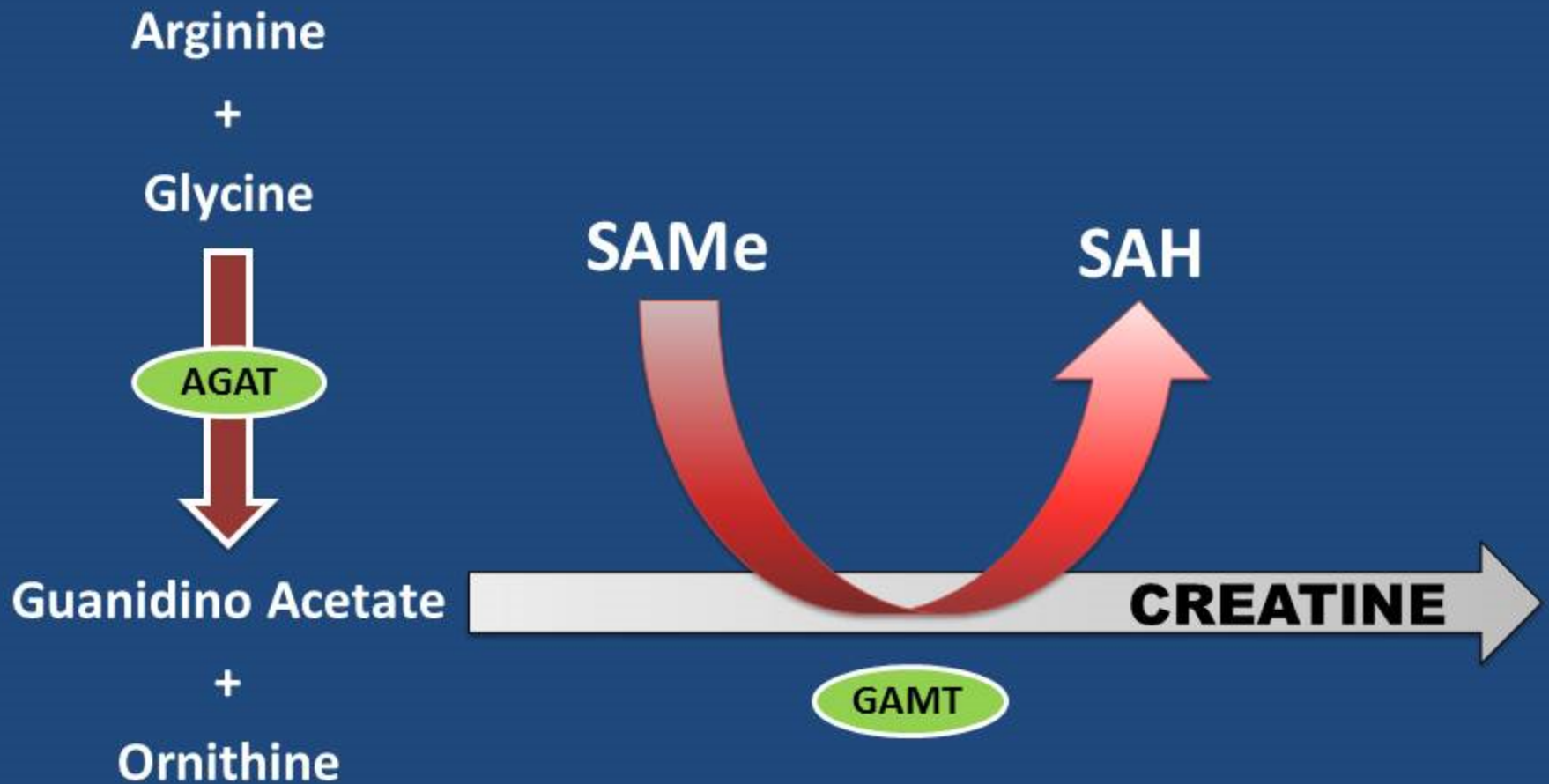
Methylation Cycle Enzymes



SAMe Utilization



Creatine Synthesis



Primary Causes of OVERmethylation

1. Impaired Creatine Synthesis

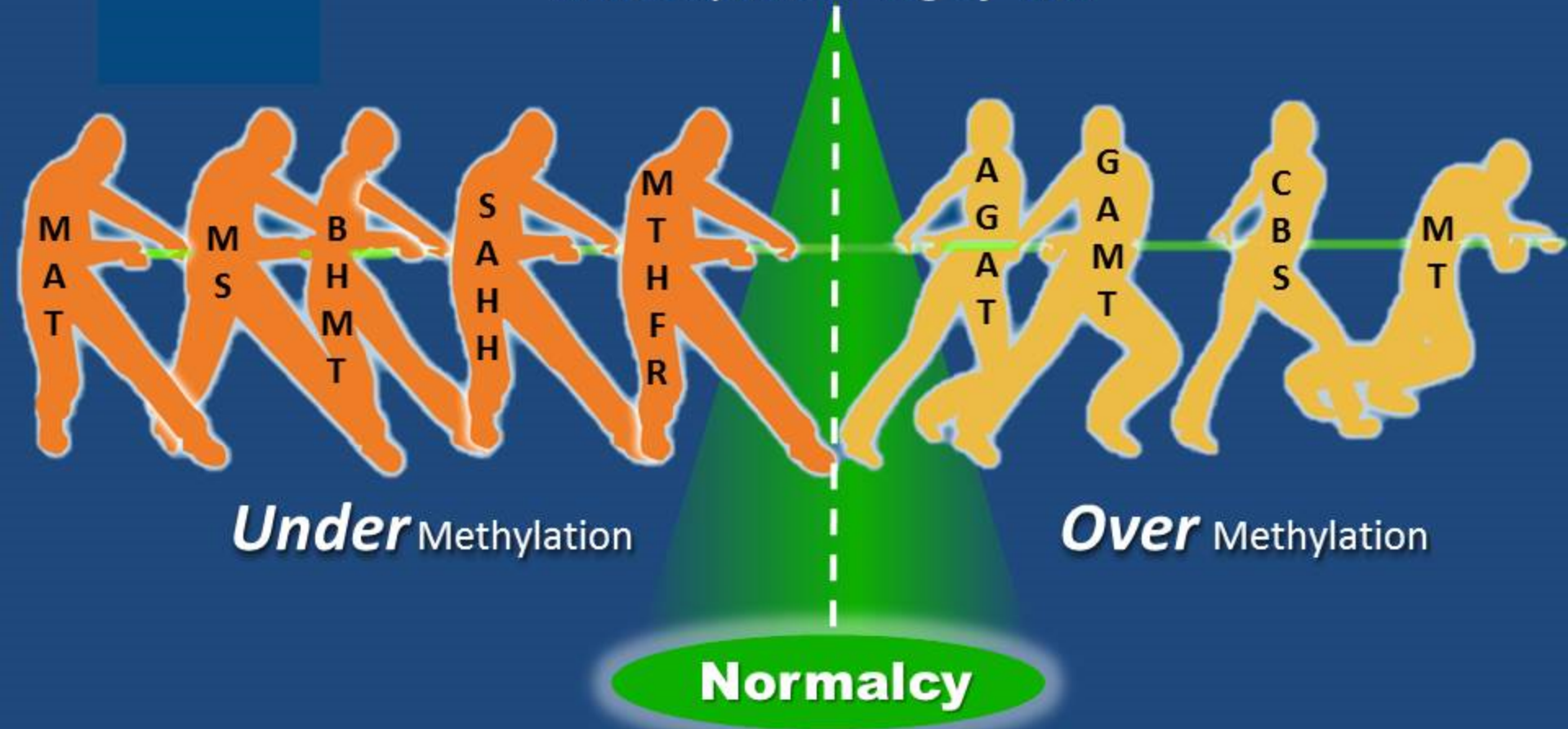
- AGAT or GAMT SNP's
- Arginine or Glycine Deficiency

2. Impaired Cystathionine Synthesis (CBS SNP)

3. Methyltransferase SNPs

Enzyme Mutations and Methylation

A Methylation Tug of War



Lab Tests for Methylation Status

1. SAME/SAH Ratio (limited availability)
2. Whole-blood histamine (methylation marker)

Note: Present genetic tests (MTHFR, etc.) cannot determine ***net effect*** of SNPs that enhance/depress methylation

Under Methylation: Symptoms & Traits

Partial List

- Very strong-willed, oppositional to authority
- Seasonal inhalant allergies
- Competitive in sports or games
- Calm demeanor but high inner tension
- High fluidity (tears, saliva, etc.)
- OCD tendencies, controlling behavior
- Good response to SSRIs
- High libido

Over Methylation: Symptoms & Traits

Partial List

- High anxiety, panic tendency
- Hyperactivity, nervous legs, pacing
- Sleep disorder
- Low libido
- Absence of seasonal allergies
- Food, chemical sensitivities
- Dry eyes and mouth
- Excellent socialization, empathy
- Non-competitiveness in sports, academics
- Adverse reaction to SSRIs, anti-histamines

Methylation and Epigenetics

- Methylation is a dominant factor in epigenetic processes.
- SAMe, methionine and folates have a powerful epigenetic impact on neurotransmitter activity at synapses.
- More than 60% of ADHD, anxiety, depression and psychosis patients exhibit a serious methylation imbalance.

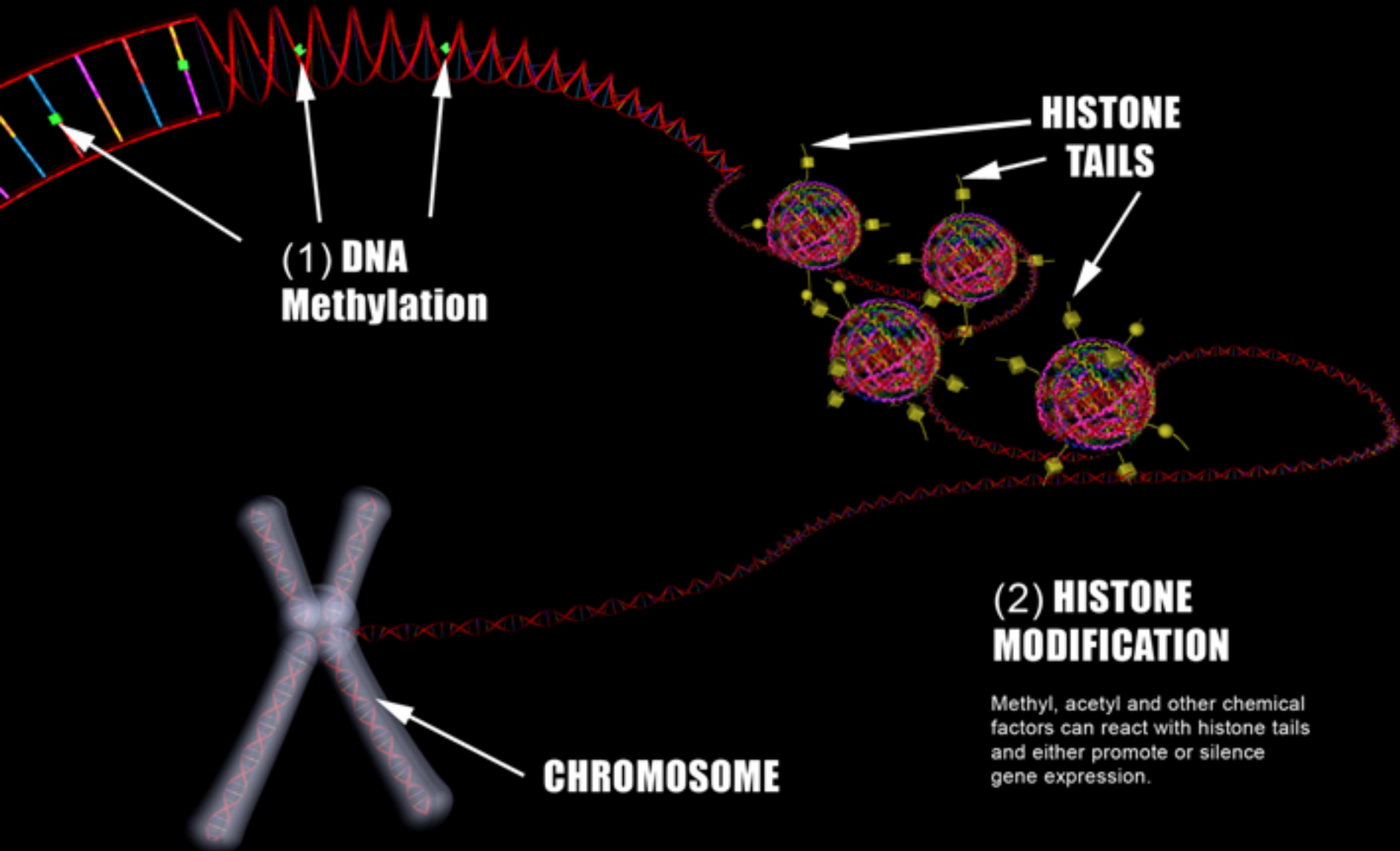
Epigenetics

- >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 alter gene bookmarks and produce mental disorders and other disease conditions.

Two Epigenetic Processes

- DNA Methylation
- Histone Modification

The Two Main Components of the Epigenetic Code



DNA Methylation

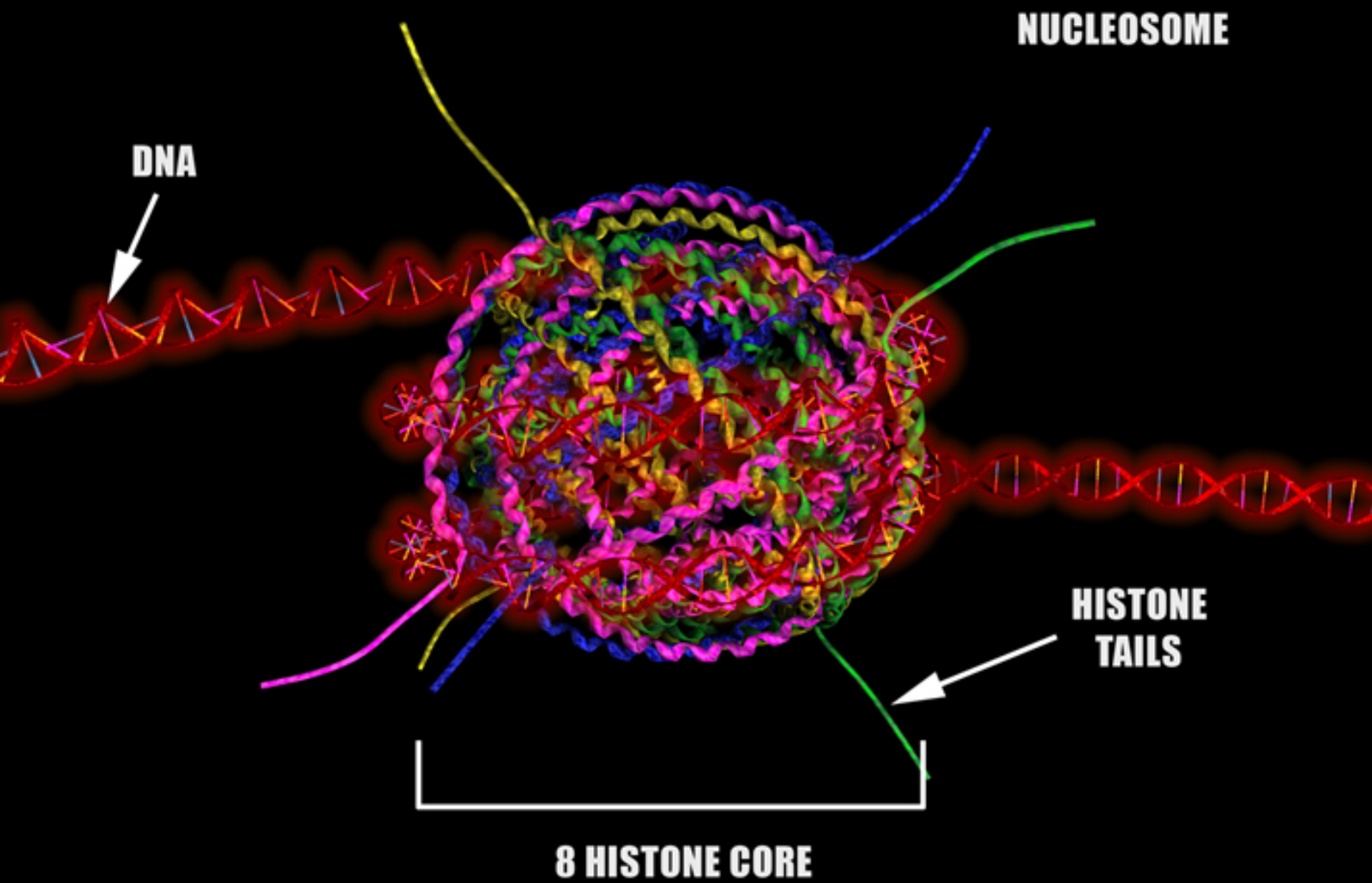
- Established in the womb.
- Methylation of cytosine at promoter CpG clusters can reduce expression (protein production) for the corresponding gene. These methyl “bookmarks” usually remain in place throughout a lifetime.
- In-utero environmental insults can produce deviant bookmarks and serious disorders or birth defects.
- Throughout life, a severe environmental insult may alter one or more gene-regulation marks and produce an epigenetic disorder, such as cancer or a mental illness.



DNA Methylation

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.
- Nutrient therapies can modify histones that control reuptake of serotonin, dopamine, and other NTs.



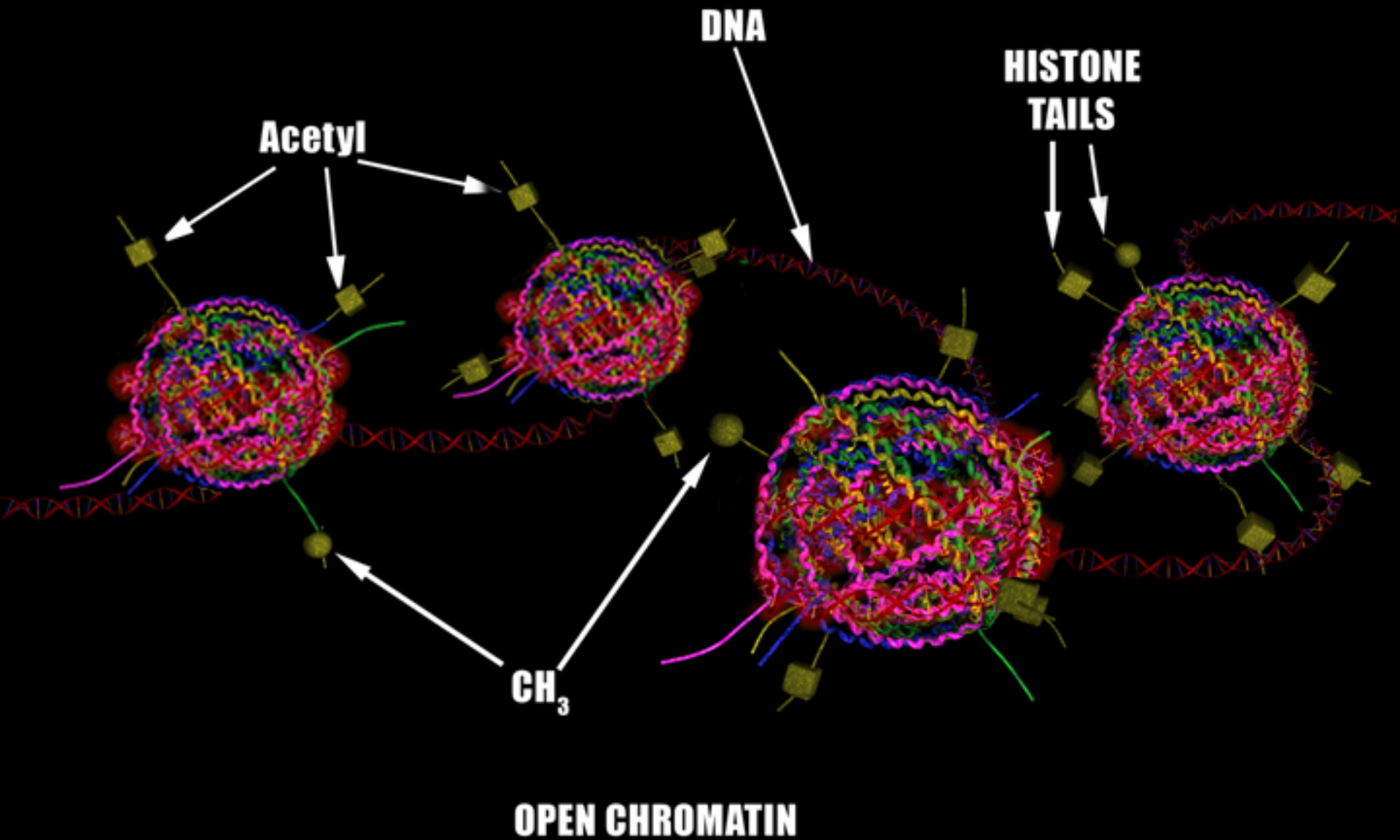
Methyl-Acetyl Competition

- 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 impact the methyl-acetyl competition and alter expression of enzymes that control serotonin and dopamine NT rates.

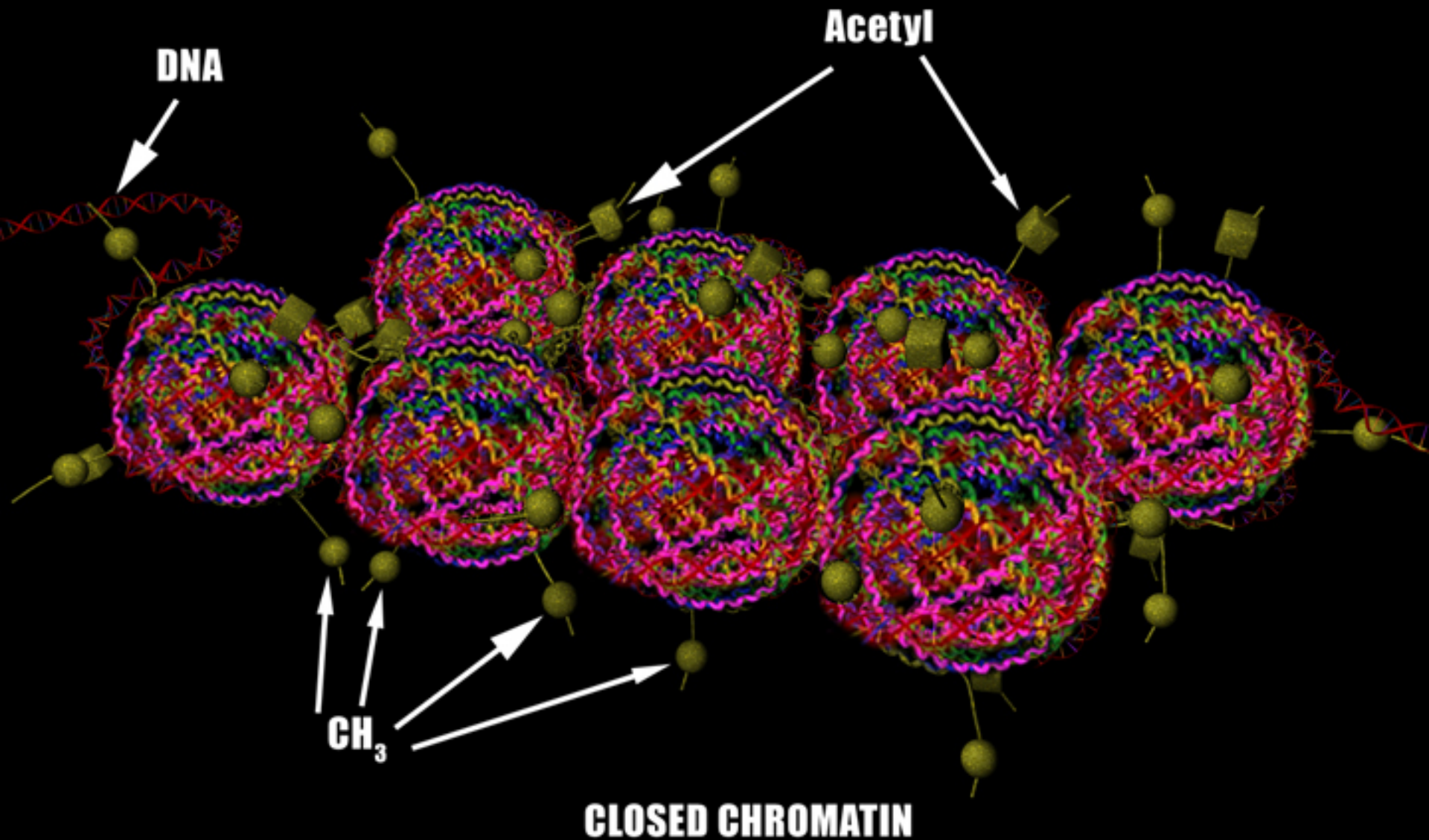
Gene Expression Requires Uncoiling of DNA

- 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



HIGH METHYLATION INHIBITS GENE EXPRESSION



Enzymes Dominate the Methyl-Acetyl Competition

- Acetyl-Coenzyme A and SAMe are the donors of acetyl and methyl, respectively – but their concentrations in brain cells are relatively unimportant.
- Acetylases, deacetylases, methylases and demethylases dominate attachment or removal of acetyl or methyl groups.
- Epigenetic nutrient therapy for adjustment of serotonin or dopamine activity concentrates on the enzymes.

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.

Nutrient Therapy Insights

- 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 glutamate activity at NMDA receptors,
- Many nutrients influence neurotransmitter activity and brain function.

FOLATES REDUCE NT ACTIVITY

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

Low Serotonin Activity Nutrient Therapy Approach

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

Characteristics of an Epigenetic Disorder

- Cases of sudden onset after normalcy
- Persistence of condition after onset
- A multitude of characteristic symptoms
- Heritable illness that violates laws of genetics
- Abnormal methylation
- Severe oxidative overload.

Apparent Epigenetic Gene-Regulation Disorders

- Cancer
- Heart Disease
- Schizophrenia
- Autism
- PTSD
- Wilson's Disease
- Bipolar Disorder
- Alzheimer's Disease

Epigenetic Disorders

- High Degree of Difficulty -

- Autism, schizophrenia, bipolar disorder, PTSD
- Numerous dysregulated genes
- Many systems need correction: immune function, biochemistry, G.I. tract, oxidative stress, brain neurotransmission, etc.
- Multiple interventions often needed.
- Progress usually partial in nature; complete recovery relatively rare.

Non-Epigenetic Disorders

- Moderate Clinical Difficulty -

- ADHD, behavior disorders, anxiety, depression
- Normalization of one to three chemical factors is usually sufficient.
- Outcome studies indicate 70-90% efficacy.
- Medication support usually unnecessary.

Massive Chemistry Database for Behavior Disorders and ADHD

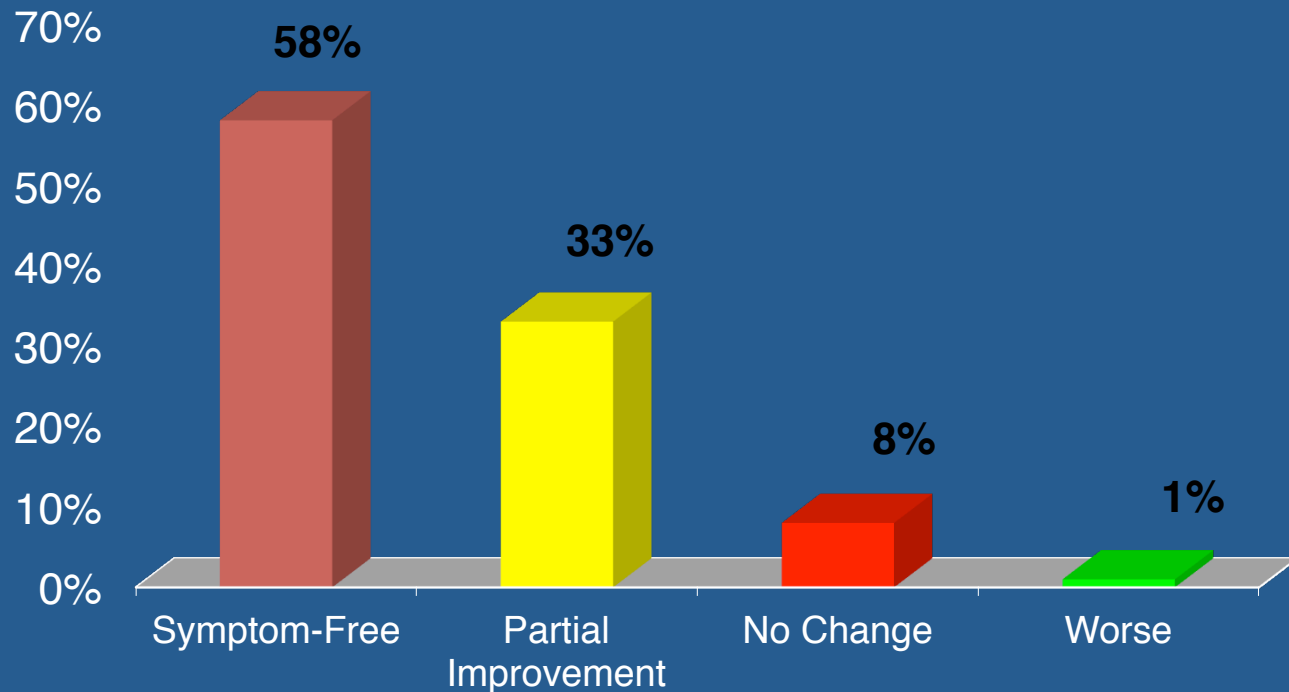
- More than 1.5 million blood/urine/tissue test results for persons diagnosed with behavior disorders and/or ADHD.
- Striking chemistry differences between these populations and the rest of society.

Outcome Study

Walsh, et al. *Physiology & Behavior*, 82:835-839 (2004)

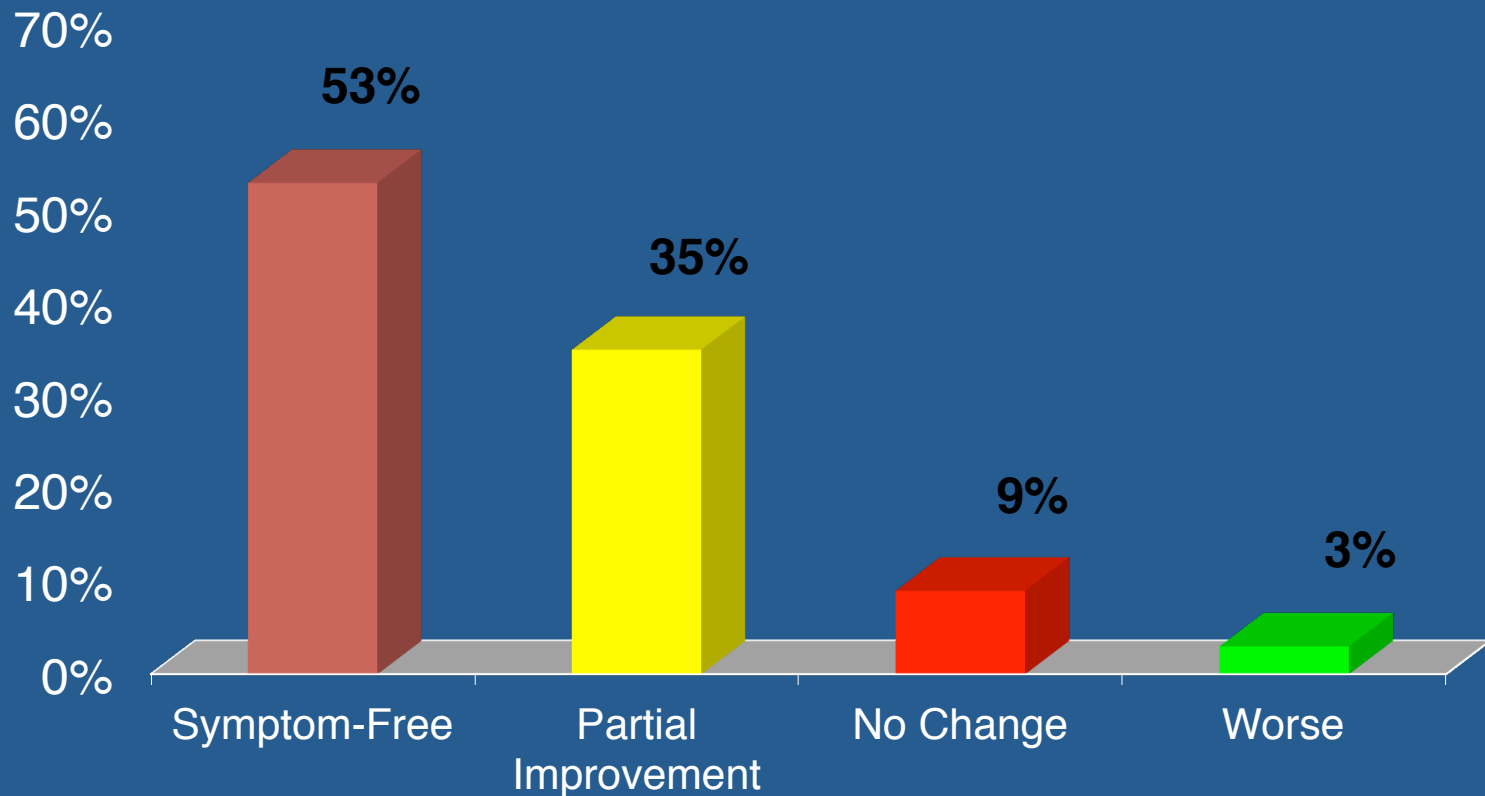
- 207 behavior-disordered subjects
- Identification of biochemical imbalances
- Individualized nutrient therapy to correct imbalances
- Measurement of frequency of physical assaults and property destruction before & after treatment

Treatment Outcomes: Compliant Assaultive Subjects



Treatment Outcomes

Compliant Destructive Subjects



Behavior Outcomes vs. Age

1. Disappointing results for adult criminals who continued abusing drugs & alcohol.
2. Excellent results for violent children and teens.

Since 1990, treatment focus has been on youths.

CLINICAL DEPRESSION

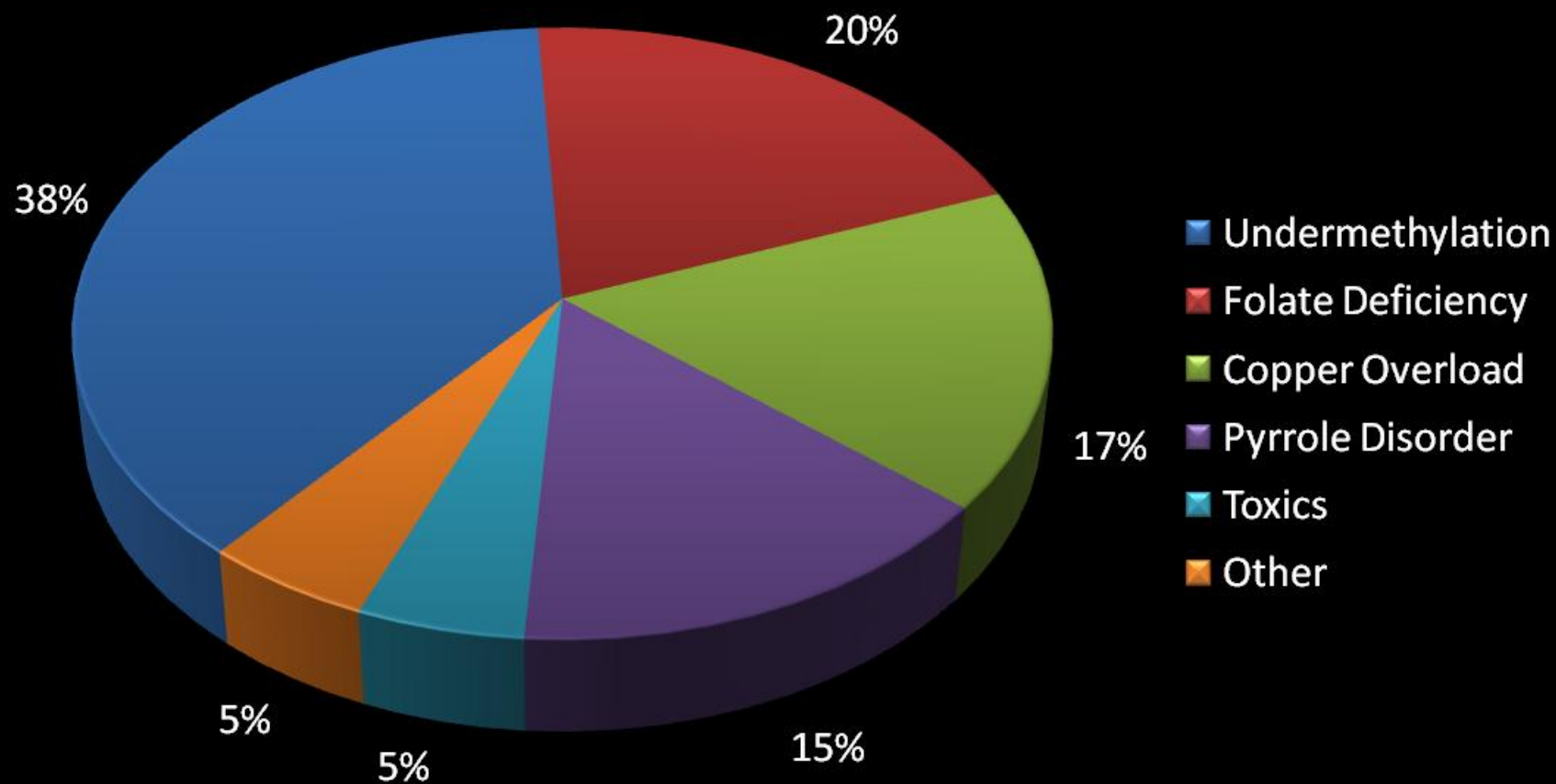
Mainstream Psychiatry Misconception

- 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 represent completely different disorders, each with unique neurotransmitter imbalances and symptoms.
3. Separate treatment approach needed for each biotype.

Depression Biotypes



Phenotype #1

Undermethylated Depression

- Strong-willed
- OCD tendencies
- Calm exterior, but inner tension
- Competitive & perfectionistic
- Seasonal allergies (75%)
- High libido
- Seasonal affective disorder
- SSRI medications usually effective

Phenotype #2

High-Copper Depression

- Elevated norepinephrine, reduced dopamine
- More than 95% are female
- Inability to eliminate excess copper
- High anxiety, tendency for panic
- Onset during hormonal event
- High incidence of post-partum depression
- Estrogen intolerance
- Tinnitus (ringing in the ears)
- Sensitive skin, intolerance to cheap metals
- SSRI antidepressants ineffective

Phenotype #3

Pyrrole Depression

- Severe mood swings
- Explosive anger
- Extreme anxiety, fears
- Poor short-term memory
- Reading disorder
- Little or no dream recall
- Sensitivity to light, noise
- Very poor morning appetite
- Abnormal fat distribution
- Fair response to SSRI antidepressants

Phenotype #4

Toxic Metal Depression

- Absence of trauma or emotional triggers
- Abdominal distress
- Unrelenting depression
- Cognitive deficits (children only)
- Metallic taste in mouth, bad breath
- Irritability, anger
- Food sensitivities
- High oxidative stress
- SSRI antidepressants ineffective

Phenotype #5

Low-Folate Depression

- Tendency for high anxiety, panic
- Non-competitive in sports or games
- Absence of inhalant allergies
- Food/chemical sensitivities
- High musical or artistic ability
- Underachievement
- Sleep disorder
- Low libido
- Adverse reaction to SSRI medications

Treatment Example (160 lb Adult)

Undermethylated Depression

- SAMe and/or methionine (reduce SERT expression and inhibit serotonin reuptake)
- B-6 (enhance synthesis of serotonin and glutathione)
- Antioxidant support (Zn, Se, Vitamins C, E, etc.)
- Augmenting nutrients as indicated (Biotin, Ca, Mg, Cr, TMG, Inositol, Serine, Vitamins A, D)

Biochemical Treatment of Clinical Depression

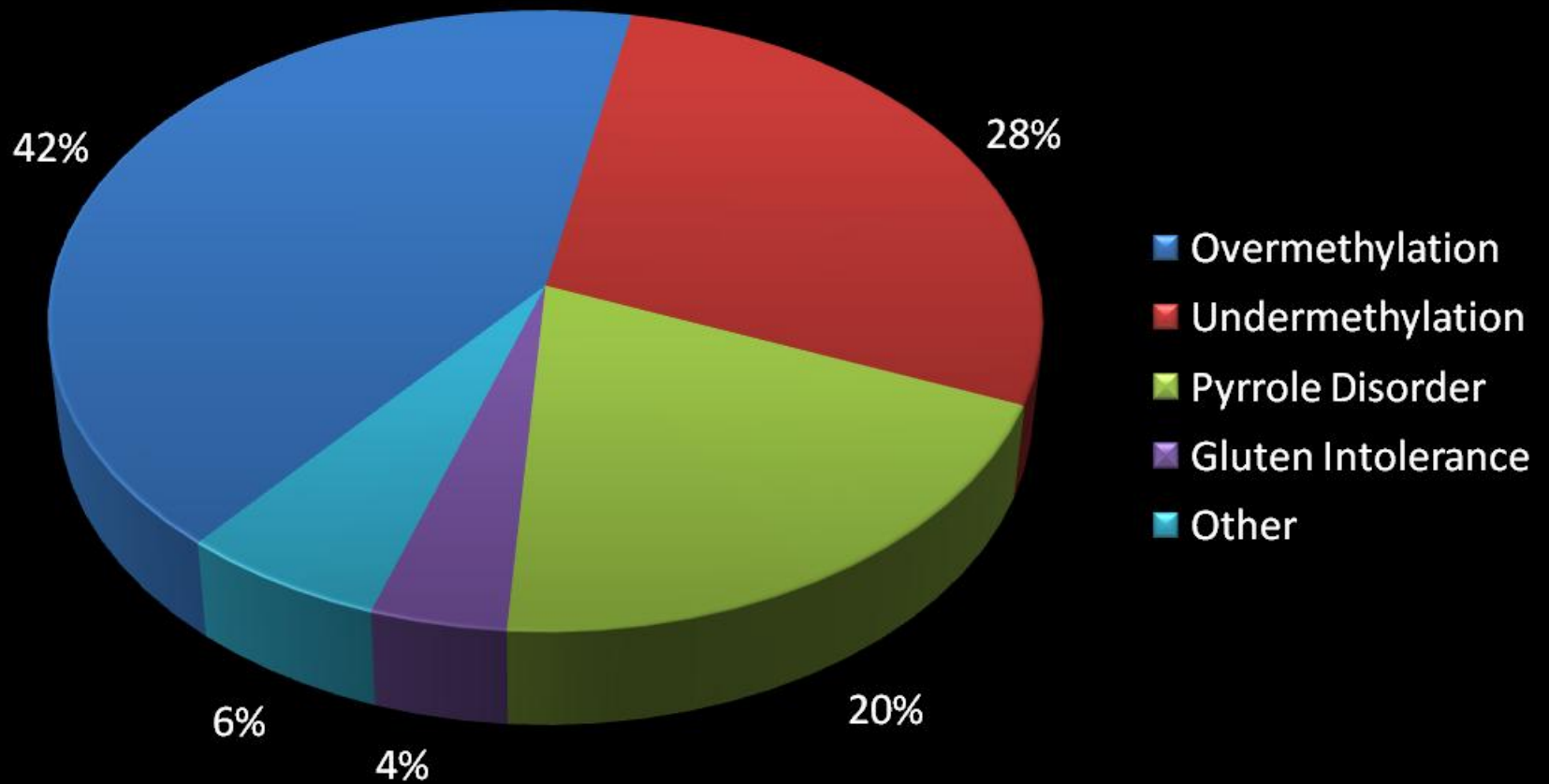
- Therapy using vitamins, minerals, amino acids, and other chemicals that are natural to the body (drug-free)
- Separate treatment approach for each biotype
- 80% of families report major improvements and ability to eliminate psychiatric drugs.

SCHIZOPHRENIA

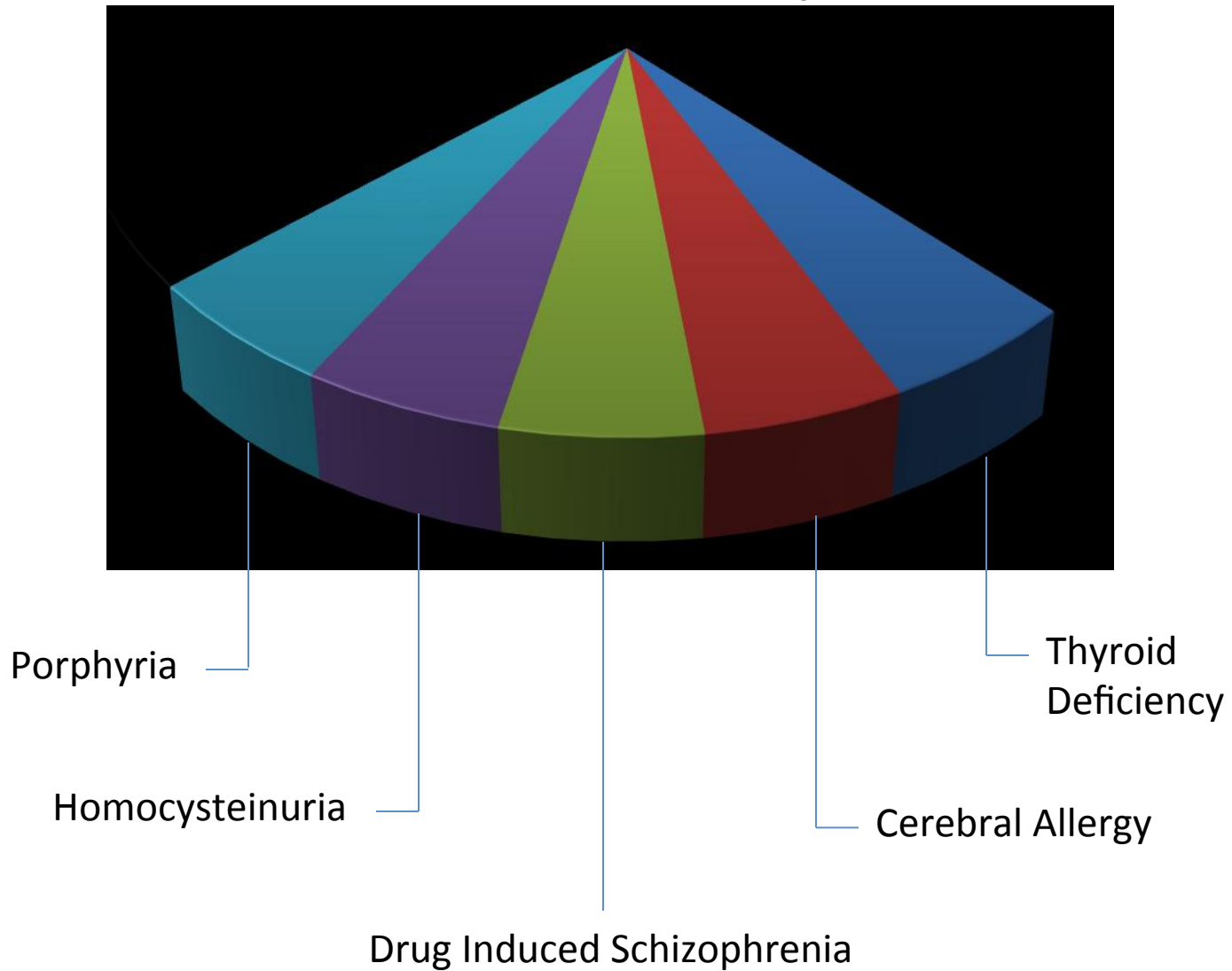
Chemical Classification of Schizophrenia

1. Our database studies have verified Carl Pfeiffer's three major high-incidence schizophrenia biotypes.
2. The biotypes represent very different disorders, each with unique neurotransmitter imbalances and symptoms.
3. Separate treatment approach needed for each biotype.

Schizophrenia Biotypes



Other Forms of Schizophrenia



Undermethylated Schizophrenia

- Severe Delusions
- Obsessive/Compulsive Behaviors
- Social Isolation
- High Internal Anxiety; Calm Exterior
- Catatonic Tendencies
- Phobias

Pyroluric Schizophrenia

- Severe Deficiency of B-6 and Zinc
- Onset During Severe Stress
- Mixed Psychotic Symptoms
- Extreme Anxiety & Fear
- Explosive anger
- Severe Mood Swings
- Morning nausea
- Abnormal Fat Distribution
- Preference for spicy foods

Gluten Intolerance

- 4% of Psychosis Cases
- Incomplete Breakdown of Gluten Proteins in the G.I. Tract
- Short Peptides with Opioid Properties

Treatment: Dietary Avoidance of Wheat, Oats, Barley, and Rye

Biochemical Treatment of Schizophrenia

- Therapy using vitamins, minerals, amino acids, and other chemicals that are natural to the body (drug-free)
- Separate treatment approach for each biotype
- 85% of families report major improvements, reduced dependence on medication, and lessened side effects.

Schizophrenia: Evidence of an Epigenetic Disorder

- Abnormal methylation or severe oxidative overload in more than 95% of SZ individuals
- Relative normalcy prior to the mental breakdown event
- Persistence of illness after the breakdown
- Schizophrenia violates classical laws of Mendelian genetics.

Epigenetic Insights Into Schizophrenia 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, glutathione, d-serine, d-cycloserine, glycine increase NMDA activity.
- Numerous other nutrients influence neurotransmitter activity and brain function.

Excessive Dopamine Activity Nutrient Therapy Approach

- Support acetylation of histones with folic acid and niacinamide (powerful deacetylase inhibitors).
- Augmenting nutrients DMAE, zinc, selenium, chromium, Vitamins B-6, B-12, C, D, E.
- Excessive dopamine activity has been observed in about 40-50% of schizophrenics, 18% of depressives, and 60% of persons with generalized anxiety disorder.

Treatment Example (160 lb adult) Excessive Dopamine Activity

- Folic Acid, 2400 mcg/day, and Niacinamide, 1000 mg/day to support acetylation of histones and promote reuptake of dopamine.
- Augmenting nutrients DMAE, zinc, manganese, selenium, chromium, Vitamins B-6, B-12, C, D, E.
- Especially promising for ADHD, depression, anxiety and schizophrenic patients who exhibit excessive dopamine activity.

A Look at the Future

- Identification of misbehaving genes in cancer, autism, schizophrenia, and other epigenetic disorders will be achieved in the near future. Therapies to normalize deviant gene expression will eventually be developed.
- Epigenetic therapies of the future may enable a cure for persons who develop these disorders.
- Future newborn babies may be screened for epigenetic errors and receive treatment to prevent these disorders.

2015 Nobel Prize – Chemistry

Modrich, Lindahl, Sancar

- Groundbreaking research on DNA repair mechanisms
- Potentially the most important scientific advance since Watson and Crick's discovery of the DNA double helix
- New therapies to maintain DNA integrity may slow the aging process and enable prevention of cancer, autism, schizophrenia, heart disease, and many other illnesses.

Summary

- Nutrient imbalances play a critical role in most mental disorders.
- Recent research in methylation and epigenetics is providing a roadmap for advanced nutrient therapies.
- Nutrient therapy represents an effective weapon in the arsenal of a mental health practitioner.

THANK YOU!

William J. Walsh, PhD

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