# MTHFR and Mental Health: Understanding the Overall Effect of Individual Genetic Mutations (SNPs)

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This lecture is presented by Albert Mensah, M.D. and was originally hosted as a webinar. The archive is available on YouTube. Use these outline notes in this PDF file as a guide while you listen to the recorded talk.



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**Methylation** is a biochemical process responsible for dozens of chemical reactions in the body and the brain. Not only is it essential to physical and mental health, but also influences an individual's characteristics and traits. For example, undermethylation is associated with perfectionism, high accomplishment, OCD tendencies, and seasonal allergies. Persons who are overmethylated have a tendency to have excellent social skills, artistic or musical abilities, chemical and food sensitivities, and high anxiety. Severe methylation imbalances can also contribute to serious mental health disorders.



The popular genetic testing for MTHFR, MS, and other

SNPs, are qualitative in nature but are limited in their ability to accurately determine the overall effect of individual genetic mutations. Learn how overall methylation status is critical for the treatment of autism, anxiety, behavioral/ learning disorders, depression, bipolar, eating disorders, and schizophrenia.

**Dr. Albert Mensah** is an internationally recognized physician-specialist in metabolic treatment approaches for patients with developmental, behavioral, learning and mental health issues. He is the president and co-founder of Mensah Medical, a biomedical outpatient clinic of physicians and nurses who encompass the best of traditional medicine and natural medicine based on biochemical evaluation, evidence-based research and clinical experience. Dr. Mensah utilizes a non-drug, nutrient approach targeted to correct biochemical imbalances that may be associated with anxiety, fears, autism, ADHD, learning disabilities, eating disorders, bipolar disorder, depression, school phobias, mood swings, aggressive or violent behavior, childhood and adult schizophrenia, Alzheimer's disease and Parkinson's Disease. Patients can be seen at our main clinic located just outside of **Chicago**, and in select cities at U.S. Outreach Clinics located near **San Francisco** and **Los Angeles**, and in **Annapolis, Maryland**, **Scottsdale, Arizona**, and **Fort Lauderdale, Florida**.

### The Brain is a "Biochemical Factory"

- Given the proper supply of building blocks and co-factors, the brain creates biochemical processes essential for normal brain function.
- Serotonin, dopamine, norepinephrine and other neurotransmitters are synthesized in the brain.
- The raw materials for neurotransmitter synthesis are nutrients: <u>vitamins, minerals,</u> <u>and amino acids.</u>
- Genetic expression (production) of key transporters is enhanced by certain nutrients and inhibited by others. **Methylation** of chromatin proteins is a primary mechanism for "silencing" genes that produce neurotransmitter transporters.
- By understanding the methylation cycle, SNPs, and enzymes, advanced nutrient therapy aims to heal the brain and correct methylation imbalances.

# Why is Methylation Important?

- The methylation cycle is essential for good mental health. Basic nutrients are necessary for normal function of this cycle.
- Excessive nutrient overloads and deficiencies disrupt methylation pathways in the brain. Additionally, severe oxidative stress can lead to poor immune function and disruption of the methylation cycle.
- To explain: The body's methyl groups turn genes off or on by affecting interactions between DNA and the cell's protein-making machinery genes.
- Too much or too little of important methyl groups can cause a methylation imbalance.
- Altered DNA methylation (epigenetics) during early fetal development, can predispose individuals to cancer, depression, schizophrenia, autism, and other disease conditions including Alzheimer's.

# **DNA Methylation**

- We share 99.9% of our DNA with everyone of the same gender -- it's the 0.1% that makes us different.
- More than 10 million single-nucleotide polymorphisms (SNPs) have been identified in the human genome. These are also called **gene mutation**.
- Most humans have more than 1,000 SNPs or genetic mutations. And most people function without any physical or cognitive difficulty despite these mutations.
- There are SNPs that tend to **reduce** methylation and others that **increase** methylation. <u>A patient's methyl status depends on the overall combined</u> <u>impact of these SNPs.</u>

# The Truth About Genetic Mutations (SNPs)

- The impact of an individual SNP varies from person to person
- Certain strategically-placed SNPs can significantly weaken enzyme function
- Most SNPs have little or no effect on enzyme function
- The larger the molecule, the less significance a SNP has on that enzyme's function
- The smaller the molecule or enzyme, the greater the significance a SNP has on enzyme function















### Massive Chemistry Database and Evidence-Based Research

- The Walsh Research Institute database contains more than 3 million chemical test results for patients diagnosed with autism, ADHD, depression, bipolar disorder, schizophrenia, and behavioral/learning disorders.
- Striking blood/urine chemistry differences between these patient populations and normal controls.
- Methylation status has been determined for 30,000 actual mental health patients over a thirty year period.

Walsh, William J. Nutrient Power. New York: Skyhorse Publishing, 2012.



Image Credit: "The Role of Methylation and Epigenetics in Brain Disorders" by William J. Walsh, PhD

## **Did You Know?**

- In the general population, 70% exhibit normal methylation, 22% are undermethylated and 8% are overmethylated.
- About **70% of persons with mental disorders** exhibit a serious <u>methylation disorder</u>.

#### **Incidences of Undermethylation**

•	Autism Spectrum Disorder	<b>98</b> %
•	Antisocial Personality Disorder	95%
•	Schizoaffective Disorder	90%
•	<b>Oppositional Defiant Disorder</b>	85%
•	Anorexia	82%
•	Depression	38%
•	Behavioral Disorder/ADHD	37%

Walsh, William J. Nutrient Power. New York: Skyhorse Publishing, 2012.

### **Undermethylation Symptoms/Traits**

- Obsessive/compulsive tendencies
- Seasonal inhalant allergies
- History of perfectionism
- Low tolerance for pain
- Prior diagnosis of OCD or ODD
- Ritualistic behaviors
- Very strong willed
- Social isolation
- Poor concentration endurance
- Low levels of serotonin
- Good response to SSRIs

- History of competitiveness in sports
- Frequent headaches
- Family history of high accomplishment
- Calm demeanor, but high inner tension
- Delusions (thought disorder)
- Slenderness
- Phobias
- Addictiveness
- High libido
- Suicidal tendencies
- Noncompliance with therapies

### Primary Causes of Undermethylation

- Undermethylation usually results from SNPs that weaken MTHFR or other enzymes in the methylation cycle in utero prior to birth.
- Enzyme Mutations (SNPs) in Methylation Cycle (MTHFR, MS, COMT, just to name a few...)
- Histamine Overload
- Protein Deficiency or Malabsorption

Source: "The Role of Methylation and Epigenetics in Brain Disorders" by William J. Walsh, PhD

#### Methylation Cycle Enzymes



Image Credit: "The Role of Methylation and Epigenetics in Brain Disorders" by William J. Walsh, PhD

#### **Incidences of Overmethylation**

- Panic or Anxiety Disorder
- Paranoid Schizophrenia
- ADHD 289
- Behavior Disorders
- Depression
  I8%

Walsh, William J. Nutrient Power. New York: Skyhorse Publishing, 2012.

28% 30% 18%

64%

52%

### **Overmethylation Symptoms/Traits**

- High anxiety or panic tendency
- Nervous legs, pacing
- Food/chemical sensitivities
- Sleep disorder
- Depression
- Self mutilation
- Dry eyes and mouth
- Adverse reaction to SSRI's
- Excellent socialization
- High empathy for others
- Postpartum depression

- High pain threshold
- Low motivation in school
- Absence of seasonal allergies
- Artistic or musical ability
- Paranoia
- Hyperactivity
- Belief that everyone thinks ill of them
- Obsessions without compulsions
- Low libido
- Antihistamine intolerance
- Estrogen intolerance

### **Primary Causes of Overmethylation**

- Overmethylation is generally caused by enzyme weaknesses (SNPs) in the SAMe utilization pathways.
- Impaired Creatine Synthesis
  - AGAT or GAMT SNP's
  - Arginine or Glycine Deficiency
- Impaired Cystathionine Synthesis (CBS SNP)
- Methyltransferase SNPs

Source: "The Role of Methylation and Epigenetics in Brain Disorders" by William J. Walsh, PhD



Image Credit: "The Role of Methylation and Epigenetics in Brain Disorders" by William J. Walsh, PhD

#### **Creatine Synthesis**



Image Credit: "The Role of Methylation and Epigenetics in Brain Disorders" by William J. Walsh, PhD



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#### **Testing for Methylation Status**

#### **Recommended**: Whole Blood Histamine or SAMe/SAH ratio

- Overall methylation status is a critical component when it comes to determining one's biochemistry. The whole blood histamine test can measure the net effect of the various SNPs, whereas genetic testing focuses on individual SNPs. For example, most persons with the 677T MTHFR SNP are undermethylated, but others are overmethylated.
- Elevated blood histamine indicates undermethylation and low histamine is evidence of overmethylation.
- Antihistamine treatments can artificially lower blood histamine and should be avoided for several days prior to sampling.

### Why Not Genetic Testing?

- Genetic testing can identify predispositions for many disorders such as breast cancer and Alzheimer's disease.
- However, the reliability of genetic testing such as "23andMe" for assessing methylation is not quite limited at present it is not targeted to any one condition in particular, therefore, it is not a guide to treatment therapies.
- Identifying SNP weaknesses in MTHFR and other methylation-cycle enzymes does not necessarily mean that individual is undermethylated since there are SNPs that produce overmethylation.
- Since genetic testing is qualitative and not quantitative, it is improbable by genetic testing alone to either determine the net methylation potential (under or overmethylation) or to direct treatment management.

### **Epigenetics and Methylation**

- What is **epigenetics**? Epigenetics involves the alteration in gene expression due to chemical factors in the womb and the influence of environmental factors throughout life.
- Every cell in our bodies has the potential for expressing any of the 20,000+ genes in our DNA. The production of gene proteins or "gene expression" can be switched on or off (gene silencing or "bookmarking").
- These epigenetic processes are more vulnerable to environmental factors such as radiation, temperature, pesticide exposure, dietary choices, toxic metals, viruses, stressful life events, etc.
- EMF/sleep disturbances

#### **Other Nutrient Imbalances**

- A genetic or epigenetic imbalance in a nutrient can alter brain levels of key neurotransmitters and result in abnormal brain chemistry.
- Vitamin D deficiency has been associated with depression, schizophrenia, ADHD and other mental disorders.
- **Pyrrole Disorder** is an abnormality in biochemistry resulting in the overproduction of pyrrole molecules. Symptoms of **pyroluria** include severe inner tension, extreme mood swings, severe depression, high irritability and temper.
- **Copper overload** tends to lower dopamine levels and increase norepinephrine in the brain. Imbalances in these important neurotransmitters have been associated with paranoid schizophrenia, ADHD, bipolar disorder, postpartum depression and violent behavior.
- Fatty acid imbalances has been associated with depression, ADHD, schizophrenia, bipolar disorder and dementia.
- In many cases, persons exhibit more than just one biochemical imbalance.

#### **Comprehensive Evaluation**

- What is out of balance?
  - Nutrient overloads and deficiencies
- Metal regulation and metal dysregulation
- Gastrointestinal (GI) issues including food allergies/ sensitivities and malabsorption
- Testing for methylation disorders
  - Whole blood histamine evaluation
- Pyrrole Disorder: Zinc/B-6 imbalances
  - Oxidative Stress/Inflammation

#### **Overview of Treatment**

- Physical Examination
- Extensive Patient History



- Specialized Laboratory Testing (blood and urine)
- Diet and Gastrointestinal (GI) issues
- Advanced Nutrient Therapy protocols are prescribed at the appropriate therapeutic level to target the patient's specific needs in order to correct underlying biochemical imbalances.
- Nurse/Physician Follow-Up Care

#### NOW AVAILABLE IN PAPERBACK!

#### **NUTRIENT POWER**

By William J. Walsh, PhD Nutritional Scientist and President of the non-profit Walsh Research Institute 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



