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**Methylation, folate and the brain: Dr William Walsh on "healing biochemistry"**

# Methylation, folate and the brain: Dr William Walsh on autism, PANDAS and the five depressions

“Heal your biochemistry and heal your brain” is one of Dr William Walsh, PhD’s catch-phrases. One of our most popular conference speakers, he is founder and president of the Walsh Research Institute and an international expert on nutrient-based psychiatry, including approaches to methylation. **SHEILA ROGERS DEMARE, MS**, director and founder, ACN Latitudes, puts a series of FAQs.

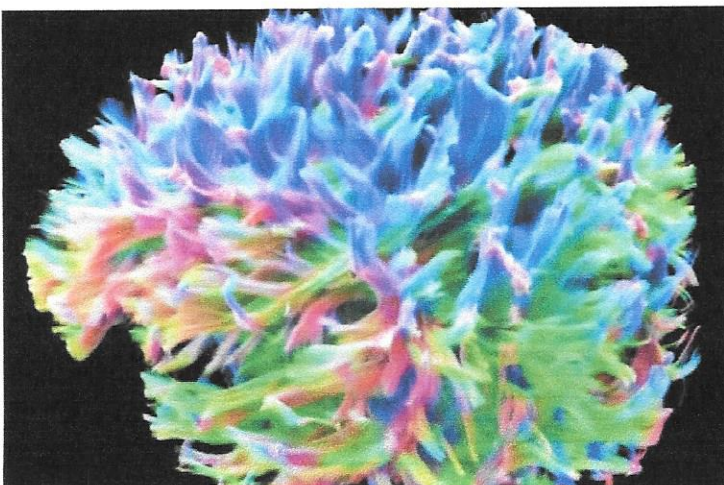
**Do you think autism is reversible, and if so, what approach does your research suggest would be most effective?**



**Dr Walsh:** Autism is very treatable, and complete recovery is possible in young persons whose brains have not completed the early development process.

I’ve worked with thousands of patients with an autism spectrum disorder and seen hundreds who achieved full recovery after biochemical therapy and a special diet. Early intervention is essential. We can make more progress in a month with a two-year-old than in six months with an eight-year old.

It’s becoming increasingly clear that autism is an epigenetic gene-regulation disorder in which environmental insults



INSIDE the brain: Cardiff University Brain Research Imaging Centre (CUBRIC) is producing stunning new images of the brain using Ultra high field MRI that allows scientists to study brain cells of 1,000th of a millimetre across.



alter DNA methylation.

Treatment success requires powerful antioxidant therapy, a toxic-free environment, and coping with GI tract problems. I believe the greatest progress can be made with brain-directed therapies that promote development of brain neurons and synapses to enable improved cognition, speech, and socialization. My personal favorite is metallothionein-promotion therapy.

**Obsessive-compulsive disorder (OCD) is another growing problem. Would you summarise your take on the role of histamine in OCD?**

**Dr Walsh:** More than 90% of OCD patients are undermethylated, with low neurotransmission at serotonin and dopamine receptors. In addition, many have low activity at N-methyl-D-aspartate (NMDA) receptors.

For years we have used whole blood histamine as a laboratory marker for methylation status. Another good lab test for methylation status is the SAME/SAH ratio test offered by Doctors Data, Inc. Neither of these lab tests is perfect, but they are more reliable than present genetic testing for determining

if a patient is under-methylated, over-methylated, or in the normal range.

**If someone seems to have symptoms of low histamine, are there ways to increase histamine levels? And if histamine is too high, what should be done?**

**Dr Walsh:** About 30 years ago, the great Carl Pfeiffer, MD, PhD, believed that histamine's role as a brain neurotransmitter was a central factor in schizophrenia and other mental disorders. Since Pfeiffer's death in 1988, we've learned this is not correct and that methylation imbalances (a) cause abnormal histamine levels and (b) have a major epigenetic effect on mental health.

Methylation is the primary process for metabolising (destroying) histamine, and there is a convenient inverse relationship between histamine levels and methylation status. Our treatments are not aimed at normalising histamine, but in dealing with the brain disorders associated with over-methylation or under-methylation.

Nutrient therapies for treating under-methylation are well-known, but great care must be used in the case of under-methylated

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persons with low serotonin activity. Folic acid, folic acid, and methylfolate all act as serotonin reuptake promoters by an epigenetic mechanism, the opposite of what these patients need.

There is increasing evidence that folates act as deacetylase inhibitors that enhance gene expression of SERT reuptake proteins known as “transporters”. Serotonin reuptake is a far more dominant factor than the amount of serotonin present. Folate supplements (together with B12) are very effective in improving methylation in most under-methylated persons. However,

## PANDAS and PANS – when a child’s behavior suddenly crashes

PANDAS is often suspected when a child suddenly develops “neuropsychiatric” symptoms – such as obsessions and compulsions, involuntary tics, or mood changes – after a strep infection.

Defined in the mid-90s by Dr Susan Sweden, PANDAS stands for “paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections”. The simple explanation of this long term is that a strep infection is causing an immune response that’s affecting the brain of a child, causing changes in behaviour.

PANS (paediatric acute-onset neuropsychiatric syndrome) is a newer term that explains similar sudden symptoms caused by strep as well as other infections and non-infectious triggers. (PANDAS is a type of PANS).

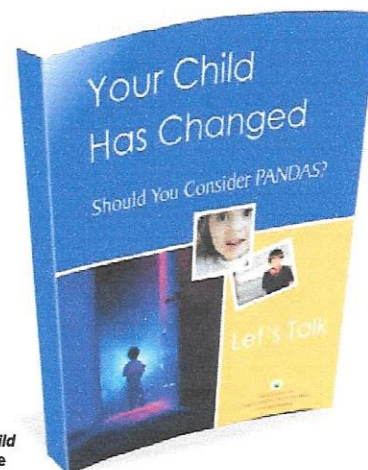
In addition to challenges a family faces in dealing with a child’s symptoms, PANS in general

and PANDAS in particular is difficult because:

- Numerous types of triggers can cause similar symptoms
- Some in the medical community insist PANDAS does not exist.
- A controversy exists on how to diagnosis PANDAS and PANS.
- Many physicians are not familiar with the conditions, and it is difficult to find expert help.
- Research has not yet defined the best treatment approaches.
- Some of the recommended therapies are expensive and, in the US, are not covered by insurance.

The good news is that progress is being made, and children can be treated successfully.

• ACN latitudes resources on PANS include the e-book *Your Child Has Changed*. Should you Consider PANDAS? Let’s Talk, and are at <https://latitudes.org/category/conditions/pandas-pans>.



folate supplements should be avoided for under-methylated patients who suffer from depression, anxiety, or other mental disorders that involve low activity at serotonin receptors.

Recent advances in epigenetic science have provided a road map for effective natural therapies that can regulate activity of serotonin, dopamine and other neurotransmitters without the side-effects associated with anti-depressant drugs. I believe that the need for drug therapies will gradually fade away as brain science advances.

**Have you seen any children with a PANDAS/PANS diagnosis, and do you think there is a nutritional way to avoid or treat such severe behavioural and neurological reactions to bacterial, viral, or other types of infections?**

**Dr Walsh:** PANDAS/PANS has many characteristics of an epigenetic gene-regulation disorder especially

- (a) sudden onset,
- (b) a multitude of serious symptoms,
- (c) being difficult to treat, and
- (d) being a condition that can persist for years after onset.

Epigenetic disorders are caused by environmental insults that alter DNA methylation or other gene-regulation factors.

I’ve only seen a few dozen children diagnosed with PANDAS and do not consider myself an expert in this disorder. I HAVE noticed that most of these children exhibit severe under-methylation and oxidative stress. Also, a high percentage had elevated pyrroles and zinc deficiency. It’s hard to believe that nutrient therapies to correct these imbalances would not result in significant improvement. However, I have no outcome data for PANDAS/PANS.

**Your research shows there are five types of depression, and you recommend that a different treatment approach should be taken for each type. How do you evaluate people to learn which type of depression they may have, and then offer suitable treatment?**

**Dr Walsh:** We have identified five chemical biotypes of clinical depression that represent about 95% of cases.

Our classification system is based on studies of 2,800 patients, including more than 250,000 blood/urine chemistry results and in-depth medical histories. Until now, most mainstream experts have regarded depression as a single condition with variations along a central theme – low activity at serotonin receptors.

We have observed low serotonin activity in two of the biotypes, with different brain disorders dominating the other cases. We reported these findings at the annual American Psychiatric Association (APA) meeting in New York City this spring.

The under-methylation (38%) and pyrrole disorder (15%) biotypes involve low serotonin activity, with many reports of improvement after SSRI antidepressants. However, these patients also respond to individualised nutrient therapy.

High-copper (17%) depressives showed little response to anti-depressants, but reported great improvement after copper-lowering nutritional supplements.

The low-folate (20%) biotype consisted of patients who reported severe intolerance to SSRIs, but thrived on supplements of folates and B12.

The smallest biotype (5%) involved toxic metal overloads such as lead, mercury, cadmium, etc.

At the APA we recommended inexpensive blood/urine tests for all depression patients, and different treatment approaches for each biotype. This is a medical procedure that requires a practitioner experienced in these protocols. We are actively engaged in continuing medical education (CME) educational programs to enable doctors to incorporate these methods into their practices.

**In your opinion, do people fall into either an over-methylated or under-methylated status, or can you be an under-methylator in certain areas of the methylation cycle and an over-methylator in other areas of the cycle? If someone has some traits of an under-methylator and some traits of an over-methylator, what would you recommend?**

**Dr Walsh:** Based on my massive chemistry database, about 22% of the population is under-methylated and 8% over-methylated.

These are inborn tendencies that usually persist throughout life. Under-methylation usually results from single nucleotide polymorphisms (SNPs) that weaken MTHFR or other enzymes in the methylation cycle. Over-methylation is generally caused by enzyme weaknesses (SNPs) in the SAME utilisation pathways.

Nutritional supplements, certain drugs, and special diets can adjust methylation, but the inborn tendency usually remains. We have evaluated the methylation status of more than 25,000 patients and controls and identified dozens of distinctive symptoms and traits associated with methylation imbalances. For example, most under-methylators report allergies to ragweed and have a history of strong will, perfectionism, competitiveness,

and OCD tendencies.

Over-methylators are usually characterised by excellence in music and art, empathy, excellent socialisation, high anxiety, and food/chemical sensitivities. All of these traits are generalities with many exceptions, and very few persons exhibit all of the traits associated with their methylation biotype. However, an experienced practitioner can usually predict the methylation lab results after a good medical history.

What are your thoughts on using genetic testing, such as 23andMe, to create an individual methylation road map/treatment plan.

Dr Walsh: Genetic testing is quite inexpensive, highly accurate, reliable, and will certainly grow in importance in future years. These tests can already identify predispositions for many disorders, such as breast cancer and Alzheimer's, and may soon make obsolete the need for pap smears.

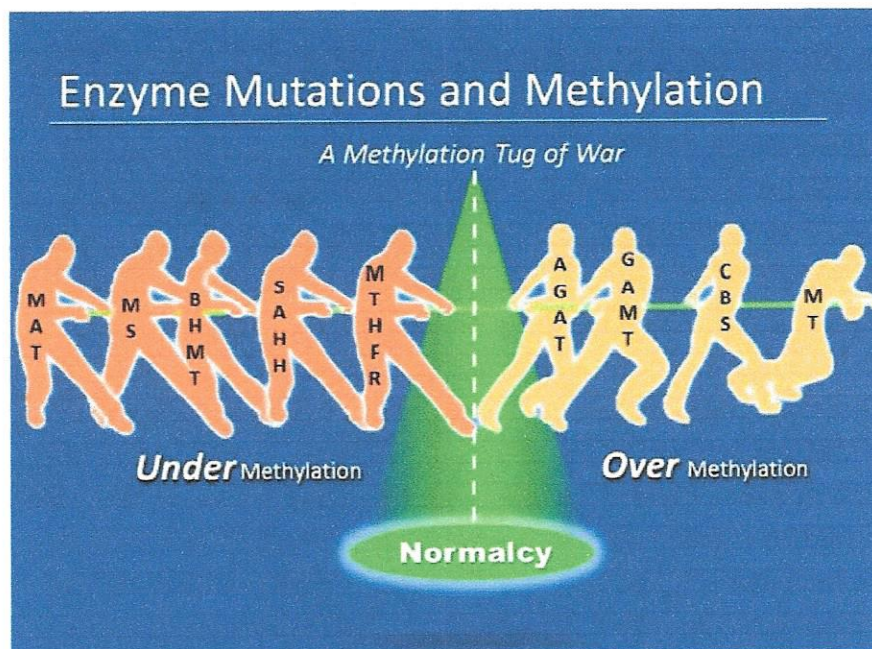
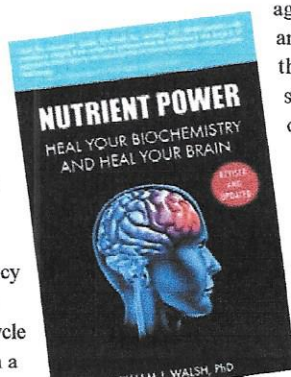
However, the reliability of genetic testing for assessing methylation is quite limited at present. Identifying SNP weaknesses in MTHFR and other methylation-cycle enzymes does not necessarily mean that individual is under-methylated. There is a "tug-of-war" competition between enzyme SNPs that weaken methylation and SNPs in the SAME utilisation pathway that can produce over-methylation.

Since the genetic information is qualitative and not quantitative, it is often impossible to determine the net methylation potential from genetic testing. Fortunately there are blood tests that can test for overall methylation status (the net effect of the competing SNPs), and I greatly prefer to use them – SAME/SAH ratio and whole-blood histamine.

In addition, blindly using methylfolate (Deplane) for patients with 677T MTHFR or other weakened enzymes can produce negative results in patients affected by low serotonin activity. Folate supplements including Duplin tend to drive serotonin activity even lower by an epigenetic mechanism (see previous question).

The benefits from improving methylation are overwhelmed by weakened serotonin neurotransmission for these persons.

Methylfolate supplements are a clever approach for coping with under-methylation in persons with MTHFR enzyme weaknesses. However the potency of methylfolate has been greatly exaggerated. The methylation cycle spins constantly, with more than a



(Graphic courtesy of the Walsh Research Institute: <http://www.walshinstitute.org>.)

million methylation reactions per second.

The methylation cycle somewhat resembles a speedway circuit, with traffic constantly spinning around the track. Methylfolate is what I call a "suicidal" nutrient, that is, a nutrient that acts only once. After a single pass through a portion of the cycle, methylfolate loses its identity and becomes part of the garden-variety THF pool. Methylfolate is somewhat more effective than folic acid and fulminic acid, but is not as effective as advertised. The bottom line is that methylfolate and other folate supplements are very effective in enhancing methylation for autism and other conditions that are not dominated by low serotonin activity.

In your book *Nutrient Power*, you frequently use the term "methyl" as in the methyl/folate balance and in giving methyl to address neurotransmitter imbalances. What is methyl? Do you mean methylcobalamin? Dr Walsh: The occasional use of "methyl" in my book is shorthand for methyl donors such as methionine and SAME. 20 years

ago I presented a paper at the annual APA meeting describing the opposite effects of folate supplements and methyl donors on neurotransmitter activity and began using the term methyl/folate ratio. I believe it's time to find a better expression for this factor.

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## About the author

Sheila A. Rogers Demario is a leader in the field of integrative therapies for neuropsychiatric disorders. She is founder and director of the international non-profit Association for Comprehensive NeuroTherapy (ACN latitudes) and editor of the website Latitudes.org. She communicates regularly with physicians, families, and organisations to learn and share new findings on treating neurological

conditions with integrative medical methods. She served on the advisory board for Health Journal Television for several years during its production (hosted by General Alexander Haig). Sheila is author of the Amazon best-seller *Natural Treatments for Tics and Tourettes*, distributed by Random House. A national speaker on Tourette syndrome she is co-author of the study "Nutritional supplements and complementary/alternative medicine in Tourette syndrome" (*J Child Adolesc Psychopharmacol*). A certified school psychologist, she served as Mental Health Liaison for the School District of Palm Beach County, and was program developer for highly successful children's service programs in Palm Beach County. She is also a consultant on the childhood obesity epidemic.

• <https://latitudes.org>.