Personalised Methylation Report

Made For (Client's name)

Dear (Client's name)

Welcome to your Methylation report!

You've taken a great step on your personalised wellness journey by exploring the science of methylation.

Understanding your body's unique needs is key to long-term wellness. Methylation, a critical biochemical process influenced by your genetics, plays a pivotal role in numerous bodily functions.

Your Methylation report will reveal how your unique genetic makeup affects your methylation capabilities, guiding you in optimising your nutrient intake for enhanced methylation activation.
This personalised insight empowers you to tailor your lifestyle and nutrition choices to boost your overall health and wellbeing.

Within your report, you'll discover the importance of key nutrients in methylation, how your DNA impacts your needs, and actionable steps to optimise your methylation pathways.

Read on to find out more about you.

What is Methylation?

Methylation refers to the process where methyl groups are transferred between molecules, altering their structure and function.

A methyl group is made up of one carbon atom and three hydrogen atoms, hence the alternative term "one carbon metabolism". Methylation can be thought of as the process of turning a raw material into a form that we can use, and is involved in almost every biochemical reaction in every cell in our body, occurring billions of times per second. Understanding methylation and its impact on health is crucial for managing and optimising these vital biochemical processes. Genetic variations in key genes involved in the methylation cycles can significantly influence individual health outcomes, necessitating personalised approaches to nutrition and supplementation.

Methylation is essential for a multitude of processes within our body, without which we simply wouldn't function. The regulation of gene expression, energy production, fat metabolism, protein function, immune responses and cell membrane repair all rely on methylation. Additionally, methylation plays a key role in the production and metabolism of neurotransmitters that regulate mood (and other neural processes) and so has a huge impact on our mental function. It also aids in detoxification processes that neutralise toxins, thereby promoting overall health.

What other factors influence Methylation capabilities?

Several factors can influence methylation, including diet, toxin exposure, and stress. Deficiencies in key dietary cofactors involved in the methylation cycles such as vitamins, minerals, and amino acids can impair the methylation process. In turn this can increase susceptibility to chronic conditions such as impaired immunity, fatigue, cardiovascular disease, neurological disorders, multiple cancers, and mood and psychiatric disorders.

Methylation and your DNA

We all carry genes that are involved at various stages within the methylation pathways, and variants in these genes can significantly influence their function. By assessing these genetic variants, or single nucleotide polymorphisms (SNPs), we can understand their potential impact on how that gene functions and identify any inhibited methylation pathways.

In turn, this can help us identify an individual's specific nutritional support needs or lifestyle interventions which could reduce potential risks and contribute to better overall health. Although you can't change your genetic code, the expression, synthesis, and function of your genes can be modulated and supported once we are armed with the right knowledge!

Helpful Terms

You'll see some of the same terms come up many times throughout your report. Here are some definitions you can refer back to:

Methylation

A biochemical process involving the transfer of methyl groups between molecules, crucial for regulating gene expression, protein function, and detoxification. Methylation occurs billions of times per second in every cell. Impaired methylation can lead to health issues such as cardiovascular disease, neurological disorders, and impaired detoxification, while overactive methylation can cause abnormal gene expression and potentially cancer.

One Carbon Metabolism

A network of biochemical pathways that involve the transfer of one-carbon units (methyl groups) between molecules. This process is essential for DNA synthesis and repair, amino acid metabolism, and the regulation of gene expression.Methyl GroupA chemical group consisting of one carbon atom bonded to three hydrogen atoms (CH3). Methyl groups are transferred between molecules in methylation reactions, influencing gene expression, protein function, and metabolism. Imbalances can disrupt numerous biological processes.

Homocysteine

A sulphur-containing amino acid that is an intermediate product in the metabolism of methionine and cysteine. Elevated levels of homocysteine, known as hyperhomocysteinaemia, can increase the risk of cardiovascular diseases, cognitive decline, and other health issues. Low levels are uncommon and usually not problematic, but they may indicate a deficiency in related nutrients such as folate or vitamin B12.

Methionine

An essential amino acid obtained from dietary protein that plays a key role in methylation. Methionine is converted to S adenosylmethionine (SAMe), the body's primary methyl donor. Deficiency can impair methylation and detoxification processes, while excess methionine intake can lead to elevated homocysteine levels, increasing the risk of cardiovascular diseases.

SAMe (S-adenosylmethionine)

A compound derived from methionine and ATP that serves as the primary methyl donor in numerous biochemical reactions, including DNA methylation, neurotransmitter synthesis, and detoxification. Low levels can impair these processes, while high levels may indicate excess methionine intake or dysregulated methylation.

SAH (S-adenosylhomocysteine)

A byproduct of methylation reactions where SAMe donates a methyl group. SAH is subsequently hydrolysed to homocysteine and adenosine, and high levels of SAH can inhibit methylation. Elevated SAH can indicate impaired methylation and contribute to elevated homocysteine levels.

SAMe:SAH Ratio

The SAMe:SAH ratio is commonly used as an indicator of cellular methylation potential. A higher ratio suggests a favorable environment for methylation reactions, implying that there are sufficient methyl groups available. Conversely, a lower ratio may indicate a reduced capacity for methylation, possibly due to lower levels of SAM or higher levels of SAH.

Cofactors

Non protein chemical compounds that bind to enzymes and are necessary for their activity. Cofactors can be metal ions (such as magnesium or molybdenum) or organic molecules (such as vitamins). Deficiency in cofactors can impair enzyme function, while excessive intake can sometimes disrupt metabolic balance.

Neurotransmitters

Chemical messengers that transmit signals across synapses between neurons and other cells. Key neurotransmitters include serotonin, dopamine, norepinephrine, and acetylcholine, which play vital roles in mood regulation, cognition, and bodily functions. Imbalances can lead to mental health issues, while normal levels are crucial for healthy brain function.

Neurotransmitter Metabolism

The processes involved in the synthesis, release, reuptake, and breakdown of neurotransmitters. Proper metabolism is essential for maintaining neurotransmitter balance and function, which affects mood, cognition, and overall neurological health. Disruptions can lead to neurological and psychiatric disorders.

Oxidative Stress

A state where there is an imbalance between the production of free radicals (like superoxide radicals) and the body's ability to detoxify them with antioxidants. This imbalance can lead to cellular damage, inflammation, and contribute to various diseases, including cardiovascular and neurodegenerative disorders. Managing oxidative stress is essential for maintaining overall health.

Free Radicals

Highly reactive molecules with unpaired electrons that can cause cellular damage through oxidative stress. Free radicals are produced during normal metabolic processes and in response to environmental factors. Excessive free radicals can lead to chronic diseases, while very low levels may affect normal cellular signalling.

Superoxide Radicals

A type of free radical formed when oxygen gains an extra electron. Superoxide radicals are highly reactive and can damage cellular components, contributing to oxidative stress and inflammation. High levels are harmful, while very low levels might impair certain cell signalling pathways.

Atheroprotective

Refers to substances or actions that protect against the development of atherosclerosis, the buildup of fatty plaques in the arteries that can lead to cardiovascular disease. Lack of atheroprotective factors can increase cardiovascular risk, while enhancing these factors can improve heart health.

Vasodilation

The widening of blood vessels, which decreases blood pressure and improves blood flow. This process is mediated by various factors, including nitric oxide, and is important for maintaining cardiovascular health. Impaired vasodilatation can lead to hypertension and cardiovascular disease, while excessive vasodilatation can cause dangerously low blood pressure.

Vitamin B9

An essential B vitamin encompassing both folate and folic acid, crucial for numerous metabolic processes including DNA synthesis and repair, and methylation.FolateThe natural form of vitamin B9 found in food sources such as leafy greens, legumes, and fruits. It is involved in DNA synthesis and repair, and the conversion of homocysteine to methionine. Deficiency can lead to anaemia and neural tube defects, while excess intake from supplements may mask vitamin B12 deficiency.

Folic Acid

The synthetic form of vitamin B9, commonly found in supplements and fortified foods. It needs to be converted to its active forms (methylfolate) in the body. High intake of folic acid can potentially mask a vitamin B12 deficiency, and lead to a variety of possible health risks.

Cobalamin

Another name for vitamin B12, an essential vitamin that plays a crucial role in the methylation of homocysteine to methionine, red blood cell formation, and neurological function. Deficiency can cause anaemia and neurological disorders, while high intake is generally considered safe as excess is excreted.

Molybdenum

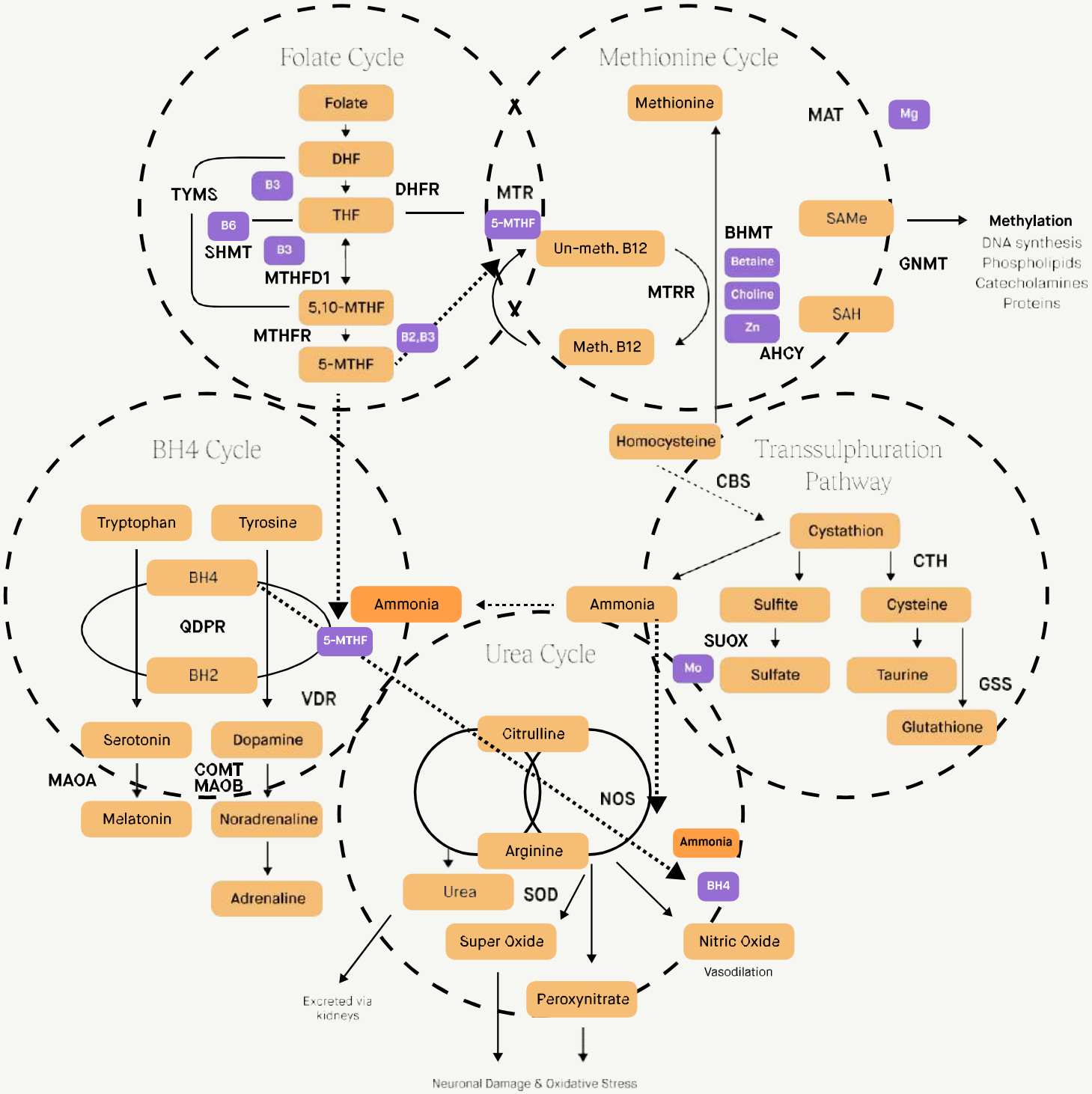
Highly reactive molecules with unpaired electrons that can cause cellular damage through oxidative stress. Free radicals are produced during normal metabolic processes and in response to environmental factors. Excessive free radicals can lead to chronic diseases, while very low levels may affect normal cellular signalling.

Superoxide Radicals

A trace mineral that acts as a cofactor for several enzymes, including those involved in the detoxification of sulphite and the metabolism of certain amino acids. Deficiency is rare but can lead to metabolic disturbances, while excessive intake may cause toxicity.

The Methylation Cycles

When assessing your genetic variants related to methylation, we will look at them in relation to 5 key metabolic pathways, or "cycles", that occur within your body every day.



The Folate Cycle

The Folate Cycle

Your Folate Cycle results show a Moderate Efficiency

NORMAL | MODERATE | IMPAIRED

Gestational/Pregnancy health | DNA synthesis and repair | Energy production | Inflammation control

Detailed Summary

The Folate Cycle is the first stop for dietary folic acid/folate that enters our bodies. It is here that we convert folate into usable forms for numerous important processes occurring elsewhere in the body, including the other pathways detailed later in this report.

Folate, also known as vitamin B9, enters the body in two different forms: either as naturally occurring folate from dietary sources, or as the synthetic form known as folic acid, which is found in supplements and fortified foods. Folate is then transported into our cells where folate is first converted to dihydrofolate (DHF) and then into tetrahydrofolate (THF), with the support of vitamin B3.

The Folate Cycle is in fact two linked cycles: in a process which catalyses three sequential reactions in the interconversion of THF metabolites, utilising vitamins B3 and B6. These metabolites are crucial for synthesising purine, thymidine (nucleotides), and methionine. The reactions are reversible and once THF is converted into 5,10-methylene THF it is then used in one of 2 ways:
i) supporting the methylation process during the formation of DNA that is required for proper cell division, or
ii) converted to methylfolate (5-MTHF), the "active" form of folate.

Methylfolate is an important product of the folate cycle: firstly, it provides a methyl group (CH3) to The Methionine Cycle when converted back to THF in a process involving vitamin B12 and Zinc; secondly, it is used to drive the conversion of BH2 to BH4 to support The BH4 Cycle which is an important component of neurotransmitter metabolism.

Considerations

Alongside your folate cycle result, it may be important to test serum and erythrocyte (red blood cell) folate levels. As serum folate levels are sensitive to recent dietary or supplementary intake, red blood cells (RBC) levels may be more indicative of tissue folate stores. Ensure adequate intakes of all B vitamins - particularly vitamins B9 (folate) B2, B3 and B6. Methylated or other forms of B vitamins (e.g. 5-MTHF) may be appropriate depending on SNPs and environmental factors.

Key Genes

DHFR - This gene is involved in the assimilation of folate from all sources, as well as the conversion of DHF to THF - a methyl group transporter necessary for the synthesis of purines, thymidine and nucleic acids and ultimately methylfolate for use in The Methionine Cycle. The deletion variant of this gene impacts folic acid metabolism, which can reduce the availability of 5-MTHF. In DD genotypes, high intakes of folic acid (>500mcg) are linked to higher circulating levels of unmetabolised folic acid, and low intakes (<250mcg) are associated with low red blood cell folate levels. Antifolate drugs work by blocking DHFR, therefore reducing THF levels and suppress purine/pyrimidine synthesis.

MTHFD1 - This gene codes for an enzyme that catalyses conversion of THF to 5,10-Methylene THF via 3 distinct,

sequential and reversible reactions. The intermediate metabolites are required for the synthesis of purine (for DNA synthesis & repair), thymidine (for nucleotide biosynthesis) and methionine (via The Methionine Cycle), and so variations in this gene can impact all these processes.

MTHFR - A key regulatory enzyme responsible for converting folate to its "active" form: 5-MTHF (methylfolate). 5-MTHF is needed for the remethylation of homocysteine to methionine (i.e. The Methionine Cycle), as well as the metabolism of neurotransmitters, phospholipids and proteins (via the BH4 cycle).
Variants in C977T can cause lower activity: 40% reduction for heterozygotes (CT), and 70% for homozygotes (TT). The A1298C variant does not impact 5-MTHF levels as much, but is associated with BH4 depletion, which can impact neurotransmitter synthesis and The Urea Cycle function.

MTR - transfers methyl group from methylfolate (5-MTHF) to B12. The folate is then recycled back to THF. Methylated vitamin B12 is then used in converting homocysteine in The Methionine Cycle. Variants upregulate ctivity, therefore lower homocysteine levels, but higher activity could also pull folate to The Methionine Cycle at the expense of other needs (e.g. purine/nucleotide synthesis).

Your Genetic Results

The below table shows the genes analysed in relation to your Folate Cycle Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
DHFR	rs70991108	Not Found	-
MTHFD1	rs2236225	Not Found	-
MTHFR (A1298C)	rs1801131	AA	-
This genotype is not associated with reduced MTHFR enzyme activity. You do not carry the genetic mutation that can impact BH4 levels.			
MTHFR (C677T)	rs1801133	CT	●
This variant is associated with a 40% reduction in MTHFR enzyme activity. About 30% of the population possess at least one T allele, and it is associated with an increased risk of high homocysteine & low folate levels.			
MTR	rs1805087	AA	●●
You do not carry an "upregulating" allele for this gene, meaning lower MTR function and potentially higher homocysteine levels than carriers of the G allele.			

Specific Gene Advice

Based on specific gene results we also have the following recommendations:

Gene	Recommendation
MTHFR (C677T)	You can support your MTHFR gene activity by increasing your intake of vitamin B-rich foods such as dark leafy greens. If supplementing, choose methylated folate (e.g. 5-MTHF), as well as vitamins B2 (riboflavin) and B3 (niacin). Monitoring levels of these vitamins as well as homocysteine, SAM and SAH is advisable.
MTR	It is important to consider your MTR result in conjunction with MTHFR to assess overall impact. As your genetic result is associated with elevated homocysteine levels, consider monitoring this as well as folate and vitamin B12 levels.

Advice for You

Here's some recommended lifestyle tips and practices based on your result:

With these genetic results it is important to consider your intake of all B vitamins - paying particular attention to B9 (folate) B2, B3 and B6. Look for methylated forms (e.g. 5-MTHF for folate) as these are the "active forms" and will be more readily utilised.

Blood testing is a great way to monitor potential risks associated with methylation - homocysteine levels, SAMe:SAH ratio and B vitamin levels are useful markers to track.

If taking a blood test, pay attention to folate levels. Serum folate levels can be easily affected by recent intake (dietary or supplementary) and so erythrocyte (red blood cell) folate levels may be a better indicator of tissue status.

The Methionine cycle

Methionine Cycle

Your Methionine Cycle results show a Moderate Efficiency

NORMAL | MODERATE | IMPAIRED

Gestational health

Amino acid synthesis

Metabolic health

Detailed Summary

The Methionine Cycle involves some of the most well-researched methylation genes. It is often referred to simply as The Methylation Cycle, and one of its key products is SAMe, which functions as a methyl donor across a multitude of important methylation processes in the body. Crucially, The Methionine Cycle is also responsible for recycling homocysteine back to methionine.

This cycle is a vital biochemical process that metabolises methionine, an essential amino acid, through a series of steps to support various cellular functions. In the first step, methionine is converted to S-adenosyl-methionine (SAMe), which uses ATP. SAMe is the main source of methyl groups for most biological methylations and is known as the master methyl donor. Once SAMe donates it's methyl group to become S-adenosyl-homocysteine (SAH), adenosine is removed to become homocysteine. The accumulation of SAH can inhibit methylation, so cells must maintain low SAH levels.

There are two ways that homocysteine can be recycled back into methionine: the 'long route' and the 'short route'. These involve different genes and cofactors as explained below. This reaction is also required for the irreversible oxidation of choline and significantly contributes to the body's choline supply, supplementing dietary intake.

Homocysteine can also be pulled from The Methionine Cycle into The Transsulphuration Pathway.

Considerations

When assessing The Methionine Cycle, it is also recommended to test homocysteine, methionine, vitamin B12 and SAMe levels. The ratio of SAH:SAMe is also a useful indicator of SAMe conversion.

Key Genes

MTR - This gene encodes methionine synthase, an enzyme that catalyses the remethylation of homocysteine to methionine via the 'long route', using 5-methyltetrahydrofolate (5-MTHF) from The Folate Cycle as a methyl donor, resulting in the formation of methylated vitamin B12 (methylcobalamin).

MTRR - This gene is responsible for regenerating MTR via a methylation reaction that utilises SAMe as a donor. Additionally, MTRR aids in maintaining MTR activity by recycling and converting vitamin B12 to its methylated form (methylcobalamin).

FUT2 - This gene regulates the expression of H antigens on the gastrointestinal mucosa, determining an individual's secretor status. The absorption of vitamin B12 depends on the secretion of the glycoprotein intrinsic factor (IF) by gastric cells, the binding of IF to vitamin B12, and a functional gastrointestinal absorption system.

TCN2 - This gene encodes transcobalamin II, a protein responsible for binding and transporting vitamin B12 into cells.

PEMT - This gene encodes an enzyme that converts phosphatidylethanolamine to phosphatidylcholine through methylation, thereby providing a source of choline. Oestrogen stimulates the expression of the PEMT gene, enabling premenopausal women to produce more of their necessary choline internally compared to postmenopausal women and men.

BHMT - This gene encodes an enzyme that facilitates the remethylation of homocysteine to methionine through the 'short route', utilising betaine as a methyl donor upon conversion to DMG (dimethylglycine). The BHMT pathway relies on zinc and requires sufficient levels of TMG (trimethylglycine or betaine) for optimal functioning. This process is essential for the irreversible oxidation of choline. BHMT activity may also be influenced by cortisol levels (stress) and could potentially impact norepinephrine levels, thereby contributing to ADD/ADHD.

Your Genetic Results

The below table shows the genes analysed in relation to your Methionine Cycle Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
MTR	rs1805087	AA	●●
You do not carry an upregulating allele for this gene, which is associated with lower MTR function and potentially elevated homocysteine levels. This can in turn reduce methionine levels, which can influence cancer risk and tumor growth, as approximately 50% of cancer cell types depend on methionine.			
MTRR	rs1801394	AG	●
You carry one copy of the G allele, which downregulates the activity of the MTRR gene and reduces the ability to re-methylate the vitamin B12 needed for MTR to function in the methionine cycle. This can contribute to high levels of homocysteine.			
BHMT	rs3733890	Not Found	-
PEMT	rs7946	Not Found	-
FUT2	rs601338	AA	-
You carry alleles that are indicators of an inactive FUT2 gene and non secretor status. About 20% of people are non secretors. This result reduces susceptibility to H. pylori infection and gastrisis linked to reduced vitamin B12 absorption.			
TCN2	rs1801198	CC	-
You carry neutral alleles for this gene, meaning normal TCN2 function with no impact on ability to absorb and transport cobalamin (vitamin B12).			

Specific Gene Advice

Based on specific gene results we also have the following recommendations:

Gene	Recommendation
MTR	Take into account both your MTR and MTRR results to evaluate the overall effect on your vitamin B12 levels. Since your genetic results are linked to elevated homocysteine levels, consider monitoring this. You can support MTR activity by supplementing with the methylated form of vitamin B12 (e.g. methylcobalamin)
MTRR (A66G)	Hydroxycobalamin (the injectable form of vitamin B12) may be the preferred form for this result. Additionally, maintain sufficient antioxidant intake with foods like berries, kale, and various herbs and spices to reduce oxidative stress. Support methylation with B2 from foods such as eggs, almonds, and spinach, and B3 from foods like chicken, peanuts, and brown rice. Both smoking and secondary exposure to tobacco smoke should be avoided, as smoking is known to increase homocysteine levels.

Advice for You

Here's some recommended lifestyle tips and practices based on your result:

With these genetic results it is important to consider your intake of folate (green leafy veg), vitamin B12, betaine (beetroot) and choline (eggs). SAMe supplementation may be considered.

Functional testing of homocysteine, methionine, vitamin B12 and SAMe levels may be considered. The ratio of SAH: SAMe is also a useful indicator of SAMe conversion.

Prioritising your gastrointestinal health by integrating probiotics into your diet—whether through foods like yogurt, kefir, kimchi or sauerkraut or via supplementation—and increasing fiber intake from sources like legumes, grains, fruits, and vegetables is advantageous.

The Transsulphuration Pathway

Transulphuration Pathway

Your Transsulphuration Pathway results show a Normal Efficiency

NORMAL | MODERATE | IMPAIRED

Oxidative stress reduction

Vascular/circulatory functioning

Neuroprotective roles

Telomere protection

Detailed Summary

The Transsulphuration Pathway is a metabolic process that offers an alternative pathway for the conversion of homocysteine where it is converted to cysteine via the intermediate cystathionine. Cysteine is a precursor of glutathione (a major antioxidant), and taurine (an essential amino acid). Cystathionine is also a central component of sulphur etabolism. This involves the oxidation of sulphite, which is produced from cystathionine, to sulphate and is catalysed by a molybdenum-dependent enzyme, helping to detoxify sulphites in the body. Sulphites can increase cortisol and cause brain fog while sulphate is less toxic and can be excreted in the urine.

Once homocysteine is converted to cystathionine, it is then converted into cysteine which requires vitamin B6 as a co-factor. This conversion process generates ammonia (which in large amounts can deplete BH4 - see The BH4 Cycle) as a by-product. Glutathione synthesis in the liver is dependent upon the availability of cysteine and is important for ealthy detoxification as well as protecting cells from oxidative damage by free radicals, detoxifying xenobiotics, and facilitating membrane ransport. Cysteine can also be further converted into taurine through a series of enzymatic reactions. Taurine is an important amino acid that plays various roles in bile salt formation, cellular osmoregulation, and neurotransmission. The pathway also involves the creation of succinyl-CoA, a reaction that depends on adenosylcobalamin (vitamin B12) as a cofactor. Succinyl-CoA is a critical intermediate in The Krebs Cycle and is crucial for the synthesis of ATP, heme, cytochrome P450s, and nucleotides.

Considerations

When evaluating the effectiveness of The Transsulphuration Pathway, conducting plasma amino acid profile can provide valuable insights. With these tests it's possibly to assess homocysteine, taurine, glutathione, ammonia, and sulphur-containing amino acids like cysteine and methionine. Additionally, a urine dipstick test can be used specifically or detecting sulfur.

Key Genes

CBS - This gene encodes an enzyme that catalyses the initial step of The Transsulphuration Pathway, converting homocysteine, derived from methionine in The Methionine Cycle, to cystathionine with vitamin B6 and heme as cofactors.

GSS - This gene encodes an enzyme that governs the second phase of glutathione synthesis, facilitating the transformation of cysteine into glutathione with the aid of ATP.

Your Genetic Results

The below table shows the genes analysed in relation to your Transsulphuration Pathway Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
CBS	rs234706	AG	●
This genotype slightly upregulates CBS gene activity and can "pull" more homocysteine from The Methionine Cycle into The Transsulphuration Pathway. Therefore, this result is associated with lower homocysteine levels and can counteract inhibited MTHFR activity. However, this can reduce SAMe synthesis, deplete vitamins B6 & B12, and may also lead to low glutathione production.			
GSS	rs6088659	Not Found	-

Specific Gene Advice

Based on specific gene results we also have the following recommendations:

Gene	Recommendation
CBS (C699T)	Increasing your intake of cofactors such as zinc (e.g. from lentils), betaine (wholegrains), and choline (chicken, broccoli) will promote the homocysteine recycling via the BHMT 'shortcut' pathway. Reduce ammonia levels by limiting animal protein intake, enhancing gut health, or consider using activated charcoal. Ensure adequate intake of vitamins B6 and B12.

Advice for You

Here's some recommended lifestyle tips and practices based on your result:

Although genetically your Transsulphuration Pathway is working efficiently, it is still important to ensure sufficient intake of vitamins B2, B6, B12, choline, zinc, and betaine.

Animal proteins and by-products such as beef, chicken, fish, eggs, and milk are excellent sources of vitamins B2, B6, B12, choline, and zinc, although excessive intake can elevate ammonia levels. Betaine can be found in beetroot, green leafy vegetables, and wholegrains like quinoa.

Urine and plasma amino acid profile testing is a great way to monitor potential risks associated with homocysteine metabolism. It may be beneficial to check levels of homocysteine, taurine, glutathione, ammonia, and sulfur-containing amino acids such as cysteine and methionine.

Neurotransmitter Metabolism

BH4 Cycle

Your BH4 Cycle results show a Moderate Efficiency

Neurotransmitter metabolism Thyroid health Inflammation Oxidative stress

Detailed Summary

The BH4 Cycle is essential for various processes in the body, including neurotransmitter metabolism, specifically in the production of key neurotransmitters such as dopamine, serotonin, melatonin, norepinephrine, and thyroid hormones.

In this cycle, BH4 or Tetrahydrobiopterin is regenerated from dihydrobiopterin (BH2). An enzyme catalyses the regeneration of BH4 from BH2, a reaction requiring active folate (5-MTHF) from The Folate Cycle. Phenylalanine is converted to tyrosine with the help of BH4. Tyrosine is then converted into a precursor of dopamine and subsequently into dopamine itself, with BH4 acting as a crucial cofactor in this process. Similarly to tyrosine, tryptophan is converted into a serotonin precursor, and then into serotonin, again requiring BH4. Serotonin is then oxidised into melatonin, a process that requires SAMe from The Methionine Cycle and vitamin B2 as cofactors. Norepinephrine from dopamine is converted to epinephrine in the adrenal medulla, also requiring SAMe as a methyl donor. BH4 also plays a role in The Urea Cycle and is vital for neutralising ammonia and generating nitric oxide. Low levels of 5-MTHF and SAMe can negatively influence neurotransmitter levels and low (or indeed high) neurotransmitter levels can result in mood imbalances, poor memory, concentration issues, sleep disturbances, and aggressive behaviour.

Considerations

When investigating the efficiency of The BH4 Cycle, testing your neurotransmitter balance and SAH:SAMe ratio could be beneficial. Assessing the amino acids tryptophan and tyrosine, vitamins B2, B6 and D, and methylfolate levels is also helpful. Environmental factors can also have a strong effect: stress both physical and mental, and diet (e.g., stimulants or toxicity of heavy metals).

Key Genes

VDR - This gene encodes the nuclear hormone receptor for vitamin D3 (the active form of vitamin D in the body). This catalyses the conversion of tyrosine into dopamine.

COMT - This gene plays a role in the metabolism of dopamine, noradrenaline, and adrenaline. These neurotransmitters play significant roles in regulating mood, cognition, and the body's response to stress.

MAOA - This enzyme catalyses the breakdown of monoaminergic neurotransmitters serotonin, melatonin, noradrenaline, and adrenaline. MAOA is found on the X chromosome, hence males possess only one allele inherited from their mother. We, therefore, present results for males as homozygous, as they do not inherit a 'balancing' allele.

MAOB - The primary enzyme responsible for breaking down phenethylamine (PEA), benzylamine, histamine, dopamine, tyramine, and tryptamine. Just like MAOA, MAOB is found on the X chromosome, hence males possess only one allele inherited from their mother. We, therefore, present results for males as homozygous, as they do not inherit a 'balancing' allele.

MTHFR - A key regulatory enzyme responsible for converting folate to its "active" form: 5-MTHF (methylfolate). The particular SNP looked at here (A1298C) regulates the conversion of MTHF to BH4 which is vital in the metabolism of neurotransmitters, phospholipids and proteins.

Your Genetic Results

The below table shows the genes analysed in relation to your BH4 Cycle Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
MTHFR (A1298C)	rs1801131	AA	-
This allele result is associated with normal BH4 levels needed for neurotransmitter synthesis. Methylfolate is pulled from the methionine cycle more readily, so ensure folate levels are adequate to support this and avoid negatively impacting homocysteine recycling.			
COMT	rs4633	CT	●
This genotype is associated with reduced COMT activity, leading to higher dopamine and norepinephrine levels. This can counteract the effects of low VDR activity and result in normal levels. However, with raised VDR activity, the resulting high dopamine levels can increase susceptibility to mood disturbances like anxiety, panic attacks, anger and bipolar disorder. Reduced COMT activity may also raise the risk of endometrial cancer due to its role in oestrogen metabolism, especially with prolonged oestrogen exposure, low folate, and high homocysteine. Low SAMe and high SAH levels can further decrease COMT activity.			
VDR	rs731236	TT	-
Your genotype is associated with normal VDR expression, and therefore no increased risk of vitamin D deficiency. However, low vitamin D levels and stress (cortisol) can reduce enzyme activity, irrespective of genotype. Carriers of variants associated with lower COMT activity may be susceptible to mood swings and intolerance of methyl donors due to high dopamine production and slow breakdown.			
MAOA	rs6323	Not Found	-
MAOB	rs1799836	Not Found	-

Specific Gene Advice

Based on specific gene results we also have the following recommendations:

Gene	Recommendation
MTHFR (A1298C)	You do not carry variants for this particular SNP, and so methylfolate is pulled into the BH4 cycle at a normal rate.
COMT (H62H)	Although your gene activity is only moderately reduced, it's still benefical for you to support SAMe synthesis by consuming adequate amounts of B vitamins (wholegrains and eggs), zinc (beef, chickpeas, and sunflower seeds), potassium (avocados, oranges, and spinach), and magnesium (dark chocolate, quinoa, and cashews). Additionally, incorporate antioxidant-rich foods such as citrus fruits, tomatoes, and spices like cinnamon and cloves to help reduce oxidative stress. Monitor your oestrogen levels.
VDR (TaqI)	To ensure adequate vitamin D intake, incorporate foods like salmon, mackerel, egg yolks, dairy products, and fortified mushrooms into your diet. Managing stress can be beneficial as cortisol has a negative effect on enzyme activity.

Advice for You

Here's some recommended lifestyle tips and practices based on your result:

With these genetic results it is important to consider your intake of the B group vitamins and important cofactors such as vitamins D and C. SAMe levels are also important, if found to be low then supplementation may also be considered, as it is not possible to increase through dietary changes.

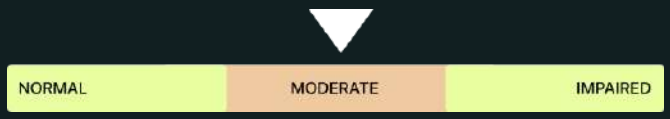
Doing a urine test to check neurotransmitter balances as well as a plasma SAH:SAMe ratio test may be considered.

Focus on eliminating heavy metals from your system, particularly mercury, lead, and aluminum. These toxic metals can accumulate in the body and disrupt biological processes. Mercury is found in fish like tuna, swordfish, and king mackerel. Lead exposure can come from old paints, contaminated water, and certain pottery and aluminum is often present in food additives, some cosmetics, and cookware.

Urea Cycle

Urea Cycle

Your Urea Cycle results show a Moderate Efficiency



Detoxification Cardiovascular function Muscle function

Detailed Summary

The Urea cycle, or ornithine cycle, is a series of biochemical reactions that convert toxic ammonia into urea, which the kidneys can then excrete. This essential process occurs in the liver with the help of enzymes located in both the mitochondria and the cytosol of the cell.

First, ammonia (from The Transsulphuration Pathway) is converted into a compound that combines with ornithine to produce citrulline. Citrulline then moves from the mitochondria to the cytosol, where it combines with aspartate to form arginosuccinate. Arginosuccinate breaks down into arginine and fumarate. Fumarate enters another cycle to become aspartate again while arginine is broken down into urea and ornithine. Ornithine returns to the mitochondria to restart the cycle. Urea is the only new product, while all other molecules are recycled.

Nitric oxide (NO) is a crucial mediator that protects against atherosclerosis and helps regulate vasodilation. It is produced from arginine with the co-factor tetrahydrobiopterin (BH4) from The BH4 Cycle. Adequate levels of BH4 are essential for the proper functioning of nitric oxide synthase (NOS). Without sufficient BH4, NOS produces harmful free radicals such as peroxynitrite and superoxide instead of nitric oxide, leading to compromised cardiovascular function and increased risk of vascular diseases.

Considerations

When investigating the efficiency of The Urea Cycle doing a Blood Urea Nitrogen (BUN) Test to test kidneys efficiency at excreting urea, as well as a blood test to test ammonia levels could be beneficial.

Key Genes

NOS3 - The gene encodes endothelial NOS (eNOS), one of three enzymes responsible for converting L-arginine and molecular oxygen into nitric oxide (NO), utilising BH4 as a cofactor. eNOS mainly makes nitric oxide (NO) in the lining of blood vessels. It is important because it helps widen blood vessels, which regulates blood flow and pressure. It also affects other processes like cell growth, the stickiness of white blood cells to blood vessel walls, and the clumping together of platelets in blood clotting. This function is vital for cardiovascular health, aiding in blood pressure regulation and the transportation of oxygen and nutrients throughout the body.

SOD2 - SOD (superoxide dismutase) enzymes form a group that catalyses the conversion of superoxide into oxygen and hydrogen peroxide, safeguarding cells against the damaging effects of superoxide.

Your Genetic Results

The below table shows the genes analysed in relation to your Urea Cycle Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
NOS3	rs1799983	GT	●
You carry one copy of the T allele, which associated with low NOS3 enzymatic activity, impaired ammonia breakdown and reduced nitric oxide production. This effect can be compounded by low BH4 levels and excess ammonia.			
SOD2	rs4880	CT	●
You carry one copy of T allele, which is linked to reduced superoxide dismutase activity. This diminished ability to breakdown the free radical superoxide may increase your susceptibility to oxidative stress.			

Specific Gene Advice

Based on specific gene results we also have the following recommendations:

Gene	Recommendation
NOS3	Ensure adequate intake of folate (B9) from foods such as leafy greens, beans, citrus, and liver; riboflavin (B2) from sources like milk, eggs, and liver; and niacin (B3) from foods such as chicken, liver, and tuna. These nutrients support the production of 5-MTHF and help maintain sufficient levels of BH4. Antioxidants (including vitamin C) are especially important to reduce damage from oxidative stress.
SOD2	Try including more manganese-rich food sources in your diet such as brown rice, spinach, pineapple and whole wheat bread to support SOD activity, and increase your antioxidant intake by including more colourful fruit and vegetables as well as herbs and spices in your diet to reduce oxidative stress.

Advice for You

Here's some recommended lifestyle tips and practices based on your result:

The production of nitric oxide is dependant on BH4, so it is important to support this process by ensuring adequate BH4 levels. Folate intake is especially important in this regard, so aim for plenty of green leafy vegetables or a folate supplement (e.g. 5-MTHF).

With a slightly higher risk of damage from oxidative stress and free radicals, it is important to ensure you are consuming enough antioxidants, including vitamin C, and manganese. You can get antioxidants from foods like berries, citrus fruits, spinach, and nuts, and vitamin C from oranges, strawberries, and bell peppers. Manganese can be found in foods like wholegrains, nuts, and leafy green vegetables.

Consider getting a Blood Urea Nitrogen (BUN) Test to check your kidneys' efficiency in excreting urea, and a blood test for ammonia levels. High ammonia can inhibit nitric oxide production, leading to issues with blood vessel dilation and inflammation, increasing heart risks in people with autoimmune diseases. In chronic kidney disease, high ammonia can worsen vasodilation, raise blood pressure, and accelerate atherosclerosis, especially in diabetic patients.