Nutri Notes

"Integrating the Nutrition-Health connection" **Vol 12, #1**

Epigenetic/Nutritional Influences on Health and the Brain

Or, when you can't change DNA…

It can be intimidating to see words we don't recognize. What is epigenetic? Well, **Epigenetic** is defined as an influence that changes the way your genes are expressed, and this is powerful!

We can't change our genes, we were dealt that hand at birth. However it is becoming increasingly evident that **we can change the way our genes are expressed.** This environmental influence is termed "epigenetic". Amazingly enough, nutrition elements have been discovered as factors that can change the way our genes are expressed. Since nutrition can change the way our genes are expressed, and some of those genes determine our health status in the body, **nutrition is one of the important epigenetic influences on our health and the health of our brain!**

We may not be able to change DNA, but we can change the way it is expressed!

We live in an exciting era, where scientific discoveries are pointing us in a direction to optimize our genetic expression. Those discoveries are happening every day. This issue of the Nutri-Notes takes a look at some of those discoveries in the area of nutrition, how nutrition affects epigenetic changes, and how the changes from these epigenetic influences subsequently improve our life and guide us along a healthy pathway.

An example of a nutrient that has the ability to effect epigenetic changes is **Curcumin.** Curcumin (diferuloylmethane) is a component of the spice turmeric and has recently been determined to induce epigenetic changes (epigenetic changes include DNA methylation changes without any change in DNA sequence).

Scientists claim that this can be an important mechanism "by which dietary components can selectively activate or inactivate gene expression" and furthermore that **curcumin** needs further investigation to determine novel and effective strategies **for clinical use as a regulator of epigenetic changes,** (Simone Reuter et al. Genes Nutr. 2011 May; 6(2): 93–108.) Kalani A. et. al also name **curcumin** as an epigenetic agent with "**remarkable medicinal properties**" (Metab Brain Dis. 2015 Apr;30(2):427-35.)

Importance of Epigenetic influences on Gene Expression:

"It is known that lifestyle, environmental conditions and nutritional compounds influence gene expression. Gene expression states are set by transcriptional activators and repressors and are often locked in by cell-heritable chromatin states. Only recently, it has been observed that the environmental conditions and daily diet can affect transgenerational gene expression via "reversible" heritable epigenetic mechanisms. Epigenetic changes in DNA methylation patterns at CpG sites (epimutations) or corrupt chromatin states of key inflammatory genes and noncoding RNAs, recently emerged as major governing factors" **(Nature or nurture: Let food be your epigenetic medicine.** Katarzyna SvS et al. Biochemical Pharmacology 80(12), 15 December 2010, Pages 1816–1832.

Ginkgo and epigenetic influences on the brain

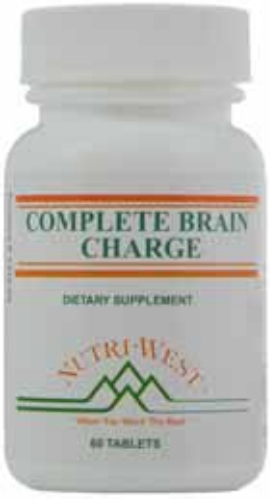
Ginkgo was one of the herbs studied for its epigenetic pharmacological effects in a report titled, "Herbal medicine…: A review of psychopharmacology and clinical evidence" by Jerome Sarris et al. (European Neuropsychopharmacology 2011 (21 (12): 841–860). Researcher explored the use of herbals and how to increase their clinical validation via the use of "omic" genetic technologies. One of the "omic" fields is proteomics, (study of the structure and function of proteins), and another is genomics (study of the structure and function of genes). A new term proposed by these researchers when the study is in the field of phytotherapy and herbals, is "herbomics", which describes the epigenetic influences that herbal proteins have on gene expression.

Ginkgo was one of the herbs studied, and researchers (Sarris et al. 2011) determined that ginkgo does have an influence and a supportive ability related to cholinergic and monoamine pathways in the body. It also has high antioxidant power and supports normal GABA and nitric oxide production.

Nutri-West Presents: *Complete Brain Charge*

Ingredients:

A proprietary blend of **Alpha Glycerylphosphocholine,**
Curcumin, Ginkgo biloba extract
(standardized 24% Ginkgosides 6% Terpene Lactones),
Sunflower lecithin (17% phosphatidylcholine),
Phosphatidylserine, CDP choline and Choline
(derived from soy but does not contain soy protein).

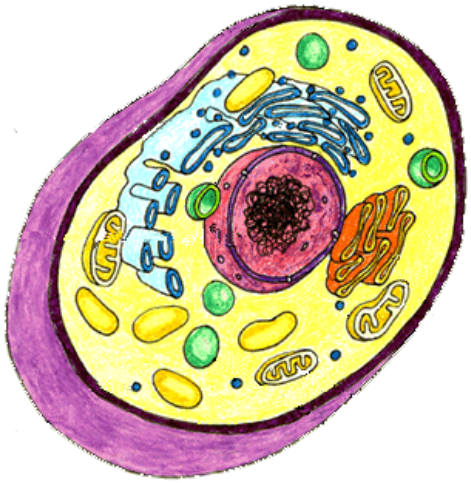


Several nutrients can help support brain function, while phosphatidylcholine and phosphatidylserine can help absorption.

Epigenetic Implications for Choline:

Single-nucleotide polymorphisms (known as SNPs) in choline metabolic pathways can change the requirement for choline (increasing the need). SNPs are inherited, and they change the RNA code and lead to difference in protein function. Certain SNPs can also change the ability to synthesize choline, ***thereby also increasing the need for choline****. Additionally, SNPs that alter the folate pathway can make someone more dependent on choline for SAM (S-adenosyl methionine) production.*

Several studies have shown that "**choline, folic acid, vitamin B12, zinc, selenium, and dietary polyphenols** are capable of interacting with epigenetic mechanisms and ultimately gene expression." (Neurochem Int. 2014 Dec;78:105-16. **Alzheimer's disease and epigenetic diet.** Sezgin Z, Dincer Y.)



Choline is a necessary element and building block for the structural components of cell membranes and helps account for fluidity and communication within those membranes. Choline is essential for **phosphatidylcholine and sphingomyelin**, which are the two major phospholipids in cell walls. Choline is the precursor molecule for the neurotransmitter **acetylcholine**, which is involved in many functions of the brain and muscles.

Choline has to be consumed through the diet for the body to remain healthy, yet it has been estimated that the **recommended dietary intake of choline by postmenopausal women is only met by 2% of that population** (Fischer, LM, et al. 2010. Dietary choline requirements of women: effects of estrogen and genetic variation". American Journal of Clinical Nutrition **92** (5): 1113–1119.)

Designer cholines:

We have always recognized the essential role for choline, but choline has many forms, several of which have been called "designer cholines" because they exhibit properties above and beyond regular choline. Two of these designer cholines are known as **alpha-GPC**, or **alpha glycerylphosphocholine, and CDP choline, or** cytidine 5'-diphosphocholine.

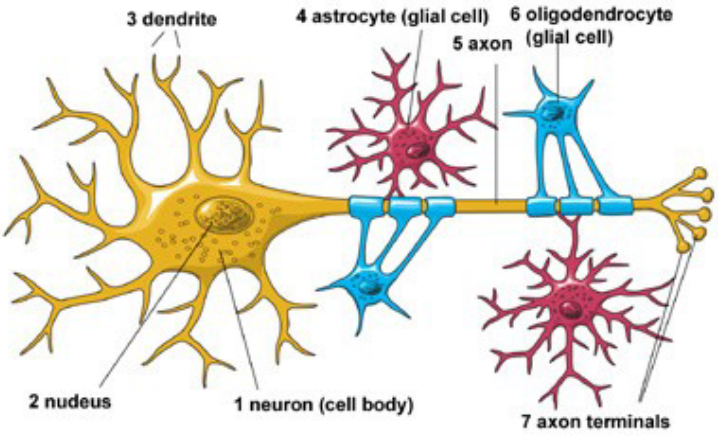
Alpha glycerylphosphocholine demonstrated a support benefit for patients in a number of clinical studies conducted on the brain and maintenance of brain function. In fact, the researchers, "being impressed not only with results but in lack of side effects, recommended that it is desirable to reconsider **alpha glycerylphosphocholine** in larger carefully controlled studies … for the maintenance of brain function" (Scapicchio PL. Revisiting choline alphoscerate profile: a new, perspective, role…? Int J Neurosci. 2013 Jul;123(7):444-9.)

CHOLINE INCREASES ABSORPTION!

Phosphatidylcholine is a normal constituent of bile, which facilitates fat emulsification, absorption and transport. Recently, phosphtidylcholine has been discovered as a nutritional addition to help boost the absorptive power of other ingredients that are given in conjunction with phosphatidylcholine, for example **ginkgo and curcumin.**

"Supplementation with alpha-GPC and CDP choline (cytidine 5'-diphosphocholine) has **proven to be much superior than supplementation with just basic choline for brain support and normal neurotransmitter production**. It is theorized that these **designer cholines are able to be better incorporated and stored into the phospholipids in the brain**, and therefore make better precursors for acetylcholine" (Amenta F, Tayebati SK. Pathways of acetylcholine synthesis, transport and release. Curr Med Chem. 2008;15(5):488-98.)

Epigenetic influences of nutritional factors on brain health:



Evidence suggests that **Bacopa** is an **effective herbal that may possess epigenetic qualities**. It was shown to **change the expression of neuronal and glial plasticity markers in the brain** (Konar, A. et al. "Bacopa monniera (CDRI-08) Upregulates the Expression of Neuronal and Glial Plasticity Markers in the Brain…" Evidence-Based Complementary and Alternative Medicine, Article ID 837012, in press, accepted Jan. 2015. Animal study).

A variety of randomized, double blinded, placebo-controlled clinical trials confirm the efficacious support for brain maintenance and function. For example: 1. Pase MP. et al. …Bacopa monnieri: a systematic review of randomized, controlled human clinical trials. J Altern Complement Med. 2012 Jul;18(7):647-52;

2. Morgan A, & Stevens J. Does Bacopa monnieri improve… performance in older persons? Results of a randomized, placebo-controlled, double-blind trial. J Altern Complement Med. 2010 Jul;16(7):753-9;

3. Calabrese C. et al. Effects of a standardized Bacopa monnieri extract… : a randomized, double-blind, placebo-controlled trial. J Altern Complement Med. 2008 Jul;14(6):707-13.

Glucoraphanin comes from cruciferous vegetables, and results in sulforaphane production. Glucoraphanin "**may target epigenetic alterations**" … reversing aberrant changes in gene transcription through mechanisms of histone deacetylase inhibition, global demethylation, and microRNA modulation" (Antioxid Redox Signal. 2014 Nov 3. Dietary Sulforaphane…: The Role of Epigenetic Regulation and HDAC Inhibition. Tortorella SM. et al.)

Other researchers "highlight more recent evidence supporting these phytochemicals as **epigenetic modulators**" and note that **glucoraphanin** has the ability to modulate the activity of enzymes controlling the **epigenetic status of cells** (AAPS J. 2013 Oct;15(4):951-61. … W Watson G. et al.)

Curcumin has "recently shown to exhibit **epigenetic modulatory properties**. Epigenetic studies include DNA methylation, histone modifications and RNA-based mechanisms which **regulate gene expression without altering nucleotide sequences**." (Metab Brain Dis. 2015 Apr;30(2):427-35. Epigenetic impact of curcumin... Kalani A. et al.)

Ashwagandha (*Withania somnifera*) root: Ashwagandha inhibits NF-kB (a protein complex/transcription factor that is one of the main players involved in inflammatory responses). It accomplishes this inhibition by way of a mutation of Cys179 residue of the DNA in the kinase involved in the synthesis. The epigenetic target of Cys 179 in DNA is believed to be an anti-inflammatory mechanism of action for Ashwagandha (Biochem Pharmacol. 2014 Oct 15;91(4):501-9. Withaferin A inhibits NF-kappaB activation by targeting cysteine 179 in IKKβ. Heyninck K et al.)

Epigenetic influences of nutritional factors on brain health (cont'd):

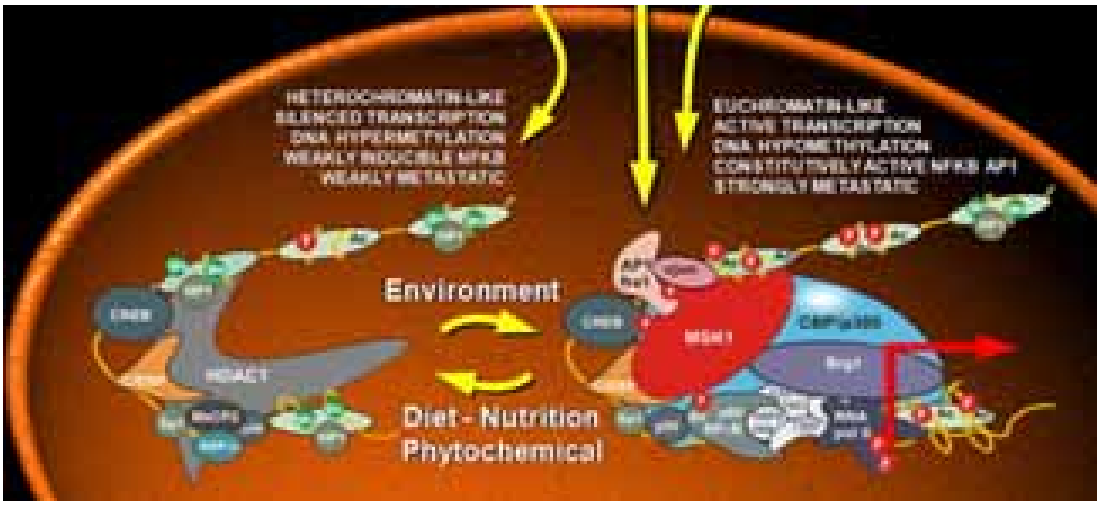
Blueberries for the brain - epigenetic regulation of antioxidant enzymes!

Trans pterostilbene is a natural dietary compound related to resveratrol and is the concentrated, **primary antioxidant component of blueberries**. Researchers report extremely high antioxidant activity with **increased lipophilic and oral absorption** for use in a wide varety of health areas, including neuronal support. The same researchers demonstrated that various cell lines treated with trans pterostilbene have shown **increased expression of the antioxidants** catalase, total glutathione (GSH), glutathione peroxidase (GPX), glutathione reductase (GR), and superoxide dismutase (SOD), meaning that trans pterostilbene can change the expression of the genes that code for these endogenous enzymes (epigenetic= changing gene expression). (A review of pterostilbene antioxidant activity ... McCormack D, McFadden D. Oxidative Medicine and Cellular Longevity. 2013;vol. 2013: article ID# 575482.)

Trans pterostilbene was shown to have 80% bioavailability compared to 20% for resveratrol, making it a very potent antioxidant (I. M. Kapetanovic, M. Muzzio, Z. Huang, et al., "Pharmacokinetics, oral bioavailability, and metabolic profile of resveratrol and pterostilbene…" Can, Ch and Pharmacology, vol. 68, no. 3, pp. 593–601, 2011.)
This blueberry-derived compound exerts **supportive effects on neurons** by **crossing the blood brain barrier and impacting central nervous system signals** (Andres-Lacueva, C. et al. Anthocyanins in aged blueberry-fed rats …," Nutritional Neuroscience, vol. 8, no. 2, pp. 111–120, 2005.) No wonder we are told to eat blueberries for brain power!

Berberine, known to possess potent support characteristics for fungal pathogens, **significantly affected the expression of more than 2,000 genes, such as those involved in translation, transcription, intracellular communication, lipid metabolism, and the cytoskeleton** (PLoS One. 2014 Oct 10;9(10):e109863. Berberine is a potent antifungal agent that inhibits the growth of Cryptococcus neoformans by regulating gene expression. Bang S. et al.)

Other nutrients with epigenetic effects include **L-theanine** (ScientificWorldJournal. 2014;2014:419032. Effects of L-theanine... Ceremuga TE), **cinnamon** (PLoS One. 2013 Dec 13;8(12): Anderson RA et al.) and **resveratrol, ashwagandha, red beet root, sulforaphane, quercetin, silibinin (milk thistle), DIM, and myricetin (from berries)**



The various epigenetic influences of these Nutritional Phytochemicals and the pathways affected are discussed in:

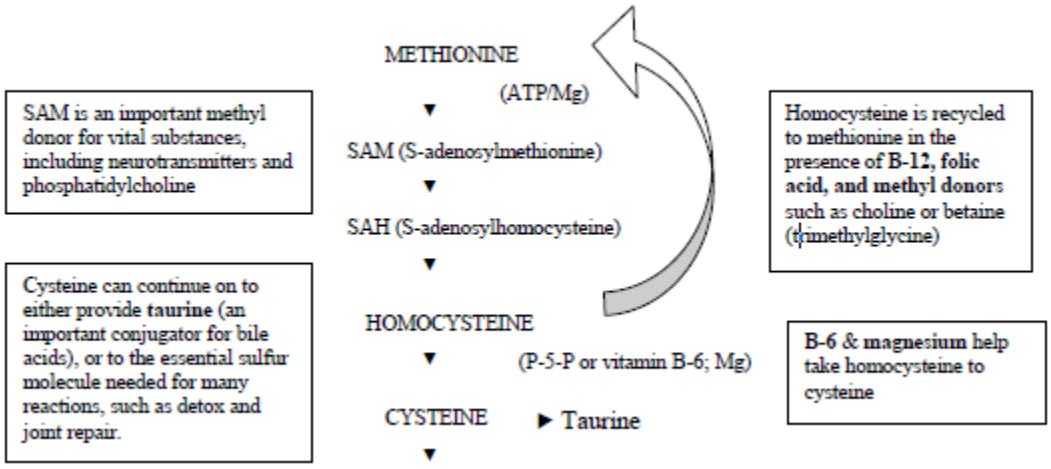
Nature or nurture: Let food be your epigenetic medicine. Katarzyna Szarc vel Szic et al. Biochem Pharmacol. 2010 Dec 15;80(12):1816-32.

Methylation Supports the Brain and has Epigenetic Influences:

*"DNA **methylation** is one of several **epigenetic** mechanisms that cells use to control gene expression."*
- Phillips, T. (2008) The role of methylation in gene expression. Nature Education 1(1):116

What is methylation? Well, **methylation** is a process in the body that adds carbon groups to substances and activates them; methylation is responsible for many of the life-sustaining pathways that keep us alive and keep us healthy. Methylation is critical for forming signaling peptides, neurotransmitter production, and hundreds of biochemical pathways. We have established on the first page that nutrition can exact epigenetic influences on health and the brain. The methylation process obviously impacts brain health with everything that methylation activates.

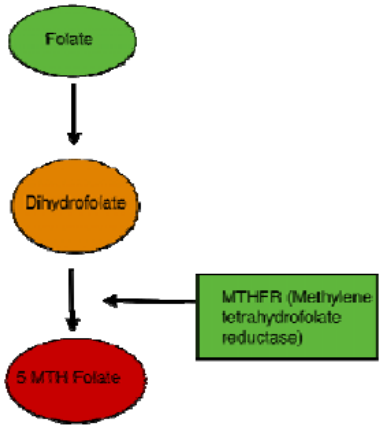
When the homocysteine pathway is facilitated, methylation is accelerated. To facilitate the homocysteine pathway where the major methylator is made (**SAM** or S adenosyl methionine), the active form of folic acid is necessary (**5 MTHF**), along with **vitamin B-12**, preferably in the active methyl B-12 form, which help recycle the toxic homocysteine back to methionine. There are several other nutrients which support/accelerate the methlation process, for instance, **vitamin B-6** (active form P-5-P), which assists the flow down the pathway to cysteine (used for processes like detox) or further down to sulfur. **Molybdenum** prevents stagnation at the step of toxic sulfite, and moves the process along to produce the sulfur molecule essential for joint health (sulfur is usedas a building block for glucosamine sulfate, chondroitin sulfate, etc.) **Magnesium** is necessary to bring methionine down the pathway to **SAM**.



Additionally, **green tea catechin, sulforaphane, N acetyl cysteine, phosphatidyl choline, choline, curcumin, intrinsic factor, dimethyl glycine, trimethyl glycine, and beet root** are exceptional synergistic nutrients to pump up methylation processes.

Active Folic Acid (5MTH Folate)

Folic acid must be converted to its active forms, folate and **5-MTHF**, to be used by the body. Approximately half of the U.S. population may have a genetic glitch that makes it difficult for them to convert folic acid into active 5-MTHF. For these individuals and many others, 5-MTHF supplementation may be a more effective method of folate replenishment.



Nutri-West Presents:

*5-MTH FOLATE

Each Tablet Contains:
Folate (as L-5 methyltetrahydrofolate)
500 mcg

HOMOCYSTEINE REDUX

Includes:
Folate (as L-5 methyltetrahydrofolate) 500 mcg
P-5-P (active B-6)
Methyl B-12
Vitamin B-6
Vitamin E
Niacin
Magnesium
Molybdenum
Zinc
Selenium
Dimethylglycine
Trimethylglycine
Beet root
N-acetyl cysteine
Choline

AND:

METHYL RENEW

The ultimate in methylation optimization!

Each Tablet Contains:
Folate (as L-5 methyltetrahydrofolate)
P-5-P
Methyl B-12
Niacin
Biotin
N-Acetyl cysteine (NAC)
Phosphatidylcholine
Green tea catechins
SAM-e
Curcumin
Intrinsic factor
Sulforaphane

COMPLETE SYNAPSE

Nutrition for the brain

Bacopa
Trans pterostilbene
Glucoraphanin (sulforaphane)
Ashwagandha (*Withania somnifera*) root
Sunflower Lecithin
3-acetyl-7-oxo-dehydroepiandrosterone
DHA vegetarian (organic spirulina (at 7% DHA))
Alpha KG (keto-glutaric acid)

Piper nigrum, berberine, L-theanine, thyme, oregano, blueberries, cinnamon, TMG (trimethylglycine)

Also:
5-methyltetrahydrofolate, P-5-P (active vitamin B-6) and Methyl B-12

For more information, visit: *www.nutriwest.com* for webinars on methylation, fact sheets on Nutri-West products, seminars, etc. You must receive a code from your Nutri-West distributor (distributors posted on website) to gain access to the website.

1-800-443-3333
(PAID ADVERTISEMENT)

Nutri-Notes/ ed. Dr. Lynn Toohey
drtoohey@nutri-west.net

Specific B vitamins are involved in the methylation pathway.

B vitamin support has been extensively studied, and it is well-known that B vitamins, specifically three B vitamins in particular, help maintain methylation pathways and provide epigenetic support for the brain. In a groundbreaking two year randomized controlled trial of 156 subjects, Douaud G. et al. published a report on May 20, 2013 in the journal Proc Natl Acad Sci U S A. that named three major B vitamins for supporting brain activity and cognitive processes. Those B vitamins were: **Vitamin B-6, vitamin B-12, and folic acid.** Although the study did not distinguish between the active forms of the vitamins, the active form of folic acid (5 MTHFolate) is powerful and beneficial to people who are impeded in their methylation capabilities (about 50% of the population), methyl B-12 is the active form of vitamin B-12, and P-5-P is the active form of vitamin B-6.

The study determined that daily amounts of folic acid (800 mcg) along with vitamin B-12 (500 mcg) and vitamin B-6 (20 mg) provided excellent support for brain function, brain volume, and normal cognitive processes. Their conclusion, in approaching brain support, was that an effective way to modify nongenetic influences (in other words epigenetic effect), was to utilize a supplement plan containing these amounts of the B vitamins.

Several studies have shown that folic acid, vitamin B12, choline, zinc, selenium, dietary polyphenols are capable of interacting with epigenetic mechanisms and ultimately gene expression. Epigenetic mechanisms resulting in neuronal dysfunction may be modified by diet. Therefore manipulation of epigenetic mechanisms via dietary nutrients may affect influence the vulnerability of neurons to degeneration…" (Sezgin Z. Dincer Y. Neurochem Int. 2014 Dec;78:105-16.)