THE AFIB REPORT
Your Premier Information Resource for Lone Atrial Fibrillation
Publisher: Hans R. Larsen MSc ChE

VIRTUAL LAF CONFERENCE

Proceedings of 20th Session
December 21st –

SUBJECT: Methylation

Ho, Ho, Ho, Yes it's me again.

I just keep finding more and more information that is starting to fall into a pattern that correlates to all of us. If I remember correctly, PC had problems with allergies - histamine. Some have problems with tyramines, and yet others with MSG, including myself, PC, Fran and more. This article ties it all together and is about methylation. Thanks to Jackie, she prompted me in this direction, but said Erling prompted her. Jackie, pay particular attn. to the fact that MSM depletes molybdenum, which is important in this methylation process. Fortunately, I have quit taking it, and was not taking MSM during my testing phase. You will read that the amino acid histadine is converted to histamine, and excess histamine causes allergies, hence people take anti-histamines. This data suggests that the reason too much histamine is there is because s-adenosyl methionine is not present to donate its methyl group to stop this reaction. Other reactions from histamine are food sensitivities, such as tyramines and MSG, yep MSG and sulfites/nitrates. So in a sense, Fran, molybdenum does help with free glutamate toxicity in the pathway of methylation. Methylation is also important for neurotransmitters. Another thing I couldn't figure out with myself, was the fact that I was low in methionine and cysteine. I was also low in B12, so I should have had high levels of homocysteine, but I didn't. Where was the methionine and cysteine going? It was attaching to the higher levels of mercury that I had, as you will read, and was rendering it useless, or maybe carrying it out of my body. I have always had this strong feeling that sulfur aminos were somehow playing a huge role in our problems, partly because of pollution and our environment, partly because of eating sick animals using up their own stores to fight their illnesses, fish using their stores to rid themselves of mercury, and by eating pesticide laden fruits and vegetables that require the body to constantly try to maintain a toxic free environment.

Maybe, just maybe, the body has to use what stores of sulfur, B12, B6, folic acid, and magnesium it has, in a cyclic manner. Today it lets the neurotransmitters do their jobs, tomorrow it tries to cleanse the liver, and the next day it works on the kidneys. It's given up on histamine, because the antigens are just not as important as the running of the organs, therefore leaving many with food sensitivities or allergies.

I had to quit taking Lipotain, made by Metagenics, as it was giving me headaches. This article states that if one is a slow methylator, then one should not take higher doses of niacin, because niacin requires methylation, and this taxes the already low methylation process, further. I also had to quit taking tryptophan for the same reason. I first need to build up my B12 and molybdenum stores. For me, I was normal in Mg, so only take 200mg daily, and my folate was trapped due to low B12. We are all different, however. Dimethylglycine is also important, as it is already methylated, and I believe that the glycine was equally important in the Mg glycinate that some have found advantageous here.

PC, here's an excerpt on histamine:
Methionine is a methyl carrying amino acid + ATP/magnesium = SAMe.

SAMe goes throughout the body delivering methyl groups to over 400 different reactions.

One way histamine is de-activated (eliminated) is by receiving a methyl group from SAMe. So if there is low methylation, there is low SAMe, and the histamine levels are higher because of the lack of methyl groups to deactivate it. If there is high methylation, there is higher amounts of SAMe, and lots of histamine can be deactivated.

Here's the first link, that I believe you would all find very interesting and make sure you click on the links within the text, to get a further understanding.
http://www.enzymestuff.com/methylation.htm

Here's an excerpt, Jackie, from a link within the text:
Additionally, resources such as Jonathan Wright, MD point out that MSM can create a molybdenum deficiency because exogenous, (outside) sources of sulfur will drain molybdenum resources because the molybdenum is essential for sulfur metabolism. On the contrary, NATURAL provision of sulfur makes what the body needs, and does not create an excess pool which then must drain molybdenum to be metabolized.

Pls. let me know what you all think, and if you see a commonality to yourself in this article.

Richard

Richard

It makes sense. However, a while back on an orthomolecular site I was conversing with one of the Dr's on the board. He seemed to think I overmethylated. There was a site I remember which gave the symptoms of under and over methylation. Over methylation certainly fitted my symptoms.

Now maybe, just maybe - as you tend to lean to adrenergic and I too vagal - undermethylation = adrenal and over methylation = vagal.

Maybe a long shot but I think not.

Fran

Fran,

In case you didn't read, this article speaks of over methylation, as well. That's a good point, about under and over. I still think somehow, that molybdenum plays a part in your genetics. I would have to further say, that I would have to guess you are an under methylator because of your smoking. That depletes enormous amounts of sulfur aminos and Vit C, and B's. Even though you have a grasp on your AF through diet, damage is still being done, and excessive stores of sulfur are being used up. Why do you suppose the doctor thought you were an over methylator?

Richard

I pulled this from the archives 2/11/03, that Erling wrote, using the word "methylation".

Hi Jackie, and Lorraine,

Jackie, your comments are always to the fact-filled point, and they are very much appreciated. In an earlier post you said that "DNA irregularities definitely influence membrane ion channels and pumps," and that in Metagenics seminars "they emphasize the major influence that nutritional factors have on healthy gene expression, protein synthesis and metabolism with their goal being the achievement of optimal genetic expression."

Your statements bring up the subject of adequate "methylation" to limit DNA mutations and enhance gene expression.

This might be of great interest to you, Lorraine, since you had said "I would like to know what I can do to improve the functioning of my calcium ion pump which I'm assuming may be faulty because my intracellular calcium level is 5.5 which is above the range upper limit of 5.0." Craig Cooney, PhD biochemistry, UC Davis, has become a leading researcher and writer on the subject of methyl metabolism. His book Methyl Magic (1999) is written in a laypersons style, very easy to read and understand. He writes, "Methylation... it starts at the moment of conception (even before, actually) and continues, billions of time every second, until the day we die... methylation is a vital key to how we feel - physically, mentally, and emotionally. Lets put it as simply as possible: Methylation helps give life, and it can take it away. In fact, without methylation there would be no life at all. So what is methylation? Technically it starts with the small parts of molecules called methyl groups. A methyl group is a carbon atom with three hydrogen atoms attached to it. Any other molecule that adds this methyl group, whether it be a molecule of DNA or a protein molecule - any of the body's enormous inventory of molecules - is considered methylated. Methylation is so crucial a part of our body's machinery that it has a name of its own: methyl metabolism. Methyl metabolism refers to the making of methyl groups and their passing from one molecule to another. Methylation happens in everything that's alive - sponges, birds, bees, chimps, mice, and humans. As we said, without methylation there is no life - period. Methylation helps regulate the switching on and off of genes (technically this is known as gene expression) - one of the most crucial regulators of health and life itself. When gene expression goes awry the results can be horrifying: birth defects, cancer, and maybe even autoimmune diseases such as lupus. When other aspects of methyl metabolism go awry the downside can be equally terrible: heart disease, mental retardation, and diseases of the nervous system, among others."

(It will not surprise me at all to someday learn that derangements of the complex structures of ion pumps and channels (proteins) from lack of adequate methylation can bring about cardiac arrhythmias)

"Among the most important of methylation's many functions is the maintenance and protection of DNA, the basic stuff of heredity and of life itself. Adding methyl groups to DNA is enormously important in maintaining healthy cells. Many other proteins need periodic repair, and methylation is essential for this crucial repair work. Methylation, to put it in a nutshell, is vital to the healthy functioning of all our body's calls. Why? Because it makes the membranes that surround each of our cells more fluid. This in turn allows better regulation of life sustaining minerals like sodium and potassium into and out of our cells, so that a healthy balance of these minerals is maintained. In most people the fluidity of cell membranes decreases with age, and this loss of fluidity may be one of the features that defines aging itself."

"Obviously methylation is a key player in giving us life, keeping us healthy, and perhaps enabling us to live longer, more vital lives. Scientists have known this for quite some time, but I still find it amazing that there's been so little discussion of methylation in the popular press and in the media. It's a shame, and we scientists bear much of the responsibility for not making the public aware of what we know."

So this subject is the closest thing that I've come across to a real way of protecting, perhaps rebuilding, faulty ion pumps and channels (proteins all), and membranes (the fluidity of which is also enhanced with good fats such as DHA and EPA fish oils, and the elimination of bad fats such as hydrogenated oils and many plant oils). The book goes on to explain that the way to determine if ones methyl metabolism is adequate for repair and maintenance is with a determination of homocysteine (HCY) levels in the blood, a routine and quite inexpensive test (the recommended upper limit is 7 micromoles per liter of blood -- above that lie all sorts of health problems). And if ones HCY level is too high, the book lays out the methyl metabolism enhancing supplements that are needed and the recommended doses: trimethylglycine (TMG), choline, inositol, folic acid, vitamins B6, B12, and E, zinc, selenium, fish oils.

The following are highly recommended reading:

Book, Methyl Magic by Craig Cooney, ISBN 0-8362-3585-1
Article, http://www.lef.org/magazine/mag98/dec98_meth.html
Article, http://www.lef.org/magazine/mag2001/apr2001_briefs.html
Article, http://www.lef.org/magazine/mag99/mar99-report2.html (this article shows the desirable HCY level)

Richard

Because of the symptoms Richard.

http://www.alternativementalhealth.com/articles/walshMP.htm

Conditions associated with undermethylation: Anorexia, Bulemia, shopping/gambling disorders, depression, schizo-affective disorder, delusions, oppositional-defiant disorder, OCD.

Conditions associated with overmethylation: Anxiety/Panic disorders, anxious depression, hyperactivity, learning disabilities, low motivation, "space cadet" syndrome, paranoid schizophrenia, hallucinations. (Oct 3, 2003)

A. **Undermethylation**: This condition is innate & is characterized by low levels of serotonin, dopamine, and norepinephrine, high whole blood histamine and elevated absolute basophils. This population has a high incidence of seasonal allergies, OCD tendencies, perfectionism, high libido, sparse body hair, and several other characteristics. They usually respond well to methionine, SAMe, calcium, magnesium, omega-3 essential oils (DHA & EPA), B-6, inositol, and vitamins A, C, and E. They should avoid supplements containing folic acid. In severe cases involving psychosis, the dominant symptom is usually delusional thinking rather than hallucinations. They tend to speak very little & may sit motionless for extended periods. They may appear outwardly calm, but suffer from extreme internal anxiety.

B. **Overmethylation**: This condition is the biochemical opposite of undermethylation. It is characterized by elevated levels of serotonin, dopamine, and norepinephrine, low whole blood histamine, and low absolute basophils. This population is characterized by the following typical symptoms: Absence of seasonal, inhalent allergies, but a multitude of chemical or food sensitivities, high anxiety which is evident to all, low libido, obsessions but not compulsions, tendency for paranoia and auditory hallucinations, underachievement as a child, heavy body hair, hyperactivity, "nervous" legs, and grandiosity. They usually respond well to folic acid, B-12, niacinamide, DMAE, choline, manganese, zinc, omega-3 essential oils (DHA and EPA) and vitamins C and E, but should avoid supplements of methionine, SAMe, inositol, TMG and DMG

I know we have discussed the fact that I have always maintained I had high seratonin levels etc and never considered myself depressed. Perhaps my smoking (very little now) keeps the methylation rate down and is a reason why I find it difficult to stop that final few. Interesting about undermethylators being told to avoid folic acid.

Fran - who has no libido, boundless energy, no seasonal allergies but lots of food sensitivities, and with AF had to work on anxiety levels, paranoia and had to keep on top of keeping my legs still, not to mention dyslexia, ADD etc etc. Have to say that I don't have the body hair though.... and the voices - well I have an inner voice I always listen too - I call it my conscience.

Fran

Fran,

Very interesting. I do fit mostly into the undermethylator, but fit some of the over categories, as well. I do not have OCD, seasonal allergies, or perfectionism. But this is an exact representation of me: They tend to speak very little & may sit motionless for extended periods. They may appear outwardly calm, but suffer from extreme internal anxiety. The latter only happens, when business goes awry or my wife gets mad.

On the other hand, I fit some of the categories of over-methylators, such as an under-achiever as a child, but not as an adult, and chemical and food sensitivities.

I consider myself mixed, so wonder if your perception of vagal, adrenergic, and mixed would come into to play here. It will be interesting to read other's comments, as to how they relate.

Thank you, Fran.

Are you back in your own home now, and working to get all that done? I know you had recently moved, and then went

to house sitting. You've been busy!!!

Have a wonderful Christmas, Fran!!
Richard

Richard....ho ho ho, yourself! You are challenging me to rethink some of the reasons why I take MSM.... I'll be re-reading Methyl Magic soon and will seriously evaluate what you've said - especially about the MO stores.

You could be on to something here. (in my case) ..although, I have to tell you that for about 2 months, I haven't taken the MSM and I'm feeling some fibromyalgic symptoms - but this could be from other sources.

Thanks for the heads up...and thanks for pulling up the past post by Erling. He was the one that turned me on to methylation.

This is were it's "at." Very important. We are all just a bunch of biochemical reactions.... and the methylation process is crucial.

Thanks for revving up the topic again.

Jackie

Oh - forgot to mention, I was put on SAMe a while back but haven't been tested recently. That will be coming up after I get my all clear from the ablation procedure. Then we will begin again fine-tuning whatever else is left to tune. :)

Richard

I have been wondering if it is possible to both under and overmethylate in different parts of the body. I don't know enough about it to make an educated judgement though. I do have a perfectionist trait and fall far short of my own mark and perhaps a bit of oppositional-defiant disorder, although I would not call it a disorder in my case. So like you I have traits in the other camp. But sometimes our little traits must just be personality rather than symptoms.

I know that overmethylation has been connected with cancer as a side note.

We have moved now, but I think it will be after the new year before I get properly settled. Did most of my Xmas shopping today and only got a tree today - talk about being late. Also bought the most expensive turkey in the whole world (£50 for 13 lbs)- but am really looking forward to it. A very Merry Xmas to you too.

Fran

Hans,

Thank you for putting this topic in the conf. room. I felt it was extremely important, and that feeling was further justified by a conversation with an old friend, Dr. Jonathan Wise, last night at a Christmas party I attended. He is a research microbiologist for Natural Alternatives International in the San Diego area and was in town for the holidays. I wish I could have spoken with him all night, as the information was very interesting. What he thought to be the most important issue to key in on, for our group, was methylation and detoxifying the liver/spleen. He said that most people are low in methionine, therefore low in s-adenosyl methionine. He stated that the methylation process in the body is complicated, but the key factors we should concentrate on are B6/P5P, methylB12, folic acid, magnesium, methionine, N-acetyl cysteine and trimethylglycine. Of course all of the nutrients are important, but these are key. He's also sending me a liver detox formula of sarsaparilla and artichoke. They did a 30 day trial in Mexico, of which he said wasn't long enough, but they have found it to work so well, that people are using this formula to be able to consume alcohol, and not have any hangover effects. He also stated that when cleansing the body it is imperative to use saunas, massage, and moderate exercise to help with elimination of toxins of the lymphatic system and deep muscle tissue, which is

where many toxins are stored. He also felt everyone needs the assistance of digestive enzymes, but not much else was said, as the party atmosphere didn't lend itself to this serious discussion. I hope to meet with him again, to go further in depth of his knowledge and opinions. He has been studying nutrition for years and is fascinating to talk with. His past studies were on the common cold, and found Vit C and zinc to be crucial. Here's the website of his company. http://www.nai-online.com/management.html

Fran,

Now my wife has a new term for me; now I'm an oppositional defiant, neurotransmitter deficient old fool. I guess if the shoe fits, wear it. Ha. From what I've read, and am still reading, it would seem that there are different pathways for methylation.

To All,

Unless one gets tested, it's a guessing game, but I do feel that we could all be served by boosting our methylation and sulfation pathways, irregardless of testings, because we are all probably lacking somewhere, due to constant assaults. Here's a Great Smokies website on this issue, and an excerpt.

Note that having a big toxic methylation load is not good because it results in lots of homocysteine and less methylation capacity for adrenal catecholamines which influence mood and behavior. Biochemicals or toxics that are methylated include: cobalamin, histamine, adrenal catecholamines (epinephrine, norepinephrine), serotonin, phosphatidylethanolamine (successive methylation produces choline), tryptamine, tyramine, amphetamine, aniline, benzidine, imidazole, arsenic, antimony, selenium, and hydrogen sulfide.
http://www.gsdl.com/news/nmnewsletter/issue2-2/index3.html
click on all pages of this link, esp. pg.4 for sulfation

Pg 4 excerpt--Excessive urinary taurine, cysteine and/or cystine may occur in molybdenum insufficiency, sulfite oxidase weakness and sulfite excess.

Back when having my urine analysis, I had extremely high levels of taurine, but chalked it up to taking 1200-1500mg per day. The fact of the matter is that I was just urinating it out, because of my Mo deficiency.

So I am lacking in methylation and the back up system of sulfation. I'm a toxic time bomb. The only good thing, is my homocysteine levels are low.

Dr. Wise didn't mention selenium, but there is a methyl form, and I know I'm low. It is common knowledge for my demographics, because our soils are low in selenium. Another thing I have to focus on, is that I have high levels of methylhistamine. For some reason I am methylating histamine and maybe this is where my sulfur stores or methylation processes are going. Still reading on this one. In order for me to save my body from having to methylate nutrients, I'm going to focus on a good multivitamin with the addition of any methylated nutrient I can i.e. methylcobalamin, trimethylglycine, tetrohydrafolate, methionine, methylated selenium and N-acetyl cysteine. Hans, choline forms betaine, and then somehow betaine is methylated to trimethylglycine. Dr. Wise touched on this, but I can't remember exactly what this process was.

Here's an interesting link on chemical sensitivities for anyone interested.

Vitamin C can improve tolerance to many chemicals, however in a few individuals it can increase chemical toxicity. In these individuals Alkali, one hour after meals may be of great benefit.
Digestive enzymes should be taken with every meal.
Hydrozyme or Apple cider vinegar one teaspoon in water with meals may aid stomach digestion.
Fish oils or linseed oil, 1 or 2 dessertspoons per day may reduce inflammation.
Ginger is a thromboxane synthetase inhibitor and can reduce inflammation.
Vitamin B5 and taurine may reduce formaldehyde sensitivity.
Vitamin B6 and C reduces MSG sensitivity.
Vitamin B12, Glycine and Molybdenum supplementation may reduce metabisulphite and sulphite sensitivity.
Try neutralizing dose of quercetin and rutin.

Zinc supplementation for tartrazine sensitivity.
Alkali may need to be taken in between meals to improve digestion.
http://www.geocities.com/nutriflip/Diseases/ChemicalAllergies.html

I'll try to sneak some more studying in, esp about sarsaparilla and artichoke. This may not end our arrhythmias, but it sure is a good place to begin for anyone.

Richard

Richard

I would be fascinated to learn of the different pathways in methylation. I hope you don't think that this is a case of oppositional defiant disorder (smile). It's just that I don't read myself the way you see me. I thank you for all the work you are putting in for me and for everyone else. But this is my take on me and maybe others who do not seem to get the benefits out of supplements but seem to get worse...

I am still convinced that I overmethylate, this is compounded by the reactions I have had to supplements - the B ones in particular to methylation. My negative experiences with antidepressants would also indicate I have very high levels of serotonin etc.

I would be fascinated also to learn as to why the Pfeiffer centre think that folic acid etc (precursors to methylation) should be avoided in undermethylators. I always think of the Pfeiffer clinic as the leading edge in this sort of research. I do think there is more to all this than meets the eye.

It maybe that a higher percentage of people undermethylate, but for me my reactions to everything is upside down to the "normal" reaction. I learned a long time back that what is right for most people is not right for me.

I have negligible homocysteine levels and a very efficient liver (shown when ever I have had liver function tests and how quickly my liver gets rid of meds and I suppose toxins). And as I have said on numerous occasions I don't think I have any problem with digestion or a lack of enzymes. And as my metabolic typing indicates I do not need to alkalise. In fact my experience with Waller Water showed what too much alkaline can do to me.

Most of the literature focuses on how to speed up methylation, not how to slow it down. This I think would be of help to me. The only thing that springs to mind - and this is stupid - is toxins.

I am wondering if there is a connection between metabolism/oxidation and methylation rates. I am such a fast metaboliser and could eat a Sumi wrestler under the table and not put on an inch.

I think I will ask for a histamine test to see exactly what my histamine levels are. It they are low than that would seem to be the gold standard to discovering whether an over or undermethylator. I can't remember but were your histamine levels high?

Have a great Christmas

Fran

Hello Fran,

You could very well be an overmethylator, but it still astounds me that your smoking isn't destroying a lot of your sulfur aminos and B's, even though you said you have cut back presently. My understanding, however, of what Dr. Wise told me, was that methionine first goes to s-adenosyl methionine, and this is the first step of methylation. Then from there, the breakdown proceeds to s-adenosyl homocysteine, and then to cysteine and so on. Because methionine is a precursor to taurine, this is where your pathway could be disrupted. Read Jackie's post on the BB, answering Peggy's post to diarrhea. Taurine is very helpful to MSG toxicity, but it is necessary to have Mo, or taurine is wasted, which is

what was happening to me. See Great Smokies link above. So, what I'm trying to say, is that all your sulfur is being diverted to methylation, because your pathway to taurine is possibly disrupted, hence MSG sensitivity. I'm theorizing here, but it makes sense.

I don't know my levels of histamine, but am trying to figure it out based on by-products of my testings. I was low in histadine, but high in 1-methylhistadine and even higher in 3-methylhistadine. So for some reason, I'm methylating histadine in greater amounts, so it would seem that my methylation is being wasted all in this direction for some reason, or there's a reason for it, that eludes me, but I'm still searching.

Thank you for the link, Fran. I'll have to read later, as my daughter is hollering for me to watch a movie with her.

To All,

I failed to mention an interesting fact that Dr. Wise presented to me. I told him of my levels of packed red blood cells. He said that wasn't a good way to find out what one's intracellular levels of electrolytes and minerals were. They have proven that the better way to determine one's levels is to take bucal (sp?) cells from the tissue of the mouth and test these. They have taken heart tissue samples and compared with bucal cells, and they very closely relate. So now I need to get yet another test. Oh boy!!

As the plot thickens,
Richard

Richard

Here is a link to the site where you can go through the symptoms of over and undermethylation along with Pyroluria.

http://www.nutritional-healing.com.au/articles-content.php?heading=Major%20Mental%20Illness%20Biochemical%20Subtypes

One more post on overmethylation. It is more commonly known as Histapenia (Histamine Low). High histamine or undermethylators is known as Histadelia.

The fascinating thing in respect of low histamine is that it is known that high copper levels decrease histamine (now was high copper not a factor in my diet?). Maybe I should try to cut back.

http://www.digitalnaturopath.com/cond/C376401.html#G1000

Serum copper levels in these patients are abnormally high. Since copper is a brain stimulant and destroys histamine, the elevated serum (and presumably brain) copper level probably accounts for many symptoms, including the low blood histamine level. This is also called a condition of overmethylation or being over-methylated.

Behavioral symptoms in high-copper histapenia include paranoia and hallucinations in younger patients, but depression may predominate in older patients. The patient is usually classified as having chronic or process schizophrenia. Some studies of schizophrenics have revealed high blood copper, as seen in histadelia, with low urinary copper (showing that copper is being retained) as well as low blood zinc.

Histapenia, is characterized by elevated levels of serotonin, dopamine, and norepinephrine, low whole blood histamine, and low absolute basophils. This population is characterized by the following typical symptoms: Absence of seasonal, inhalent allergies, but a multitude of chemical or food sensitivities, high anxiety which is evident to all, low libido, obsessions but not compulsions, tendency for paranoia and auditory hallucinations, underachievement as a child, heavy body hair, hyperactivity, "nervous" legs, and grandiosity.

The treatment program consists of the administration of zinc, manganese, vitamin C, niacin, vitamin B12, and folic acid. With this treatment the high blood copper is slowly reduced and symptoms are slowly relieved in several months' time.

Symptoms - General Good pain tolerance

Counter-indicators:
Poor pain tolerance [I have really high pain tolerance and often don't feel pain when I hurt myself]

Symptoms - Hair
High body hair quantity [don't have this]

Symptoms - Metabolic
Hyperactivity [Absolutely have this]

Not having headaches - Headaches are usually not experienced by those with low histamine levels (histapenia). [used to suffer this all the time but have not in long time]

Symptoms - Mind - General
An overstimulated mind [absolutely]

Symptoms - Reproductive - General
Difficulty achieving orgasm [what's one of these?]

Histapenia tends to cause obsessions but not compulsions.

What are the most common obsessions?
Fear of contamination
Fear of causing harm to another
Fear of making a mistake
Fear of behaving in a socially unacceptable manner
Need for symmetry or exactness
Excessive doubt

[this is me to a T always worrying about what I might inadvertently do and I do worry when next to people or unsanitary conditions in case I might catch it and I always have a need to balance ornaments, pictures or if I scratch one side of my face need to have the same feeling on the other side - the same goes for situations - if I feel someone is being picked on I need to balance the situation to even the odds - despite maybe not even believing or liking the out of balance side....]

Amino Acid / Protein Histidine
Not recommended:
Phenylalanine
Methionine
Tryptophan / 5 HTP
Tyrosine

Botanical
Not recommended:
St John's Wort (Hypericum perforatum)

Diet
High/Increased Protein Diet

Lab Tests/Rule-Outs
Test Copper Levels
Test Histamine Levels
Test for Manganese Levels
Test Zinc Levels

Mineral
Manganese Copper levels are usually elevated in patients with histapenia. Manganese and zinc supplementation increase copper excretion.

Not recommended:
Copper Excess copper may be acquired from commercial vitamins and minerals or drinking water flowing through copper pipes. Distilled water may occasionally be needed to reduce copper intake.

Nutrient
Essential Fatty Acids

Not recommended:
Inositol
TMG (Tri-methyl-glycine) DMG and TMG (dimethyl and trimethylglycine) or SAMe may cause adverse reactions in some.

Vitamins
Vitamin Folic Acid The rationale underlying this treatment is that folic acid in conjunction with vitamin B12 injections raises the blood histamine while lowering the degree of symptoms.

Vitamin B3 (Niacin)
Vitamin C (Ascorbic Acid) Zinc and manganese with vitamin C remove copper from the tissues. Copper destroys histamine and therefore as copper levels decrease, histamine levels should return towards normal.

Vitamin B12 (Cobalamine)
Vitamin B6 (Pyridoxine)

Heres the link to undermethylation.

http://www.digitalnaturopath.com/cond/C446553.html

And the reason why not to take folic acid -

"Histadelics should avoid supplemental folic acid as it can produce excess histamine. In fact, anti-folate drugs may be required. Folic acid increases depression in histadelic patients and a trial of folic acid could be used to distinguish between histapenics and histadelics. In extreme cases, folic acid in food or in multivitamins is enough to produce the adverse effects"

Recommendations for Histadelia (Histamine High):
Amino Acid / Protein Methionine Methionine supplements lower blood levels of histamine by increasing histamine breakdown.

Not recommended:
Histidine

Diet
Vegetarian/Vegan Diet Nutritionists recommend a low-protein, high complex carbohydrate diet. Histidine, which is more common in animal proteins, should be avoided as it can be converted into histamine.

Lab Tests/Rule-Outs
Test Copper Levels Testing serum or hair copper levels is usually adequate for evaluating copper status when low levels of copper are suspected and hair contamination with copper can be ruled out. When in doubt, it would be better to use more accurate tests such as the 24 hour urine copper or serum ceruloplasmin.

Test Histamine Levels

Test Folic Acid Levels Under certain conditions, such as anticipated or actual pregnancy, a simple lab test for serum folate levels is advisable. If the test results show low levels, supplementation should be considered to prevent potential birth defects.

Test Zinc Levels
Test for Manganese Levels

Mineral
Calcium
Magnesium
Manganese
Copper - Copper levels may be low to normal in patients with histadelia. Copper is part of the enzyme histaminase, which is involved in the metabolism of histamine. Some suggest that copper should be avoided when bipolar symptoms are present. Testing will help confirm a person's status.

Nutrient
Not recommended:
Lecithin / Choline / GPC
DMAE

Vitamins
Vitamin B6 (Pyridoxine)
Vitamin C (Ascorbic Acid)

Not recommended:
Vitamin Folic Acid Histadelics should avoid supplemental folic acid as it can produce excess histamine. In fact, anti-folate drugs may be required. Folic acid increases depression in histadelic patients and a trial of folic acid could be used to distinguish between histapenics and histadelics. In extreme cases, folic acid in food or in multivitamins is enough to produce the adverse effects.

Interesting that they say high histamine types do better on veggie or vegan diets??

I must say that I thought it strange that Mg was not mentioned as a supplement for over methylation - only under methylation. I wonder if as an overmethylator it is not needed - and hence my reactions.....

Hope this stimulates some feedback.

Fran

Fran, I capped my response.

Poor pain tolerance [I have really high pain tolerance and often don't feel pain when I hurt myself] I'M A BIG BABY, SO I'M TOLD.

Symptoms - Hair
High body hair quantity [don't have this] NEITHER DO I

Symptoms - Metabolic
Hyperactivity [Absolutely have this] DO NOT HAVE THIS

Not having headaches - Headaches are usually not experienced by those with low histamine levels (histapenia). [used to suffer this all the time but have not in long time] I ALWAYS HAD HEADACHES, BUT NO LONGER DO, EXCEPT WHEN I WAS TAKING NIACINAMIDE B3 AND TRYPTOPHAN. STOPPED.

Symptoms - Mind - General

An overstimulated mind [absolutely] ME, TOO, BUT CAN TURN IT OFF WHEN DESIRED.

Symptoms - Reproductive - General
Difficulty achieving orgasm [what's one of these?] NO PROBLEM WHEN MY WIFE OBLIGES.

Interestingly, I am both high in copper and zinc, in the red zone, on my hair analysis, and normal on both, in packed red blood cell. My hair manganese was a bit low, but intracellular was a bit high.

Histapenia, is characterized by elevated levels of serotonin, dopamine, and norepinephrine. I DO NOT HAVE THIS EITHER, according to the end by products being low.

Basically, one needs to have certain testings to know whether they are over or under methylators. In your case, Fran, you can't do any thing different than you already are. I guess the only thing I would be most interested in, in your case, is your molybdenum levels. Your methylation detox pathway may be over active because your sulfation pathway is having problems. I need to chart this out on paper, in my case, but the pattern seems to exist that I am an under methylator and under sulfator. I'm mixed. Hmmmm?

Thank you for the info.
Richard

Fran wrote:
But sometimes our little traits
> must just be personality rather than symptoms.

I wonder if the difference is just the degree of severity sometimes - still much to learn.

This I think is interesting

http://www.univ-lille1.fr/lea/Menu_du_Site/Publications/Acrobat/Placebo2002.pdf

Fran, is the big trip still a happening thing? I hope so.

Angus

Hi Angus

You may have something there with the severity of symptoms.

I have started to read the article and it looks fascinating - the placebo effect and self deception. That to me sounds very much like the mind over matter attitude and sometimes I often wonder if I went into a denial about my AF and have to check that I am not secretly afibbiing - but it is not the case. I definitely think there is something in it. But will need more time to read the article.

The big trip is hopefully still on - but my Mums estate is taking longer than we thought to be finalised. I cant' book it until I know when it is coming. I am really looking forward to it and can't wait to meet you and your family and experience some real weather.

Fran - sick of the gales, the sleet, the rain and the horizontal rain and hail, and grey skies.

Hello Fran,

Well, I took the test and seem to fall more in between an under-methylator and pyroluria (still not sure what this is). I

only went down to dental health when scoring.

I scored 10 out of 18 on under; 4 out of 18 on over; 8 out of 18 on pyroluria. I would mark both categories if they both applied, such as inhalant and food and chemical sensitivities. Maybe you could take the test, as well, and mark all that apply, and see where you fall.

In any event, I'm still wondering why histamine is such a crucial marker. I can't find much on methylhistadine or what the end metabolite is, so am still searching.

Here's a bit on histadine. It's interesting to note, that taking histadine actually lowers histamine.

Histidine is an essential amino acid during infancy, and its synthetic pathways in older children and adults are poorly understood. According to "Nelson's Textbook of Pediatrics" the clinical signs of a lack of the enzyme which acts in the metabolism of histadine can include impaired speech, growth retardation or mental retardation. However, whether these findings are actually related to lack of histidine is unclear since children who are deficient in histidine can be completely normal.

The importance of the amino acid histidine lies in the fact that the body uses it to manufacture histamine, and histamine is responsible for a wide range of physiological processes. It is common knowledge that histamines cause the swelling and reddening in many inflammations and allergic reactions. Doctors therefore often prescribe antihistamines in the treatment of inflammations and infections, as well as allergies.

Histidine is a metalloprotein that can bind and transport several metals, including copper and iron. It also increases calcium absorption, reduces histamine levels, and in turn controls diarrhea. (Too much histidine will actually cause constipation, and this is overcome by taking zinc and GLA in the form of primrose, borage, or black current oil.) Since diarrhea causes dehydration and loss of electrolytes, histidine can greatly enhance performance by countering this effect. Histidine is also an important mechanism in clotting factors and can minimize internal bleeding from microtrauma.

As the major component of zinc-binding proteins, histidine is essential for zinc absorption and transport to tissues. One study showed that histidine supplementation stimulated growth by increasing zinc absorption, which in turn thickened the growth plate in bone. Zinc is also a factor in insulin sensitivity, prostaglandin synthesis, and immune function. Another critical role for histidine is myelin basic protein. Because of this protein's zinc-binding properties, myelin is compacted and provides more nerve-insulating protection.

Less known is the important role, histamines play in sexual functions. By and large it is histamines that regulate ejaculations and orgasms. Men suffering from premature ejaculations often show increased histamine activity. They may be helped by an amino acid which counteracts the formation of histamine from histidine, or the activity of histamine, namely methionine.

Contrarily, men and women having difficulties achieving orgasms may be helped by histidine supplementation, as this may result in increased histamine levels in the sexual tract, which in turn may make orgasms and ejaculations easier. Older men who experience a slow down in sexual response may also ask their doctors about histidine upplementation.

An additional pro-sexual effect of histidine may lay in its vasodilating effect, thus making blood flow to the sex organs easier.

Apart from its sexual functions, histidine is involved in many other physiological processes. It is necessary for the production of red and white blood cells and supports the activity of suppressor T cells.

Histidine is used as a supplement for sufferers of rheumatoid arthritis, since it has been shown that in these patients, histidine levels are low. And last but not least, histidine is, like many other amino acids, important for growth and general tissue repair.

In the heart, the ability of histidine to act as an electron donor and, thereby, to neutralize singlet oxygen and the hydroxyl radical results in improved contractility and heart function during heart attack and cardiac procedures such as

angioplasty, heart bypass, heart transplant. Cellular (tissue) damage occurs in a wide variety of medical conditions, including infectious diarrheal diseases, ophthalmic surgery, idiopathic bowel diseases, cardiac conditions, transplant surgery, the central nervous system, and the administration of radiation therapy and chemotherapeutic agents.

Histidine has been administered to both animals and humans in dozens of studies for numerous conditions. The metabolic pathway, pharmacokinetics, and safety of histidine are all well known. Preclinical studies by CYTOS have demonstrated that histidine is very effective in preventing cellular (tissue) damage in a wide variety of ischemic and inflammatory conditions.

Histidine protects cells by the following:

Scavenging reactive oxygen species called singlet oxygen and the hydroxyl radical;
Inhibiting lipid peroxidation;
Preserving glutathione levels;
Protecting the nitric oxide (NO) cycle; and
Reacting with and inactivating inflammatory mediators such as cytokines and prostaglandins.
Histidine is able to protect cells (i.e., tissue) during inflammation by using one or more of these biochemical processes simultaneously.
http://www.geocities.com/nutriflip/Nutrients/Histidine.html

I remember posting a while back on the topic of irradiation, that of all the nutrients for protection of this, NASA used histidine most commonly.

I've been doing my diet since Feb. 03, yet both urine and serum amino tests, one done 4/03 and the latter done 7/03, still indicate I fell at the bottom of the ref. range.

Richard

Richard - how very fortunate and timely to have had that conversation with Dr. Wise. I hope you remain in contact with him especially for the liver cleanse.

My functional medicine MD follows along the lines you outlined from Dr. Wise's observations.... I've done and continue to do the Great Smokies Testing...and all of the supportive supplements you mentioned. I've also done a liver cleanse based on the Metagenics supportive formula and will probably be doing it again. This is not a thing that normalizes quickly - I'm finding out. Perhaps again, it is the biochemical individuality issue we frequently mention.

However, I'm delighted to hear from another knowledgeable source that answers can lie in both liver detox and methylation. I'm sure that if I had had another few years to tinker, I could have resolved the a/f without ablation.... but that's history now and I'm still in need of making sure other systems are functioning optimally.

This is good information. Thanks.

Jackie

Richard - in one or two of these posts, you mentioned elevated levels of copper and zinc.... be sure to read some of the articles written in Life Extension. In fact, the current month is commenting again on the need to reduce the levels....

check this:
http://www.google.com/search?hl=en&ie=UTF-8&oe=UTF-8&q=lef+copper++zinc+alzheimer%27s&btnG=Google+search

Jackie

Jackie,

Thank you so much for those links. Strangely, carnosine is derived from histadine and alanine, both of which I was really low in hair analysis, but low in serum on alanine, and marginally low in histadine. I really wasn't exactly sure why I was elevated in both copper and zinc, in hair, but the levels of the aminos could explain why. Being that I was in the red zone on my hair analysis, could tell me that I'm having a problem in the brain area with these minerals. I went to www.jomarlabs.com to see if they sell carnosine and they do, but here's what they had to say about it.

L-Carnosine is an endogenous (naturally occurring) di-peptide that is composed of one molecule each of Histidine and Alanine. This product is said to be a potent antioxidant; it accelerates wound healing and promotes the chelation of heavy metals. Since it also functions as a buffer of lactic acid in muscle tissue, L-Carnosine is said to increase physical performance during strenuous activities (e.g. weight lifting, sprinting, etc).

According to a study done by the American Physiological Society, L-Carnosine helps the heart muscle to contract more efficiently by regulating intracellular calcium. L-Carnosine is also known as an anti-aging agent. It can prevent protein oxidation and the cross-linking of collagen and other proteins (which cause skin wrinkling). L-Carnosine concentrates in the lens of the eye where it is reported to work to prevent cataracts. Existing gastric ulcer formations are said to be reduced and the creation of new ulcers are said to be prevented with the use of L-Carnosine.

Soooo, I'm gonna get me some of that stuff.
Thank you, Jackie!!!
Richard

By the way, I found it rather coincidental and profound, to speak with Dr. Wise, as well, and find that he felt methylation was of the upmost importance. One of those things that makes you want to say Hmmmmm??!!

Jackie,

Look at this picture of the catabolism of sulfur containing aminos. Serine is needed to convert homocysteine to cysteine. I was pretty low in serine, so I'm still confounded, as to why I didn't have elevated homocysteine. I'm starting to wonder if the tests were correct, yet I had two.

http://oregonstate.edu/instruct/bb450/winter2002/ch21/fi21p11.htm

Richard

Richard

I did a quick run down and tested myself. I scored 3 on undermethylation (sparse hair, body fat dist, long fingers), 18 on over methylation and 1 in pyroluria (salivery flow - normal)

Interesting that RA sufferers are often low in histamine too. Its probably worth noting that I never react to midge bites which bring everyone else up in big angry red lumps. I get a tiny little red pin prick that does not raise and disappears in about 5 minutes - low histamine?

What I am going to try is some histadine. Next time I'm in the big city I am going to get some. Hopefully it will bring my libido back - I look on that as my total health mark.

Here is a bit about pyroluria

http://www.diagnose-me.com/cond/C372380.html

Pyroluria

Often such people have pale skin that easily burns, eyes that are sensitive to light, white flecks/marks on their nails, and stretch marks on their skin. They tire easily, are anemic, have poor dream recall, prefer not to eat breakfast, notice upper abdominal pain when stressed, and experience a "stitch" in their side if they run. They have a tendency to become loners as they age. Mental symptoms are aggravated when undergoing stress. In fact, pyroluria flares up when the individual is undergoing prolonged stress, such as during a chronic and debilitating illness.

Pyroluria may occur along with other imbalances as seen in some subtypes of schizophrenia such as histapenia (low histamine), histadelia (high histamine), high copper levels or cerebral allergies. It is the primary imbalance for 20% of schizophrenics.

Alcohol use is one way for pyrolurics to shut off their anxiety, feel more sociable, de-stress, and experience a short time when they feel more normal. Without a knowledge of this chemical imbalance, those who try to quit alcohol use must face coexisting with their symptoms. If additional antianxiety support is needed, GABA, tryptophan, chromium and inositol should be considered.

Fran

This is an interesting study about histamine and its effects on G proteins, acid secretion and the heart.

www.duc.auburn.edu/~deruija/hist_intro.pdf

Richard

I hope I don't wear you all out on methylation, but here a bit of interesting information. Just more proof of why I was high intracellularly in folate, but low in B12. It was indeed trapped, as was my methylation process. As you'll read further down, because my folate was trapped, my choline, which should have been making acetylcholine, was possibly being used as a methyl donor.

5,10-Methylene tetrahydrofolate (TH4) is required for the synthesis of nucleic acids, while 5-methyl TH4 is required for the formation of methionine from homocysteine by the vitamin B12-dependent enzyme, methionine synthase. Methionine, in the form of S-adenosylmethionine, is required for many biological methylation reactions, including the methylation of DNA. Vitamin B12 deficiency traps folate in a form that is unusable by the body for DNA synthesis and results in a reduced capacity for DNA methylation.

At this link, there is a diagram of B12 and Nucleic Acid metabolism.
http://lpi.oregonstate.edu/infocenter/vitamins/vitaminB12/figure9_2.html

A recent study of 21 men and women fed diets that varied in folate and choline content indicated that choline is used as a methyl group donor when folate intake is low, and that the de novo synthesis of phosphatidylcholine is not sufficient to maintain adequate choline nutritional status when dietary folate and choline intakes are low (5).

http://lpi.oregonstate.edu/infocenter/othernuts/choline/

Here's the link to a lot of studies on methylation. I haven't begun to read much, as it is late, but thought I'd share.

http://search.oregonstate.edu/web/?query=methylation&btnG.x=11&btnG.y=11

Richard

Hans,

In case you read this, I wanted to let you know that I took 2 capsules of the following, and went out of rhythm within 15

minutes.

2 caps =
200mg phosphatidyl serine
200mg choline from choline bitartrate
100mg inositol
Other ingred. rice flour, mg. stearate, and silica Mfg by NOW Foods

My daily multi has 40 mg of the same choline and 24 mg of inositol in 2 caps, of which is all I take of these particular nutrients daily, but the above amt. could have put me over the edge. I don't know much about the serine, other than I was fairly low on my amino testings. Either the problem is the methylation process of these particular nutrients, or the choline/inositol themselves. I just can't believe that they could have affected me that quickly, unless my liver enzymes in that area are depressed or nonexistant. I had, had nothing else to eat since breakfast, nor had I taken any other vitamins with them. Do you believe, in your opinion, that choline could have affected my heart that quickly?

Richard

Merry Christmas Eve to All,

I hope all of you enjoy your holidays and stay in NSR.

In light of what happened yesterday, when taking the above mentioned supplement, it put me on a search for what might have been the cause. The only thing different that I did was take phosphatidyl serine (PS). I want to add, that my wife also took the same supplement and dosage, and had a reaction, as well. She was extremely hyper and edgy and her blood pressure and pulse increased to much higher levels. Her systolic and diastolic readings were erratic. It took longer to affect her than it did me, but remained with her for a longer period. I converted in about 1.5 hrs. by taking an extra 50mg of flecainide and 12.5mg of Toprol. I used the latter because my pulse was fast. We won't be taking that supplement any longer.

Anyway, while searching I found this very important study on homocysteine and methylation. Homocysteine is a potent neurotoxin and induces Ca influx through the N-methyl-d-aspartate channel which stimulates Glu toxicity. Measurement of PS is indicative of cell death, apoptosis. I don't know how this plays into why I had a reaction to PS. Homocysteine (HC) reduces cellular levels of s-adenosyl-methione (SAM) and treatment with SAM reduced apoptosis by 50%. HC is usually controlled by remethylation back to methionine and is dependent on B12 and folic acid, but folic acid is dependent on adequate levels of B12. HC neurotoxicity is due in part to DNA damage and the DNA repair enzymes undergo a 2-fold increase in activity when subjected to HC and the resultant increase depletes neuronal energy reserves.
http://www.uml.edu/Dept/Biology/tshea/JNR.pdf

Here's a link to the possible explanation of my PS problem.

Phosphatidyl Serine is an important part of all nerve cell membranes and enables the release of the neurotransmitters acetylcholine and dopamine. It increases the number of neurotransmitter receptors to youthful levels, and improves the binding of glutamate and glycine to the receptors, resulting in greater signal intensity, speed, and quality of neural transmission. Phosphatidyl Serine plays a key role in nerve cell communication between synapses, and reverses loss of membrane fluidity associated with age related mental decline. A clinical study with the elderly showed increased memory in just four weeks and cognitive improvement equal to twelve years of reversed brain aging within just twelve weeks after using 300 mg of PS per day. Phosphatidyl Serine also has an anti-cortisol stress hormone effect. Phosphatidyl serine improves glycine and glutamate nerve binding.
I don't think I want improvement of nerve bindings by Glu.

http://www.lifespandynamics.com/403_5.htm

Hopefully we haven't experienced neuronal death, and if so, how can we rebuild the cells. Keeping availability of SAM and N-acetyl-cysteine should help, coupled with higher levels of B12 and folate, to at least preserve what we have.

Methylation is very important to DNA rebuilding, so maybe taking higher doses of these important nutrients, could have reversal effects. That's my next step of study.

Richard

Just a shot in the dark Richard but was the Phosohatidyl serine from a soy base product? I ask only because that's what the PS that I was taking was from and the ND told me to avoid soy products. I didn't notice any reactions while I was taking it but then again I am in mild afib about 60% of the time so it's hard to get a handle on any triggers. I am no longer taking it.

Peace and Silent Nights

Adrian

Richard,

That is a very interesting although somewhat uncomfortable observation - what we all endure in the name of research :~)

The fact that it affected you wife as well certainly points to a pretty powerful reaction. I wonder if the product could have been contaminated with something. Adrian's idea about a connection to soy certainly makes sense especially if you and your wife are allergic to soy products. I still find it hard to believe that such a relatively small amount of supplement could have such a strong effect. You mentioned that you had had nothing to eat since breakfast. How long did you actually go without food? Could it have been partly a hypoglycemic reaction?

I find this reaction most intriguing and hope we can figure out the mechanism somehow. Anyway it is good to hear that it was a short episode. I hope it will be your last in 2003.

Merry Christmas and all the best for 2004

Hans

Hans and Adrian,

Although the product says nothing about not containing soy, neither my wife nor I have ever had any reactions to soy based products, even though we avoid them. Both of us, on the other hand, do have reactions to MSG, mine being arrhythmia and hers being the edgy overstimulated feeling. My wife had such a reaction to the supplement, she has thought about having it tested, because she felt the same way as you do, about the possibility of it being contaminated. It was a supplement that was prescribed and purchased from a naturopath here, in Tacoma, not by Dr. Gersten. I do not believe it was a hypoglycemic reaction, as I had a late breakfast, around 11 am, and then ate around 4:30pm. That's not unusual for me. The fact that my wife reacted to the supplement makes me believe it had something to do with free glutamate. The product does state that it does NOT contain yeast, wheat, gluten, corn, milk, sugar, salt, preservatives, or color. Strangely, my wife takes supplements all the time, and has never had this reaction, and as Fran has said, most supplements contain free glutamate. So either the product is contaminated or its the phos. serine, because that's the only thing that's not in any of my other supplements.

Thank you for your responses,

Hmmmmm???
Richard

Merry Christmas Eve to All,

I hope all of you enjoy your holidays and stay in NSR.

In light of what happened yesterday, when taking the above mentioned supplement, it put me on a search for what might have been the cause. The only thing different that I did was take phosphatidyl serine (PS). I want to add, that my wife also took the same supplement and dosage, and had a reaction, as well. She was extremely hyper and edgy and her blood pressure and pulse increased to much higher levels. Her systolic and diastolic readings were erratic. It took longer to affect her than it did me, but remained with her for a longer period. I converted in about 1.5 hrs. by taking an extra 50mg of flecainide and 12.5mg of Toprol. I used the latter because my pulse was fast. We won't be taking that supplement any longer.

Anyway, while searching I found this very important study on homocysteine and methylation. Homocysteine is a potent neurotoxin and induces Ca influx through the N-methyl-d-aspartate channel which stimulates Glu toxicity. Measurement of PS is indicative of cell death, apoptosis. I don't know how this plays into why I had a reaction to PS. Homocysteine (HC) reduces cellular levels of s-adenosyl-methione (SAM) and treatment with SAM reduced apoptosis by 50%. HC is usually controlled by remethylation back to methionine and is dependent on B12 and folic acid, but folic acid is dependent on adequate levels of B12. HC neurotoxicity is due in part to DNA damage and the DNA repair enzymes undergo a 2-fold increase in activity when subjected to HC and the resultant increase depletes neuronal energy reserves.
http://www.uml.edu/Dept/Biology/tshea/JNR.pdf

Here's a link to the possible explanation of my PS problem.

Phosphatidyl Serine is an important part of all nerve cell membranes and enables the release of the neurotransmitters acetylcholine and dopamine. It increases the number of neurotransmitter receptors to youthful levels, and improves the binding of glutamate and glycine to the receptors, resulting in greater signal intensity, speed, and quality of neural transmission. Phosphatidyl Serine plays a key role in nerve cell communication between synapses, and reverses loss of membrane fluidity associated with age related mental decline. A clinical study with the elderly showed increased memory in just four weeks and cognitive improvement equal to twelve years of reversed brain aging within just twelve weeks after using 300 mg of PS per day. Phosphatidyl Serine also has an anti-cortisol stress hormone effect. Phosphatidyl serine improves glycine and glutamate nerve binding.
I don't think I want improvement of nerve bindings by Glu.

http://www.lifespandynamics.com/403_5.htm

Hopefully we haven't experienced neuronal death, and if so, how can we rebuild the cells. Keeping availability of SAM and N-acetyl-cysteine should help, coupled with higher levels of B12 and folate, to at least preserve what we have. Methylation is very important to DNA rebuilding, so maybe taking higher doses of these important nutrients, could have reversal effects. That's my next step of study.

Richard

Just a shot in the dark Richard but was the Phosohatidyl serine from a soy base product? I ask only because that's what the PS that I was taking was from and the ND told me to avoid soy products. I didn't notice any reactions while I was taking it but then again I am in mild afib about 60% of the time so it's hard to get a handle on any triggers. I am no longer taking it.

Peace and Silent Nights

Adrian

Hello All,

Nothing much new, as I haven't had much time to study, but did notify www.consumerlab.com, a testing lab for vitamins that Jackie recommended and I became a member of, to let them know of the effects of the vitamin I took. Dr. Cooperman responded back, and thought the likely culprit was choline, because it has been known to cause vomiting and profuse sweating, and if it could do this, then it could very well affect the heart. I'm still not sure what to think.

I also wanted to re-post this link about the different pathways of toxins in the liver, that I posted on the BB a little while ago, for ease of future reference.

http://www.garynull.com/Documents/Continuum/LiverOfTheMatter.htm

I've got to get through the holidays before I can get back into this important issue.

Richard

Richard

What are the ingredients on the supplement bottle? Include the inactive ingredients. I might be able to help with determining if they include free glutamate. But that reaction is my reaction to most supplements including Solgar's Mg citrate.

Fran

Fran,

Besides the nutrient content as stated above, the other ingredients are: rice flour, Mg. stearate (vegetable source), and silica.

It says it contains NO yeast, wheat, gluten, corn, milk, sugar, salt, preservatives or color.

Thank you Fran, for responding to anything you may see in this.

Richard

Richard - I have just read and not studied these recent posts of yours, but the one statement .... Homocysteine is a potent neurotoxin and induces Ca influx through the N-methyl-d-aspartate channel which stimulates Glu toxicity....jumps out at me... Anything that increases the Ca in cells is highly likely to stimulate afib....based on the other things I've read.....so for those with elevated HCY, it could be an important influence.

Again, a faulty methylation process could be at the base of it all. This is very complicated and most likely since no one is doing studies on afib and the link between faulty methylation, we won't find any documentation but it seems to be a reasonable assumption to me.

I know that once I stepped up the amounts of trimethyglycine,and other nutrients as recommended in Methyl Magic and along with the other stepped up supplements of mag glycinate and taurine, the breakthrough arrhythmia began to subside until it was on hold with the current dose of flecainide....so I have to feel I was on the right track. Of course, the experiement was stopped since my ablation date arrived, but had I been able to continue, I definitely feel I could have successfully eliminated the use of flecainide. We'll never know.

Happy New Year - and Peaceful Hearts in 2004

Jackie

On the topic of the reaction to P/S, I'm wondering if it was the gelatin in the capsule..... remember when we had that discussion about capsules and free glutamate? Perhaps this particular manufacturer's capsule is the culprit. How would one ever know? I take P/S in a gel capsule and have had no reactions at all.... but that doesn't say anything, really.

I'll get back to the methylation issue and contribute once the holidays are over. I'm helping critique a book a friend is writing and it is taking up most of my reading time... once done with that, my eyes and brain aren't ready for thinking about methylation. ;)

Jackie,

I agree, that the homocysteine study is very important, especially as it pertains to glutamate and calcium. Something I've been pondering, is that we know the liver stores B12; up to six years worth. Here are a few facts about myself, that I have re-hashed, before I go on.

1) Normal B12 in vitamin analysis.
2) Somewhat high methylmalonic acid which indicates B12 deficiency.
3) High formiminoglutamatic acid which indicates low folate and B12.
4) Very high folate in vitamin analysis.
5) Niacinamide normal in vitamin analysis and gives me headaches, if I take, because it has to be methylated, and apparently I don't have enough methyl donors to donate.
6) Low B12 traps folate inside cell.
7) Low in methionine and its breakdown sulfur aminos, cysteine and taurine.
8) Taurine has to be sulfated by the molybdenum dependent sulfite oxidase enzyme.
9) Low in molybdenum.

There should have been no way that I was low in B12, given the amount of proteins I have been eating, esp. red meat, and indeed, the vit. analysis showed normal levels. I do know that the body methylates B12, just as it does niacin, therefore I can only deduce that my B12 isn't being methylated, as well, rendering it trapped just as folate is.

Now how would one know if on some days they have higher homocysteine levels than other days. Maybe the building up to AF, that so many speak of, is really all about how much methylation process is going on, or not going on, at any one time, depending on their methylated nutrient status. I should have had higher homocysteine levels, and maybe I did, right before I went into AF/flutter. It's never been measured at these times. In your case, Jackie, maybe you HCY levels went up even further, right before an episode. This doesn't explain Fran's episode of a Burger King hamburger, stress, and the AF she experienced right after, however.

I'm just thinking out loud again, as it helps me sort some of this out in my mind.

And STILL thinking and searching!!!
Richard

Here's some important studies:

Protective effects of a vitamin B12 analogue, methylcobalamin, against glutamate cytotoxicity in cultured cortical neurons
Akaike A Tamura Y Sato Y Yokota T, **Eur J Pharmacol** *(1993 Sep 7) 241(1):1-6*

The effects of methylcobalamin, a vitamin B12 analogue, on glutamate-induced neurotoxicity were examined using cultured rat cortical neurons. Cell viability was markedly reduced by a brief exposure to glutamate followed by incubation with glutamate-free medium for 1 h. Glutamate cytotoxicity was prevented when the cultures were maintained in methylcobalamin-containing medium. Glutamate cytotoxicity was also prevented by chronic exposure to S-adenosylmethionine, which is formed in the metabolic pathway of methylcobalamin. Chronic exposure to

methylcobalamin and S- adenosylmethionine also inhibited the cytotoxicity induced by methyl-D-aspartate or sodium nitroprusside that releases nitric oxide. In cultures maintained in a standard medium, glutamate cytotoxicity was not affected by adding methylcobalamin to the glutamate-containing medium. In contrast, acute exposure to MK-801, a NMDA receptor antagonist, prevented glutamate cytotoxicity. These results indicate that chronic exposure to methylcobalamin protects cortical neurons against NMDA receptor-mediated glutamate cytotoxicity.

Methylcobalamin and Diabetic Neuropathy

Clinical usefulness of intrathecal injection of methylcobalamin in patients with diabetic neuropathy
Ide H Fujiya S Asanuma Y Tsuji M Sakai H Agishi Y, **Clin Ther** *(1987) 9(2):183-92*

Seven men and four women with symptomatic diabetic neuropathy were treated with methylcobalamin (2,500 micrograms in 10 ml of saline) injected intrathecally. Treatment was begun when patients had good metabolic control, as determined by measurements of plasma glucose and hemoglobin, and was repeated several times with a one-month interval between injections. Three patients were re-treated one year after the last intrathecal injection. Symptoms in the legs, such as paresthesia, burning pains, and heaviness, dramatically improved. The effect appeared within a few hours to one week and lasted from several months to four years. The mean peroneal motor-nerve conduction velocity did not change significantly. The mean (+/- SD) concentration of methylcobalamin in spinal fluid was 114 +/- 32 pg/ml before intrathecal injection (n = 5) and 4,752 +/- 2,504 pg/ml one month after intrathecal methylcobalamin treatment (n = 11). Methylcobalamin caused no side effects with respect to subjective symptoms or characteristics of spinal fluid. These findings suggest that a high concentration of methylcobalamin in spinal fluid is highly effective and safe for treating the symptoms of diabetic neuropathy.

Nerve Regeneration with Methylcobalamin

Ultra-high dose methylcobalamin promotes nerve regeneration in experimental acrylamide neuropathy.
Watanabe T Kaji R Oka N Bara W Kimura J, **J Neurol Sci** *(1994 Apr) 122(2):140-3*

Despite intensive searches for therapeutic agents, few substances have been convincingly shown to enhance nerve regeneration in patients with peripheral neuropathies. Recent biochemical evidence suggests that an ultra-high dose of methylcobalamin (methyl-B12) may up-regulate gene transcription and thereby protein synthesis. We examined the effects of ultra-high dose of methyl-B12 on the rate of nerve regeneration in rats with acrylamide neuropathy, using the amplitudes of compound muscle action potentials (CMAPs) after tibial nerve stimulation as an index of the number of regenerating motor fibers. After intoxication with acrylamide, all the rats showed equally decreased CMAP amplitudes. The animals were then divided into 3 groups; rats treated with ultra-high (500 micrograms/kg body weight, intraperitoneally) and low (50 micrograms/kg) doses of methyl- B12, and saline-treated control rats. Those treated with ultra-high dose showed significantly faster CMAP recovery than saline-treated control rats, whereas the low-dose group showed no difference from the control. Morphometric analysis revealed a similar difference in fiber density between these groups. Ultra-high doses of methyl-B12 may be of clinical use for patients with peripheral neuropathies.

Methylcobalamin, Bell's Palsy

Methylcobalamin treatment of Bell's Palsy
Jalaludin MA, **Methods Find Exp Clin Pharmacol** *(1995 Oct) 17(8):539-44*

Bell's palsy patients were assigned into three treatment groups: steroid (group 1), methylcobalamin (group 2) and methylcobalamin + steroid (group 3). Comparison between the three groups was based on the number of days needed to attain full recovery, facial nerve scores, and improvement of concomitant symptoms. The time required for complete recovery of facial nerve function was significantly shorter in the methylcobalamin and methylcobalamin plus steroid groups than in the steroid group. The facial nerve score after 1-3 weeks of treatment was significantly more severe ($p < 0.001$) in the steroid group compared to the methylcobalamin and methylcobalamin plus steroid groups. The improvement of concomitant symptoms was better in the methylcobalamin treated groups than the group treated with steroid alone.

Nerve Terminal Regeneration

Methylcobalamin (methyl-B12) promotes regeneration of motor nerve terminals degenerating in anterior gracile muscle of gracile axonal dystrophy (GAD) mutant mouse.
Yamazaki K Oda K Endo C Kikuchi T Wakabayashi T, **Neurosci Lett** *(1994 Mar 28) 170(1):195-7*

We examined the effects of methylcobalamin (methyl-B12, mecobalamin) on degeneration of motor nerve terminals in the anterior gracile muscle of gracile axonal dystrophy (GAD) mutant mice. GAD mice received orally methyl-B12 (1 mg/kg body wt/day) from the 40th day after birth for 25 days. In the distal endplate zone of the muscle, although most terminals were degenerated in both the untreated and methyl-B12-treated GAD mice, sprouts were more frequently observed in the latter. In the proximal endplate zone, where few degenerated terminals were seen in both groups of the mice, the perimeter of the terminals was increased and the area of the terminals was decreased significantly in the methyl-B12-treated GAD mice. These findings indicate that methyl-B12 promotes regeneration of degenerating nerve terminals in GAD mice.

Fighting Neurotoxicity

Protective effects of methylcobalamin, a vitamin B12 analogue, against glutamate-induced neurotoxicity in retinal cell culture.
Kikuchi M Kashii S Honda Y Tamura Y Kaneda K Akaike, **Invest Ophthalmol Vis Sci** *(1997 Apr) 38(5):848-54*

Purpose: To examine the effects of methylcobalamin on glutamate- induced neurotoxicity in the cultured retinal neurons. Methods: Primary cultures obtained from the fetal rat retina (gestation days 16 to 19) were used for the experiment. The neurotoxicity was assessed quantitatively using the trypan blue exclusion method. Results: Glutamate neurotoxicity was prevented by chronic exposure to methylcobalamin and S-adenosylmethionine (SAMe), which is formed in the metabolic pathway of methylcobalamin. Chronic exposure to methylcobalamin and SAMe also inhibited the neurotoxicity induced by sodium nitroprusside that release nitric oxide. By contrast, acute exposure to methylcobalamin did not protect retinal neurons against glutamate neurotoxicity. Conclusions: Chronic administration of methylcobalamin protects cultured retinal neurons against N-methyl-D- aspartate-receptor-mediated glutamate neurotoxicity, probably by altering the membrane properties through SAMe-mediated methylation.

Methyl Donor Effects

Effect of cobalamin derivatives on in vitro enzymatic DNA methylation: methylcobalamin can act as a methyl donor.
Leszkowicz A Keith G Dirheimer G, **Biochemistry** *(1991 Aug 13) 30(32):8045-51*

Methylcytosine synthesis in DNA involves the transfer of methyl groups from S-adenosylmethionine to the 5'-position of cytosine through the action of DNA (cytosine-5)-methyltransferase. The rate of this reaction has been found to be enhanced by cobalt ions. We therefore analyzed the influence of vitamin B12 and related compounds containing cobalt on DNA methylation. Vitamin B12, methylcobalamin, and coenzyme B12 (methylcobalamin) were found to enhance significantly the de novo DNA methylation in the presence of S-adenosylmethionine for concentrations up to 1 microM, but at higher concentrations these compounds were found to inhibit DNA methylation. Methylcobalamin behaves as a competitive inhibitor of the enzymatic methylation reaction (Ki = 15 microM), the Km for S-adenosylmethionine being 8 microM. In addition, the use of radioactive methylcobalamin shows that it can be used as a methyl donor in the de novo and maintenance DNA methylation reactions. Thus, two DNA methylation pathways could exist: one involving methylation from S-adenosylmethionine and a second one involving methylation from methylcobalamin.

http://www.nutritionaltest.com/methyl.html

Richard

A few more tidbits from my meanderings on the net.

I have found another possible correlation to my B12 problem. Not only could the problem be a lack of methylation, but lithium is know to transport B12, of which I'm at the bottom of the scale on my hair analysis. Ref range .007-.023/ result .004, which put me at the lowest part of the red zone. Here's a take from GSDL, along with some other interesting reading on minerals and hair analysis.

Lithium
Hair appears to be a reliable indicator of lithium status, and hair lithium is often low in violent offenders. A direct association was observed between hair lithium and cobalt concentrations, suggesting a role for lithium in the transport and distribution of vitamin B12. Hair lithium levels increase in response to supplementation, but lithium is a marker only in some subjects.69-71 It may be that certain behavioral defects, depression, and learning disabilities are caused, or aggravated, by low nutritional lithium intake coupled with marginal deficiencies of B12 and folic acid, whose transport is also modulated by lithium. (I was low, but in ref range on cobalt and NO, I'm not a violent offender, at least not yet)
http://gsdl.com/assessments/elemental/appguide/index4.html

Scientists investigating the ability of folate, vitamin B12 and pyridoxal-5'-phosphate (P5P) to lower the body's levels of homocysteine - a potential risk factor in cardiovascular disease - discovered an interesting fact: rather than lowering homocysteine across the board, each of these vitamins interacted with specific types of homocysteine. Consequently, folate and vitamin B12 reduced fasting hyperhomocystinemia, whereas P5P lowered homocysteine only after the administration of high doses of methionine, the amino acid from which homocysteine is metabolized.

P5P's specialized ability could have implications for those consuming diets high in methionine, an essential amino acid found in meats (especially red meats) and dairy products. That P5P can lower methionine-induced elevated homocysteine levels is an important argument to support its protective role against myocardial infarctions (heart attacks), arrhythmias, and other cardiovascular diseases. Furthermore, P5P deficiency has been linked with hypertension and pancreatic and cervical cancer.
http://www.vrp.com/articles/353.asp

On the basis of the collective data gathered by the Rotterdam Study, it was concluded that vascular risk factors and indicators of vascular disease, particularly in elderly subjects, have an established association with AD.15,16 The risk factors for AD reported thus far in the Rotterdam Study, many of which have been confirmed by other independent studies, include the following: (1) diabetes mellitus,17 (2) thrombotic episodes,18 (3) high fibrinogen concentrations,19 (4) high serum homocysteine,20 (5) atrial fibrillation,16,21 (6) smoking,22,23 (7) alcoholism,24 (8) low level of education,25 and (9) atherosclerosis26 (Table). All these conditions have a vascular involvement and are known to reduce cerebral perfusion.27
http://stroke.ahajournals.org/cgi/content/full/33/4/1152

Here's an interesting article on **sulfur and the sulfur aminos**.

In the United States, low-sulfur soils are found in the Pacific Northwest (this is where I live) and the Great Lakes region.1 Glutathione is a source of dietary sulfur, with fruits and vegetables contributing over 50 percent of dietary glutathione, while meats contribute less than 25 percent.18
http://www.thorne.com/altmedrev/.fulltext/7/1/22.html

Here's a good link that shows and explains the **metabolism of folate and B12**.
http://www.hscbklyn.edu/SUNY/Biochem/ALCOHOL/alcohol_folate_bkgd.html

In 1975, several studies were published on SAM-e for liver disease, cirrhosis and chronic hepatitis. A study by Dr. Labo was conducted with over 50 patients who had liver disease and cirrhosis. The patients who were treated with SAM-e had significant improvements in liver function. In a study published in 1975, Dr. Cantoni treated 70 patients who had chronic hepatitis and cirrhosis. At the end of the study the patients treated with SAM-e had virtually all of their liver proteins restored. A study also published in 1975 by Dr. Ideo with 15 patients found the production of albumin returned to normal in SAM-e treated patients. Studies done in 1989 and in 1992 found SAM-e as a positive solution for the treatment of liver disease, hepatitis and cirrhosis.
http://www.bettersam-e.com/liver-disease.html

Richard

Here's a bit on the **advantages of methylcobalamin**.

Evidence indicates methylco-balamin is utilized more efficiently than cyanocobalamin to increase levels of one of the coenzyme forms of vitamin B12. Experiments have demonstrated similar absorption of methylcobalamin following oral administration. The quantity of cobalamin detected following a small oral dose of methylcobalamin is similar to the amount following administration of cyanocobalamin; but significantly more cobalamin accumulates in liver tissue following administration of methylcobalamin. Human urinary excretion of methylcobalamin is about one-third that of a similar dose of cyanocobalamin, indicating substantially greater tissue retention.1

Heart Rate Variability: Heart rate variability is a means of detecting the relative activity and balance of the sympathetic/parasympathetic nervous systems. Methylcobalamin produces improvements in several components of heart rate variability, suggesting a balancing effect on the nervous system.10

Dosage

The dosage for clinical effect is 1500-6000 mcg per day. No significant therapeutic advantage appears to occur from dosages exceeding this maximum dose. Methylcobalamin has been administered orally, intramuscularly, and intravenously; however, positive clinical results have been reported irrespective of the method of administration. It is not clear whether any therapeutic advantage is gained from the non-oral methods of administration.

http://www.thorne.com/altmedrev/.fulltext/3/6/461.html

Richard

The role of histidine in the anemia of folate deficiency.

Cooperman JM, Lopez R.
Department of Community and Preventive Medicine, New York Medical College, Valhalla, NY 10595, USA.
coopermanjmr@aol.com

The amino acid histidine is metabolized to glutamic acid in mammalian tissue. Formiminoglutamic acid (FIGLU) is an intermediary in this reaction, and tetrahydrofolic acid is the coenzyme that converts it to glutamic acid. A test for folate deficiency concerns the measurement of urinary FIGLU excretion after a histidine load. It was observed that folate-deficient individuals receiving the histidine for the FIGLU test made hematological response that alleviated the anemia associated with this deficiency. This was unusual in that a biochemical test to determine the deficiency results in a beneficial effect for one aspect of the deficiency. The studies reported in this paper give a metabolic explanation for this phenomenon. Urine was collected for 24 hr from 25 folate-deficient subjects, 10 vitamin B(12)-deficient subjects, and 15 normal controls. Urinary excretion of histidine was a mean of 203 mg with a range of 130-360 mg for the folate-deficient subjects; 51.5 mg with a range of 30-76.6 mg for normal subjects; and 60.0 mg with a range of 32.3-93.0 mg for the vitamin B(12)-deficient subjects. All the folate-deficient subjects subsequently made a hematological response to the histidine administered for the FIGLU test. No hematological response was observed in the vitamin B(12)-deficient individuals. When folic acid was given to folate-deficient subjects who received no histidine, urinary histidine levels returned to normal levels rapidly and this was followed by a hematological response. Others have shown that volunteers fed a histidine-free diet developed anemia. In normal subjects, histidine is excreted much more in the urine than other essential amino acids are. Hemoglobin protein contains 10% histidine. Under normal conditions, dietary histidine can supply sufficient histidine to prevent anemia. When the dietary intake is diminished or the urinary excretion is greatly increased, anemia results. It is concluded that folate deficiency causes histidine depletion through increased urinary excretion of this amino acid. Feeding histidine replenishes tissue levels of histidine, resulting in hemoglobin regeneration. Folic acid administration results in return of histidine to normal urinary levels. Thus, a combination of folic acid and histidine would be beneficial for folate deficient individuals.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12486209&dopt=Abstract

My FIGlu test with GSDL indicated very high levels, which indicated a folate deficiency. This study is saying that not only is folate important, but the administration of histidine is, as well, with the latter being a neurotransmitter. My urine levels of histadine were almost at the bottom of ref range (result 290 range 270-1150). The serum test was a bit low, as well (result 8.9 range 7.9-12.1). The FIGlu result was 22.6 with the range being <=9.0. I wonder if this somehow ties into Glu toxicity.

Richard

Fran,

In going back and re-reading all the posts, for refreshment of memory, I found it interesting that over methylators should avoid inositol, and unders should avoid choline. I had the reaction to that supplement, mentioned below, so if I took a single dose of choline, and then one of inositol, would I then have a definitive answer as to which I am? My copper and zinc levels were high, esp. on my hair analysis, so the copper fits the criteria of an over mether, but the zinc does not. I'm beginning to believe I'm this mutant species. Also, it would seem that there's the possiblity that I'm a over mether, because my sulfur aminos were all low, as was my homocysteine, so I'm using it up as fast as I consume, if I'm getting enough in the first place.

Richard
