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In this issue: During Stress, Some Prebiotics Order Up B Vitamins from the Microbiome; SNiPPets: This SNP Relates to Women and Asprin's CVD-Preventive Influence; With Brain Plasticity, Even Personality Can Flex

**During Stress, Some Prebiotics Order Up B Vitamins from the Microbiome**

The experience of stress—whether physical, mental, emotional, or metabolic—can shift the immunometabolic response into a more pro-inflammatory, protective stance. While this may be good in the short run if there truly is a valid threat, over time it can be destructive, and a more moderate response is more adaptive during chronic challenge. A recent animal study has discovered that certain prebiotic oligosaccharides given prior to a stressful experience (exposure to an aggressor) may moderate the immune response to it in an interesting way: cultivating the growth of gut bacteria that upregulate the synthesis of B vitamins that help limit cytokine production and maintain immune tolerance.

Researchers gave animals a combination of galactooligosaccharides (found in dairy foods), polydextrose (a synthetic dietary fiber), and sialyllactose (a breastmilk saccharide also found in cow’s milk). They found that the combination as well as sialyllactose alone were each able to reduce production of the potent pro-inflammatory cytokines TNFα, IL-1β, and IL-6 and immunoreactivity to lipopolysaccharides (the most common source of which is digestion of lipid- and carb-rich junk-type foods) that can trigger immune intolerance and inflammation.

Upon analyzing and genome-sequencing the gut microbiomes of stressed versus non-stressed animals, researchers noted many changes in microbial populations (especially reduced abundance of lactobacilli) and metabolism of amino acids, proteins, and B vitamins. Stressed animals provided the saccharides, however, showed greater abundance of bifidobacteria that produce various forms of B vitamins, and that their levels related to lower circulating levels of IL-6. While these results need to be confirmed in humans, they reveal intriguing links among stress, dietary choices, and health outcomes.
**SNiPpets**

How significant to health are particular single nucleotide polymorphisms, also known as SNPs? SNiPpets is an ongoing exploration of this topic.

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**In Women, These SNPs May Alter Aspirin's CVD Preventive Influence**

Aspirin is widely recognized and commonly prescribed as preventative against some forms of cardiovascular disease (CVD). COMT (catechol-O-methyltransferase) is an extremely crucial enzyme related to neurotransmitter metabolism and methylation function, especially in the nervous system, and integral to vascular regulation of blood flow and the heart’s rhythm in cardiovascular function.

Research focusing on women is increasingly discovering divergence in symptoms, treatment effects, and prevention strategies between women and men, and the study below has found that aspirin may not be indicated for CVD prevention in women as widely as has previously been assumed.

In both men and women, having the major G allele at the rs4680 locus of the gene that codes for COMT shows a protective effect against cardiovascular dysfunction; in women, this protection manifests as reduced risk for myocardial infarction as well as overall total CVD. Yet in one study of women possessing this most common genetic pattern at this genetic location, taking aspirin negated this beneficial effect in them, and these women receiving aspirin showed a higher risk for CVD than those receiving a placebo. Women with this common G variant also showed a lower (and statistically insignificant) increase in CVD risk if they received vitamin E. (Dosages in this study were the following taking over a period of at least 10 years: 100 mg aspirin every other day; 600 IU α-tocopherol every other day.) However, among women having the minor variant G-to-A SNP (single-nucleotide polymorphism) at this rs4680 gene locus, taking aspirin significantly reduced their CVD risk by about 40%, and taking vitamin E reduced it by about 47%.

This study also examined effects of aspirin and vitamin E on genetic variations at a closely-located SNP in the same COMT coding region involving a C-to-G substitution at its rs4818 locus. Among women with the major C allele, aspirin and/or vitamin E showed protective effects. However, in those with one G variant (a CG haplotype at this locus), taking aspirin was slightly less protective and protection from vitamin E was abolished, and in those with two G variants (a GG haplotype here), taking aspirin alone resulted in an almost-tripled increased risk for CVD, while taking vitamin E with or without aspirin resulted in an almost-doubled risk.

While the conclusions drawn from this study should probably be confirmed by further research, women having one or two G alleles at the rs4680 (for which G is the major variant) or rs4818 (at which G is the minor variant) loci of the COMT gene may wish to discuss with a Functional Medicine practitioner personalized lifestyle strategies for long-term cardiovascular function, and especially whether or not aspirin or supplementation with vitamin E is recommendable.
With Brain Plasticity, Even Personality Can Flex

Genes contribute to around 40% of individual personality distinctions, and environmental influences on personality increase with age. It is estimated that 50-67% of Americans are extroverted while 33-50% are more introverted, and it can be amusing and insightful to take a personality test to find out which type you gravitate towards. However, personality traits constitute very complex response patterns to living situations, and behavior can be more flexible than ‘either-or’ naming suggests. Even more revealing is to re-take personality tests over time to see how your responses have adapted and evolved according to what you have learned and experienced from your life.

Genetic components of social orientation relate to how you process, analyze, and act upon information from the environment (based upon what worked well for your ancestors), and these are all responsive to new inputs from your culture, lifestyle habits, social contacts, and exposures to chemicals, nutrients, and events. Here are two examples:

- **Introversion is influenced** by variations in the gene that codes for a critical nerve cell factor (BDNF) that affects memory, learning, and neuron growth, remodeling with new experience, and rejuvenation (plasticity), especially in the hippocampus, which mediates memory and stress response; these variants interact with the mood-related serotonin system.
- Gene mutations for the motivation-related neurotransmitter dopamine, which is linked to extroversion, have been associated with better nutritional status in nomadic men yet poorer status in those living in stable, settled societies.

There is an enormous amount of body activity and brain processing taking place, for example, between watching others’ interactions and deciding what (or what not) to do or say in response. The body’s main functional team members related to cognitive adaptivity include:

1. Nerve cells in the brain, spine, and body, their synapses (communication links among neurons and their networks), and environmental/lifestyle influences on their growth, remodeling, rejuvenation, and death
2. The energy-producing mitochondria fueling nerve cell activity and driving cells’ life-and-death decisions
3. The specialized immune cells that normally protect but in metabolic dysfunction can also damage nerve cells and synapses
4. The body’s glucose and fat processing and storage systems—and how efficient they are at accessing and delivering appropriate energy substrates as needed to maintain optimal cellular function
5. Your senses and perceptions, and how they are translated into chemical messaging that impacts hormones, the stress response, and energy metabolism

Cognitive processing of incoming information can adapt to ‘normal’ as well as suboptimal experiences of living conditions; some traits are more adaptive in stressful circumstances with fewer available resources and opportunities, while others are more functional in neutral or supportive situations. Here are a few examples of cognitive/behavioral aspects of personality:

- Enjoy pursuing risky high rewards versus prefer waiting for less-risky opportunities
- Higher versus lower activation in different brain areas from sensory, social, and emotional inputs
- Responding quickly versus observing and reflecting before acting
- Being more concerned about goals than mistakes versus taking time to study mistakes
- Actively seeking others’ input versus more independent thinking
- Enjoying competition versus preferring collaboration
- Preferring shorter or more varied tasks versus enjoying longer, more complex tasks
- Being better at or more comfortable talking versus listening

Staying flexible between behavioral extremes may aid long-term health and function,
but doing so involves training body, mind, and will to maintain a broader range of potential responses; in other words, brain plasticity. The Human Connectome Project is exploring how individual brains show different patterns of regional activity and inter-regional connectivity. Neuronal plasticity relates to all four major quadrants of function:

- Physical, through how physical activity integrates multiple brain networks; if intense enough, it even helps trigger innate cellular ‘housekeeping’ and stem cell rejuvenation programs
- Metabolic, through how cell-to-cell communications related to diet, immune and hormonal balance, and toxic exposures impact neurons’ ability to make, maintain, and remodel connections
- Cognitive, through how perceptions and thought patterns program which brain networks are built, maintained, or dismantled
- Behavioral, through how emotions are influenced by past experiences yet may be retrained through mind-body practices and reflection

Ways to Help Maintain Brain Plasticity

- Spend time in quiet and/or natural settings, and enjoy new experiences that challenge your mind and body: visit new places, do volunteer work, learn a new language, summer or winter sport, craft, or game, etc.
- Consider journaling to reflect on your day-to-day thought patterns, observations, assumptions, expectations, and what you have learned, and experiment with a few brain plasticity apps that sound interesting to you; possibilities include Active Memory, Peak, Lumosity, or Elevate, though you could also try ones like Headspace or Moodspace.
- Enjoy regular, sweat-inducing, and periodically intense physical activity to encourage formation of new nerve cells and synapses, and consider body-mind practices that help re-set the stress response, like martial arts, yoga, or meditation.
- Increase the overall nutrient density of your diet: total nutrient, fiber, and phytonutrient contents versus calories; you might consider adopting a Mediterranean-style eating approach, and discuss with a Functional Medicine practitioner whether you might benefit from periodically observing a Fasting-Mimicking Diet.
- Enjoy foods and nutrients that mimic the effects of caloric restriction, including green and black teas, berries, fiber, resveratrol, and anthocyanidins, and avoid caloric foods and beverages for at least 3-4 hours before you go to bed.
- Maintain healthy weight and body composition, and especially limit belly fat, yet be sure to get enough omega-3 fatty acids, vitamin D, lutein, and zeaxanthin, and adequate but not excessive amounts of zinc, B-complex vitamins, iron, and magnesium.
- Consider supplementing with nutrients that help support mitochondrial function and membrane integrity, such as coenzyme Q10, N-acetylcysteine, L-carnitine, astaxanthin, and vitamin E, and discuss with a Functional Medicine practitioner the ReCODE protocol for optimizing brain plasticity, developed by Functional Neurologist Dale Bredesen, MD.
- Keep good, regular sleeping habits and a sleeping environment that is quiet, cool, dark, and free from electromagnetic fields, and learn about how medically-supervised metabolic detoxification and/or sauna therapy can reduce your body’s toxic burden.
- Consider being evaluated for these important contributors to brain function: glycemic response, nutritional adequacy, hormonal balance, toxic exposures, and chronic inflammation; you might also consider testing for genetic variants that can impact long-term cognitive function (such as ApoE4), in order to help guide lifestyle approaches.

The wise might encourage us “not to believe everything we think.” Improving how we live and biologically age means challenging assumptions about people (especially ourselves), the world, and the meaning of events. The life of a Citizen Scientist is a kind of ongoing N-of-1 experiment in discovering what is behind appearances and perceptions.