Using organic acids to resolve chief complaints and improve quality of life in chronically ill patients

Part VI

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“An understanding of the nature of stress is fundamental to the rational design of nutrient mixtures to feed patients whose homeostasis has been altered by one or more stressors.”

“All stresses may be presumed to be associated with characteristic modifications in the metabolism of lipids, carbohydrates, amino acids, and micronutrients.”


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Using the Organic Acids Test – Part 6
Dr. Jeff Moss

Considerations for the Catabolic Patient

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Reducing Inflammation

- Reduce inflammation
- Address food allergies

Optimizing Insulin Sensitivity

- Watch carbohydrate/protein ratios
- Fasting glucose

Optimizing GI Function

- History, changes, supplementation of digestive aids

Presented by: Moss Nutrition - Tools for True Healing

Su KP. Biological mechanism of antidepressant effect of omega-3 fatty acids: How does fish oil act as a ‘mind-body interface’? Neurosignals, Vol. 17, pp. 144-152, 2009

"The study population consisted of 182 diabetic patients and 50 body composition- and age-matched controls. We assessed anthropometric and metabolic parameters and mitochondrial function by evaluating mitochondrial oxygen (O₂) consumption, reactive oxygen species (ROS) production, glutathione (GSH) levels, GSH/GSSG ratio, mitochondrial membrane potential, and mitochondrial complex I activity in polymorphonuclear cells from diabetes type 2 patients."
• “The pathogenesis of mitochondrial dysfunction in obesity or diabetes-related disease is multifactorial and includes mitochondrial uncoupling and oxidative damage.”

• “There is considerable evidence that a chronic, low-grade inflammatory response is ongoing in and actually precedes type 2 diabetes and related syndromes, and this inflammation may be due, in part, to the effects of hyperglycemia or other metabolic abnormalities on white blood cells.”

• “The results of this study demonstrate, as expected, an increase in waist circumference and fasting levels of triglycerides, IL-6, TNF-α, homocysteine, US-CRP, HbA1C, glucose, [and] insulin…in type 2 diabetic patients.”

• “Furthermore, we have demonstrated that grade of mitochondrial function impairment in PMNs that takes place during type 2 diabetes.”

• “This effect was evident in the decrease in mitochondrial O₂ consumption, the increase in ROS production, the enhanced TNF-α levels and the decrease in GSH/GSSG ratio related to oxidative stress, the drop in GSH levels, and the diminished mitochondrial membrane potential that we observed in these patients.”
• “Recently, it has been reported that insulin signaling per se also regulates mitochondrial O$_2$ consumption and ATP synthesis rates.”

• “…our study also supports previous observations of mitochondrial dysfunction as a complication of hyperglycemia- and hyperlipidemia-induced ROS production in skeletal muscle from mice.”

• “…the increase in the production of ROS, decrease in GSH levels and GSH/GSSG ratio, and reduction in the mitochondrial membrane potential—all characteristics of diabetes-point toward a dysfunction within the respiratory chain that compromises the functioning of the mitochondrion as a source of energy.”
• “ROS are highly toxic to various sites of the mitochondrial respiratory chain, and inhibition of complex I would seem to be the most likely consequence of the toxicity.”
• “Furthermore, a reduction of complex enzyme activity leads to an accumulation of electrons in the initial part of the transport chain (complex I and coenzyme Q), which facilitates the direct transfer of electrons to molecular \( \text{O}_2 \). This ultimately results in the generation of ROS.”

“These data support the hypothesis that mitochondrial activity, and concretely mitochondrial complex I, may represent an important new pharmacological target for the prevention and treatment of type 2 diabetes.”
**Organic Acids**

**Neurotransmitter Metabolism Markers**

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<td>Body composition, Blood glucose, Insulin sensitivity, Testosterone, Body mass index</td>
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<td>Reduce inflammation</td>
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<td>Fasting glucose, Fasting insulin, Cravings</td>
<td>Metabolic Syndrome (DHF)</td>
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<td>Serum 25 OH vitamin D, Fatigue/symptom index, Zinc status test</td>
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Controversy:

Urinary neurotransmitters vs. urinary neurotransmitter metabolites

- “Accurately determining the central nervous system (CNS) level of neurotransmitters has proven difficult.”
- “This may be in part because neurotransmitters are rapidly formed and degraded in nervous tissue, leaving neurotransmitter concentrations in other tissues largely unrelated to CNS levels.”
- “An exception is the reflection of CNS levels of serotonin by platelet or platelet-rich plasma serotonin concentrations and corresponding associations with serotonin-related pathologies.”
• “**Even when 24-hour collection specimens are used, urinary serotonin is found to vary widely among healthy males under clinically controlled conditions.**”

• “Regarding dopamine, even in the extreme chronic elevation conditions of neuroblastoma, direct urinary dopamine to creatinine ratios were far less revealing than the dopamine catabolite vanilmandelic acid.”

• “In a retrospective study of 5,933 adults and 467 children conducted over a 57-month period, high 24-hour urinary dopamine levels were found in less than 3% of adults, and those instances were associated with overcollection, drug effects, and neural crest tumors.”
• “...studies specifically seeking evidence of dysregulation of dopaminergic activity in the brain have failed to find any relationship with urinary dopamine levels.”
• “Therefore, whatever clinical utility may be claimed for measurement of urinary neurotransmitter concentrations should not be associated with any effects related to actual levels in brain or spinal cord neurons.”

Catecholamines:

Vanilmandelate (VMA)

Homovanillate (HVA)
• “Vanilmandelate, also known as vanilmandelic or vanillyl-mandelic acid (VMA), is the main urinary metabolite of the catecholamines, epinephrine, and norepinephrine.”
• “Homovanillate (HVA) is the main metabolite of dopamine that appears in urine.”
• “In controlled laboratory animal experiments, low urinary levels of VMA and HVA have been associated with low CNS levels of these neurotransmitters.”

• “Low levels of these neurotransmitters are associated with symptoms that include depression, sleep disturbances, anxiety and fatigue.”
• “Because these neurotransmitters are products of the amino acid tyrosine, treatments aimed at improving protein digestion and supplementation with tyrosine may normalize CNS levels.”
• “Elevated levels of VMA and HVA signal an increased rate of synthesis and degradation in normal tissue or abnormal production by tumor tissue.”
• “In absence of such disease processes, increased catecholamine synthesis results from the synergism of pituitary adrenocorticotropic hormone (ACTH) and adrenal cortisol.”

The Stress Response: An Expanded Definition

“The stress response is characterized by a stimulation of the sympathetic nervous system and increased secretion of both epinephrine from the adrenal medulla and glucocorticoids from the adrenal cortex. All these stimuli can be expected to reduce insulin sensitivity.”

The Stress Response: An Expanded Definition

“The Mental stress significantly enhances plasma catecholamines and cortisol concentrations, but does not acutely impair insulin sensitivity. It can, however, be postulated that repeated mental stress may lead to chronic alterations in cortisol and catecholamine concentrations, and to insulin resistance.”


The Stress Response: An Expanded Definition

“For several decades, on the basis of experiments performed on rats, it had been thought that circulating epinephrine acted directly on the pituitary to control the release of ACTH. In this formulation the first step in the adrenal ‘stress response’ was thought to be the liberation of epinephrine; this in turn released ACTH, leading to hypersecretion by the adrenal cortex.”

The Stress Response: An Expanded Definition

“However, subsequent experiments on humans failed to demonstrate any consistent effect of circulating epinephrine on ACTH secretion. Hence, it is no longer believed that epinephrine controls glucocorticoid secretion. Rather, the converse is true; glucocorticoids control epinephrine synthesis, and thereby affect its secretion.”


The Stress Response: An Expanded Definition

“A common mechanism links the secretion of these hormones, even though the adrenal medulla and cortex have different embryologic origins and biochemical properties and very different mechanisms controlling their activities…”

The Stress Response: An Expanded Definition

“This mechanism is made possible by an intra-adrenal portal vascular system, which provides the medulla with uniquely high concentrations of glucocorticoids. These high concentrations are needed to induce the medullary enzyme, phenylethanolamine-N-methyltransferase (PNMT), which controls the synthesis of epinephrine from norepinephrine.”


The Stress Response: An Expanded Definition

“...prolonged chronic stress can enhance epinephrine synthesis and secretion within the adrenal, the brain, and both organs.”

The Stress Response: An Expanded Definition

“Our hypothesis suggests that high levels of glucocorticoids should, if anything, reverse the actions of catecholamines.”


Sympathetic Compensation

“When stress is prolonged the repeated cortisol peaks during occasions of stress cause elevated cortisol secretion, which eventually is followed by a decreased ‘winding down’ of the stress-induced cortisol peaks, followed by a decreased, rigid cortisol secretion, a ‘burn-out,’ where low morning cortisols are a hallmark.”

Sympathetic Compensation

“At this stage sympathetic nervous system activity is increasing, which might be considered as a compensatory phenomenon to maintain homeostasis or allostasis in various somatic systems.”


Sympathetic Compensation

“Patients with posttraumatic stress disorder (PTSD) have decreased cortisol and increased catecholamine secretion.”

Sympathetic Compensation

"Exaggerated norepinephrine responses and heart rate increases, as well as delayed ACTH release, were observed among female fibromyalgia patients compared withagematched female controls. Delayed ACTH release after IL-6 administration in fibromyalgia is consistent with a defect in hypothalamic CRH neuronal function."


The Damaging Power of “Uncontrollable” Stress

Some final points on HVA and VMA

- “Dietary copper deficiency results in higher dopamine and lower norepinephrine levels in rats due to lower activity of dopamine-β-monooxygenase, even though copper deficiency leads to greater production of the enzyme as well as tyrosine monooxygenase.”

- “Interpretation of urinary HVA must take into account dietary influences. A large fraction of ingested quercetin is metabolized by intestinal bacteria to homovanillic acid.”
• “…urinary HVA levels can also be raised by ingestion of bananas, which have concentrations of dopamine relative to other foods.”
• “Both urine VMA and HVA levels were higher in the workers exposed to aluminum, although serum aluminum was not significantly different.”
• “Compared with controls, the exposed workers in this study had significant differences in neurobehavioral tests.”

Thank you!!