The TRIADSM Panel in Cases of Depression and Migraine Headache

The TRIAD℠ Profile in Depression and Migraine Headache: A Case Study

Standard medical treatments for major depressive disorder and migraine headache are only partially effective. Clinical improvement requires correction of underlying metabolic difficulties. This case illustrates the power of multiple markers to focus on key metabolic issues. With a little training any practitioner can learn to see the patterns that emerge from a TRIAD℠ report where organic acids, amino acids and food-specific IgG4 antibodies are reported. Organic acids provide insight into metabolism, cellular energy production, neurotransmitters, phase 1 and phase 2 hepatic detoxification, glutathione status, and xylene exposure. Other markers indicate overgrowth of small intestine bacteria or yeast. The amino acid profile identifies amino acid precursors for neurotransmitters and energy production. It also shows digestion, absorption, long-term depletion, and utilization of amino acids. The IgG4 results identify potentially antigenic foods that may be causing patient symptoms. The following case study of Maggie, who suffered with depression and migraine headaches, demonstrates the progress that can be made when treatment is guided and monitored by functional medical testing.
**Medical History:** Maggie, a 40-year-old female, suffered from severe depression as far back as she could remember. She never used antidepressants but had migraines triggered by exercise around the time of menstruation. She took fish oil and a multi-vitamin. She took Relpax for frequent, severe migraines. Relpax, or elitriptan hydrobromide, is effective for migraines because it is a 5-hydroxytryptamine (serotonin) receptor agonist.

**Lab Results:** In October 2006, a fasting plasma specimen revealed a general pattern of low essential amino acids (Figure 1). In particular, tryptophan and tyrosine were very low. Phenylalanine was low-normal. Vanilmandelate (VMA) and homovanillate (HVA), were low-normal; 5-hydroxyindoleacetate (5-HIA) was low (Figure 1). The other organic acids (not shown) were within normal limits. Maggie showed food antibodies to many foods (Figure 2), although she did not complain of Gi symptoms. The clinician was surprised to find so many food reactions.
Background Biochemistry: VMA is the break-down product of norepinephrine and epinephrine. HVA is the break-down product of dopamine. 5-HIA is the break-down product of serotonin. Norepinephrine, epinephrine, and dopamine are all derived from the essential amino acid phenylalanine, later converted to tyrosine (Figure 3). Serotonin is derived from tryptophan (Figure 4). Due to these biochemical relationships, patients with psycho-emotional disorders should have amino acids and organic acids evaluated as part of a standard work-up. Note that the prognosis of positive response to amino acids is greatly strengthened by examining both the metabolic precursors and products of neurotransmitter pathways. Maggie may have experienced a vicious cycle of maldigestion and malabsorption along with depression leading to poor appetite and little hope for achieving wellness. Daily dosing with free-form amino acids requires no digestive power. Amino acids quickly enter the blood and can enhance production of these catecholamine neurotransmitter compounds.

Moderate to severe antibody production to many foods shows that Maggie may have leaky gut or increased intestinal permeability. This means that large food peptides cross the intestinal membrane into circulation where the immune system recognizes them as foreign, thereby producing antibodies against the peptides. Maggie may have had poor amino acid absorption due to the intestinal permeability which may have also been aggravated by low amino acids. It is possible that Maggie’s reactions to foods created maldigestion and malabsorption, ultimately leading to depletion of amino acids and serotonin with resulting depression and migraines. Treatment for increased intestinal permeability includes nutrients for the enterocytes (glutamine, zinc, pantothenic acid), anti-inflammatory medical food, and eliminating allergens. The massive metabolic task of maintaining tight small intestinal cell-cell junctions requires sustained levels of plasma essential amino acids during overnight fasting when anabolic processes are maximal.

Treatment: The clinician encouraged the dietary changes as directed in the TRIAD rotation diet plan and gave Maggie a basic amino acid blend (Metabolic Maintenance) starting at ¼ teaspoon in the morning and increasing ¼ teaspoon until reaching ½ tsp in the mornings. In addition, Maggie took one teaspoon of glutamine twice daily. She eliminated all foods with IgG4 levels of +, +4, and +5 for 1 month and then rotated them sparingly into her diet. In the first month of treatment with the elimination diet and amino acid therapy, Maggie’s headaches were triggered when some of the reactive foods were reintroduced. Maggie was started on Moducare (Thorne) which is a plant sterol product that is an immune modulator. Thereafter, she avoided the allergic foods but occasionally rotated them into her diet.

Clinical Follow-up: After maintaining this regimen for 90 days, the clinician reported that the patient was feeling more energetic and more positive. Previously, she took Relpax once every week for migraines, but after treatment, Maggie was able to reduce the Relpax to just once per month. For her most recent 3 migraine headaches, she only had to take the Relpax once. The use of free-form essential amino acids, glutamine and Moducare, resulted in less severe and less frequent migraine headaches. Her depression was also much improved. Maggie’s affect had dramatically changed. Initially she had a flat affect because she was in chronic pain and depressed, the clinician explained. In January, Maggie said that running still triggered migraine headaches. Maggie was steadily improving at the time of her last visit at which time the clinician planned a follow-up visit in 3 months. The follow-up testing confirmed Maggie’s metabolic improvement.
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Lab Results: The second TRIAD panel, completed in April 2007, shows some essential amino acids were still low, but improved (Figure 5). Fasting phenylalanine, and especially tryptophan, have risen and are within normal limits. Tyrosine was still low, as well as other amino acids. In the interim, reference ranges changed, so quantitative results cannot be compared directly. Low, normal or high results may be compared relative to their previous quintile positions. Maggie should continue on amino acid supplementation as well as protein digestion and absorption support.

Other organic acids were elevated (Figure 6). Previously she did not show B-vitamin or CoQ10 need. This is commonly seen after supplementing amino acids in an amino-acid deplete individual because amino acids are the precursors of organic acids. Further, the higher rates of protein synthesis, due to additional amino acids, places new strain on cofactor pools such as B vitamins and CoQ10. In the second TRIAD panel, Maggie showed need for CoQ10 and B vitamins to support the new levels of tissue maintenance and neurotransmitter synthesis.

An analogy can be made comparing the body’s metabolism with a car. A car must have gas in order to see if the transmission is working properly. If the car is out of gas, then one can only assume the transmission is in good working order. However, once gas is put in the car and the engine is running, the underlying transmission problem can be identified. When Maggie put more amino acids (fuel) into her energy production and biosynthesis pathways, underlying deficiencies of B vitamins and CoQ10 (or problematic transmission) were discovered. The changes in her laboratory data inform the clinician of Maggie’s need for added support during this transitional rebuilding phase. As the needed cofactors are supplied, the dosing with free form amino acids may be increased to twice daily to enhance progress.

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**Figure 3.** Dopamine, norepinephrine, and epinephrine production. Tyrosine is the amino acid precursor of dopamine (catabolized to homovanillate) and norepinephrine and epinephrine (catabolized to vanilmandelate). Some cofactors in these reactions are shown: tetrahydrobiopterin (BH4), pyridoxine (B6), copper (Cu), vitamin C, and SAMe. Phenylalanine is the essential amino acid precursor to tyrosine, not shown here.

**Figure 4.** Serotonin production. Tryptophan is the amino acid precursor to serotonin which is catabolized to 5-hydroxyindoleacetate. Cofactors shown in these reactions are tetrahydrobiopterin (BH4), pyridoxine (B6), riboflavin (B2) and copper (Cu).
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5-Hydroxyindoleacetate was low before but in the second test, 5-HIA was normal, showing a stimulation of serotonin production and utilization. Normalized serotonin probably explains Maggie's reports of fewer and less severe migraine headaches with less reliance on the serotonin agonist medication. Her previously low vanilmandelate and homovanillate, due to phenylalanine and tyrosine depletion, shifted to normal and even fifth quintile, respectively. The increased bacterial and fungal activity in the gut, indicated by high bacterial and fungal compounds in urine, may be further signs of the generally increased nutrient intake and digestive system activity.

Food antibodies dramatically improved, attesting to a strengthened physical barrier to antigen penetration (Figure 7). After treatment, Maggie showed only mild and moderate IgG4 production to milk, egg, and mustard greens. Although her intestinal permeability appears to have improved, Maggie still needs to be vigilant with her GI health by using probiotics and prebiotics and eliminating or rotating IgG4-positive foods. There may be fluctuations in food antibodies and dysbiosis markers as gut mucosa and microbiota are restored to healthy balance.
### Organic acid results for Maggie in April 2007. Markers for CoQ10 and B vitamins are elevated.
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Conclusions: The TRIAD includes 20 amino acids, 90 food allergens, and 45 organic acids and can be used to evaluate multiple aspects of digestion, absorption, GI membrane permeability, long-term food reactions, small intestinal dysbiosis, energy metabolism, vitamin deficiencies, neurotransmitters and biotransformation. This case illustrates how simple dietary modification and focused nutrient interventions can bring relief from life-long depression and severe migraine headaches. The patient experienced great improvement in symptoms and decreased her reliance on prescription medication because she addressed the underlying causes of her illness, rather than the symptoms alone. While this approach takes time and patience, Maggie has been given tools for her body to achieve long-term normalcy and health. This not only improves Maggie’s health in the short-term but may decrease her risk of developing complex, chronic disease as she ages.

![Figure 7. IgG4 antibodies found in Maggie’s serum in April 2007.](image)

If you have an interesting case you would like to see developed into a case study by the Metametrix Science and Education Department, please contact us at 800.221.4640 or e-mail to memo@metametrix.com.