Neurotransmitters and Amino Acids

Neurological disease (and there are many diseases that are, at their root, neurological, even though the symptoms are systemic) is often associated with deficiencies of monoamine neurotransmitters. The two categories of monoamine neurotransmitters are catecholamines, (including dopamine, norepinephrine, and epinephrine), and serotonin. The drugs used to treat depression, anxiety, Parkinson's disease, and so forth, are not neurotransmitters, since neurotransmitters do not cross the blood-brain barrier. The pharmacological approach to increasing activity of these neurotransmitters involves prescribing uptake inhibitors. As the neurotransmitters are secreted by the presynaptic neuron into the synapse, these drugs prevent the reuptake of the neurotransmitters, thus keeping a higher quantity of them in the synapse between the presynaptic and postsynaptic neurons.

Many studies show that these uptake inhibiting drugs work no better than a placebo for depression in 90% of cases. Why, after sometimes giving short-term anti-depressant effects, are they so ineffective long-term? The problem is that as drugs increase the length of time neurotransmitters spend in the synapse, those neurotransmitters are subject to enzymatic action by the MAO (Monoamine Oxidase) and the COMT (Catechol-O-Methyltransferase) enzymes in the synapse that catabolize those neurotransmitters. So, by keeping larger quantities of neurotransmitters in the synapse, these drugs actually cause the enzymatic degradation of, and ultimately the depletion of, those neurotransmitters.

Since the net effect of reuptake inhibitors is the depletion of neurotransmitters in the brain, astute clinicians have taken a different approach to elevating catecholamines and/or serotonin. These neurotransmitter levels can be increased by providing their amino acid precursors, which do cross the blood-brain barrier, and are subsequently synthesized into the neurotransmitters. Tyrosine is the amino acid precursor to the catecholamines dopamine, norepinephrine, and epinephrine, while tryptophan (or 5-HTP) is the precursor to serotonin.

Supplementation with high doses of tyrosine and/or 5-HTP, as advocated by many researchers and clinicians, would seem to be the effective way to correct depression, anxiety, attention deficit disorder, chronic fatigue, memory loss, and a myriad of other neurologically-based diseases. However, most of these attempts fail miserably. Why the universal failure? Few proponents of amino acid therapy recognize that the same enzyme (aromatic amino acid decarboxylase) is shared by both the catecholamine and the serotonin metabolic pathways. The shared enzyme creates competitive inhibition between these metabolic pathways. In other words, giving tyrosine

supplementation will inhibit serotonin synthesis, and giving 5-HTP supplementation will inhibit catecholamine synthesis. Administering only one amino acid neurotransmitter precursor dominates the shared enzyme, not just in the brain, but everywhere in the body.

Often amino acid therapists make comments such as, "Some patients develop a resistance to 5-HTP." What they are undoubtedly running into is that their 5-HTP supplementation is depleting patients of catecholamines, with disastrous clinical consequences.

There is more to this competitive inhibition between catecholamines and serotonin than applies to their synthesis. The same competitive inhibition occurs in the kidneys with respect to their relative retention and excretion. All the neurotransmitters --- dopamine, norepinephrine, epinephrine, and serotonin --- enter the renal tubules, and so do the amino acid precursors --- tyrosine, L-DOPA, tryptophan, and 5-HTP. What does the kidney do with these neurotransmitters and with their amino acid precursors?

The kidneys can take neurotransmitter metabolism in both directions. The kidneys can synthesize serotonin and synthesize dopamine from their amino acid precursors, but, the kidneys can also catabolize the four neuro-transmitters. Using the same catabolic enzymes, MAO and COMT, that are used in the brain, the catabolism of the three catecholamines results in homovanilic acid, while the degradation of serotonin results in 5-hydroxy indolacetic acid. These end products of catabolism are dumped into the urine. From the reverse process, the synthesizing of serotonin and dopamine in the kidneys, some of these synthesized neurotransmitters are excreted in the urine, but much of them are reabsorbed though the renal vein back into the systemic circulation.

Now, here is the critical consideration as regards MAO and COMT in the kidney. The levels of these two enzyme systems fluctuate in response to changing neurotransmitter levels. When any of the neurotransmitters are increased, enzymatic activity also increases. Clinically this is a problem, since if you administer catecholamines and serotonin, or administer uptake inhibitors that increase concentration of these neurotransmitters in the systemic circulation, or administer the amino acid precursors that increase the systemic level of these neurotransmitters, the increased quantities of these neurotransmitters entering the kidneys upregulates the catabolic enzymes.

Again, the competitive inhibition is at work. If tyrosine alone or catecholamines alone are supplemented, with a resulting increase in catecholamines, the renal action of MAO and COMT will increase dramatically. But, since there is no increase in serotonin, the serotonin that the patient naturally produces, will be degraded, causing a systemic depletion. The reverse is true if 5-HTP or an SSRI is supplemented without tyrosine. In

summary, administration of tyrosine or 5-HTP unopposed or improperly balanced with the amino acid precursor of the other pathway will deplete that other pathway because of increased MAO and COMT, decreased synthesis, and uptake competition.

This uptake competition needs further elaboration. --- The production of neurotransmitters requires that the amino acid precursors undergo uptake in the cells performing the synthesis. This synthesis occurs throughout the body, most particularly in the central nervous system, the kidneys, the liver, the GI tract, the mesentery, the lungs, and the peripheral nerves. Administration of an amino acid precursor to one system will overwhelm and compete with the uptake of the amino acid precursor from the other system.

All these aspects of competitive inhibition between the catecholamines and serotonin as regards catabolism, synthesis, and uptake, is understood by very few. Almost all amino acid therapy advocates are totally in the dark. In ignorance, and with no objective means of evaluation, they recommend amino acid supplementation with the potential to imbalance or even deplete neurotransmitters, potentially doing even more harm than drugging with uptake inhibitors.

One erroneous assumption that leads many therapists astray is that using urine neurotransmitter levels prior to therapy is an objective means of evaluating neurotransmitter status. The neurotransmitters in the urine are <u>not</u> filtered by the kidneys and excreted into the urine; they are synthesized by the kidney and excreted into the urine (or, secreted into the system via the renal veins). In other words, the urinary levels of these neurotransmitters have absolutely nothing to do with their levels in the brain. Remember, monoamine neurotransmitters do not cross the blood-brain barrier, so any neuro-transmitters filtered from the blood by the kidneys are not necessarily related to brain levels. Prescribing amino acids or reuptake inhibiting drugs based upon high or low urinary neurotransmitters almost certainly exacerbates or creates neurotransmitter imbalances. (At the same time, it will create NUTRI-SPEC Metabolic Imbalances.)

Where does NUTRI-SPEC stand with respect to amino acid supplementation to affect neurotransmitter function?

NUTRI-SPEC understands that balance between amino acid neurotransmitter precursors is an important part, but only one small part, of brain function facilitation. We recognize that neurotransmitter precursor supplementation can have devastating effects on the Fundamental Metabolic Balance Systems. NUTRI-SPEC also understands that 5-HTP and its derivative serotonin, when even slightly in excess, totally derange many metabolic systems. Similarly, excess supplementation with tyrosine(or even phenylalanine) can cause depletion of vitamins B6, B12, and folic acid, and the amino acids methionine

and cysteine, and can reduce the body's production of the essential antioxidant glutathione. The monkey-brained doctors playing with amino acids while focused on only one system of the body are potentially causing major Metabolic Imbalances.

And, as just mentioned, the amino acid precursor considerations are only one small part of addressing normal brain function. Each of the NUTRI-SPEC Metabolic Imbalances affects brain function, and each in several ways …

- Anaerobic/Dysaerobic Imbalances can cause anxiety and/or depression.

- Anaerobic Imbalance can cause somnolence; Dysaerobic Imbalance can cause insomnia.

- Glucogenic/Ketogenic Imbalances can cause anxiety and/or depression.

- Sympathetic/Parasympathetic Imbalances can cause anxiety and/or depression.

- Sympathetic/Parasympathetic Imbalances can cause somnolence and/or insomnia.

- Sympathetic Imbalance can cause tremors.

- All 10 NUTRI-SPEC Metabolic Imbalances can cause brain fog, memory loss, and cognitive decline.

There are three other equally important considerations …

- unhealthy microbiota
- excitotoxicity
- fatty acid balance

Any deficiencies or imbalances in the intestinal microbiota will cause severe ImmunoNeuroEndocrine Stress. That INE Stress virtually always affects one or more brain centers. The connection between microbiota and brain function is the most exciting branch of ImmunoNeuroEndocrine research. More and more studies are published identifying the various branches of what has come to be known as The Gut-Brain Axis. ----- Supplementation with IMMUNO-SYNBIOTIC is essential for all patients.

(The topics of excitotoxicity and brain fatty acid balance are for another day.)