



## **UNDERSTANDING THE BRAIN & METABOLIC ASSESSMENT FORMS**

The information that is presented below is not meant as a substitute for medical care. It is to provide information on relationships and symptoms only. There is much more information to be presented on the topics, and this is only a small amount to present an introductory or basic understanding.

### **HEALTH QUESTIONNAIRE (NTAF)**

#### **Section A – General Brain Function**

This section categorizes symptoms associated with general loss of neurotransmitter and brain function. These symptoms are not specific to any neurotransmitter in general, but rather reflect symptoms found in common with a decline in response of any of the neurotransmitters. Relevance of these symptoms may also indicate early signs of brain aging and degeneration. Symptoms alone cannot determine the degree of neuronal death versus the amount of deficit associated with loss of neurological integration, secondary to loss of neurotransmitter responses and other physiological factors that hinder brain performance. The subsequent sections will help determine potential areas of deficit leading to general loss of central nervous system outcome.

Prevalence of these symptoms should alert us to the potential for progressive loss of brain health. Immediate attention should be placed on preventing further degeneration and improving existing neuronal potentials. It is important to understand that brain function is not solely limited to cognitive attributes, but to autonomic, endocrine/metabolic, and immune function, as well. A loss of central nervous system integrity has global impacts on health and may contribute to hypertension, erectile dysfunction, digestive disorders, constipation, insomnia, etc.

In this area it is important to reduce inflammation and increase blood flow to the brain in addition to providing nutritional support for general brain function. This includes a rich source of essential fatty acids and what is called methyl donors. The brain is comprised of phospholipids and requires rich sources of fatty acids such as EPA and DHA. Methyl donors are important for many neurotransmitter biochemical processes and are also used for the production of myelin (the sheath around our nerves that protects them).

#### **Section B – Stress**

This section categorizes symptoms associated with an ACTIVE stress response. Stress is the most aggressive challenge to the neuro-endocrine-immune system and is a major cause for the loss of neurotransmitter-endocrine-immune integrity. Prevalence of these symptoms signifies people are either pushing themselves or being pushed past a normal degree of health. Despite the person's ability to make lifestyle and career choices, attempts to modulate (manage) stress physiology should always be considered.

Stress physiology profoundly alters the central nervous system neurotransmitter balance. Providing a high dose of phosphatidylserine and adrenal adaptogens (herbs that work either way the body needs – hypo vs. hyper) helps to modulate alteration of neurotransmitters from stress.

### **Section C1 – Reactive Hypoglycemia**

Reactive hypoglycemia alters brain neurochemistry due to drops and fluctuations in brain chemistry. A drop in blood sugar promotes surges of epinephrine, norepinephrine, and dopamine. Additionally, a sudden increase in blood glucose promotes surges of serotonin and GABA. Additionally, the brain needs constant glucose for normal function.

Reactive hypoglycemia must always be managed in order to assure healthy brain and neurotransmitter function. A diet consisting of frequent low-glycemic meals and snacks to manage blood glucose should also be considered if the person has a prevalence of C1 symptoms.

### **Section C2 – Insulin Receptor Site Insensitivity (Insulin resistance)**

Symptoms in this section are associated with insulin receptor site insensitivity leading to insulin surges after meals. Insulin surges promote spikes of serotonin and dopamine directly and shifts dopamine, epinephrine, and norepinephrine indirectly. Insulin resistance promotes elevations of cortisol, glycosylated end products (GEP), and inflammatory cytokines, all of which promote neurodegeneration of the brain. Additionally, the brain needs constant glucose for normal function.

Insulin receptor site sensitivity must always be managed in order to assure healthy brain and neurotransmitter function.

### **Section 1 – S – Serotonin**

Serotonin is a monoamine neurotransmitter and is also called 5-hydroxytryptamine or 5-HT. Serotonin is found in the central nervous system and in the peripheral nervous system. Serotonin produced in the central nervous system is associated with functions such as anger regulation, level of joy or enthusiasm, body temperature, mood, sleep, vomiting, and appetite. Serotonin in the peripheral nervous system has been associated with gastrointestinal (GI) tract motility, pain modulation, vasoconstriction (blood vessel), and as a promoter of cell division. Serotonin synthesis is linked to pineal gland production of melatonin. Imbalances in these pathways may lead to insomnia, altered sleeping cycles, behavioral changes in response to the cycles of the seasons, sexual activity and thermogenesis.

Conditions associated with low levels of serotonin include increased anger and aggressiveness, depression, obsessive-compulsive disorder (OCD), migraines, irritable bowel syndrome, tinnitus, fibromyalgia, bipolar disorders, anxiety disorders, and intense religious experiences. High levels of serotonin include shyness, inferiority complex, nervousness, being self-vulnerable to criticism, afraid of being disliked, desire for social contact but afraid.

### **Section 1 – D – Dopamine**

Dopamine is a neurotransmitter that is found both in the central nervous system and in the peripheral glands, such as the adrenal medulla and the kidneys. Dopamine has numerous functions in the brain related to motor coordination, motivation and reward, cognition, regulation of prolactin, mood, attention, and learning. Dopamine is associated with the “pleasure system” of the brain and promotes feelings of

enjoyment and reinforcement to motivate performance. Dopamine is usually thought of as a transmitter of arousal of physical and psychological activity.

Low levels of dopamine are associated with depression, Parkinson's disease, anhedonia (inability to experience pleasure), social anxiety, heavy menstrual cycles, male secondary hypogonadism, depressed libido, learning disorders, ADD, and chemical addictions. High levels of dopamine are associated with psychosis, schizophrenia, hyper-social activity, and increased libido.

### **Section 1 – G – GABA (Gamma-aminobutyric acid)**

GABA is the chief inhibitory neurotransmitter of the nervous system. The great majority of GABA is found in the central nervous system, although there are trace amounts in the pancreatic islet cell and in the kidneys. The trace amounts of GABA produced outside of the central nervous system cannot cross the blood-brain barrier (BBB). GABAergic responses are linked with relaxation, anti-anxiety, and anti-convulsive effects. GABA has also demonstrated some properties in modulating the release of human growth hormone.

Conditions associated with low levels of GABA include anxiety, insomnia, and depression.

### **Section 1 – ACH – Acetylcholine**

Acetylcholine is produced both in the central nervous system and in the peripheral nervous system. In the central nervous system, acetylcholine is used to promote excitatory actions for cognition, memory, and arousal. In the peripheral nervous system, acetylcholine is a major neurotransmitter for the autonomic nervous system released at all pre- and post-ganglionic parasympathetic neurons and all pre-ganglionic sympathetic neurons, which promote the release of epinephrine and norepinephrine from the adrenal medulla. Acetylcholine is also used to activate muscles by promoting opening of ligand sodium channels in the cell membrane of muscles that lead to muscle contraction. Acetylcholine induces contraction of skeletal muscles; however, it diminishes contractions of cardiac muscles as well. This difference is promoted due to the differences of receptors found in these different muscle tissues.

Conditions associated with acetylcholine imbalances include Alzheimer's disease, dementia, and myasthenia gravis. Low levels of acetylcholine are associated with memory lapses, calculation difficulties, decreased arousal, impaired creativity, diminished comprehension, and impaired judgment.

## **METABOLIC ASSESSMENT FORM**

Each of these functions is controlled by various hormones secreted by the endocrine glands, but it is the brain that tells the hormones and neurotransmitters what to do. The important thing to remember is that if any of these systems are dysfunctional for an extended period of time, immune system responses occur and the ultimate result is degeneration of the brain (neurodegenerative disease).

It is important for a moment to talk about the immune system, or the Immune Barrier System. This system is the immune system's first line of defense against foreign microbes or substances (things that shouldn't be there). The innate and adaptive immune systems become involved primarily when the immune barrier's system is infiltrated. The barrier system includes the skin, the respiratory mucous membranes, the GI mucosa membrane, and the blood-brain barrier (BBB.) The skin is typically

penetrated only by cuts or trauma, however, the other barrier systems can be compromised by physiological and chemical responses.

The mucosa barrier systems of the lung and GI tract are covered and protected by SIgA cells. These cells serve as a barrier lining for the mucosa, but unfortunately are susceptible to physiological stress responses. The stress response severely hinders the production of SIgA cells and function of the lung and GI mucosa barrier system. The stress response has also been shown to cause loss of BBB integrity.

Clinically, this is important because if an individual is in a stress response and has antigenic (allergy) exposure by respiration or by digestion, they'll be prone to have antigen infiltration and immune responses. For example, an individual that works in a mold-antigen infested environment may have greater risk to respiratory infection if they have suppressed SIgA cells, versus times when they have adequate SIgA. Constant exposure of an antigen to the mucosa can also cause depletion of SIgA cells. For example, chronic parasitic infection may result in low SIgA cells, leading to infiltration of their antigens to the GI immune system known as the "gut associated lymphoid tissue" (GALT). It is not uncommon to see a history of chronic stress followed by antigenic exposure with individuals suffering from an autoimmune disease.

To make this short, antigen exposure to the immune system creates a series of responses. The immune response will be simplified to serve as an introduction to immunology:

1. As the antigen bypasses the barrier system, it comes into contact with macrophages (blood cells that clean and destroy). The antigen is immediately attacked by a macrophage and becomes an "antigen-presenting cell (APC)".
2. The APC releases interleukin-1, which signals T-helper cells to mature and replicate. T-helper cells release cytokines to activate both TH-1 and TH-2 systems. Interleukin-2 and interferon (IFN) are used to stimulate the innate immunity. These cytokines increase the production and activity of natural killer cells and cytotoxic T-cells to destroy the antigen. T-helper cells also produce interleukin-4 and -10 to increase B-cells activity and production of antibodies against the antigen.
3. As soon as the antigen is recognized by the macrophage, it becomes attacked. Shortly after attack by the APC, the APC sends out signals (IL-1) to T-helper cells which then send out signals (IL-2 & IFN) to bring in natural killer cells and cytotoxic T-cells to also attack the antigen. As soon as messages were sent to T-helper cells from the APC, signals were also sent (IL-4 & IL10) to B-cells to produce antibodies.
4. After a few days, if the antigen has already not been destroyed by the TH-1 system, antibodies are produced by B-cells and start attaching to the antigen. Once the antigen is tagged with an antibody protein, it is easily recognized and destroyed by natural killer cells and cytotoxic T-cells.

This is the normal process. When the brain gets "confused," it can respond this way to basic nutrients, hormones, receptor sites, and transmitters, treating them as invaders rather than required elements in our body. NAET helps us return the brain's programming to normal rather than abnormal functioning.

### **Category I – Colon**

The colon moves waste products out of the body. If constipation occurs, waste products have the opportunity to find their way back into the body and create a toxic effect. Symptoms can include bloating, distention, and inflammation, followed by brain fog. If there is inflammation in the colon, there is inflammation in the brain. The hindbrain actually controls the colon's activity through neurotransmitter activity.

**Category II – Stomach hypochlorhydria (not enough stomach acid)**

The stomach is the second section of the digestive process. It uses stomach acid (HCl) to break down food for the small intestine to process. Too little stomach acid will cause reduced effectiveness in the breakdown of the food in preparation for the small intestine. Symptoms can include excessive gas, bad breath, difficult bowel movements, and undigested food in the bowels.

**Category III – Stomach hyperchlorhydria (too much stomach acid)**

Too much stomach acid will cause the digestive process to move so quickly that nourishment is impaired and antacid use will become more frequent to be comfortable.

**Category IV – Small Intestine**

The small intestine completes the digestion process by moving nutrients from the digested food into the blood stream and passing the waste product to the colon for removal from the system.

**Category V – Gallbladder**

The gallbladder stores bile, which is used to break down fats in the digestive process. It passes bile to the liver through the bile duct to aid in the digestive process.

**Category VI – Reactive Hypoglycemia**

(See Section C1 above)

**Category VII – Insulin Resistance**

(See Section C2 above)

**Category VIII – Hypo Adrenal (underactive)**

In this case, the adrenal glands are not producing enough of one or more of the following hormones to signal brain activity. Aldosterone, androgens (eg. testosterone), cortisol, dehydroepiandrosterone, adrenaline (epinephrine), and noradrenalin (norepinephrine)

**Category IX – Hyper Adrenal (overactive)**

In this the case, the adrenal glands are sending too much of the above listed hormones and over stimulating the brain.

**Category X – Hypo Thyroid**

The thyroid is one of our first mechanisms of defense with the immune system response. It also regulates our body temperature and metabolism. Thyroid hormones promote plasticity or flexibility of the brain and healthy brain aging in addition to helping manage the stress response. When the thyroid is underactive (hypo) it is providing these functions at a lower level than required, or not at all.

**Category XI – Hyper Thyroid**

In this condition, the thyroid is providing too many signals, over-stimulating the system.

**Category XII – Hypo Pituitary**

The pituitary is one of the main control endocrine glands. When it is not functioning properly, many other endocrine systems become compromised. In this case, the pituitary is not sending enough of one or more of the following hormones: adrenocorticotrophic, follicle-stimulating, growth hormone, lutenizing, prolactin, thyroid-stimulating, and antidiuretic (vasopressin) which releases oxytocin.

**Category XIII – Hyper Pituitary**

In this case the pituitary is sending too many of one or more of the above hormones.

### **Category XIV – Prostate**

The prostate is affected by hormones including testosterone, dihydrotestosterone, and inhibin. The prostate is also affected by the bladder and urinary tract and can impact sexual performance.

### **Category XV – Andropause**

Andropause is the condition that occurs when male hormones are too low in men. The hormones are the same as listed in the prostate section. Testosterone is important for healthy aging in males and very important for neuron health. Loss of testosterone in men can include associations with basic memory, cognitive function, and dementia. Testosterone affects dopamine storage and uptake. Low testosterone has been linked as a risk factor by Alzheimer's disease.

### **Category XVI – Progesterone & Estrogen Utilization**

This category relates to menstruating women as the progesterone and estrogen levels should be higher than in menopausal women. Incorrect levels of female hormones will cause more difficulties with the menstrual cycle. The effects of estrogen in the central nervous system extend far beyond its predominant role in orchestrating reproductive behavior and have been linked to such mental properties as verbal and spatial memory, fine motor skills, and depressive illness. Estradiol causes an increase in the excitatory drive on pyramidal neurons, leading to new dendritic spines with higher density of glutamateric receptors and increased synaptic activity among neurons. In other words, it increases electrical activity in the brain.

Although estrogen can act directly on neurons to alter their behavior, it is now understood that glial cells (cells that hold the brain together) may also be targets of gonadal hormone action. Estrogens play a role in brain inflammation and degeneration and menopause. Estrogen plays an important role in serotonin signaling, pain transmission, headaches, dizziness, nausea, bone density, vascular function and immune cell self-recognition, and depression.

### **Category XVII – Progesterone (Menopause)**

It is expected for menopausal women that estrogen levels should be lower than menstruating women. Incorrect levels of female hormones will cause more difficult menopausal symptoms. Progesterone appears to have the ability to activate GABA receptors which induces a calming effect. It has also demonstrated physiological significance in the regulation of stress, post-partum depression, memory, cognition, PMS, and depression, to name a few. Progesterone receptors in the brain appear to be modulated by dopamine. Progesterone appears to have very powerful protective properties on neurons and has a known anti-inflammatory effect.

### **Following are clinical strategies to modulate the brain-immune axis from *A FUNCTIONAL MEDICINE PERSPECTIVE*:**

#### **Reduce Inflammation**

##### **1. Optimize Methylation – Reduce homocysteine**

Elevated homocysteine increase the brain-immune response in two ways. First, it promotes loss of integrity of the blood-brain barrier (BBB) that leads to potential crossing of pathogenic organisms and haptens into the central nervous system. Second, elevated homocysteine itself has been shown to promote neurodegeneration due to its inflammatory properties. Serum homocysteine should be evaluated in all clients not just for its associated cardiovascular risk, but for its associations for brain health. Methyl donors and Methylation pathway cofactors are needed to support this. Methyl-SP

and vitamin B12 sublingual. The most common cause of methyl donor absorption is hypochlorhydria. The most common cause of hypochlorhydria is secondary to H. Pylori antigens. It should be noted that methyl donor depletion is commonly found with females taking estrogen replacement. The most common sources include Premarin and oral contraceptives. These individuals should always have their homocysteine levels measured.

## **Reduce Stress Levels**

### **2. Modulate Stress Physiology and HPA Axis**

The hypothalamus-pituitary axis (HPA) and stress responses have several critical influences on the brain-immune response. Activation of the HPA has been strongly correlated with the integrity of the BBB. Activation of the HPA has been shown to degrade the BBB and dampening of the HPA response has been shown to restore the BBB. HPA modulation is critical for healthy BBB and support to enhance its modulation and feedback go far beyond adrenal gland nutritional support. The stress response also releases cytokines that disrupt immune cycle coordination, decreased the product of natural killer cells and promotes general inflammation. Lastly, chronic stress activity with elevations of cortisol are linked to the promotion of brain degeneration and loss of cognitive function. Compounds such as Adrenacalm which contain a high dose of liposomal phosphatidylserine, have been shown to enhance the integrity of the HPA and modulate stress physiology. The site of action of phosphatidylserine is not on the adrenal glands, but on the central nervous system. It is a powerful antioxidant for the brain and helps modulate neurotransmitter activity of the HPA. Adaptogenic herbs have also been found to have anti-inflammatory influences on the brain and also modulate neurotransmitter physiology for the HPA.

## **Balance Blood Sugar Levels**

### **3. Reduce Advanced Glycosylated End Products**

When serum glucose levels are abnormally high and cannot be taken into the cell efficiently as in diabetes or insulin resistance conditions, the glucose in the bloodstream becomes oxidized by free radicals and produces an extremely inflammatory compound called advanced glycosylated end products (AGEs). AGEs are destructive and inflammatory to many tissues, but especially to the vascular epithelium and to the brain. AGEs can cross the BBB and activate microglia to form amyloid plaques. This mechanism can be a major contributor to neurodegeneration, and elevations of serum glucose must be taken seriously. The chief complaint when people have elevated glucose is fatigue and sugar cravings after meals.

## **Reduce Inflammation**

### **4. Optimize Prostaglandin Balance**

Prostaglandin balance is very important for inflammation modulation systemically, and the BBB and brain are no exceptions. Increased production of pro-inflammatory prostaglandins have the ability to promote loss of integrity of the BBB, increase inflammatory cytokine responses, promote neuroinflammation and dysregulate microglia communication and modulation. The use of cod liver oil and emulsified vitamin D has powerful anti-inflammatory influences and helps enhance regulatory T-cell responses (immune system)

### **5. Provide Antioxidant Support**

Antioxidants are critical for balancing free radical excess and inflammation. The two major areas for antioxidant concern are the BBB and the mitochondria. Oxidative damage to neuronal mitochondria promote further propagation of mitochondria loss and neurodegeneration. The main

antioxidants for mitochondria loss and neurodegeneration are glutathione, super oxide dismutase (SOD), and alpha lipoic acid.

#### 6. Identify Microglia-Lymphocyte Antigen Products

Once the BBB has been breached by an antigen or hapten, the microglia immediately recognize the foreign invader and initiate attack against the compound. The microglia also release cytokines across the BBB to bring across T-cells and macrophages across the BBB to help destroy the antigen (B-cells cannot cross the BBB). The macrophages and T-cells send signals to B-cells on the other side of the BBB to develop memory against the pathogenic compound. This creates a memory of pathogenic compounds that may harm the brain. Then in the future, even if the BBB is not breached by the compound, if the immune cells outside of the central nervous system recognize that antigen, the macrophages and T-helper cells will release cytokines to alert the microglia about their presence across the BBB. This in turn signals microglia to become active and results in the promotion of neuroinflammation without breach of the BBB. Once the organisms are found, all attempts to decrease their exposure to the immune system should be considered.

#### 7. Optimize GALT Activity

Gut-associated lymphoid tissue (GALT) is a collective term for the gastrointestinal immune system and the gastrointestinal barrier system. Activation of the GALT in general by pathogenic organisms or by large protein molecules from a leaky gut syndrome alone will create a systemic inflammatory response. This inflammatory response may change the tone of the entire immune system and promote inflammation that may degrade the BBB. Additionally, many times the BBB and the GALT have lost their integrity together and microglia-lymphocyte antigen relationships have been developed, as stated previously. When this occurs, that antigen exposed to the BALT breaches the microvillus layer and may promote activation of microglia cell by cytokine production from the GALT that crosses the BBB. The integrity of a healthy gut barrier is crucial to decrease activation of the GALT. The use of anti-inflammatory programs that support hepatic (liver) detoxification pathways nutritionally, provides anti-inflammatory compounds, supports regeneration of the gut microvillus, and provides an anti-inflammatory diet can be supplied with the three-week Clear Vite program. During this three-week program, dietary changes are conducted in conjunction with the Clear Vite program, metabolic powder formulation. The use of nutritional compounds that support restoring the integrity of the gastrointestinal epithelium such as Gastro-ULC should also be considered.

#### 8. Optimize BALT activity

The bronchial-associated-lymphoid tissue (BALT) is a collective term for the lung immune system and epithelium barrier. Activation of the BALT in general by pathogenic organisms or by large environmental compounds from a leaky lung syndrome alone will create a systemic inflammatory response. This inflammatory response may change the tone of the entire immune system and promote inflammation that may degrade the BBB. Additionally, many times the BBB and BALT have lost their integrity together and microglia-lymphocyte antigen relationships have been developed as stated in the previous paragraph. When this occurs, that antigen exposed to the BALT breaches the microvillus layer and may promote activation of microglia cell by cytokine production from the BALT that crosses the BBB. The integrity of a healthy lung barrier is crucial to decrease activation of the BALT. Clinical strategies such as decreasing smoke and harmful gas exposure, in conjunction with nutritional support to enhance the lung epithelium barrier, should be considered. A rich source of emulsified vitamin A and alpha lipoic acid may be supportive for the lung epithelium barrier system.

#### 9. Optimize T and B-Cell Modulation

The immune system is a very tightly orchestrated set of responses generated by cytokines, chemokines, and other messenger proteins generated from the immune cells. Healthy activity of T-Cells and B-Cells are necessary for healthy coordinate immune activity. The compounds found in X-Viromin may nutritionally support T-cells and natural killer cells. The botanicals found in X-FLM may nutritionally support B-cell activity and anti-inflammatory cytokine release. The glutathione and super oxide dismutase found in OxiCell and the EPA, DHA and high dose emulsified vitamin D found in Ultra D complex may be beneficial in nutritionally supporting regulatory T-cells. In autoimmune response, careful attention should be given to these compounds since they promote further immune activation. X-Viromin appears to enhance the TH-1 pathway and X-FLM appears to enhance the TH-2 pathway.

#### 10. Support Brain Synaptic Activity

General activity and firing of the brain is not only crucial for cognitive responses, but also very important for enhancing glial cells and astrocytes. Both glial cells and astrocytes maintain their firing rate and metabolic activity from surrounding neurons. The importance of healthy brain activity by various forms of stimulation – exercise, reading, math, art, music, stretching, learning, etc. – are crucial for brain health. Additionally, neurotransmitter substrates needed for neuronal signaling are critical for healthy neuronal synapses and firing rates of the brain. The use of the Neurotransmitter Assessment Form (NTAF) can help identify subjective indications to related neurotransmitter imbalances. Healthy neurotransmitter activity in conjunction with stimulation of the brain can promote reactions to help maintain the health of the microglia cells.