Neurotransmitters *Fact Sheet*

Neurotransmitters are chemical messengers that regulate many physical and emotional processes including movement, stress response, cognition, emotions, energy, cravings, pain and more.

Functioning in the central nervous system (CNS), as well as in the periphery, neurotransmitters facilitate communication between the brain and the body's glands, organs and muscles. They are released from neurons and travel across a small space, called a synapse, to reach receptors on target cells. Inadequate neurotransmitter function disrupts the signal to target tissue and has a profound influence on overall health and well-being. In fact, imbalances in certain neurotransmitters are associated with many of the prevalent symptoms and conditions seen in doctors' offices today including:

- **Mood Disorders: depression, anxiety**
- **Adrenal Dysfunction: fatigue, insomnia**
- **Loss of Mental Focus: ADD, ADHD, cognitive fog**
- **Addiction and Dependency**
- **Hormonal Imbalances: E2 dominance, E2 deficiency, low androgens**
- **Loss of Appetite Control: obesity and insulin resistance**

These symptoms are often compounded by the use of bioactive substances including caffeine, alcohol, nicotine and prescription medications that can contribute to neurotransmitter depletion and worsening of symptoms by suppressing or artificially stimulating neurotransmitter receptor function.

When functioning properly, the neurotransmission system has natural checks and balances in the form of excitatory and inhibitory neurotransmitters. These are classified according to their effects on the receptor site on the postsynaptic neuron. Excitatory neurotransmitters cause depolarization of the membrane, causing that neuron to "fire" and send a signal. Inhibitory neurotransmitters cause hyperpolarization, preventing the neuron from forwarding a signal.

Labrix currently offers two profiles for testing neurotransmitter balance: The Neurobasic Profile and The Comprehensive Neurotransmitter profile. The Neurobasic profile measures nine markers that commonly play a role in primary symptomatic conditions.

Neurobasic Profile:

SEROTONIN is a key neurotransmitter that is involved in the regulation of sleep, appetite and aggression. Serotonin imbalance is a common contributor to mood problems, and pharmacologic agents that alter serotonin levels are among the most commonly used class of drugs prescribed for anxiety and depression.

High stress, insufficient nutrients, fluctuating hormones and the use of stimulant medications or caffeine can all contribute to the depletion of serotonin over time. When serotonin is out of range, depression, anxiety, worry, obsessive thoughts and behaviors, carbohydrate cravings, PMS, difficulty with pain control, and sleep cycle disturbances can result.

GABA is the major inhibitory neurotransmitter found in the CNS and, as such, is important for balancing excitatory action of other neurotransmitters. High levels of GABA may be a result of excitatory overload, or a compensatory mechanism to balance the surplus excitatory neurotransmitter activity. These high levels result in a 'calming' action that may contribute to sluggish energy, feelings of sedation, and foggy thinking. Low GABA levels are associated with dysregulation of the adrenal stress response. Without the inhibiting function of GABA, impulsive behaviors are often poorly controlled, contributing to a range of anxious and/or reactive symptoms that extend from poor impulse control to seizure disorders. Alcohol as well as benzodiazepine drugs act on GABA receptors and imitate the effects of GABA. Though these substances don't cause an increase in GABA levels, understanding their mechanism can give us additional insight into the effects of GABA.

DOPAMINE is largely responsible for regulating the pleasure/reward pathway, memory and motor control. Its function creates both inhibitory and excitatory action depending on the dopaminergic receptor it binds to. Memory issues are common with both elevations and depressions in dopamine levels. Caffeine and other stimulants, such as medications for ADD/ADHD, often improve focus by increasing dopamine release, although continual stimulation of this release can deplete dopamine over time.

Common symptoms associated with low dopamine levels include depression, loss of motor control, cravings, compulsions, loss of satisfaction and addictive behaviors

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including: drug and alcohol use, smoking cigarettes, gambling, and overeating. These actions often result from an unconscious attempt to self-medicate, looking for the satisfaction that is not occurring naturally in the body.

Elevated dopamine levels may contribute to hyperactivity or anxiety and have been observed in patients with schizophrenia. High dopamine may also be related to autism, mood swings, psychosis and attention disorders. L-DOPA is a precursor to dopamine, and is used therapeutically for low dopamine conditions such as Parkinson's disease. These medications can cause elevations in dopamine.

NOREPINEPHRINE, also called noradrenaline, is an excitatory neurotransmitter produced in the CNS, as well as a stress hormone produced in the adrenal medulla. Norepinephrine is involved in a wide variety of actions including attention, focus, regulating heart rate, affecting blood flow, and suppressing inflammation. Involved in arousal, it prepares the body for action by relaying messages in the sympathetic nervous system as part of the autonomic nervous system's fight-or-flight response. High levels of norepinephrine are often linked to anxiety, stress, elevated blood pressure, and hyperactivity, whereas low levels are associated with lack of energy, focus, and motivation.

EPINEPHRINE, often better known as adrenaline, is synthesized from norepinephrine in both the CNS and the adrenal medulla. Much like norepinephrine, this excitatory neurotransmitter helps regulate muscle contraction, heart rate, glycogen breakdown, blood pressure and more, and is heavily involved in a stress response.

Elevated levels of epinephrine are often associated with hyperactivity, ADHD, anxiety, sleep issues, and low adrenal function. Over time, chronic stress and stimulation can deplete epinephrine stores leading to difficulty concentrating, fatigue, depression, insufficient cortisol production, chronic stress, poor recovery from illness, dizziness and more.

The Norepinephrine:Epinephrine Ratio is an indicator of the conversion of norepinephrine to epinephrine. Because cortisol stimulates the enzyme responsible for this conversion, low cortisol, in addition to depletion of cofactors including magnesium and SAMe can inhibit this conversion, leading to an elevated ratio.

GLUTAMATE is an excitatory neurotransmitter and is considered to be the most abundant neurotransmitter in the nervous system. Glutamate is involved in most aspects of normal brain function including cognition, memory and learning, although high levels of can cause excitotoxicity, a process where nerve cells are damaged by excessive stimulation. Elevated glutamate levels are commonly associated with panic attacks, anxiety, difficulty concentrating, OCD and depression, whereas low glutamate levels may result in agitation, memory loss, sleeplessness, low energy levels and depression.

GLYCINE Glycine is inhibitory and plays dual roles as both a neurotransmitter and an amino acid that serves as a building block of proteins. Glycine improves sleep quality, calms aggression, and serves as an anti-inflammatory agent. Glycine has been shown to boost mental performance and memory. Elevated glycine levels may be associated with compromised cognitive processing. Low levels of glycine may contribute to poor sleep, poor cognitive function, and issues with memory.

HISTAMINE Histamine is an excitatory neurotransmitter involved in the sleep/wake cycle as well as the inflammatory response. Histamine plays a dual role in the body as a neurotransmitter and immunomodulator that increases metabolism, promotes wakefulness, attention, circadian rhythms, learning, and memory. Elevated levels may be associated with allergy-like symptoms, gastro-intestinal concerns, and inflammation. Elevated histamine can interfere with sleep, contributing to insomnia. Low histamine may affect digestion and appetite control, learning, memory, and mood, and may result in drowsiness.

PEA (PHENYLETHLYAMINE) PEA promotes energy, elevates mood, regulates attention and aggression, and serves as a biomarker for ADHD. Elevated PEA may contribute to anxiety, with very high levels having amphetamine-like effects. Elevated PEA levels may be associated with higher cortisol levels. Low PEA may be associated with ADHD, depression, Parkinson's disease and bipolar disorder.

Comprehensive Neurotransmitter Profile:

For providers who want a more comprehensive look at neurotransmitter secretion and the metabolism of these markers, consider the Comprehensive Neurotransmitter Profile. This panel includes all of the markers listed above, as well as:

DOPAC: DOPAC is the primary metabolite of dopamine formed via the actions of the MAO enzyme. When DOPAC is elevated, and dopamine is low/low range, slowing the activity of the MAO enzyme may help to increase dopamine levels.

3-MT: 3-MT is formed by direct metabolism of dopamine by the COMT enzyme. Very high levels of 3-MT may have stimulant qualities. When 3-MT is elevated, and dopamine is low/low range, slowing the activity of the COMT enzyme may help to increase dopamine levels.

Normetanephrine: Normetanephrine is a metabolite of norepinephrine formed via the actions of the COMT enzyme. When normetanephrine is elevated and norepinephrine is low/low range, slowing the activity of the COMT enzyme may help to increase/maintain norepinephrine levels.

Metanephrine: Metanephrine is a metabolite of epinephrine formed via the actions of the COMT enzyme. When metanephrine is elevated and epinephrine is low/low range, slowing the activity of the COMT enzyme may help to increase/maintain norepinephrine levels.

5-HIAA: Clinically, urinary 5-HIAA is an indicator of serotonin synthesis and metabolism by the MAO enzyme. Some medications as well as dietary consumption of foods rich in serotonin (plantain, pineapple, banana, kiwi fruit, plums, tomatoes, walnuts and hickory nuts) may elevate 5-HIAA levels. It is recommended to avoid these foods for 3 days prior to sample collection. When 5-HIAA is elevated, and serotonin is low/low range, slowing the activity of the MAO enzyme may help to increase serotonin levels.

Tryptamine: Tryptamine is a trace amine derived directly from tryptophan by a B6-dependent enzyme. Trace amines (tryptamine, tyramine, PEA) may have stimulant effects at high levels. Tryptophan supplementation may increase tryptamine levels. Decreased tryptamine levels may be associated with depression. Tryptamine is normally metabolized by MAO; low enzyme activity may increase tryptamine levels.

Tyrosine: Tyrosine is the amino acid precursor for dopamine, norepinephrine and epinephrine. Low tyrosine levels may increase irritability, and lower mood, mental performance, energy levels, body temperature and thyroid function. Tyrosine hydroxylase converts tyrosine into the dopamine precursor L-DOPA.

Tyramine: Tyramine is a trace amine derived directly from tyrosine by a B6-dependent enzyme. Trace amines (tryptamine, tyramine, PEA) may have stimulant effects at high levels. Foodstuffs such as hard cheeses and red wines contain large amounts of tyramine. Decreased tyramine levels may be associated with depression. Tyramine is normally metabolized by MAO; low enzyme activity may increase tyramine levels.

Taurine: Taurine is an essential amino acid that has an inhibitory effect on neurons; it is important for balancing the action of excitatory neurotransmitters, particularly glutamate. Symptoms of elevated taurine may include apathy, sleep changes, irritability, recklessness, poor concentration, aches and pains, or social withdrawal. Taurine is an ingredient in many “energy drinks.” Decreased CNS taurine synthesis has been reported in individuals with autoimmune and neurodegenerative diseases, including rheumatoid arthritis, Parkinson’s disease, Alzheimer’s disease, and motor neuron diseases such as amyotrophic lateral sclerosis (ALS). Naïve vegetarians or individuals with digestion or malabsorption disorders may have low taurine levels. Taurine does not cross the blood brain barrier (BBB) easily and must be synthesized within the CNS, which requires a functional methylation pathway.

Putting It All Together

Neurotransmitter imbalances can be easily identified with a single noninvasive urine sample. Testing provides a tool to understand each patient’s specific neuroendocrine imbalances, which can be corrected with targeted nutritional therapy, BHRT, diet, and lifestyle interventions. Because it is especially important to understand the interrelationships of the neurotransmitters as well as their relationships with adrenal and sex hormones, an optimal approach measures each of the neurotransmitter levels identified here in addition to a full hormone panel. Changes in sex hormones and adrenal hormones can lead to neurotransmitter imbalances, while conversely neurotransmitter imbalances can affect hormone production and function. Testing both neurotransmitters and hormones provides a comprehensive view of the body’s functional neuroendocrine status, and brings to light additional factors that may be contributing to symptoms.

References:

[1] Bear MF, Connors BW, Paradiso MA. Neuroscience Exploring the Brain, second edition