NeuroLab
A Division of Sanesco International

The foremost reference laboratory for the measurement of biomarkers associated with HPA-T axis function.

HPA Profile (1) (Hypothalamic-Pituitary-Adrenal Axis)

Franklin Cook
ID#: 360524
Gender: M Age: 71

Brian Popiel, ND
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Date Reported
11/09/2015

Date Collected
10/18/2015

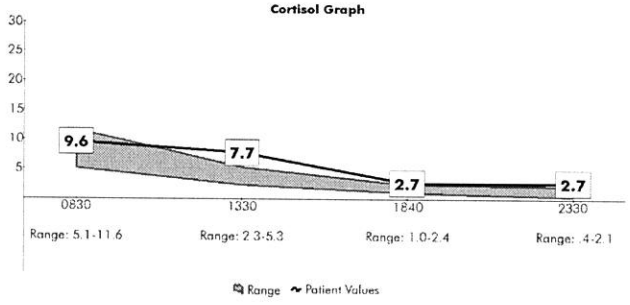
Date Received
10/23/2015

Lab Final
10/29/2015

Report Final
11/09/2015

Marker	Values	Optimal Range	Reference Range
INHIBITORY NEUROTRANSMITTERS			
SEROTONIN	**725.8** (H)	200-415 mcg/g Cr	50-250 mcg/g Cr
GABA	**182.6** (L)	600-1100 mcg/g Cr	150-700 mcg/g Cr
EXCITATORY NEUROTRANSMITTERS			
DOPAMINE	**115.0** (L)	250-400 mcg/g Cr	100-350 mcg/g Cr
NOR-EPINEPHRINE	**109.1** (H)	30-50 mcg/g Cr	13-70 mcg/g Cr
EPINEPHRINE	**9.1** (L)	10-15 mcg/g Cr	3-20 mcg/g Cr
GLUTAMATE	**2.4** (L)	5-10 mg/g Cr	2-12 mg/g Cr
ADRENAL ADAPTATION INDEX			
NOREPI/EPI RATIO	**12.0**	N/A	<13
ADRENAL HORMONES			
CORTISOL (0830)	**9.6**	N/A	5.1-11.6 nM
CORTISOL (1330)	**7.7** (H)	N/A	2.3-5.3 nM
CORTISOL (1840)	**2.7** (H)	N/A	1.0-2.4 nM
CORTISOL (2330)	**2.7** (H)	N/A	.4-2.1 nM
DHEA-s (0830)	**1.7**	N/A	1.0-3.0 ng/ml
DHEA-s (1840)	**1.8**	N/A	1.0-3.0 ng/ml
OTHER MARKERS			
CREATININE, URINE	**46.1**	N/A	mg/dL

Creatinine is used to calculate results and is not intended to be used diagnostically.
(L) and (H) are based on optimal ranges



Whenever laboratory data conflict with clinical findings or impressions, clinical judgment should be exercised and additional evaluation undertaken.

Results Processed By CLIA #: 34D1054007, NeuroLab Asheville, NC

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CORRELATION ANALYSIS REPORT

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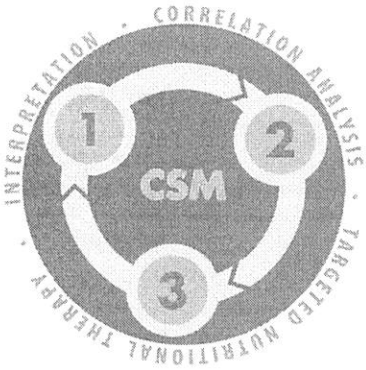

The CSM And Your Patient

The Communication System Management Model is designed to give you an analysis of neurotransmitter and adrenal hormone values and an observation of how they affect one another. This approach targets the underlying cause of chronic symptoms by addressing the root imbalance. In the next section, we will observe trends in the lab values, correlating those with the symptoms that were marked by the patient.

The patient has indicated the use of medications and supplements that may have an effect on the results.

The patient's laboratory results show a high serotonin paired with a low GABA. The high serotonin may be due to the indicated 5HTP supplementation. Despite the high serotonin, inhibitory system function may be compromised based on the presence of anxiety, irritability and sugar cravings. Typically, low serotonin is associated with sugar cravings. However, as serotonin and GABA function together to support balanced moods, consider incorporating support formulas targeted towards optimizing inhibitory system function. In addition, adjusting current serotonin supplementation is also recommended to normalize inhibitory values. Furthermore, the catecholamines are also imbalanced, as dopamine and epinephrine levels are decreased, while norepinephrine is high. This pattern can stem from excess copper, methylation complications, and/or underlying inflammatory conditions. Once the source of this pattern is determined, protocol may be implemented to restore balance to the excitatory system. Moreover, the patient's adrenal panel reveals cortisol levels to be elevated throughout the majority of the day. Therefore, the patient may further benefit from a cortisol modulator, such as phosphatidylserine, as excess cortisol can dampen inhibitory regulation. To monitor the norepinephrine to epinephrine ratio, system response, formula efficacy and patient concerns, reassessment is advised in six weeks.

This report was written for you by Alexis Rachkovsky. We strive to create the highest quality reports, and encourage our practitioners to contact our Clinical Support Specialists with any questions or concerns. We can also arrange for an Interpretation of the patient's results, based on your schedule and availability. To reach the report writer directly, dial 866-670-5705 ext. 305.

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CORTISOL (1330)	**7.7** (H)	2.3-5.3 nM
CORTISOL (1840)	**2.7** (H)	1.0-2.4 nM
CORTISOL (2330)	**2.7** (H)	.4-2.1 nM
DHEA-s (0830)	**1.7**	1.0-3.0 ng/ml

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DHEA-s (1840)	**1.8**	1.0-3.0 ng/ml

Adrenal Comments

Cortisol levels are elevated throughout most of the day. Surges throughout the day may result from stress, high glycemic meals, excess caffeine or nicotine, adrenal glandulars, supplemental or prescriptive cortisone products, pain and/or viral infections. The elevated levels during the day would be indicative of multiple stressors and/or poor stress management skills that are upregulating the HPA-T axis. This patient is stuck in fight or flight mode. Sustained cortisol elevations however, do indicate adequate adrenal reserve. Elevated cortisol may partially depress serotonin levels throughout the day, further contributing to the patients inability to handle stress. The late evening cortisol levels may also result from stress, high glycemic meals, excess caffeine or nicotine, pain and/or viral infections. This is also a pattern seen frequently in depressed patients. Nearly half of insulin resistant patients demonstrate elevated evening cortisol levels. Elevated levels can contribute to poor sleep and increased sleep latency, i.e. difficulty falling asleep.

Normal DHEA indicates this patient is in an adaptive phase. During a sustained stress response which requires continual cortisol secretion, the adrenal glands will begin to compensate. Prior to the alarm, DHEA levels may have been low and have now increased to normal as a result the alarm or stressor. Another possibility is that as a result of the Pregnenolone Steal, the DHEA levels have been shifted to normal and were elevated previously. As time goes on, and the stressors continue, the adrenals will start to lose their ability to compensate (maladaptive phase) and testing may show increased cortisol and decreased DHEA.

STRESS has system-wide effects on the body's communication system. Chronic stress can become cumulative and may have an especially deleterious effect over time. The perception of stress stimulates immediate release of epinephrine and norepinephrine, followed shortly by release of cortisol and DHEA. The effects of these hormones are beneficial in a short-term, life-threatening situation. Chronic stress, however, generates a cascade of effects. Prolonged stress leads to elevated levels of norepinephrine and epinephrine, and decreased turnover in the synaptic space, with chronically high cortisol levels. DHEA levels rise initially but soon decrease. This is significant because DHEA plays a role in protecting nerves from the neurotoxic effects of glucocorticoids, benefiting stress tolerance and resilience. Low levels of DHEA have been associated with chronic illnesses ranging from CFIDS to depression to rheumatoid conditions. Continuously elevated cortisol levels contribute to the aging process and are associated with declining immune function. An increased cortisol/DHEA ratio is specifically thought to interfere with T-cell immunity. Elevated cortisol may damage the overall regulation of the Communication System by interrupting the natural mechanisms of recovery. In addition, elevated cortisol is associated with promoting insulin resistance and weight gain. GABA is the primary inhibitory neurotransmitter. GABA's regulating and calming role is supported by adequate serotonin. Initially, GABA will make a compensatory rise to counter excitatory hormones and neurotransmitters. However, over time, a toll may be taken on GABA stores leading to a state of deficiency. When this happens, feelings of stress and anxiety may not be alleviated. Supporting both GABA and serotonin is recommended. Avoid supporting excitatory neurotransmitters, even when decreased, before replenishing serotonin and GABA. DHEA support may also be considered.

*The following are additional recommendations to assist in recovery from or to prevent adrenal fatigue: Adequate nutrient intake including multivitamin/multimineral, B-vitamin (Pantothenic Acid), Vitamin C, Magnesium, and Omega 3 Fatty Acids. Consider hormone support if necessary for DHEA, Pregnenolone, Progesterone, as well as adrenal support. Supportive lifestyle factors include structuring proper sleep hygiene with 8-10 hours per night; avoid stimulants and limit coffee, soda, nicotine, and caffeine; eat a balanced diet of small meals interspersed throughout the day and include lean protein, unprocessed carbohydrates, and healthy fats; increase water consumption to at least 64 oz per day; gentle exercise; make time for quietude.

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Neurotransmitter Comments

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Inhibitory Neurotransmitters

Patient indicated symptoms of ANXIETY and IRRITABILITY, which are often the result of decreased inhibitory neurotransmission and/or excess excitatory neurotransmission. As this patient has a high serotonin level, it may indicate higher loss in the urine; we understand that patient symptoms of anxiety or irritability may result from low serotonin function in the face of high loss. High loss may be due to receptor blockage (medication or heavy metal toxicity/neuron damage), 5-HTP supplementation, or high neurotransmitter turnover. In these cases, we recommend treating the patient, not the numbers. As the main inhibitory neurotransmitters, GABA and glycine function to promote calm and prevent over excitation. As GABA is the primary inhibitory neurotransmitter, it can be thought of as "the great balancer" of the nervous system. Also, serotonin often functions as a modulator of GABA activity. Depletion of GABA alone may cause anxiety. Research indicates that inositol and glycine supplementation may be beneficial for those suffering from anxiety, especially acute anxiety and panic disorders. Avoid supporting excitatory neurotransmitter function before restoring serotonin and GABA levels. Elevated adrenal hormone levels are known to contribute to the presence of anxiety and irritability concerns. If adrenal hormones levels are elevated, consider identifying and appropriately managing stressors, dietary components and/or medication, which may be contributing to up-regulated adrenal function and the presence of mood concerns. When up-regulated, thyroid hormones may also generate feelings of irritability and anxiety for the patient; therefore, consider a comprehensive thyroid hormone assessment.

SUGAR CRAVINGS may be the result of several factors. Inadequate levels of serotonin can often be a cause. Where serotonin is low, serotonin support is needed. When there is insulin resistance, adequate blood sugar is not getting into the cells. This can result in cellular signals to the CNS to increase carbohydrate intake. At times, an overgrowth of candida yeast can cause sugar cravings. Consider ruling out this possibility. The adrenal hormones play an important role in blood sugar homeostasis, and glucose/insulin balance; therefore, dysregulation of the adrenal gland can result in sugar cravings.

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Excitatory Neurotransmitters

Patient symptom questionnaire indicates ANDROPAUSAL SYMPTOMS of LOW LIBIDO and/or LOW STAMINA. Often adrenal function (DHEA, cortisol and the catecholamines - norepinephrine and epinephrine) is depressed in andropause. Cortisol and catecholamine depletion is commonly a consequence of adrenal fatigue. This is particularly true when Metabolic Syndrome or insulin resistance is present. Testosterone levels are inversely related to insulin levels. Consider repletion when assessment indicates deficiency. In addition, the patient may benefit from a low glycemic diet and increased exercise. In cases where either or both are high, the adrenals have not reached Selye's Exhaustion Phase, their reserves are not yet depleted and support is useful in the face of

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continuing stressors. Literature review finds a documented positive relationship between testosterone and dopamine. When both are adequate, healthy vigor, libido and drive are present. Patients who present with low dopamine in conjunction with symptoms of andropause may be candidates for a comprehensive sex hormone profile.

Patient indicated excess APPETITE. The appetite control center is located in the hypothalamus. Imbalances in the Appetite Regulating Network (ARN) (made up of complex signals from hormones, neurotransmitters, and neuropeptides) can lead to overweight and obesity. A multi-factorial approach is needed for achieving balance. The interrelationship between white adipose tissue (WAT), neurotransmitters such as serotonin and dopamine, and ARN hormones like cortisol, ghrelin, and leptin contribute to hunger signals or satiation. Low serotonin levels can increase cravings, especially for carbohydrates. Sufficient dopamine is necessary for a feeling of satiation. Chronic stress can lead to elevated cortisol, which can decrease serotonin, suppress thyroid hormones, and increase levels of ghrelin, thus increasing appetite. Elevated cortisol levels may also interfere with proper sleep. This can allow ghrelin levels to rise and appetite to increase. Decreased cortisol can lead to fatigue, which can increase food intake in an effort to restore energy. As excessive appetite is often present in hyperthyroid patients, and thyroid function controls metabolism, dysfunction of the thyroid gland can result in changes in appetite; therefore, consider assessing thyroid hormone levels.

Patient checked FATIGUE/DECREASED STAMINA on the questionnaire. Chronic fatigue can be caused by numerous conditions, the most common of which are 1) inadequate sleep (consider sleep pathologies), 2) low or high blood sugar, 3) hypothyroidism, and 4) adrenal fatigue, usually demonstrated by inadequate cortisol, particularly low morning levels (87% of patients indicating fatigue of moderate or severe intensity measure low a.m. cortisol). Low stores of excitatory neurotransmitters, such as norepinephrine, epinephrine, and glutamate, can also influence energy levels. Other reasons for fatigue involve inadequate dietary protein or B vitamins, dysregulation of mitochondrial function, anemia, depression, acute or chronic illnesses, heavy metal toxicity as well as acute and chronic environmental toxins, and certainly many medications. Assessment of thyroid, iron status, blood sugar, diet and adrenal function are all warranted.

Patient indicated exhaustive DEPRESSION as a concern. There are multiple pathways in the central nervous system where imbalance can produce depressive symptoms, the most well-known of which are the bioamine (serotonin, norepinephrine, dopamine) pathways. Low serotonin levels are often associated with depression, particularly depression with concurrent anxiety, dread, and insomnia. If patient shows normal or high serotonin, consider that serotonergic or overall inhibitory function is not adequate; inhibitory support may beneficial despite the normal urinary levels. High urinary levels of serotonin may be indicative of high loss, which may be due to receptor blockage (medication or heavy metal toxicity), 5-HTP supplementation or high neurotransmitter turnover. Depression can also be associated with low dopamine and/or norepinephrine, especially those with vegetative depressions that involve lack of adequate drive, ambition, focus, or energy and typically present with lethargy, fatigue, excess sleep and lowered HPA function.

If the patient has normal or high urinary bioamine levels, indicating high loss, function may still be low. High loss may be due to receptor blockage (medication or heavy metal toxicity), supplementation or high neurotransmitter turnover. Depression can also be associated with low blood RBC, low serum ferritin levels, and low levels of the essential fatty acid EPA. Bioamine repletion (if necessary) and EPA supplementation (e.g., fish oil) may be warranted with the addition of co-factors required for the pathways, such as B6 as P5P.

Optimal thyroid function is paramount to comprehensive treatment of depression. Medical research is replete with references regarding mood and thyroid function; consider adding a comprehensive thyroid assessment.

Additionally, depression is associated in the literature with elevations in cortisol, particularly evening elevations. It is well known that Cortisol Releasing Factor (CRF) is increased in healthy patients with depression, which lead to increased cortisol levels. The medical

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literature also supports the fact that unmedicated unipolar and bipolar depressed patients have a 'hyperresponsive' noradrenergic system (with elevated NE levels and turnover). This is a common pattern along with low serotonin levels. In addition, much research suggests that both hypothalamic and extrahypothalamic CRF activates the locus ceruleus in the brain, leading to an increase in norepinephrine. Thus, high CRF activity might lead to both elevated cortisol and norepinephrine levels seen in depressed patients. In cases of low DHEA, supplemental DHEA administration is warranted, as supplemental DHEA has been associated with improvement in symptoms of depression.

The patient's questionnaire indicated GENERAL PAIN and JOINT PAIN to be an issue. Approximately 70% of patients who marked moderate or severe pain issues measure low serotonin. Both serotonin and norepinephrine are known to provide an inhibitory influence on pain, and under stressful conditions, may provide nearly complete pain inhibition. Norepinephrine can also reduce pain by stimulating beta-endorphin release. If the level of serotonin is deficient, pain perception increases. Often norepinephrine is elevated (if adrenal function is adequate), likely responding to the stress of the painful experience. Another possible area of imbalance is dopamine function. Research indicates altered dopamine activity at the receptors, and an abnormal dopamine response in the experience of pain. Replenishing serotonin, supporting dopamine, and balancing norepinephrine can often be helpful in cases of pain. At times, if pain is severe, the body may perceive this pain as stress, resulting in the up-regulation of adrenal hormone levels.

Patient indicated POOR MEMORY. Memory is dependent upon balance among many central neurotransmitters. Adequate glutamate is required for learning and memory; 60% of patients marking moderate or severe memory issues have low/low normal glutamate. Adequate dopamine is also necessary; low levels can impair working memory, in particular. 70% have low or low-normal dopamine. Norepinephrine is also required-both short-term memory and long-term memory depend on adequate NE levels. Acetylcholine is a primary neurotransmitter for the laying down of memory traces and, though not measured, can be supported by increasing dietary choline or supplementing with phosphatidylcholine or DMAE. Serotonin is also required for proper memory (acute tryptophan depletion can directly impair memory). There is evidence in the literature, however, that extreme excesses of norepinephrine, glutamate and serotonin can also impair memory. Additionally, chronic elevations of cortisol damage the hippocampus, center for short-term memory. DHEA should be repleted when low, since it is known to be neuroprotective to the hippocampus. Balance, then, among the neurochemicals, is of utmost importance for establishment and maintenance of memory. Decreased thyroid function is known to impede cognitive function; therefore, consider assessing thyroid hormone levels.

The patient indicated HAND TREMORS. Imbalances between excitatory and inhibitory neurotransmitters can lead to stress, anxiety, heightened emotional state and/or fatigue that can be causes of hand tremors. High cortisol may also be present, contributing to hand tremors, as over-excitation often results in shakiness. Dietary causes may include excess caffeine, other stimulants and alcohol or other substance withdrawal. Blood sugar and thyroid disorders should be ruled out through appropriate testing. Studies have shown that a genetic variance in dopamine function or heavy metal toxicity may contribute to this condition. Neurological conditions that affect the brain function, such as stroke, multiple sclerosis, and traumatic brain injury, can contribute to hand tremors. Proper balancing of excitatory and inhibitory neurotransmitters is recommended. A persistent fine tremor is the most common movement abnormality that presents in thyrotoxicosis, a syndrome resulting from the excess of circulating FT4 and/or FT3; therefore, consider assessing thyroid hormone levels, for more insight into the cause of this symptom.

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THERAPEUTIC RECOMMENDATIONS

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Patient is in: Initial Phase

The following therapeutic protocol is based on conclusions derived from patient lab results, clinical data, gender, age, etc, and symptoms listed on the patient questionnaire. The goal of this protocol is to help the doctor begin the three-phase process of restoring balance in the HPA-T axis, while also improving symptoms for patient optimum well-being. The Initial Phase is the beginning of the patients rebuilding process, where TNT is introduced to help move lab values in the right direction. Leaving the patient on the Initial protocol longer than necessary may unbalance the patient. Retesting initiates the Restoration Phase. It provides significant two-fold value in that it serves as a guide in adjusting or fine-tuning the therapy. In addition, it allows for monitoring of progress as the patient rebalances their signaling biochemicals on the path toward optimum well-being.

Overall Summary and Recommendations

Lentra ***x 1 daily for GABA support; may increase to x 2***
Contains: GABA-A agonists: Magnesium Taurate, Suntheanine, and Lactium

Retesting is an important part of this process. NT levels need to be monitored. Retesting for this patient is recommended in 6 weeks.

Additional Recommendations

* It is recommended that all patients on a program to balance HPA axis function should also supplement with B complex, a multi-mineral and multi-vitamin as well as EPA/DHA.

Disclaimers
* These statements have not been evaluated by the Food and Drug Administration. These products are not intended diagnose, treat, cure, or prevent any disease.
*The statements above are recommendations to the clinician. All final therapeutic decisions are the responsibility of the treating physician.
* Please call Sanesco International at 866-670-5705 with your technical and clinical questions. For further reading and references, please refer to Sanesco's Technical guide and Clinical guide.