Brain Gut 16: Adrenal Fatigue Rx

Readers Summary:

1. What is adrenal fatigue really?
2. What is the PVN?
3. How do hormones play a role in all this?
4. What is the adrenal fatigue Rx?
5. Is there a real clinical example of how this all ties together?

Adrenal Fatigue = an inhibited PVN.

What is Adrenal Fatigue at its core? Many websites will tell you it is an adrenal gland function problem that is best assayed by a salivary adrenal stress panel. I wont and I do not. The cause of adrenal fatigue is a brain injury at the hypothalamus all caused by bad signaling. My Adrenal Fatigue Rx is best called ***Metabolic Neurosurgery***: It is all about energy and energy utilization that allows for perfect signaling of environmental signals. When your energy is bad your signaling falls off a cliff. The ASI is just like a gauge on a car. It tells you some info but it does not tell you why it is happening. How we understand adrenal dysfunction in 2012 has radically changed because of a relatively new science called neurohumoral-immunology. What does this mean?

It means adrenal fatigue at its core is a brain illness and not an adrenal gland problem.

What is the PVN? How do we know if our PVN is shut off? What are some of the symptoms? We can't sleep, our guts do not work, our body composition goes way off, we sweat at the wrong times, we develop cognitive haze, blurred vision, migraines, and reactive hypoglycemia. Many times fatigue is only relieved by eating foods we should not. It also means we have lost allosteric control of leptin!

You might be wonder how does leptin play a role here? Because leptin is secreted by adipose tissue cells and enters the hypothalamus at midnight, it was originally thought to signal information about the size of body fat stores. We now know it is more complicated than that. Rapid and profound declines in leptin were soon observed in response to intermittent and long term fasting and calorie restriction in many papers. Soon thereafter, many extreme increases in leptin were observed in Amgen's trials in response to overfeeding and re-feeding states after energy was restricted for sometime.

In these cases all these effects occurred in humans, before changes in adiposity could occur. So we knew leptin has other fast acting properties in the brain. These observations led to the revised theory that leptin might actually signal information about dietary energy intake to the brain to alter hormone signaling. Since this reformulated hypothesis, however, we have found in research that the leptin level and diurnal rhythm of leptin actually depend on energy availability and that exercise itself has no suppressive effect on leptin beyond the impact of its energy cost on energy availability.

Leptin is one of the main signals of what is going on in the parasympathetic system of the brain. The vagus nerve connects the gut to the brain at the area postrema in the 4th ventricle of the brain. It is bathed in "Cerebrospinal Fluid" (CSF) fluid. You will learn more about that in this blog too.

When I learned these bits of knowledge about leptin in 2006,

I knew exercise was not the key to losing weight many others thought it was. I knew that at its core obesity was an inflammatory brain condition of bad signaling. This is why the Leptin Rx avoids exercise initially.

So what else did this data on leptin imply to me? It meant that energy availability and not body fat stores determine the secretion of leptin by fat cells. In other words if energy balance is off leptin signaling is also off at the fat cells and in the brain. This is how the brain samples energy balance in humans. When the balance is off the tell tale signs will show up in the person's altered hormone panels. An altered hormone panel tells us the brain can no longer sense its environment well. When it can not sense its environment well it loses the ability to signal properly and illness begins to show up in all systems body wide. In other words, humans have a ***whole body physiology*** all tied directly to energy balance. When the system is out of balance, the brain loses the ability to signal in many areas. Adrenal Fatigue is one of those systems.

Let us discuss this further. Where in the brain does all this go on?

1. Hippocampus: this is located in the deepest part of your temporal lobe in the brain and this part of the brain makes most of the new neurons in our brain. It requires optimal diurnal cortisol levels for this to happen with two special chemicals called BDNF and NGF. The hippocampus is also where memory starts and ends. The processing of memory however requires optimal melatonin signaling that the brain is responsible for by sensing light and dark properly. It also is where the circadian rhythmicity of the HPA axis is controlled in the brain. When your hippocampus is off you are off in a big way in more ways than one.

2. Hypothalamus: Most of you know about this part of the brain if you read my blog. One of the most important functions of

the hypothalamus is to link the central nervous system to the endocrine system and the immune system via the pituitary gland. There is a small nucleus there where all three of these systems converge on one another. This area is called the paraventricular nucleus (PVN). The PVN is in ultimate control over the secretion or suppression of cortisol from the adrenal gland based upon the marching orders the brain gives it. This implies that the PVN is the source of adrenal fatigue and not the adrenal gland. This is a new truth you might need to hear a few more times to buy. This blog is going to show your the details why that is the case.

3. Mesencephalic Reticular Formation (MRF): This is part of the oldest part of brain stem. It is not part of the cortex of the brain where consciousness and memory live. Most of our uniqueness as humans are located in our cortex and not our brain stem. Simple life forms also have a brain stem. It controls vegetative or automatic functions in us. This part of the brain controls the sympathetic outflow of our brain. It does this by altering excitation signaling of the intermedio-lateral cell column (IML) in the spinal cord, which stimulates the adrenal medulla to release epinephrine and norepinephrine. You will learn about this in the **Geek** portion coming later in this blog. That is the basic anatomy you need to know before you learn about the **Adrenal Fatigue Rx.**

What is Adrenal Fatigue really? AF is an alteration in cortisol's normal diurnal pattern. So let us take a look at the most common clinical findings we see today: **Chronically elevated cortisol is the first sign of AF:**

Adrenal Fatigue Rx: For Cortisol Elevation

1. Control of cytokine response by controlling the fast acting eicosanoid hormone system: Here is where the Leptin Rx, the Cold Thermogenesis Protocol, and supplements or foods

containing curcumin, quercetin resveratrol, pycnogenol, green tea extract might be considered. Trouble for your hormone panel down the road is always signaled first in the fast acting eicosanoid system. Alterations in leptin signaling is the first clue something is a miss. These things are rarely checked by any practitioner because few even know about how it integrates into the hormone panel and is coded for in the brain.

2. Phosphatidyl choline and serine tend to work well here because the brain needs them for cell membrane signaling to properly occur.

3. Neurotransmitter support best monitored by organic cation testing. I covered this topic in a webinar this summer. Chronic elevated cortisol stimulates neurotransmitter depletion as time elapses. The brain can not signal well with poor NT stocks in the brain. We must have good NT to sense our environment well and transmit the signals of the outside world to our cells in our body. When you think about cancer now you will begin to understand why it always seems to occur when stress is a major player. It alters our ability to signal. Cancer is not really a genetic disease of our original template. **Our first genomic draft is built by our parents and the environmental experience we obtain builds the revisions of this original draft.** This implies that cancer at its core is epigenetic and at its core is a loss of an ability to signal.

4. The adaptogenic supplements/herbs can be considered now here as a last option not a first option as it appears in most websites over the internet.

Adrenal Fatigue Rx: Chronically

depressed cortisol: The more common clinical situation we see in AF:

When the body is under chronic stress, pregnenolone, the precursor to all other steroidal hormones, is diverted to produce cortisol (known as pregnenolone steal syndrome). When this occurs, it is to the detriment of all other steroidal hormones, like DHEA and its metabolites, including progesterone, testosterone, and the estrogens. Vitamin D production will also be down regulated. As pregnenolone is diverted to cortisol, DHEA depletion begins quickly. The result is an elevated cortisol to DHEA ratio. A normal ratio is approximately 4:1 to 6:1 in most ASI labs. This upside down ratio is able to inhibit the PVN of the brain quickly. Why? Cortisol is needed to make new nerve cells in the hippocampus. This is the key element to the Adrenal Fatigue Rx.

The Key Problem for Healing: Re-establish the progesterone level in the brain immediately. I also do this for brain surgery cases. General anesthesia also depletes our brain of progesterone and can lead to cognitive dysfunction for a few days post op.

A. We must re establish the Progesterone level quickly to increase BDNF signaling to make new neurons to replace the damaged nerve tracts that allow for altered signaling.

B. Once the new neurons are made, they need to be connected together. This is done with optimal diurnal cortisol AM and PM levels.

C. The new neural circuits created must wire together to become “hardwired” via Hebbian learning. This is done by optimal diurnal melatonin levels at night when we are chemically reduced. This is when the brain trims bad neural

circuits and strengthens good ones to regain control of signaling. If melatonin is off you can not re wire a bad brain no matter what anyone tells you. This is why sleep is so critical to human biology.

D. Neurons that fire together wire together. This means that you should consider things that strengthen your newly built circuits when you use this Adrenal Fatigue Rx. Cold Thermogenesis, short explosive sprinting, and meditation are the best safest ways to increase chronic secretion of brain derived nerve growth factor (BDNF) and nerve growth factor (NGF) in the brain to get it to heal quickly.

E. NT building blocks and co factor supports to power the synaptic clefts. DHA and iodine are hugely important to synaptic cleft signaling. It provides the bio-energic power and antioxidant protection to explosively powerful signaling found in all neurons.

F. Strict control of all inflammatory cytokines and acute phase proteins to keep the system humming and immune system working in unison with the PVN.

G. Consider the rest of the things in my initial Adrenal Fatigue Protocol at this point. I only use this in minor cases. Most cases need a rewire as I am laying out here in detail in this blog.

Abnormal Circadian Rhythm: Reversal to regain cellular signaling in the brain

1. Cycloset use to reset the circadian cycle for a low cortisol in the AM. This is usually due to a low dopamine level in the brain. You can follow IGF-1 and salivary diurnal melatonin levels to gauge progress. You will soon learn in the new quantum biology series that Vitamin A, and not vitamin

D, is the main controller of our photoperiod that sets the clock in the SCN.

2. Use natural sunlight to reset your SCN and repair your cortisol levels every morning as soon as you rise.

3. The worse your ASI looks the more you might need to incorporate oxytocin as step two in your AM regimen after letting the sun hit your retina. After you rise you might consider using endogenous or exogenous oxytocin to exercise the new neural networks you are learning to rebuild in this blog. Why? It is coming in the GEEK section soon.

4. What next? Then eat your Big Ass Breakfast (BAB) of the Leptin Rx. That is how you start your morning to reset your circadian signaling.

5. Rebuilding neurotransmitter building blocks with the Epi-Paleo Rx: Nothing does it faster

6. At night if your case calls for it based upon the night time circadian signals, leptin, IGF-1, and melatonin levels off: When the sun sets your artificial light needs to be minimized. Blue and green light is especially problematic to PVN signaling in the human brain. Based upon testing one might consider a low dose of progesterone one hour prior to bed. The best route will have to be discussed with the clinician and is based upon your own clinical context.

7. Phopshytidylcholine and serine via diet or supplements can be used here to make sure adequate glycerophospolipids are present to adequately re establish the cell membranes in new neurons that are created in the hippocampus to this Rx. People forget the outside world is sensed in our cell membranes first. This implies that we need great cell membrane architecture and signaling to get well. DHA and iodine are also critical in this process for protection of signaling integrity from oxidation and in energy production to drive the chemical reactions of signal transduction. One of the first

signs of cell membrane problems is actually cellular overcrowding of proteins and enzymes in the cytoplasm.

When the cell loses its normal space it effects the ability to carry out enzymatic processes of the nano machinery of human biochemistry. This affects the rapidity and kinetics of how the system can signal. The more chemically oxidized we are the more crowded a cell's interior becomes and the worse cellular signaling becomes. The more chemically reduced a cell is the better is functions and signal. Circadian signaling can be fine tuned when we pay attention to these little talked about biochemical variables. The Epi-Paleo Rx takes these factors into account where most other dietary templates have not even looked at these variables in an adrenal fatigue case. They are incredibly important when you are trying to re establish brain signaling and rewiring your neural networks to regain control of the pharmacy in your hypothalamus.

As I mentioned briefly in Brain Gut 12, the single most important hypothalamic nucleus of the central autonomic network is the paraventricular nucleus (PVN). This is the source of where adrenal fatigue really resides. It is not an adrenal issue it is a brain signaling issue. Let me explain that so you get it.

Geek Alert: The PVN has two morphological classes of neurons that fall into three functional categories. The first morphological class is comprised of magnacellular (big) neurons. These neurons contain vasopressin and oxytocin and project their axons into the posterior pituitary where these hormones are released directly into the blood stream. Yes, orgasm (oxytocin release) can help heal adrenal fatigue if you know how to use it. It can be used to reset your circadian signal and produce a massive antioxidant surge to repair the damaged circuits between the posterior pituitary, PVN, and the hypothalamus so you once again reach the giant pharmacy in your head.

All of these parts of your brain makes the chemicals and drugs we need to fine tune our signaling. The second morphological class is comprised of parvocellular (small) neurons. The parvocellular PVN neurons also include a neuroendocrine-related functional subset that project to the median eminence and secrete releasing hormones into the hypophyseal portal blood stream for control of anterior pituitary hormone secretion. More on these two functional groups will be covered later in the blog series. Finally, a group of parvocellular neurons comprise the third functional group of PVN neurons with these involved in central autonomic control.

There are three types of pre-autonomic parvocellular neurons (Types A, B and C) separable based on anatomical and physiological criteria, as well as based on subnuclear location within the PVN. Pre-autonomic PVN neurons project directly onto preganglionic autonomic neurons in the dorsal motor nucleus of the vagus nerve, the autonomic relay nuclei of the brainstem (A5, rostral ventral lateral medulla) and even directly to the intermediolateral spinal columns.

I mentioned this system earlier in the blog. This is where the sympathetic nervous system lives. It starts in the Mesencephalic Reticular system mentioned above. These projections descend ipsilaterally through the brainstem and spinal cord with four points of decussation (supramammillary, pontine tegmentum, commisural part of the nucleus of the solitary tract (the major one), lamina X of the spinal cord) so that ultimately innervation is bilateral but with an ipsilateral dominance in most brains.

Key Geek Point: Thus, the PVN, unlike any other brain site, has direct influence over both sympathetic and parasympathetic outflow. Furthermore, the PVN receives direct sympathetic and parasympathetic afferent inputs from trigeminal pars caudalis (sympathetic) and the nucleus of the solitary tract (parasympathetic). This is why we use face dunks in the Cold Thermogenesis Protocol. It is the fastest way to signal an

inhibited a broken PVN. (a bad ASI) The PVN therefore is the only brain site in a closed efferent-afferent reflex loop with both the sympathetic and parasympathetic nervous systems. **This implies that the PVN is the key portion to study in the brain in all cases of adrenal fatigue. The system breaks when signaling is broken here. The PVN is a collector of environmental inputs. So if we can't sense our environment well the output of the PVN will not be reflective if what our brain is really experiencing in life.**

The summation of the excitation and inhibition is what controls the outflow of the PVN in humans. What determines this? The environment the human is in and how well it can signal those changes into the brain's neural network. This theory of neural processing is called the central integrative state. This theory states, the combination of environmental stimuli that alters our neuronal pool or ability to make new neurons, neurotransmitter levels, hormone panels, and levels of cytokines all result in an excitatory state, the result will be an elevation of cortisol. If the reverse situation is true then we will have a dramatic fall in cortisol's diurnal pattern. This explains how someone can move from an adrenal fatigue state to an adrenal exhaustion phase quickly.

So true adrenal fatigue is collection of inputs that is entirely inhibitory to the PVN. The result is a flat lined ASI. So you might be wondering what stimulates the PVN and what turns it off? High insulin levels, low Acetylcholine NT levels in the brain (Alzheimer's), elevations in epinephrine and norepinepherine. The immune modulation of the Th2 cytokineslike IL-4, IL-5 and IL-10 can also do this.

What turn's off the PVN and results in a low cortisol? Low dopamine levels in the reward circuits in the frontal lobe, low GABA levels, low epinephrine and norepinepherine output, endothelial nitric oxide, interferon or drugs that act like it, TNF alpha and beta, and Th1 cytokines IL-2 and IL-12 that control formation of NF killer cells that destroy cancer

cells.

More Deep Geekiness: Other hypothalamic nuclei in the central autonomic network include the dorsomedial nucleus, the lateral hypothalamic area, the posterior hypothalamic nucleus and the mammillary nucleus. These nuclei send and receive projections from the PVN, the dorsal motor nucleus of the vagus, the central gray matter, the parabrachial nucleus, the nucleus of the solitary tract, the lateral and ventral medulla and the intermediolateral spinal columns. The lateral hypothalamus is especially involved in cardiovascular control as well as in control of feeding, satiety and insulin release. Remember this because later I am going to give you a clinical example later in this blog how all this complex neural wiring works in you. EMF and fake light destroy the permeability of the blood brain barrier and this is how the process begins in most.

The lateral hypothalamus is bathed in spinal fluid and this where the extracellular fluid of the Ca/Mg flux is felt and the result delivered for the brain to signal. **The serum levels are never important in this fashion when we work the problem up. The chemical content of the CSF is paramount in understanding this process.** It is rarely checked. Is there another way to check it? Yes there is. Many of my members know it and many educational consultants know how to apply it to their own clinical contexts. We do it by looking at the hormones of the circadian night cycle, namely, leptin signaling, IGF-1, and melatonin levels. These are also rarely checked because they are so misunderstood.

NON GEEKS: Inflammation causes the blood brain barrier to become permeable due to cytokines. The CSF becomes dramatically altered in composition because when the blood brain barrier is permeable it allows the ions to get into the brain to disrupt signaling of the PVN. This is the true source of adrenal fatigue. It is brain signaling problem not an adrenal gland issue. If the signaling is off the output of the gland becomes altered, and as such the labs look bad.

Often this is done with a adrenal stress index, but that does not go far enough. If you look at IGF-1 and melatonin levels you will see further evidence of altered signaling at the brain level.

This was explained in Brain Gut 11. Those with true adrenal issues present like a patient with Addison's disease. Most people who are diagnosed by an integrated clinician have a brain signaling problem due to the inability to signal the exterior world's signals to the interior world in our brain that senses it and mounts a response via the adrenal gland.

If the brain signaling is off, it means it becomes less energy efficient. This is the core issue that leptin was designed to measure in evolution. When the brain is energy inefficient it steals more energy from other organs with deep supplies of energy to offset its losses. It is at heart our biggest energy hog in the body by design. This is why it has some amazing abilities. Where does the energy come from? The heart and kidneys are two of those organs the brain draws from. Let me explain how this looks clinically for you in an adrenal stress case with a bad brain, altered heart function and kidney system.

The Clinical Example of this in practice: Why is heart palpitations or rhythm issues so common today? Why are they often seen in adrenal fatigue cases? Why do many cases of adrenal fatigue also have blood pressure issue present in them? Why do many people with altered adrenal issues have issues with sleep and night time bathroom runs?

Non Geeks: Your brain is Robinhood when leptin resistance is present. It steals from the rich to give to the poor neurons in your PVN! Once your brain is filled with its brain specific nutrients we laid out in the Epi-Paleo Rx it wont have to usurp nutrients from the heart to function well and cause its dysfunction. ***You must have the brain injury first to get the disease.*** Many things cause the injury to begin with,

but that is not the focus of this blog. But rest assured the injury must exist in the brain before the illness appears in the adrenal gland. This is a foundational concept in my theory laid out in levee one of the Quilt.

For those who don’t understand how brain function can cause heart rhythm issues here is the playbook again for you to review: This contains many bits of information in the recent blog posts in the Brain Gut series.

The brain allows us to sense the epigenetics alterations in our environment well. The environment first encounter life via a cell membrane. I want you to now channel what I said about the heart and brain in Brain Gut 13 with respect to how the Na/K ATPase is affected in metabolic terms in all tissues. Then, I want you to think about the number one killer of all humans today: Heart disease. How does heart disease tie into this theory of whole body physiology? When the neuronal Na/K ATPase is off we can make that extra 60{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of energy the brain needs. When we can not do this what does the brain do? It changes the physiology of its neighbors who have the energy.

If you begin to alter your blood glucose because of dietary or any other epigenetics signal (light or temp) and cause inflammation at a cellular level by eating badly or not being mindful of circadian cycles, you start secreting large amounts of insulin from beta cells to deal with it. This alters your magnesium levels in your CSF which activate the metabolically efficient Na/K ratio because of DHA found in massive abundance in the brain. We laid this cornerstone out in Brain Gut 13.

When we have an altered Na/K (low) ratio, this in turn, simultaneously cause brain metabolism to ratcheted down because its function is directly coupled to the efficiency of the Na/K ATPase for our species. As the brain’s metabolism falters, it begins to shunt energy to itself at the determent

of other organs. It robs Peter to pay Paul. This physiologic bio-energetic “stealing” of energy alters functions everywhere in the body to satisfy the brains needs. As other organs fail slowly under this physiologic directive, this further alters brain function from the excessive 60{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} energy boon created by the DHA/ Na/K ATPase, which results in your feeling less well with less energy and you have a chronic cognitive haze. This system is entire water based and you will be hearing a lot more about this in the EMF series. Is this beginning to sound familiar to anyone yet? This is precisely what a person with adrenal fatigue presents with. Stress begets stress and causes further decline in physiologic function in many systems.

It is the modern human condition that most of us exist in chronically. As this goes on chronically, brain function is eroded (the real source of adrenal fatigue in the PVN) because there is an excess of sodium and calcium ions in neurons, which begin to alter our homeostatic brain controls of the renin angiotensin system in the kidney. When this happens this alters our Blood Pressure clinically. The renin angiotensin system target organ is the kidneys. The kidneys control the electrolyte balance of the serum and ultimately is what changes the composition of the CSF to further alter the function of our brain. CSF at its core is just an ultra-filtrate of our serum. Our brain uses the chemical composition of CSF to see what is happening in its neighbors and then mount a proper response in it efferent neural tracts.

This slow erosion of our kidney function goes on undetected for years by medicine and integrated practitioners and slowly undermines our electrical systems balance body wide. This implies that our declining kidney function, directly effects our electrical system of our heart (conduction system AV node and sinus pacemaker) to become less optimal or “foggy” in its physiologic function as well over time. As the relays in the

hearts electrical system becomes “sticky”, this can cause all kinds of unusual heart rhythms in humans. **This shows you why declining brain function always correlates with declining heart function.** Modern medicine has never made this physiologic link but they do know it exists because heart disease and brain diseases share so much homology. Why does this happen? These organs are chemically and electrically tied together by the action of the Na/K ATPase, DHA, and iodine at a foundational level physiologically in humans in our cell membranes. This all results in the many types of cardiac dys-rhythmias we see clinically. This is an early sign of major bio-energenic shifts in cells all tied to oxidation. This is metabolic neurosurgery at work. The human brain dictates how energy is partititioned because it requires so much of it.

When this goes on further brain function erodes and we can not sense any circadian signals well. It is at this time when we see dramatic changes in AM and PM cortisol, severe alterations in IGF-1 and altered melatonin. We, in essence, lose our primal sense of well being and eventually we develop an inability to sense vascular trouble before it happens clinically. Over time, this inability to sense circadian signals leads to a heart attack/palpitations, cancer or heart failure.

Adrenal fatigue or resistance is a real phenomena in us, but the way it has been described by people is very incomplete and in wrong in many respects. What is not clear to most health websites or integrated practitioners I have reviewed is the source of the problem for people relying on this information. EMF and fake light are the biggest risk factors for inhibiting the PVN. It is altered signaling in the brain that alters the function of neural pathways that control signaling of the autonomic nervous system. Most of the advice out there in “old school” and not going to lead to a reversal of function until you know about how the brain really works.

Here is a simple way to explain it: **The natural world of health communicates: things are okay as they are; you are okay just as you are; simply relax and be present.** If your

signaling sucks, your health will suffer and you will find yourself in an emergency crisis before too long because your PVN can’t translate the profound messages your body gives it. That is the Adrenal Fatigue in a nutshell. Included in this blog are the keys to deciphering it and how to attack the version of it you may have. When you know better you do better.

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- Brain Gut 11: Is Technology an Achilles Heel?
- Brain Gut 12: Dare to Disagree?
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