



## Fatigue by Daniel Nuchovich

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Fatigue is an overall feeling of tiredness and lack of energy, often associated with having poor motivation, affected thought process, sore muscles and mood changes. It is a lingering tiredness, unexplained, persistent, that affects daily activities, productive work and relationships.

And this is the time for you to learn about it. The factors we here describe interact and combine to cause fatigue. Intense or light, with or without body aches or brain fog, with or without GI problems, fatigue has different forms.

### What is fatigue?

Fatigue is more than just feeling tired. It is a state of mental and/or physical exhaustion that reduces a person's ability to perform work safely and effectively. It may also manifest itself unrelated to work, like a lack of interest for activities and even for entertainment. It might be associated with feeling tired even after sleep, mood disorders, short term memory problems, lack of enjoyment, inability to concentrate and a constant need for rest. Those affected may feel overwhelmed, withdrawn and emotionally and mentally drained.

Symptoms vary from person to person and might also include lack of motivation, irritability, weight gain secondary to stress eating or weight loss secondary to loss of appetite. Insomnia and mental exhaustion can be present as well. If left unchecked, it can lead to all sorts of serious health problems, including anxiety, depression, burnout, and even hit you with mental exhaustion.

### What causes fatigue?

The first step in addressing fatigue is making sure it is not due to a medical condition.

### Medical conditions associated with fatigue, lack of energy and feeling tired are:

Anemia, hypothyroidism, cancer, metabolic disorders, diabetes, cardiovascular disease, heart disease, lung disease, low sodium, low potassium, low magnesium, low B-12, liver disease, kidney disorder, side effects of medications (like blood pressure medication, cholesterol medication, pain killers, allergy medication, etc.), grief, nutritional deficiency, drug abuse, alcoholism, leukemia, poor sleep, tumors, cancer, side effect of over the counter medications and exercise supplements, poor adrenal function, hormonal decline, amino acid deficit, infection, depression, etc. They all need to be ruled out by a competent physician with proper tests and lab work. Don't postpone this. Once this is done, you can then focus on this publication and understand how the factors we mention here (NT, hormones, toxins, brain-hypothalamus-pituitary-adrenal axis disorder, etc) can combine to make your life difficult and make you feel tired all the time.

### Once those medical conditions are ruled out, you should consider the following eight factors:

#### Nutrient Deficit

Lack of good proteins, amino acids, vitamins and minerals are quite frequent in our country. These generate nutritional deficits

often affecting important metabolic pathways and brain chemicals production. These brain chemicals are known as neurotransmitters (NT), they control all our mental functions and they are strongly dependent on the food we eat, digest and absorb. Certain eating habits, fad diets and wrong dietary approach can generate important nutritional deficiencies that may end up causing NT decline. Mothers feeding their children artificial food should take this in account.

A quick walk through supermarket isles can reveal multiple factory-made foods commonly consumed which may not provide de quality nutrients our brain needs. Artificial (man-made) diet can end up depleting brain and body of essential nutrients, (like vitamin B-12, vitamin B-6, amino acids, omega fat, magnesium, iodine, etc). Teenagers and young adults, so much affected by the stress to succeed and who disregard proper nutrition and consume large quantity of artificial (factory-made) foods can be particularly susceptible.

#### Diet

Wrong diets can slowly cause all kind of metabolic problems. Here are some examples. A strict vegetarian diet in a person genetically set to consume animal protein may end up causing unexpected consequences. Wrong diet and a diet based on factory-made foods is an agent for nutritional decline and NT deficiency. Lack of consumption of the right type and the right amount of protein can also be a cause. A diet containing foods the person is sensitive to can be the cause as well (food sensitive test might be needed). A fat-free diet may deprive brain and body from the vital omega fatty acids.

Whether ketogenic, high carb, fat-free, carb-free diets, high protein or vegetarian, unbalanced diets with improper food composition can affect the body's energy cycle, metabolic pathways and neurotransmitters, EVEN if the person feels well and is unaware of it. Diets that use stimulants, fat burners or metabolic enhancers are even worse. Excess of caffeine and alcohol may make it worse.

Example, a breakfast of cereal or oatmeal and large coffee, later on a lunch of donuts or bagel and coffee and a dinner of pizza or pasta might be all working against you.

According to studies done by the National Institutes of Health "higher adherence to a Mediterranean Diet brings on significant metabolic improvement and slow the rate of energy decline, improving NT function, and enhancing general health. Actually, studies demonstrated that Mediterranean-like Diets improved mentation,

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cognition and intellectual outcomes. Hence, we use and recommend our Florida Mediterranean Diet (we can mail or e-mail you a copy). Without any doubt, dietary improvement, away from the Standard American Diet (SAD) should be the first step. We regularly combine this diet with our gut healing protocol. Quite often we provide a nutrition protocol based on the food sensitive test and nutrigenomics guidelines, disengaging the person from the SAD. An initial 2-3 weeks of Detoxification diet combined with high quality multivitamins offers a beneficial first step approach.

Most of the times we manage this by adapting the Florida Mediterranean Diet according to the Food Sensitivity Test and the genetic background of the person. An initial 2-3 weeks of Vital-Detox program offers a beneficial first step approach.

Example: I follow this dietary plan but I don't consume dairy, lobster, shrimps, sushi, apples, cereal, oatmeal, cream-cheese or turkey, and once a month I do a 'Vital-Detox Program' week, which includes the Vital-Detox detoxification protocol.

But Wait, We Were Addressing Fatigue, what are those neurotransmitters (brain chemicals) have to do with it?

Our brain controls every single function of our body, including walking, typing, digestion, mood, liver and kidney function, heart and lungs, hormones, body temperature, blood pressure, glands, muscles, immune system, etc. All these functions are achieved through communications between the billions of brain cells that constitute our brain. Those brain cells pass chemical-electrical information to one another through the passage of brain chemicals known as NEUROTRANSMITTERS (NT).

There is a strong relationship between NT and fatigue.

These NT are chemicals that enable transmission between brain cells (neurons) and between brain cells and organs, muscles and glands. These communications are vital and it is through these very essential neurotransmitters that proper brain function is achieved. In the brain, NT are involved in managing memory, intellect, problems solving, mood, sex drive, hunger, thirst, satiety, anger, thought process, concentration, sleep, communication, speech, reading, understanding, sensations, behavior, and many more functions. When NT decline or are in imbalance, ANY brain function can be affected. Production and utilization of energy is controlled by NT.

There are over a hundred different brain chemicals encompassing multiple functions. Of those, serotonin, dopamine, epinephrine and norepinephrine are our main concern because they are the four main NT and because of their implications in multiple medical disorders. When you take in account how much mood and psychological disorders and how much fatigue we have in this country you then realize how widespread the NT imbalance is in the general population. When NT transmitters decline, brain functions decline as well, and the resulting mental and neurological disorders are now affecting millions of Americans throughout our country. The problem is very serious and it is fomented by the lack of information of the general population.

Neurotransmitters cannot be orally consumed, nor given by injection or intravenously. The brain itself will not let them in. The only way to re-build NT is to provide efficiently NT precursors. For example, we need an amino acid called tyrosine and certain B vitamins to make dopamine in the brain; if they don't reach the brain we develop dopamine decline. And we need dopamine to make adrenaline, so here you can see how a single deficiency can cause the decline of two very vital NT. Those affected by fatigue (not caused by the above medical

conditions) frequently have NT decline caused by what is known as NT Precursors Deficit, which we can also call : Nutritional deficit of NT-Precursors.

### The Relative Nutritional Precursors Deficit

is a similar process. Individuals following a properly balanced diet, who regularly consume NT-precursors, can still develop precursors-deficit which results in NT decline or imbalance. In other words, the condition arises when adequate nutrition intake cannot meet the brain demands. In these cases, diet is good but unable to be sufficient. The cause is sometimes multi-factorial and not easy to find. Management requires precise amounts of concentrated and purified NT-precursors given following a protocol. We regularly use some of those products in our office.

Attention: humans suffering from fatigue, with or without depression, muscle aches or insomnia, are not suffering from drug deficiency; there is not such a thing as a 'prozac-deficiency-syndrome', 'medication- deficit-disease' or 'xanax-deficiency-disorder'; those people are all suffering NT decline. And NT is what they need.

Here we'll get into something else. All cells in the body produce waste products that need to be eliminated; and this is done using a molecular system called glutathione. This molecule is your 'cellular cleaning lady' and is in charge of neutralizing free radicals, eliminating toxins and waste and keeping the cell clean and functional. Decline in glutathione will allow all kind of waste to accumulate in the cells. Just imagine your sweet home with a clogged toilet for five weeks, with you inside the house.

Here comes a problem. The neurotransmitter (NT) cycle in the brain is intimately linked with this glutathione-detoxification cycle; hence we cannot affect one without the other. If we just give NT-precursors our detoxification system may decline (which is pretty bad), and if we just give glutathione-detoxification precursors then both the serotonin and the dopamine systems might deplete (and that is also pretty bad). If we just give 5-HTP or Tryptophan, we run the risk of depleting dopamine and the glutathione-detox system and we may jump from the frying pan into the fire. There can't be any guessing here; a protocol must be followed. We know that this is difficult to understand and it might need half a book to explain, but that's the way things are.

Hence, the protocol for the management of above conditions is a combination of NT-precursors with glutathione-detox precursors taken simultaneously. The periodic urine tests that we manage in our office assure that the right amount is given.

Just in case you were wondering, yes, individuals suffering from addiction, adrenal fatigue, ADD, ADHD, alcoholism, Alzheimer's Dementia, anorexia, anxiety, bipolar, panic, cognitive decline, chronic fatigue, chronic pain, chronic stress, dementia, depression, fatigue unrelieved by rest or sleep, fibromyalgia, headache, hormone dysfunction, insomnia, migraines, mental fatigue, mood disorders, OCD, Parkinson's, phobias, poor memory, PTSD, restless legs, psychological disorders, psychiatric diseases and schizophrenia, severe tiredness, may be suffering from a combination of NT-collapse combined with glutathione-detox collapse at the same time. You don't rescue those individuals with some vitamins and chicken soup nor with a one week vacation or psychotherapy. Nor with pharmaceuticals, alcohol or marihuana. You rescue them with a combined therapy of NT-precursors combined with glutathione-detox precursors.

Some people think taking plenty of 5-HTP, L-Tryptophan or

SAME is smart, but they are misinformed and they are just tilting the metabolism in the wrong direction and may end up depleting vital neurotransmitters. Some others pride themselves from getting the expensive IV glutathione, but they are just unknowingly pushing themselves to dopamine decline with all its adverse consequences. Some people take those energy drinks containing guarana, 5-HTP and caffeine, which other than temporary excitation bring the individual closer to detox failure and NT decline. The eagerness for stimulation combined with lack of information makes the picture worse. Guiding yourself by the advice of a 'beautiful website' or by the cheap 'recommendation' of a vitamin shop salesman will not make things any easier.

Make no mistake. Taking just 5-HTP or L-Tryptophan or tyrosine may deplete the glutathione-detox system and may push the person deeper into the above conditions. This is essential because the glutathione-detox system (also described as the cysteine-glutathione pathway) keeps the cellular methylation-factory working well. (We'll talk about methylation later on).

A bit of a warning: A lot of products are sold in the internet and health food stores containing 'energy' pills or drinks containing tyrosine, taurine, tryptophan, alpha lipoic, caffeine, special vitamins, and promising better energy, clearer mind, metabolic enhancement, exercise improvement, pre-workout benefits, etc. . However, the recurrent use sacrifices vital metabolic pathways and might replete both NT and the precious glutathione.

Hey, why such a fuzz about glutathione? Because, again, it is the cellular cleaner, removing toxins and free radicals that otherwise would clog the cells with waste and impair their functions. Research has shown that almost all chronic conditions are characterized by glutathione deficiency, like the ones we mention above but also asthma, cancers, cataracts, macular degeneration, glaucoma (open angle only), chronic fatigue syndrome, degenerative diseases, diabetes, autoimmune disorders, all diseases of liver, kidneys, lungs, heart, and digestive system, fibromyalgia, peripheral neuropathy, metabolic disorders, multiple sclerosis, Parkinson's, skin disorders, seizures, tumors, autism, as well as low immunity, cell mutations and poor healing after burns, physical trauma and surgery. This glutathione system, then, is essential for good health AND for prevention of multiple diseases. The combination of NT and glutathione decline is a threat to good health.

Quite often NT imbalance, fatigue, weight gain and hormone decline occur at same time. You don't rescue those individuals with some cheap vitamins and chicken soup nor with a one week vacation or psychotherapy. Nor with pharmaceuticals, alcohol or marihuana. You rescue them with a combined therapy of NT-precursors. Did I mention marihuana?

Marihuana The THC in marihuana might benefit NT and its interaction with dopamine is well known. It can also activate brain cells and alter cellular communication because of its cannabinoid chemical structure. THC can affect brain areas that influence pleasure, memory, thinking, concentration, movement, coordination, and sensory and time perception. THC is able to alter the frontal brain areas that enable a person to form new memories and shift his or her intentional focus. As a result, using marijuana causes impaired thinking and interferes with a person's ability to learn and perform complicated tasks. THC can also activate the brain's reward system, which includes regions that govern the response to healthy pleasurable behaviors such as sex and eating. It is agreed that marihuana may improve and control an enormous amount of medical conditions. The question is: does it really

heal you?

When we know that NT-decline and multiple serious metabolic disorders are caused by the interactions of the eight factors we mention here, be aware that marihuana will not heal the deep NT deficit or your dietary errors, your nutrient deficit, your hormone decline, your clogged detoxification system or the horrible effects of stress. Marihuana might give you relief, but relief is not the same as healing.

Marihuana (THC) (in any form) might benefit NT but will not heal the deep NT deficit nor your dietary errors, your nutrient deficit, your hormone decline, your clogged detox system nor the horrible effects of stress. Marihuana might give you relief, but relief is not the same as healing. However, for those who need it, for those who accept it and for those who are using marihuana (THC or cannabis) in any form, whether they have the 'marihuana-card' or not, cannabis may offer a great positive impact in symptoms-relief, may make life more comfortable, may decrease anxiety and pain / PTSD symptoms, may provide neuro-psychiatric benefits and might help 'normalize' the individual. It's alright to use it as long you understand that you have eight factors to take care of. You can use any form of cannabis on Sunday, yes, but on Monday morning when you wake up these eight factors will still be there.

In our Brain Chemicals Improvement Program (BCIP) we provide both NT-precursors with simultaneous administration of glutathione-detox precursors, easy dietary instructions, comprehensive detoxification protocol and the eight factors we here describe.

\*Fatigue is very common, but it is a symptom, not a disease. It occurs when a dopamine relative nutritional deficit induces low adrenaline (epinephrine) production. There may be a slight case or there may be an advanced state with significant fatigue (mental and/or physical).

So grab this: fatigue occurs from dopamine-adrenaline decline and severe fatigue and what we call severe adrenal fatigue suggests dopamine-adrenaline COLLAPSE. And this is bad. NT collapse is a serious condition. But attention to this: Not everybody needs to engage in a BCIP or other similar program. Medical conditions need to be ruled out. The other seven factors we mention here need to be evaluated, managed and treated first by a physician. Some of those factors could be managed with significant improvement. After those proper steps have been taken and without success, the individual should consider a brain chemicals (NT) improvement program.

In our Brain Chemicals Improvement Program (BCIP) we provide both NT-precursors with simultaneous administration of glutathione-detox precursors, easy dietary instructions and comprehensive detoxification protocol.

This is the moment to make a halt in our path and realize that

- 1) Neurotransmitters (NT) are at the control center of our life, and with their decline our head-to-toes body functions start to decline
- 2) All cells of our body need the detox system to cleanse their waste so they can continue functioning right; and glutathione has to do a lot with that.

Now imagine your muscles, your pancreas, your brain or your sex organs polluted with toxins while not getting the right NT messages. Nothing good will happen. Now open the window and look at our society. See all the people with muscle aches and back pain, all the diabetics, all the people with low hormones, erectile problems, all

the people with fatigue or addiction, all the psychiatric disorders, all the people with depression or anxiety, and all so many with cancer ?. Millions! Now you are learning why. This paper has to do a lot with the answer to this 'why'.

## Toxins

Toxins and chemicals of all kinds have been persistent and common environmental contaminants over the last several decades, and continue to be a permanent threat to human health. They come from multiple sources and invade our body regularly. They include chemicals, pesticides, plastic particles, petrochemicals, colorants, herbicides, fertilizers, some food additives, metal particles (known as heavy metal particles), chemical discharges from industrial plants, multiple air pollutants, water contaminants, colorants in drinks and snacks, etc. It is a common knowledge that 80-90% of most chronic health conditions are triggered by toxins.

From Florida to Alaska and from New York to California the water supply and the water in rivers and lakes are contaminated with chemicals of all kinds, and supermarkets carry vegetables and fruits contaminated with herbicides, pesticides and toxic fertilizers and foods prepared with chemical additives, colorants and even petrochemicals. Toxins are so widespread that you can find them even in breast milk and in the umbilical cord blood of newborns. Check the "Toxin" article in our website ([www.JupiterInstitute.com](http://www.JupiterInstitute.com)).

To certain degree, our body's own detoxification system is capable of eliminating those incoming toxic attacks. This glutathione-detoxification system is natural to us, and has been always there, helping us survive, even when there weren't antibiotics or doctors around. But things changed. For many centuries the agents attacking our body were natural, simpler and not coming in such large numbers. But among the many good things brought to us by the advances in science, industry and technology came a tremendous explosion of new toxins and man-made chemicals: new, not-natural, and in large quantities. As a result, our bodies are overwhelmed.

With progress, new dangers have come to hurt our health and wellbeing. We now have exposure to a huge variety of man-made toxins against which our detoxification system is unable to operate. Our bodies are many times not able to detoxify all the large amount and variety of chemicals to which they are exposed, leading to a continuous process of accumulation of toxins in our tissues and organs.

The accumulation of toxins causes damage in the cells of almost every organ in the body and also leads to imbalance in hormones and metabolism. Toxins, chemicals, pollutants, contaminants, metal particles (like lead, mercury, cadmium, etc) and food additives slowly accumulate and end up causing hormonal, metabolic and neurotransmitter disruption.

People need to come to terms with the fact that toxin accumulation and the disorders they produce causes health decline and numerous diseases, as stated by the National Institute of Environmental Health Sciences (NIEHS). One of the most important concepts you need to remember from this article is that toxins and chemicals from air, water and food are metabolic and Nt disruptors.

Do you think you are an exception? Do you think that this is like in the war, as long as you are far away the bullets will not hurt you? There is no 'far away' here; toxins are all around us, in the soil, vegetables, foods and drinks. We all have toxins inside.

The Environmental Protection Agency (EPA) ([www.epa.gov](http://www.epa.gov))

publishes a list of the drinking water contaminants, which include: arsenic, asbestos, antimony, cadmium, barium, benzene, carbon tetrachloride, dalapon, dioxin, phtalates, dichloroethane, endrin, fluoride, thallium, trichloroethane, oxymal, nitrates, chlorobenzene, radium, mercury, lead, PCBs and nickel. These products come from additives, discharges from refineries and waste plants, ceramics, electronics, discharges from industries, corrosion of pipes and plumbing systems, runoffs from fertilizer deposits, sewage, erosions, chemical plants, decay of man-made deposits, discharges from plastic and rubber factories, residues from all kind of electronic devices thrown in canals and rivers, etc. All these contaminate the drinking water throughout our country and are capable of damaging brain cells and their axons.

Those toxins hurt our neurotransmitters, and imbalance in NT causes mental and physical disorders. In addition to above medical disorders, NT decline can cause stress, attention deficit, hypertension, insomnia, higher sensitivity for pain, poor digestion, autism, psychosis, agitation, fatigue, restless legs, lack of motivation, poor mood, pains, difficulty losing weight, cravings, sedation, psychologic imbalances, headaches, uncontrolled appetite. The chronic stress combined with adrenal imbalance may lead to poor immunity, decreasing the defense against infections and cancer. The chronic fatigue and pains may throw the person into disability, can destroy his finances and his marriage. People end up losing their jobs for one reason or another, and all these conditions make them go from doctor to doctor, taking numerous medications and getting several side effects, without ever finding a solution, a relief or an improvement.

Aware of all these, our office teach and encourage patients to learn about toxins and practice some form of detoxification. We use 'detoxification kits' from laboratories affiliated with the Anti-Aging Academy.

## Habits, Drugs and Medications

Alcoholism, drug abuse, stimulants, opiates and multiple medications are capable of affecting NT balance. Among them are caffeine, guarana and most of the energy drink people buy over the counter and even in gas stations. Certain drugs and substances such as caffeine, nicotine, ephedra, NutraSweet, antidepressants, and some cholesterol lowering medications deplete neurotransmitter levels leading to neurotransmitter imbalances. There are multiple medications that have shown to cause depletion of serotonin and other NT. These are the medications prescribed to increase the activity of serotonin in the brain such as fluoxetine (Prozac, Sarafem), paroxetine (Paxil), sertraline (Zoloft), Luvox, Citalopram (Celexa), Lexapro, etc. The same holds true for medications that block the re-uptake of serotonin and catecholamines such as Effexor, Cymbalta, and Pristiq. Ritalin and the weight loss medication Phentermine can cause the same.

Sensory overload happens when something around us overstimulates one or more of our senses. Perceiving sounds, music and TV, for example, require neurotransmitter (NT) processing. The more intense and long the experience the more NT are used and overused. This can disrupt the neurotransmitters balance and cause unwanted consequences. There are many environmental elements that affect individuals: daily long drive to work, excessive fast driving, overuse of internet, TV, movies and cable, videogames, loud continued noises, excessive loud music. They can all adversely affect NT and cause irritability, mental fatigue, attention disorders, sleeplessness, and more. Combine that with excess of coffee, carbs abuse and stress and you are in trouble.



## Stress

Stress is a known cause of NT imbalance and decline. Emotional events and stress have an adverse reaction over the NT and on our capacity to detoxify. Fear, anger, grief, work related stress, driving stress, financial and family stress, divorce and recurrent state of anxiety produces this effect. Working as a truck driver, policeman, nurse, doctor, soldier and paramedic are just few examples of high stress occupation. Housewife stress, financial problems and work related stress are quite common. Any of these events or occupations, carried for prolonged time, can and will interfere with NT balance and our liver detoxification process, allowing toxins to accumulate. It is a fact, prolonged periods of stress can deplete neurotransmitters levels. Our fast paced, fast food society greatly contributes to these imbalances. Moreover, the sensory overload that occurs from our brain being bombarded by sounds, electronic games, cell phone overuse, rapid visual effects from television and movies, noise, artificial light, etc., does have an adverse effect on our NT. Management requires a very specific type of adaptogens (never from websites or internet) and guidance regarding stress management.

## Gut Effect

When our gastrointestinal system is not working properly then either the digestion, the absorption or the elimination work right and all kind of complications occur. The combination of artificial (man-made) foods, excess of carbohydrates, processed carbohydrates, stress, food chemicals, yeast, food sensitivity reactions, enzyme deficit, abnormal bacteria and the use of anti-acids and stomach-acid blockers causes poor digestion of foods. The lack of proper digestion causes poor absorption of nutrients and allows the food in our intestines to go through abnormal fermentation and putrefaction with consequent productions of toxins inside the intestine. This process allows abnormal bacteria and yeast to overgrow ( a process called Dysbiosis) which in turn produces local toxins, which then leak through the wall of the intestine and can spread through organs and brain. (Read the articles in our website, especially the ones titled 'mental health', food sensitivities', 'stress' and 'hormones and fatigue').

The association between food, gut and mental health is a reality. As wrong foods and food sensitivities cause dysbiosis, gut flora abnormalities and bacterial overgrowth, bad things occur. The altered gut flora can impact human brain in numerous ways:

- 1) Bacterial components, such as LPS, may produce nervous system inflammation
- 2) Bacterial proteins may stimulate dysfunctional responses of the brain
- 3) Bacterial enzymes may produce neurotoxic metabolites
- 4) Gut microbes can produce hormones and neurotransmitters that are identical to those produced by humans, causing metabolic adversities
- 5) Gut bacteria may cause all kind of metabolic alterations and neurotoxicity.

Through these varied mechanisms, gut microbes shape the architecture of sleep and stress reactivity of the hypothalamic-pituitary-adrenal axis. They influence memory, mood, and cognition and may be involved in a range of disorders, including alcoholism, chronic fatigue, fibromyalgia, restless legs syndrome, etc.

Since diet has a significant impact on composition and function of

the human gut flora, change in dietary patterns should be considered when attempting to relieve the impact of gut microbes on the brain. Don't look the other way, the food you are eating or giving to your kids might be directly or indirectly responsible of the mental health changes.

You don't fix this with probiotics. You fix it with precise food elimination guidelines, a food sensitivity test, gut healing protocol, the 'Rs' of detox (see our detox article) and functional foods. The use of NT precursors and amino acids precursors' replacement needs to be strongly entertained.

## Hormones

I'll be short here because this topic needs a whole book. Suffice to say that thyroid, adrenal and sex hormones all interact with NT. Thyroid dysfunction is known to interfere with NT function, and in addition, many studies report interactions between sex hormones and the main NT. Many brain regions have been shown to be affected by estrogen and progesterone, such as the amygdala, the hypothalamus, and the hippocampus. Research has demonstrated the critical role of sex hormones in mediating effects on memory, intellectual functions, mood, and cognition through their influence on NT. Although this is a complicated field, the take home message is that hormone changes cause neurotransmitter imbalances. The relationship between adrenal gland and brain's neurotransmitters has been studied in length. The brain-hypothalamic-pituitary-adrenal axis is a two way street through which the adrenal glands can adversely affect neurotransmitter functions.

## Combination

Toxins whether coming from the environment or leaking through the wall of the intestine into the blood stream, (a process called Leaky Gut) accumulate everywhere in the body. Individuals who suffer chronic stress, abuse carbohydrate and 'junk' food and take daily stomach acid-blockers are good candidates for this type of intoxication. In addition, all those individuals who have Dysbiosis for whatever reason, or have (without knowing) a Silent Bowel Illness (SBI) (a combination of irritation, inflammation and loss of natural protection), are also susceptible to poor absorption of NT-precursors. Individuals with unhealthy lifestyle habits, like 'junk food eaters', 'coffee abusers', those who use frequent antibiotics, those who overtake large amounts of poor quality vitamins, alcohol abusers, drugs abusers, consumers of foods known to irritate the digestive system, are all at risk of NT decline and imbalance. If in addition they develop low hormones and adrenal function disorder, they will be then affected by several problems at the same time.

Just imagine an individual affected by silent dysbiosis who is also very stressed out from work and family, who drinks plenty of coffee, abuses carbs, whose hormones start to decline and without knowing start to have a decline in neurotransmitters and adrenal function.

## Where is this fatigue coming from?

When stressful situations occurs, whether you are in danger or not, the response stems from the hormone adrenaline, also called epinephrine. Adrenaline is produced in the adrenal glands as well as some of the brain cells and is the hormone that triggers the body's fight-or-flight response. This reaction causes air passages to dilate to provide the muscles with the oxygen they need to either fight danger or flee. Adrenaline also triggers the blood vessels to re-direct blood flow to heart and lungs, and causes a noticeable increase in strength

and performance, as well as heightened awareness. Adrenaline is an important part of your body's ability to survive, but sometimes the body will release the hormone when it is under stress but not facing real danger. This can create some problems since excessively high levels of the hormone due to stress without real danger can cause metabolic and neurological disorders. However, problems can get even worse when the excess of adrenal gland work pushes it to fail. After all, the adrenal gland is a gland and can only secrete so many hormones in one day. The constant demand in an environment full of toxins, stress and bad food hurts its function and induces its failure. When people are faced with long-term stress, at work or at family, etc., their adrenal glands cannot keep up with the body's need for these hormones. When this happens, symptoms of "adrenal fatigue" (also called adrenal insufficiency) may appear. Adrenal insufficiency is caused by damage to the adrenal glands or a problem with the pituitary gland. The result is a decline in the two vital adrenal hormones: adrenaline and cortisol.

People think that we need a strong psychological blow to develop this state, however studies show that mental fatigue (and its resulting physical fatigue) can be induced by daily events in healthy people.

Additional symptoms: tiredness, weariness, not being able to finish a task, lack of energy, hard to work physically and mentally. With some kinds of fatigue, even sleep doesn't help. Fatigue is very common.

Once you ruled out medical diseases, the next step is to address fatigue as a neurological disorder centralized in the brain. Different brain structures known as hypothalamus, pituitary gland, amygdala and cortex are involved and have their neurotransmitters connections in disarray.

Stress is a reaction to a challenging event. In the short term; stress can be helpful, as it makes people more alert and gives motivation and energy to get things done. In a way, the stress reaction is good as it allows the individual to survive and accomplish the daily work. However, long-term stress can lead to serious health problems in both men and women. Somehow women are more likely than men to report symptoms of stress, including malaise, headaches and upset stomach, and are also more likely to have mental health conditions that are made worse by stress, such as foggy brain, depression or anxiety.

During stressful events, dangerous or not, the body releases hormones, such as adrenaline, which gives a burst of energy that helps the person cope and respond to that event.

Stress can range from mild and short-term to more extreme and long-lasting. Chronic (long-lasting) stress can affect our mental and physical health in many ways. Stress is a reaction to many different things. Examples of common causes of short-term stress include: driving, difficult tasks, getting stuck in traffic, arguments with boss or spouse, financial problems, deadlines, exams, grief, disease, etc. Examples of common causes of long-term stress include persisting effects of traumatic events, assault, work, sour relationships, emotional problems, poverty, etc.

On many occasions the detrimental effects of stress can be hard to notice, and individuals can go through slow and progressive changes that affect, and are affected by, the eight factors I described above. By the time the fatigue has developed, affecting activities of daily living, family life, work, studies, relationships, sex life, productivity, etc., a complex mini-storm has been brewing involving HPA (the Hypothalamic-Pituitary-Adrenal axis), NT, adrenal cortisol, sex hormones, lack of toxin cleansing and more.

Often, by that time, the metabolic adversity has become more

complex making it harder to manage. This represents a problem since patients want a quick fix to what took years to develop. But quick fix ain't going to happen, hence the frustration in dealing with those situations.

The nervous system has several divisions: The central division involving the brain and spinal cord and the peripheral division consisting of the autonomic and somatic nervous systems. The autonomic nervous system (ANS) has a direct role in physical response to stress and is divided into the sympathetic nervous system (SNS), and the parasympathetic nervous system (PNS). When the body is stressed, the SNS contributes to what is known as the "fight or flight" response. The body shifts its energy resources toward fighting off a life threat, or fleeing from an enemy. The SNS signals the adrenal glands to release hormones called adrenalin (epinephrine) and cortisol (see Endocrine System). These hormones, together with direct actions of autonomic nerves, cause the heart to beat faster (see Cardiovascular System), respiration rate to increase (see Respiratory System), blood vessels in the arms and legs to dilate (see Musculoskeletal System), digestive process to change and glucose levels (sugar energy) in the bloodstream to increase to deal with the emergency (see Gastrointestinal System).

The SNS response is fairly sudden in order to prepare the body to respond to an emergency situation or acute stress, short term stressors. Once the crisis is over, the body usually returns to the pre-emergency, unstressed state. This recovery is facilitated by the PNS, which generally has opposing effects to the SNS. But PNS over-activity can also contribute to stress reactions, for example, by promoting bronchoconstriction (e.g., in asthma) or exaggerated vasodilation and compromised blood circulation. Both the SNS and the PNS have powerful interactions with the immune system, which can also modulate stress reactions. The central nervous system is particularly important in triggering stress-responses, as it regulates the autonomic nervous system and plays a central role in interpreting contexts as potentially threatening.

Chronic stress, experiencing stressors over a prolonged period of time, can result in a long-term drain on the body. As the autonomic nervous system continues to trigger physical reactions, it causes wear and tear on the body. It's not so much what chronic stress does to the nervous system, but what continuous activation of the nervous system does to other bodily systems that become problematic.

When someone perceives a situation to be challenging, threatening, or uncontrollable, the brain initiates a cascade of events involving the hypothalamic-pituitary-adrenal (HPA) axis, which is the primary driver of the endocrine stress response. This ultimately results in an increase in the production of steroid hormones called glucocorticoids, which include cortisol, often referred to as the "stress hormone."

### The HPA Axis

During times of stress, the hypothalamus, a collection of nuclei that connects the brain and the endocrine system, signals the pituitary gland to produce a hormone, which in turn signals the adrenal glands, located above the kidneys, to increase the production of cortisol. Cortisol increases the level of energy fuel available by mobilizing glucose and fatty acids from the liver. Cortisol is normally produced in varying levels throughout the day, typically increasing in concentration upon awakening and slowly declining throughout the day, providing a daily cycle of energy. During a stressful event, an increase in cortisol can provide the energy required to deal with prolonged or extreme challenge.

The HPA axis (Hypothalamus-Pituitary-Adrenal) is affected and the adrenal gland secretion of cortisol and adrenaline is impaired as well, with resulting decline in the production and utilization of energy. Neurotransmitters like dopamine, substance-P, serotonin and norepinephrine are all involved, and their decline is a key player in the development of fatigue. The effect of consequent hormonal decline and the failure of the glutathione-detox system add up to the complexity of this condition.

Management is not easy, as brain chemicals are not well understood by the common population who wants a fast and successful relief for their fatigue. There is no instant solution here. In addition, most people

want to continue their routine without accepting that a change is needed. That may not be possible either. Management requires reviewing this publication and understanding it, then evaluating which factors are affecting you, then treating appropriately the relative nutrient decline, fixing the gut, managing hormones and thyroid, working on the stress factors, adjusting the diet, etc. . The person might be affected by several of the eight factors I describe which need to be evaluated and managed. We address this panorama of disorders step by step, doing the necessary testing, evaluating and supplying sex hormones, managing supplements and nutrition, providing NT-precursors, counseling on detoxification, working on possible stress factors, healing the gut, etc.