The Vagus Nerve’s Role in Chronic Fatigue, Depression, Obesity, and Other Common Diseases

by Chris D. Meletis, ND, and Kimberly Wilkes

Many common diseases and disorders that plague us today have their roots in a nerve that the average person doesn’t know exists. It’s called the vagus nerve, and it plays a role in everything from obesity to heart health to kidney disease and depression. In fact, new research is emerging that infections in this nerve are involved in chronic fatigue syndrome.

Vagus is the Latin word for “wandering,” because this nerve extends throughout much of the body. The largest nerve in the autonomic nervous system, the vagus nerve begins in the medulla oblongata of the brainstem and then extends into every chest and abdominal organ from the neck to the transverse colon with the exception of the adrenal glands. This nerve also regulates some skeletal muscles. The vagus nerve involves both afferent neurons (sensory neurons) and efferent neurons (motor neurons), although the majority of its neurons (65% to 80%) are afferent neurons, which send sensory information about the status of our organs to the central nervous system. Efferent vagus nerve fibers supply the pharynx and back of the throat with nerves and initiate the gag reflex.

It was once thought that the vagus nerve affected only the stomach and heart, but now we know that it casts a much wider net in the body and that it has a considerable number of functions far beyond what was initially thought. In this article, we will discuss the many ways that the vagus nerve affects your health.

Chronic Fatigue Syndrome

It has long been suspected that viral infections may trigger chronic fatigue syndrome and that an ongoing immune response may lead to the debilitating fatigue associated with the syndrome. Functional medicine has long held that it is individual susceptibility of the host that creates the ecology for a given disease state to manifest. I have long held that the vagal nerve plays a role in chronic fatigue and countless other common ailments, which has been also postulated by scientist Michael B. VanElzakker. He presents a convincing argument that infection of the vagus nerve may be responsible for this disorder.

When an infection lands on immune cells’ radar, they release pro-inflammatory cytokines, which are detected by receptors of the vagus nerve. The receptors signal the brain to initiate fatigue, fever, myalgia, depression, and other symptoms of a cold, flu, or viral or bacterial infection. VanElzakker contends that chronic fatigue symptoms are a more prolonged version of those normal sickness symptoms and that chronic fatigue symptoms are triggered when any virus or bacterium infects the vagal ganglia (a structure containing nerve cells). These virus- or bacteria-activated cells can assault the vagus nerve with proteins known as pro-inflammatory cytokines and other substances that signal the development of sickness symptoms. This hypothesis proposed that any infection of the vagus nerve can lead to chronic fatigue syndrome and that not just one virus or bacterium is responsible for chronic fatigue but rather that any pathogen can cause the disorder.

Depression, ADHD, and Other Cognitive Disorders

The vagus nerve is involved in cognitive health and emotional well-being. Vagal nerve stimulation is commonly used to treat drug-resistant epilepsy and depression. It also is used to eliminate fear and anxiety and is involved in our response to traumatic events. The vagus nerve determines how likely you are to be affected emotionally by a trauma long after it has concluded.

A marker of increased emotional sensitivity to trauma is reduced heart rate variability, an indicator that the vagal nerve is not working properly. The vagus nerve slows the heart rate during safe, nontraumatic conditions. However, in response to threats, the heart-rate inhibiting effect of the vagus nerve stops, allowing the sympathetic nervous system to mobilize defense responses and heart rate increases. Ongoing exposure to conflict and threats may impair vagal system function over time. This results in a reduced ability of the body to adapt to stressful events.

Heart rate variability that operates at a higher level during nonstressful times is thought to be a sign that a person has a healthy ability to regulate emotions and cope with stress. A vagus nerve that is operating optimally is thought to reflect psychological flexibility, emotional self-regulation, and positive adaptation. On the other hand, low resting state heart rate variability is a sign of a reduced ability to control emotional responses to stressful events. Reduced resting heart rate variability is linked to greater trauma exposure and mental disorder. It also is associated with worse physical health, PTSD, depression and anxiety, and aggression and anger. People who have reduced resting heart rate variability also are more vulnerable to stress and it takes them longer to recover from a stressful experience. In one study of 45 people with post-traumatic stress disorder (PTSD), depression, and intermittent explosive disorder and 29 controls who did not have these...
disorders, resting heart rate variability was significantly lower in the people with the mental disorders compared with the controls.  

The vagus nerve also plays a role in reducing aggressive behavior in attention-deficit hyperactivity disorder (ADHD). In a rodent model of ADHD, a substance that reduced aggression no longer worked when the vagus nerve was removed. In ADHD, the autonomic nervous system does not work properly, resulting in poor control of the heart. Cardiac vagal control is lower in children with untreated ADHD compared with healthy controls. Children with ADHD experience reduced cardiac vagal control reactivity when performing tasks involving self-regulation and regulation of emotions.

The means by which the vagus nerve affects mental health may be due to its involvement in the gut–brain axis. The vagus nerve is one of the primary means of communication between the gut and the brain. The microbiota may interact with the vagus nerve to send signals to the brain.

Weight Management and Food Intake

In the gastrointestinal tract, afferent vagus nerves control food intake. However, in obesity, GI vagal responses to stimuli are modified leading to a shift away from satiety toward increased food intake. Vagal pathways that aren’t operating properly are involved in the development of obesity and the inability to lose weight already gained. Many studies have shown that the gut microbiota is involved in weight maintenance. The gut microbiota assists in the production of short chain fatty acids (SCFAs), which in turn results in the production of substances that can then act on afferent vagus nerves to increase satiety. Specifically, the SCFA butyrate can directly activate vagal afferent nerves in the small intestine.

Gut hormones activate vagal afferent neurons, the primary neural pathway by which information about ingested nutrients reaches the central nervous system (CNS) to play a role in both GI function and satiety. Vagal afferent neurons can also become resistant to the hormone leptin, which regulates appetite. Furthermore, in a rodent model, a high-fat diet produced changes in the gut microbiota and this imbalance resulted in gut inflammation and “leaky gut.” Through toxins escaping into the bloodstream, this led to changes in the function of vagal neurons.

Another advantage of the vagus nerve is that it can counteract the inflammation that occurs as a person gains weight. The vagus nerve also has the ability to reduce insulin resistance. Researchers fed rats either a high-fat diet or a high-fat diet together with vagus nerve stimulation. The rats exposed to only a high-fat diet developed a number of damaging effects in the brain, including insulin resistance, oxidative stress, inflammation, and the cell death known as apoptosis, which all lead to cognitive decline. However, the group fed a high-fat diet together with vagus nerve stimulation had an improvement in peripheral and brain insulin sensitivity as well as reduced brain mitochondrial dysfunction and cell apoptosis. Vagus nerve stimulation also enhanced cognitive function.

Conversely, an overly active vagus nerve can play a role in bulimia nervosa. Increases in vagal afferent activity are linked to binge-eating and vomiting in this condition. Inhibiting vagal afferent activity in subjects with severe bulimia nervosa results in a rapid and pronounced decline in binge-eating and
Vagus Nerve

vomiting compared with controls as well as reduced depressive symptoms.13

Cardiovascular
Cardiovascular disease interferes with the regulatory function of the autonomic nervous system. The two branches of the autonomic nervous system are the parasympathetic and sympathetic nervous systems. These must remain in balance in order to properly regulate the heart’s electromechanical function, resulting in the ideal cardiac output after exposure to a number of environmental and metabolic stressors. Diseases such as chronic heart failure and hypertension are linked to autonomic imbalances characterized by increased sympathetic drive and reduced parasympathetic activity. Vagus nerve stimulation normalizes autonomic function and improves cardiovascular function and heart failure symptoms.14

In obese, insulin-resistant rats fed a high-fat diet, vagus nerve stimulation resulted in a pronounced decline in plasma insulin, total cholesterol, triglycerides, LDL, and visceral fat. Vagus nerve stimulation also significantly reduced blood pressure, improved heart rate variability and left ventricular function, and enhanced cardiac mitochondrial function.15 Vagus nerve stimulation also has reduced blood pressure in a rat model of hypertension.16

Furthermore, research has shown that stimulation of the vagus nerve is beneficial in stroke. Recombinant tissue-type plasminogen activator is used within 4.5 hours of a stroke. This results in a rapid reintroduction of cerebral blood flow. While this has its advantages it also leads to an excessive inflammatory response that worsens ischemic injury, which can be harmful to the patient. In animal models of endotoxemia (toxins in the blood), stimulation of vagus nerve efferents results in a significant decline in systemic levels of pro-inflammatory mediators such as tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), interleukin 1 beta (IL-1β), and the DNA-binding protein, high-mobility group box 1 (HMGB-1).17

Stimulation of the vagus nerve also is neuroprotective leading to a decrease in infarct volume during the acute phase of ischemic stroke.17 Researchers induce strokes in rodents by blocking the middle cerebral artery. When vagal nerve stimulation is begun within 30 minutes after blocking the artery, infarct volume is reduced by nearly 50%, and there is an improvement in neurological score.18

In hypertensive rats prone to developing strokes, vagus nerve stimulation prevents the endothelial dysfunction caused by high blood pressure. It also prevents the aortic stiffening that would otherwise occur in these animals.19 Researchers believe that the anti-inflammatory actions of vagus nerve stimulation may be responsible for these beneficial effects.

Immune System Support
The vagus nerve’s regulation of inflammation is involved in immune system activity. During infection or injury, sensory input triggered by inflammation travels through the afferent vagus nerve to the brainstem, from which efferent nerves send signals that terminate in the spleen and other tissues.20 This assists in communication between immune cells, indicating that the vagus nerve is important for optimal functioning of the immune system.

Roemheld Syndrome
This disorder is characterized by arrhythmia (irregular heart beat), tachycardia (rapid heart rate), gastrointestinal complaints, intestinal gas, panic attacks, confusion, anxiety, depression, blood pressure fluctuations, dizziness and balance issues, lightheadedness, fainting, nausea, and tinnitus. In this syndrome, problems in the gastrointestinal tract or abdomen trigger heart-related symptoms.

While researching the symptoms in the 1920s to 1940s, Dr. Ludwig Roemheld discovered that the vagus nerve plays an important role in the syndrome, since this nerve is connected to the brain, heart, lungs, and GI tract.21 Changes in the gut can affect the vagus nerve, causing heart rate to slow. This leads to the activation of autonomic reflexes, which increase blood pressure and heart rate.

Other Conditions Related to Vagus Nerve Function
Optimal functioning of the vagus nerve is involved in many other aspects of health. Stimulation of the vagus nerve reduces trigeminal pain, and the vagus nerve may be involved in a rare type of trigeminal neuralgia known as vagoglossopharyngeal neuralgia.22,23 Vagus nerve stimulation also reduces migraine and cluster headaches.22,24 Additionally, vagus nerve stimulation has prevented acute kidney injury in rodent studies.25 Another way in which the vagus nerve affects health is its important involvement in the reflex relaxation of the lower esophageal sphincter, which has implications for gastroesophageal reflux disease (GERD).26,27

Another interesting aspect of the vagus nerve’s involvement in health is its ability to trigger the cough reflex.28 Furthermore, inflammatory conditions respond well to vagus nerve stimulation, due to this nerve’s anti-inflammatory abilities.20 Researchers believe that vagus nerve stimulation could be used successfully in inflammatory bowel diseases, irritable bowel syndrome, postoperative ileus, and rheumatoid arthritis.29

Natural Ways to Support Vagus Nerve Function
Acupuncture is one means by which the vagus nerve can be stimulated. The reason why acupuncture produces so many beneficial effects may be because it can increase the vagus nerve’s ability to regulate inflammatory responses in internal organs.30 The autonomic nervous system is involved in acupuncture’s benefits because it is the connection between external sensory inputs and internal organ responses. Signals from many acupuncture points may travel to the vagus nerve, where they affect the function of the autonomic nervous system.31 Studies also have shown that tai chi can influence vagus nerve function.31 Heart rate variability increases immediately after both young and old men perform tai chi.32

As mentioned earlier in this article, heart rate variability is a marker of vagus nerve function. Studies have shown that a number of supplements can improve heart rate variability and vagus nerve function. For example, researchers investigated the effects of L-citrulline on resting heart rate variability and blood pressure in obese postmenopausal women.33 The researchers
randomly divided the women to receive either L-citrulline or a placebo. Supplementation with L-citrulline resulted in improvements in heart rate variability and blood pressure as well as a significant increase in vagal tone. Beetroot juice is another supplement that increases heart rate variability at rest and during aerobic exercise in addition to reducing systolic blood pressure in human subjects.34 In subjects who consumed a multivitamin-mineral preparation together with 300 mg guarana, heart rate variability remained stable, whereas in participants consuming either caffeine or a placebo, heart rate variability significantly declined.35

Omega-3 fatty acids are another nutrient shown to affect vagus nerve functioning. Higher concentrations of the omega-3 fatty acid docosahexaenoic acid (DHA) are associated with lower blood pressure and resting heart rate and higher heart rate variability.36 Another study found that higher intakes of omega-3 fatty acids were linked to higher heart rate variability during sleep-time.37 A review of the medical literature showed that short-term fish-oil supplementation enhanced vagal tone and thus improved heart rate variability.38

Conclusion
Optimal functioning of the vagus nerve can drive many aspects of our health. Chronic fatigue, depression, ADHD, obesity, cardiovascular conditions, and impaired immunity are all related to reduced function of the vagus nerve. Stimulating the vagus nerve has relieved trigeminal nerve pain and migraine and cluster headaches and prevented acute kidney injury. Through its inflammation-dampening effect, vagus nerve stimulation could also be used successfully in inflammatory bowel diseases, irritable bowel syndrome, postoperative ileus, and rheumatoid arthritis. Acupuncture and tai chi can improve vagus nerve activity; and L-citrulline, beetroot juice, multivitamins, guarana, and omega-3 fatty acids have all been shown to increase heart rate variability, a marker of optimal vagus nerve function.

Notes


Dr. Chris D. Meletis is an educator, international author, and lecturer. His personal mission is “Changing America’s Health One Person at a Time.” He believes that when people become educated about their bodies, that is the moment when true change and wellness begins. Dr. Meletis served as dean of naturopathic medicine and chief medical officer for 7 years at National College of Natural Medicine (NCCN) and was awarded the 2003 Physician of the Year award by the American Association of Naturopathic Physicians. www.DrMeletis.com.