Decoding the Research: The Neural Tourniquet
By Kelly Owens

Over the last twenty years, researchers at the Feinstein Institute have been investigating how to harness the power of the vagus nerve to treat and cure inflammatory diseases. The vagus nerve runs up and down both sides of the neck, a communication highway between the central nervous system and the immune system. The afferent limb of the nerve communicates using 80-90% of the vagus nerve's fibers upward from the peritoneal cavity (the stomach and gut) up to the brain, and the efferent limb communicates downward from the brain to the heart and spleen. This back and forth communication composes what Dr. Kevin J. Tracey has coined as 'the inflammatory reflex.'

Since discovering that electrically stimulating the vagus nerve has an anti-inflammatory effect on autoimmune/cytokine-based diseases, researchers at Feinstein continue to investigate the neural pathways to understand how the signals in the nerve communicate and what they are capable of when stimulated. These investigations led to the hypothesis that the vagus nerve can control internal and external bleeding through the use of a proprietary device called the Neural Tourniquet.

Bleeding is the most common preventable cause of death in traumatic injury, the fifth leading cause of death in this country, and the first cause of death in children and in adults up to age 45. Blood loss related to trauma, hemophilia, surgery, and post-maternal hemorrhage are areas of medicine that currently look like the wild west in terms of care, prevention, and treatment. Dr. Jared Huston has stated that bleeding is the disease no one talks about, because beyond the use of the classic tourniquet, no one has an answer for prevention and treatment.

The first use of the tourniquet during combat was at the Battle of Hydaspes in 326 BC, when Alexander the Great invaded the Indus River valley. This method of treatment wasn't named until 1718, when a French surgeon, Louis Petit, developed a screw-like device to be placed over the wound and screwed into place to stop the blood flow. From the French verb '*tourner'*, meaning *to turn,* Petit named the device a *tourniquet*.

Dr. Tracey came up with the idea for the neural tourniquet while in a meeting with DARPA. The defense agency asked if there was anything else (other than inflammation) that could be curbed by stimulating the vagus nerve, and Dr. Tracey said it could work for bleeding. He explained how when a worm is cut open, cytoplasm leaks out, bacteria gets in, and the little worm body works hard to fire neural signals at the site of the wound in order to close it as quickly as possible. He said that the same is true for the human body – nerves fire in order to draw platelets to the site of injury in order to clot and secure the wound. He hypothesized that stimulating the vagus nerve could cause it to happen faster… and over fifteen years of research later, it was proven to be the case.

Through multiple experiments using animal models with both external and internal bleeding, it was discovered that vagus nerve stimulation can reduce the amount of blood loss by up to 50% and decrease the amount of bleeding time by 40%, due to expedited clot formation at the site of the injury.

It turns out that vagus nerve stimulation increases the generation of thrombin. Thrombin is a clotting enzyme; the more thrombin in the blood, the more it will clot. Vagus nerve stimulation increases and accelerates the production of thrombin which increases clot formation, but interestingly enough, only does so at the site of the injury. Thrombin is not increased systemically throughout the body – only locally at the site of bleeding. This is important, because a systemic increase in thrombin can lead to adverse events like stroke, etc. This targeted pathway allows for things to remain stable throughout the rest of the patient's system, while focusing energy on where it's needed immediately.

So why does stimulating the vagus nerve cause this series of events that slows and stops blood loss? According to Dr. Jared Huston, the vagus nerve and the brain are educating cells in the blood as they pass through the spleen, teaching them how to respond more quickly when there is an injury.

Platelets are a type of cell that's main job is clotting. Dr. Huston and his team measured platelet activation using two known markers for platelet formation: Jon-A and P-selectin, as well as two agonists, ADP and thrombin. Think of Jon-A and P-selectin as the reactors. Now, think of ADP and thrombin as the instigators. Dr. Huston and his team used the instigators to see how the reactors would, well, *react.*

Knowing that nicotine has the anti-inflammatory effect on the cholinergic pathway, which is how the vagus nerve communicates, Dr. Huston and the team treated animals with saline or nicotine to see how the platelets would respond. An hour after treatment, the platelets were not activated for increased clotting. However, when stimulated with thrombin (our instigator), the platelets from the nicotine-treated animals activate, with an increase in both reactors Jon-A and P-selectin, showing that the 'priming effect' of platelets require both stimulation of the cholinergic pathway and the instigator, thrombin.

The other instigator, ADP, did not cause the reactors (Jon-A and P-selectin) to react, therefore showing that the priming of platelets to increase clotting at the site of injury is specific to the thrombin pathway – but where is that happening? Where are the platelets being primed to be the medics on the battlefield?

Based on the inflammatory reflex, it is happening in the spleen. When the spleen is removed, the mechanism for the Neural Tourniquet breaks down, and stimulation of the vagus nerve (or intravenous treatment of nicotine) will not prime the platelets to act as we need them to.

According to Dr. Jared Huston, the Neural Tourniquet will transform the medical field in the next ten years: from emergency trauma bleeding in the ER, at the scene of an accident, and the battlefield, to prevention via pre-surgery stimulation, post-partum bleeding, and hemophilia, the opportunities to save lives are seemingly endless with this revolutionary bioelectronic discovery.