

The Portable Neuromodulation Stimulator (PoNS™) FACT SHEET

What is the PoNS Device?

The Portable Neuromodulation Stimulator (PoNS) is an investigational non-invasive wearable medical device being studied for the treatment of neurological symptoms caused by disease or trauma. PoNS Therapy combines use of the device with physical therapy and is currently being studied in a pivotal, multicenter, clinical trial for the treatment of balance disorder related to mild to moderate Traumatic Brain Injury (mTBI). PoNS Therapy is also being evaluated in the treatment of symptoms related to other neurologic diseases such as Multiple Sclerosis (MS) and Cerebral Palsy (CP).

The PoNS device represents the first in a series of non-invasive devices -- based on the patented PoNS Therapy platform -- designed to amplify the brain's powerful ability to heal itself. This is part of a new approach being studied for "symptom treatment" for the rising number of patients who have experienced loss of function as a result of neurological disease or trauma.

What is the potential impact of the PoNS Therapy?

As a result of their disease or injury, many patients are left with disrupted neural networks in the brain that are unable to carry nerve impulses completely or efficiently. Neural impulses are the signals responsible for directing bodily functions, such as movement control or sensory perception. Researchers believe that significantly increasing activation of these neurons through electrical stimulation, combined with physical therapy, may help reorganize and reactivate the networks responsible for those functions.

While physicians and patients turn to available options to manage a host of neurological symptoms today, for millions living with these chronic disorders, limited treatment options exist that actually help patients rehabilitate lost function. The PoNS device is being studied as new potential option for the treatment of these chronic neurological symptoms of disease or trauma.

What is the growing science behind the PoNS Therapy?

The PoNS device is based on almost 40 years of research in the field of *neuromodulation* – the use of neurostimulation to intentionally change and regulate the electrochemical environment of the brain. Neuromodulation enhances *neuroplasticity*, the brain's ability to restructure or relearn in response to new experiences, sensory input and functional demands.² The process of neuroplasticity underlies all cerebral learning, training, and rehabilitation.

Other contemporary forms of neurostimulation aimed at inducing neuromodulation are costly and invasive, with the potential for adverse effects. For example, deep brain stimulation, which uses an implanted pacemaker-like electrical device to decrease tremors in Multiple Sclerosis, carries surgical risks.¹

How Does the PoNS™ device work?

In the research setting, the PoNS device delivers specially-patterned electrical stimulation developed to mirror nerve impulses to the brain through 143-gold-plated electrodes on the mouthpiece which is placed on the tongue. For 20 minutes the electrical stimulation, called Translingual Neurostimulation (TLNS) is coupled with targeted functional therapy. Therapy consists of condition-specific physical, occupational, relaxation and cognitive exercises, based on the patient's deficits. Clinical research shows that electrical stimulation of the tongue activates two major cranial nerves – the lingual nerve (part of the trigeminal nerve) and the chorda tympani (part of the facial nerve). Electrical stimulation of the cranial nerves creates a flow of neural impulses that are then delivered directly into the brain stem and cerebellum – the main control centers for many life functions including sensory perception and movement. From the brain stem, these impulses travel throughout the brain and activate or reactivate neurons and structures involved in human function – the cortex, spinal cord and potentially the entire central nervous system. How does this happen? Researchers believe that sustained stimulation initiates a sequential cascade of changes in the actual interconnected nuclei, or neuronal network, the fundamental connections between the anatomical components of the brain.³

What is unique about the PoNS device?

The PoNS device is believed to be the first non-invasive means for delivering neurostimulation through the tongue. Stimulation of the brain and brain-stem via Translingual Neurostimulation (TLNS) is hypothesized to induce neuroplasticity, or a “re-routing,” enabling the damaged brain to compensate for lost function due to trauma or disease, by recruiting existing working neurons.

Researchers believe that use of the tongue, as a gateway to the brain may be one of the most natural, non-invasive and direct ways to stimulate the brain. The tongue is an anatomically unique area, with the highest density of nerve endings and receptors projecting thousands of nerve fibers to the brainstem with two major cranial nerves. Researchers point to the intensity of the signal the brain receives when a person accidentally bites down on his/her tongue, as a good example of the power of the tongue to send intense messages directly to the brain.⁴

PoNS Therapy Clinical Studies

Data from multiple pilot studies with IRB oversight and several case studies conducted since 2007 have shown positive results in rehabilitating a range of symptoms caused by neurological disorders or injury. PoNS Therapy has shown to improve and sustain functional rehabilitation to address brain dysfunction from traumatic, degenerative, developmental, chemical, or other origins.

Clinical trials are now underway and others are planned to study the safety and effectiveness of the PoNS device including:

- Pivotal Phase III trial for the treatment of balance disorder resulting from mild to moderate traumatic brain injury (mTBI) has been completed at HealthTech Connex, Inc. in Surrey, British Columbia; the Montreal Neurofeedback Center in Canada; Oregon Health & Science University/Portland VA; Orlando Regional Medical Center in Florida; MedStar National Rehabilitation Hospital in Washington, D.C.; and Virginia Commonwealth University in Richmond, VA

- A feasibility study of chronic balance and gait deficit due to MS was completed at McGill University's Montreal Neurological Institute and Hospital and Concordia University's PERFORM Center
- Results from a pilot study, investigating the benefits of the PoNS with physiotherapy in treating symptoms of pediatric Cerebral Palsy, have been accepted for publication in a rehabilitation peer reviewed journal
- In MS, a registrational trial for the treatment of chronic gait deficit is scheduled to start in 2017

Limited Treatments for Neurologic Symptoms

The relief of neurological symptoms as a result of disease or trauma represents a high unmet need in society today including:

Traumatic Brain Injury (TBI) – is a serious public health problem in the United States.⁵ No pharmacologic or biologic treatment for improving outcomes of traumatic brain injury have been approved.⁶ Current approaches include rehabilitation to teach patients how to cope with their specific injury-related symptoms. There are approximately 5.3 million Americans living with a TBI-related disability and the consequences that can affect all aspects of an individual's life.⁷ Since 2000, more than 287,000 U.S. service members have sustained a TBI.⁸

Multiple Sclerosis (MS) - an estimated 2.3 million people are affected by MS worldwide⁹. Experts believe currently 250,000 to 350,000 people in the United States are diagnosed with MS.¹⁰ Medications help reduce inflammation in the Central Nervous System (CNS), reduce the frequency and severity of MS attacks and the numbers of lesions in the CNS, and may slow the progression of disability.¹¹ However, medication does not address the rehabilitation of loss of function.

¹ Tyler, M.E., Kaczmarek, K.A., Rust K.L., Subbotin, A.M., Skinner, K.L., & Danilov, Y.P. (2014). Non-invasive neuromodulation to improve gait in chronic multiple sclerosis, *Journal of NeuroEngineering and Rehabilitation*.

² Acharya, S. Shukla, S. Mahajan, S.N., Diwan, S.K. Localizationism to Neuroplasticity---The Evolution of Metaphysical Neuroscience. *JAPI 2012 • VOL. 60*

³ Danilov, Y.P. and Kublanov, V.S. (2014) Emerging Noninvasive Neurostimulation Technologies: CN-NINM and SYMPATOCORRECTION. *Journal of Behavioral and Brain Science*, 4, 105-113.

⁴ Y. P. Danilov, M. E. Tyler and K. A. Kaczmarek, *Vestibular sensory substitution using tongue electro tactile display*, in Human Haptic Perception: Basics and Applications, M. Grunwald, Ed. Basel, Switzerland: Birkhauser Verlag, pp. 467-480, 2008; Y.P. Danilov, M.E. Tyler, K.L. Skinner, R.A. Hogle, and P. Bach-y-Rita, *Efficacy of electro tactile vestibular substitution in patients with peripheral and central vestibular loss*, *J. Vestib. Res.*, 16:119-130, 2007;

M. Tyler, Y. Danilov and P. Bach-y-Rita, *Closing an open-loop control system: Vestibular substitution through the tongue*, *J. Integrat. Neurosci.*, 2:159-164, 2003; Bach-y-Rita P., Kaczmarek K., Tyler M. and Garcia-Lara J., *Form perception with a 49-point electro tactile stimulus array on the tongue*, *J. Rehab. Res. Develop.* 35 (1998) pp. 427-431

⁵ The Centers for Disease Control.

⁶ Society for Neuroscience, *BrainFacts*, pg. 69.-

⁷ Thurman, D., Alverson, C., Dunn, K., et. al. (1999). Traumatic brain injury in the United States: A public health perspective. *Journal of Head Trauma and Rehabilitation*, 14(6): 602-615. The Brain Trauma Foundation. The Centers for Disease Control.

⁸ The Defense and Veterans Brain Injury Center ⁹ National Multiple Sclerosis Society

¹⁰ National Institute of Neurological Disorders and Stroke

¹¹ National Multiple Sclerosis Society