

**INTRODUCTION**

The objective of this study was to investigate the efficacy of cranial nerve non-invasive neuromodulation (CN-NIM) intervention using a portable neuromodulation simulator (PoNS®) device to treat symptoms of chronic mild to moderate traumatic brain injury (mTBI) and stroke, especially functional deficits in balance, gait, cognition, and mood.

**BACKGROUND**

mTBI affects annually 1.5 million people in the US only, and costs $50.3 Billion each year in medical services. Add to these numbers the loss in productivity and quality of life for both the patient and their family and it is easy to understand the need for a viable, low-cost therapeutic intervention for this disease.

CN-NIMMs aim to directly reduce symptoms of TBI by enhancing the brain’s ability to selectively conditionally compensate for neural tissues damaged or compromised by TBI.

We have developed an electrostimulation (ETS) system for the human tongue that can be used to present information for a variety of sensory substitution applications, e.g., vision, or head orientation in balance control, or for neurorehabilitation and rehabilitation after neural injury.

The various tactile sensors in the anterior aspect of the tongue are innervated by 2 cranial nerves (CN): the trigeminal (CN-V) and the chorda tympani (CN-VII).

Additional, receptor densities are highest at the tip of the tongue, slightly lower at the lateral periphery, and progressively decline toward the posterior and ventral surface. The electrostimulation we have developed stimulates all these regions, leading to electrotactile sensations in the posterior esophagus for under the stimulation location.

The tongue is uniquely suited for electromechanical stimulation because in the protected environment of the mouth, there is no central or protective layer of skin typically found on external body surfaces (particularly the head and neck). Additionally, the cutaneous-sensory receptors are close to the surface of the tongue, and it is continuously bathed with saliva, an effective electrolyte. Consequently, the tongue is an attractive candidate for an extra-cranial electrostimulus-based intervention.

We have found that the tongue requires only about 3% of the voltage (10-20 V), and far less current (1-4 mA), than the fingertip to achieve equivalent sensation levels.

**METHODS**

The PoNS® system (ver. 2) has operational limits of 19 V (max) and 3 mA (max) on the tongue. The biphasic waveform is specifically designed to ensure zero net DC current to minimize the potential for tissue irritation.

The system delivers triplets of 0.4-0.5-millisecond pulses at 5 m/s (i.e., 200 Hz) to a 143-electrode sequentially-arranged array of gold-plated circular electrodes (1.50 mm diameter, on 2.34 mm centers) created by a photolithographic process used to make printed circuit boards. While the pulse width and timing to each electrode is programmed in the device and cannot be altered, the subject can adjust the pulse width (hence, stimulation intensity) by manipulating a pair of buttons. At any instant in time, one of 143 electrodes in each of the 9 sectors on the array is delivering stimulation. The remaining electrodes serve as the current return path to ground. This form of tongue stimulation has been used in our research for the last 12 years under multiple UW Health Sciences - IRB protocols for studies in balance, vision, and speech substitution studies.

**CN-NIM** was administered twice daily, 5 days per week for 2 weeks. Daily sessions comprised functional evaluation, flexibility and conditioning exercises, and CN-NIM training. The functional evaluations allowed the therapist to tailor the remaining tasks to the needs and abilities of the subject, which vary greatly depending on the progression of the disease and impact of brain lesions.

A key feature of this intervention is intended to produce benefical neuroplastic changes that challenge the subject at the limit of his or her abilities. Functional evaluations were performed before and after the CN-NIM training began and again at the end of the 2-week intervention.

All of the tests were performed without tongue stimulation.

**DISCUSSION**

Prolonged activation produces sustained increased neural activity in all the central and spinal nuclei of trigeminal system in the brainstem, extending from the midbrain to the nuclei of the descending spinal tracts, and the caudal part of the nucleus tractus solitarius where both stimulated nerves have direct projections. It may also increases the receptivity of multiple central circuits and accordingly impact mid-levels of homoeostatic regulation, according to our contemporary concept of synaptic plasticity. We cannot exclude that this induces similar effects of activation of somatotopic and pseudosomatotopic regulation systems of the brain as well.

The result of our approach is essentially brain plasticity on demand - a priming or up-regulating of targeted neural structures to develop new functional pathways, which is the goal of neurorehabilitation and a primary means of functional recovery from permanent physical damage caused by stroke or trauma.

**RESULTS**

Changes in the Composite score of 5 points or greater are considered clinically significant.

In our study subjects balance score improved in 52, 10, 22 and 47 points correspondingly.

Additionally, Subjects C and D have noted significant reductions in both expressive aphasia and anxiety.

Taken on the whole, the results clearly indicate that the CN-NIM intervention is changing brain activity that is apparently producing consolidated improvements in functional behavior, and on perceived magnitude of symptoms, as measured on standardized metrics.

**CONCLUSIONS**

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**References**

Wildenberg, J.C., Tyler, M.E., Danilov, Y.P., Kaczmarek, K.A., Meyerand, M.E. (2010). “Sustained cortical and subcortical activation of sensory and motor pathways, which is the goal of neurorehabilitation and a primary means of functional recovery from permanent physical damage caused by stroke or trauma.” J. Neuroimag and Behav., 31(2), 219-231.