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VAGAL NERVE STIMULATION; CURRENT AND FUTURE INTERVENTIONS

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Vagus Nerve is the 10th and the largest cranial nerve of the parasympathetic system, consist of approximately 20% efferent and 80% afferent. It is a big nerve, providing autonomous, cardiovascular, respiratory, gastrointestinal, immune and endocrine systems. The key function of the vagus nerve is to relay relaxation from the central nervous system to the body and checking homeostatic and arousal of viscera. After the introduction of vagus nerve stimulation (VNS), it has become an important therapeutic target [1]. It involves the use of an implantable device that can send electrical impulses to the vagus nerve, which in turn can send signals to different parts of the brain. American neurologist, James Corning, used VNS for the first time to treat epilepsy. And since then there have been more than 5000 articles published, benefitting more than 90,000 individuals [2].

VNS is divided into two groups, invasive or implantable, non-invasive or transcutaneous. In the invasive group the stimulating unit is positioned around the left cervical vagus nerve and the stimulating generator is put in the left infraclavicular pockets. In the transcutaneous group, with the assistance of the sterile ultrasound method, the electrode is placed through the skin and right of the carotid sheath. For signal delivery, the electrode is attached to the external signal generator. Badran et al. [3] conducted a single-blind study Including 17 adults, psarticipants had two scanning visits separated by one day by using the transcutaneous auricular VNS (taVNS) / MRI trial. All participants either received left earlobe (control) or tragus (active) stimulation at 25 Hz, 500 ms for 60 seconds (3 times in 6 minutes). Brain MRI scans were taken to see the effect in control stimulation, active stimulation, and the comparison. Also evaluated were brainstem and midbrain. Results showed that by stimulating tragus, we can activate the afferent cerebral vagus and that taVNS can be used instead of VNS.

VNS was originally approved for the therapy of epilepsy and depression owing to anti-inflammatory characteristics and was investigated in many illnesses. The use of VNS in drug-resistant epilepsy (DRE) is due to immediate VNS that reaches the nuclei of the brainstem and inhibits cortex excitability. Barbella et al. [4] researched in 20 adult patients by four hours of tVNS during the six-month (T1) and two-month (T2) washout period. They compared the frequency and type of seizures with seizures that occurred prior to study admission for 3 months. There was a decrease of more than 30 percent in seizures frequency with minimal side effects.

Multiple studies are being conducted to explore the true potential of these nervous system stimulation devices for the enhancement of human critical thinking. Beste et.al [5] explored the impact of GABAergic and Norepinephrine simultaneous stimulation on inhibitory control by using tVNS. They hypothesized that by stimulating vagus nerve NE and GABAergic activity will increase the inhibitory process in the brain helping better switching task performance and efficient response under varying levels of memory load. Fifty-one undergraduate students participated in an online study in which the effects of tVNS were studied on two different aspects of human inhibitory control. Two different models assessed the backward and mental workload response inhibition. At the completion of the study, results showed that tVNS had no effect on backward inhibition but when working memory was required to control response inhibition, tVNS showed a better effect in controlling inhibition.

In a second consecutive study, to explore the potential of the in the augmenting creative process Colzato et.al [6] asses the role of tVNS in 104 undergraduate students. The participants were enrolled via the online recruiting system, the creative performance was evaluated by assessing the divergent thinking through alternate uses task. The convergent task was assessed through remote associates test, Creative Problem Solving and Idea Selection task. At the end of the study, results demonstrated that tVNS, as compared to sham stimulation, enhances divergent thinking in individuals. Hoque et.al [7] reported a case of a 17-year-old boy with cerebral palsy and right hemiparesis being treated with VNS for the treatment of refractory focal dyscognitive seizures. After the initiation of VNS monitored with Polysomnography and EMG, snoring was completely abolished and the airflow was reduced on the nasal pressure transducer (PTAF) channel. This observation was noted during non-REM sleep but not on REM sleep.

So far the studies have proven the tolerability and efficacy of the VNS but some side effects are reported. In the systematic review by Redgrave et al. [8], they included 51 types of studies reporting side effects of tVNS. Anatomical positioning of tVNS was cervical, concha, and tragus area in 8, 14 and 11 researches respectively. All trials used 20-25 Hz average frequency and 0.25-1 ms average pulse width. The most frequently reported side effect was skin irritation. Other side effects reported were a headache, drooping facial, dizziness, nausea, nasopharyngitis, and arrhythmias. VNS associated side effects such as sleep-disordered breathing and dysphagia are well known. For better outcomes, doctors and patients are advised to report these side effects to higher authorities regulating the protocols of tVNS and the information should be available to the public

The FDA has now approved multiple VNS. In 2018, the market has been valued at around 440$ million and it is being estimated that it will surpass more than 880$ million by 2026 [9]. To explore the potential of VNS studies being conducted in different specialties. It has shown improvement in alertness, attention and psychomotor activity in a study. Similarly, VNS has shown favorable outcomes for cluster headaches and migraines. It also has anti-inflammatory properties, so it has shown beneficial outcomes in Rheumatoid arthritis (RA), Diabetes, stroke pain management, obesity, Sepsis and Cardiovascular Diseases and traumatic brain injury (TBI) [10]. Our curiosity has always helped us to find new ways to increase the longevity of human life and Stimulation devices is one example of our collective success. Future areas for vagal nerve stimulation include stroke, neurorehabilitation, gaming disorder etc. We hope to see many randomized trials using cutaneous vagal nerve stimulation involving these conditions

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