

## Effect of Vagus Nerve Stimulation in Vestibular Function among Subjects with Stroke

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### Abstract

**Background:** The background of the study is the incidence of vestibular dysfunction among stroke subjects which indirectly affects the balance function and early recovery of daily activities like sitting, standing and walking.

**Purpose:** The main objective of this study is to investigate the vestibular dysfunction using Vestibular evoked myogenic potential (VEMP) and efficiency of Transcutaneous auricular vagal nerve (TaVNS) stimulation among Middle cerebral artery (MCA) stroke survivors.

**Method:** Thirty subjects were randomly assigned into one of two groups: Group A (Transcutaneous auricular vagal nerve stimulation with conventional stroke rehabilitation) and Group B (conventional stroke rehabilitation and epley's maneuver). The pre-test measures of vestibular function were assessed by VEMP (an electrophysiological diagnostic tool). The intervention group received Transcutaneous auricular vagal nerve stimulation for 30 minutes, and a single session per day for 4 weeks along with conventional stroke rehabilitation whereas the control group received Epley's maneuver exercises along with conventional stroke rehabilitative exercises for 60 minutes, 6 days/week, and a single session per day for 4 weeks.

Weeks. The same VEMP test was measured after 4 weeks of treatment as post-test values.

**Result:** The pre and post-test values were significantly different between group A and group B ( $p \geq 0.001$ ) indicating that TaVNS has a major impact on recovery of vestibular dysfunction among stroke participants.

**Conclusion:** The transcutaneous auricular vagal nerve stimulation is found effective for improving the vestibular function and balance.

**Keywords:** Balance, vestibular apparatus, vagal nerve, VEMP.

### Introduction

Stroke is a common and most prevalent neurological condition affecting all age groups. It causes a variety of dysfunctions, impairments and

disabilities, among which balance impairment is associated with poorer functional recovery. Middle cerebral artery stroke causes postural instability and balance dysfunction more often than other arteries

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[1]. The specific mechanism behind the impairment of balance in stroke is still unclear but it is a known fact that the vestibular system has an important function of maintaining and controlling the equilibrium of the body through defined cerebellar pathways. Just like gait, tone, coordination, Balance is also a major function of the body that keeps the line of gravity within the body's base of support with minimal or no postural sway while doing day-to-day functional activities [2]. There are multiple reports stating the prevalence of balance impairments after stroke ranging as low as 16.7% to as high as 83% [10]. The balance impairment caused by stroke can be complex, but normally the brain is the major structure that sends signals to the muscles through the nerves to make them move and that when a stroke damages the brain, it will also be affecting the signals that produce and transmit. Balance impairments are commonly caused due to the ischemic changes happening in cerebellar or vestibular pathways. Finding effective acute therapy is crucial for delivering early relief and improving patient outcomes because vestibular dysfunction can be severely debilitating and have a major influence on a survivor's quality of life.

The tenth cranial nerve, vagus nerve is a main branch of the parasympathetic nervous system which has different branches and auricular branch is a branch from the main bundle which innervates the human ear. The Auricular branch of vagus nerve (ABVN) is also called Alderman's nerve or Arnold's nerve is the core system that can provide non-invasive vagal nerve stimulation, which is called as transcutaneous auricular vagus nerve stimulation (TaVNS) [3]. The brainstem has a vital structure called "the nucleus of the solitary tract" (NTS) that can control the sensory signals of cardiovascular, gustatory, respiratory and oral tactile function. This nucleus gets projected to the locus coeruleus, where Vagal nerve stimulation (VNS) is thought to be mediated [4]. A Different stimulus from the vagus nerve is transmitted to the central nervous system and cortex via this primary structure NTS. Researchers started focusing on it in the 20th century. Various studies have made assumptions about the regions of the brain that the non-invasive vagal nerve stimulation (nVNS) may activate according to the area of focus. The neuromodulatory impact starts immediately after the vagal nerve is electrically stimulated. Two

important brain neuromodulators, the noradrenergic locus coeruleus and the cholinergic nucleus basalis, are quickly activated by a VNS pulse [15]. Stimulation over cymba concha of the ear approach may be used to treat Alzheimer's disease, Parkinson's disease, dystonias and multiple sclerosis in addition to treating depression, epilepsy, headaches, and autism issues. It was found to be protective in a rat model of cerebral ischemia [6]. Hence using this place for stimulation in human beings is much safer.

The body's adaptations and motions to restore stability and keep an upright posture are referred to as postural responses. There is a strong correlation between the patients' levels of postural instability and balance issues and the severity of vestibular impairment. There are different pathways in the body that connect to the vagal nerve network. Stimulating the auricular branch will reciprocate the effect through the vagus nerve pathway and enters the vagal bundle which projects into the brain via the brainstem where the central pathway of vestibular apparatus is present. Stimulating the vagal nerve stimulates the solitary nucleus since a vagal cell body exists in it, thereby the stimulation is carried over to vestibular pathways. Though there are several neuro modulations to stimulate vestibular systems, an emerging transcutaneous auricular vagal nerve stimulation (TaVNS) is yet to be explored for its influence over vestibular pathways.

TaVNS can be used to enhance the benefit of conventional rehabilitation therapy on the recovery of disrupted balance functions, which is a sensory feedback mechanism affected by acute hemorrhagic or ischemic stroke. Hence it is essential to understand its effect on sensorimotor functions like balance.

### **Aim**

The aim is to determine the impact of vagal nerve stimulation on vestibular function and its effect on balance function.

### **Methods and Materials**

It was an experimental study conducted at Saveetha hospital. 30 Participants were selected by convenient sampling method depending on the inclusion and exclusion criteria from Physiotherapy out-patient department and Neurology In-patient

ward of Saveetha hospital with sub-acute MCA (Middle cerebral artery) stroke (>1 month). Full procedure of the study was explained to the participants and a printed informed consent was given and got signed for their willingness to participate in the study. Participants with willingness to participate in the study are only proceeded with the study methods. Entire study procedure took around 5 months, selection of participants took around 2 months and the study duration for one participant was 4 weeks (1 month) which was conducted between September 2022 to January 2023.

#### Inclusion Criteria

- Both male and female between the ages of 40 years to 60 years.
- Participants with reduced/abnormal Vestibular evoked myogenic potential (VEMP).
- Participants with the ability to stand with minimal assistance.
- Berg balance scale score of <20.

#### Exclusion Criteria:

- Participants with ear infection, ear pain, sensory loss in ear or hearing loss, other neurological or psychological diseases and cardiac complications.

#### Outcome Measure

Vestibular evoked myogenic potential (VEMP) is an electro diagnostic procedure with short-latency potential induced by vibration or sound which induces the activation of vestibular receptors. When this potential is applied to inferior oblique muscle of neck, Modulated electromyographic response from the muscle is used to measure the cervical VEMP (cVEMP). This was measured in the neurophysiology laboratory, Saveetha hospital with the help of laboratory staff. The values were obtained before the study and at the end of study (after 4 weeks).

#### Procedure

Participants were then randomly allocated into two groups (Group A and Group B) using the closed envelope method and their pre-test values are tabulated. Post-test values were measured at the end of 4 weeks.

#### Group A: Transcutaneous auricular vagal nerve stimulation (TaVNS)

TaVNS group was treated with TaVNS using TENS7000 (Figure 1) along with conventional stroke rehabilitation exercises for a period of 4 weeks. TaVNS was given through clip electrode on cymba concha of the ear (Figure 2) for a period of 30 minutes/session/day using TENS7000 (Acutens) apparatus through a clip electrode daily with the pulse ratio of 3: 1 (40 seconds of stimulation and 3 minutes interval), frequency: 25 Hz, pulse width: 60 mA, amplitude: 200  $\mu$ s, placement: cymba concha of left external ear. Intensity given during the TaVNS is adjusted according to the level above the participant's detection threshold and less than their pain threshold.

#### Group B: Control group (Epley's maneuver technique)

Control group was treated with Epley's maneuver technique: 1 time along with conventional stroke rehabilitation exercises for 6 days/week with a duration of 1 hour every day.



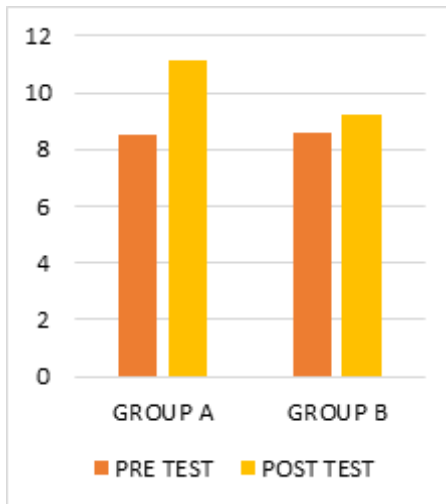
Figure 1: Transcutaneous auricular vagal nerve simulator (Acutens/TENS 7000)



Figure 2: Placement of electrode at cymba concha of the ear

## Data Analysis

Both pre-test and post-test values were recorded and statistically analyzed for their normality using the Shapiro-Wilk test. Brown Forsythe test is used for testing the equal variance. Paired t-test is used to find the significance.



**Graph 1**

INTERPRETATION: Difference of post-test mean values of GROUP A and GROUP B is 1.847, which shows that post-test mean value of Group A is higher and the group.

## Result

The study was randomly allocated to a group of 30 patients. Each group was allocated 15 participants each. The mean and standard deviation of the data were statistically analyzed. Obtaining a p-value of less than 0.001 was judged significant. The data acquired were statistically significant between the pre-test and post-test of group A, with a mean value of 8.52 in the pre-test and 11.10 in the post-test. Also, the data acquired were statistically significant between the pre-test and post-test of group B, with a mean value of 8.58 in the pre-test and 9.25 in the post-test according to the statistical analysis performed on the quantitative data for cVEMP. This indicates that both the groups have shown betterment in their vestibular function after the treatment period of 4 weeks. Between group significance was calculated using Student t-test and the mean difference between intervention group and control group was found significant with a confidence interval of 1.331 to

2.363. Thus, comparing the mean difference of the two groups, transcutaneous auricular vagal nerve stimulation group has produced better post-test values than the conventional treatment and was found to be beneficial in improving the vestibular function than conventional treatment in stroke survivors. Both Group A and Group B, showed a considerable improvement in vestibular function. But Group A had a mean value higher than group B which indicates that TaVNS is more beneficial than control group's treatment. The difference in the mean values between group A and B is greater than would be expected by chance. On comparing both the groups, significant difference in their statistics is observed ( $P = <0.001$ ).

## Discussion

The impact of trans auricular vagal nerve stimulation was having a positive result in improving the balance via vestibular function, though there is no direct way of analyzing it. There was found to be a significant improvement in the electrodiagnosis of vestibular apparatus as assessed by VEMP. According to Jai-ni-li et al., ta-VNS has a positive influence on acute stroke patients' overall neurofunctional recovery. The mechanisms of VNS action in the acute stage of stroke were thought to be nerve regeneration, neural protection, neural plasticity and angiogenesis [14]. Non-invasive transcutaneous methods of vagus nerve stimulation is a feasible alternative way to produce VNS without using any surgical implant has recently become popular. Noninvasive nVNS can be delivered in two main ways. The auricular branch of the vagus nerve (ABVN) is the focus of the first technique, known as TaVNS, which involves applying stimulation to the superficial skin of the cymba concha and tragus of the external ear. The tragus and cymba concha are the two principal locations for auricular VNS. According to recent studies, there is uncertainty regarding the vagal branches' innervation of the tragus because of discrepancies in a study using human cadavers that examined the human auricle's innervation [4]. Additionally, irregularities in electrode placement and skin contact will develop different effects on varying tissue impedance when the nerve is stimulated. This difference from person to person may hinder the effectiveness of tVNS stimulation.

For instance, the electrode might stimulate the auriculotemporal branch of the mandibular nerve, which is a neighboring nerve to the vagus nerve. This variation happens when the electrode is positioned over the auricular skin in a very limited area with dense innervation. The evaluation and interpretation of the effects of vagus nerve stimulation are made more challenging by this dual recruitment. Studies indicate that TaVNS is useful in a variety of rehabilitation problems, even though the effect is not evident [8]. Outcome measure used in this study only interprets vestibular function while TaVNS should be assessed with different parameters and in different functions. This study has shown a significant difference in the recovery and improvement in balance function when it is combined with conventional stroke rehabilitative therapy. Furthermore, studies need to be done on its individual effect over the conventional therapy, also the improvement of balance should be justified whether it is improved because of the vestibular pathway. In a rat study using taVNS stimulation, it was hypothesized that VNS stimulated the proliferation of hippocampal progenitor cells in the adult rat dentate gyrus, allowing these progenitor cells to assist in the healing of injured neurons after ischemic injury [15]. Ethically cleared rat studies are the proof that TaVNS can reverse the damage caused to the neurons of the CNS following stroke which gives an overall effect of AVNS in the rehabilitation of stroke. This again gives a hypothesis of development in vestibular function seen in this study can also be due to the reversal effect caused by TaVNS in CNS pathways that produces vestibular function.

Invasive vagus nerve stimulation's (VNS) Activity within afferent vagal projection locations was also observed in functional MRI studies, where the brainstem, postcentral gyrus, hypothalamus, hippocampus, thalamus, nucleus accumbens, amygdala, and insula are the area's most frequently impacted by taVNS and VNS [12]. Even Though there was a better improvement observed in a different conditions, it is possible that additional variables, such as coexisting illnesses, the cause of a stroke, an individual's unique anatomy, or medications or disorders that affect neuromodulatory function, could affect the effectiveness of VNS therapy. [7]. The potential for this therapy to speed-up the participant's recovery will be maximized by testing the clinical

improvement of paired VNS therapy among the vast stroke populations and by continuing to develop parameters for stimulation and rehabilitative concepts to individualize and optimize the intervention for patient sectors. When TaVNS is combined with a rehabilitative framework as opposed to giving only conventional rehabilitative training, animal models with behavioral abnormalities of chronic ischemic stroke, and traumatic brain injury and intracerebral hemorrhage shows better improvement. According to several studies, VNS increases neuronal plasticity by energizing neuromodulatory systems in tandem with training. The cholinergic basal forebrain and the noradrenergic locus coeruleus are activated physically by VNS [13]. Since neuroplasticity is the base which improves the left-over neurological pathways and returning the normal function, increasing its neuronal activity through TaVNS is a remarkable development in neurological rehabilitation. Possible explanations for the increases in proprioception seen in the patients can also be due to the improvement in range of motion and strength which has been made possible by TaVNS-assisted exercises. It's likely that the extended range of joint motions caused by the injury of the affected limb will eventually increase sensory feedback, which in turn increases neuroplasticity of sensory pathways in the cerebral cortex. When the relationship between improved motor performance and sensory feedback is taken into consideration, it is reasonable to hypothesize that motor and sensory repair are mutually reinforcing positive feedback loops. Along with this, a combination of taVNS helped in the rewiring of the neuronal pathway that produces sensorimotor feedback back to the CNS. Wide research on combining TaVNS with other different interventions is essential for incorporating this intervention into rehabilitation. TaVNS is thus a wide area that needs to be understood and can be put into rehabilitation for the betterment of the neurological population. Small sample size and treatment is initiated at different times for every participant affecting the similarity are the limitations of the study.

## Conclusion

The transcutaneous auricular vagal nerve stimulation has a positive impact and improvement of vestibular function among stroke survivors. Even

though there was no direct measure or assessment regarding the improvement of balance, the study enhanced the recovery rate and improved their functional balance.

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**Conflict of Interest:** Nil

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