RESEARCH PAPER

Analyzing the Effect of Non-Invasive Vagus Nerve Stimulation in Sensory Re-Education Training for Upper Limb Acute Stroke Patients

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Abstract
Background: Stroke is a leading cause of disability worldwide, frequently resulting in sensory impairments that adversely affect upper limb function and quality of life. Although motor rehabilitation has received considerable attention, sensory rehabilitation remains underexplored. Non-invasive vagus nerve stimulation (nVNS) has emerged as a promising adjunctive therapy for enhancing neuroplasticity and functional recovery.
Objective: To evaluate the effectiveness of non-invasive vagus nerve stimulation combined with conventional sensory re-education training in improving upper limb sensory function among acute stroke patients.
Methods: A randomized controlled study was conducted involving 40 acute stroke patients with upper limb sensory impairment. Participants were randomly allocated into an Experimental Group (n=20), receiving non-invasive vagus nerve stimulation combined with conventional sensory rehabilitation, and a Control Group (n=20), receiving sham vagus nerve stimulation with conventional rehabilitation. Participants were aged between 50 and 90 years. Both groups received 30-minute intervention sessions for five consecutive days. Outcome measures included the Sensory Component of the Fugl-Meyer Assessment for Upper Extremity (FMA-UE) and the Nottingham Sensory Assessment (NSA). Pre- and post-intervention assessments were performed.
Results: Both groups demonstrated statistically significant improvements in sensory function following intervention ($p < 0.001$). However, the experimental group exhibited greater improvements than the control group in both the Fugl-Meyer Sensory Assessment and Nottingham Sensory Assessment.
Conclusion: Non-invasive vagus nerve stimulation combined with conventional sensory rehabilitation significantly improves sensory recovery in acute stroke patients compared with conventional rehabilitation alone. These findings support the integration of nVNS as an adjunct therapeutic modality for enhancing sensory rehabilitation after stroke.

Keywords: Stroke, Non-invasive Vagus Nerve Stimulation, Sensory Rehabilitation, Neuroplasticity, Acute Stroke, Fugl-Meyer Assessment, Nottingham Sensory Assessment

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1. Introduction

Stroke is one of the leading causes of mortality and long-term disability worldwide, resulting in substantial physical, cognitive, and sensory impairments that affect millions of individuals every year. According to global estimates, stroke remains the second leading cause of death and a major contributor to disability-adjusted life years (DALYs).[1] Sensory impairment is reported in nearly 80% of stroke survivors and significantly affects upper limb function, balance, coordination, and the ability to perform activities of daily living.[2],[3] Despite its high prevalence, sensory rehabilitation has received considerably less attention than motor rehabilitation in conventional stroke management.[2]

Upper limb sensory deficits, including impaired tactile sensation, proprioception, stereognosis, and temperature discrimination, reduce functional independence and negatively impact patients' quality of life.[3] Sensory recovery is closely associated with cortical reorganization and neuroplasticity, emphasizing the importance of interventions that can enhance neural recovery following stroke.[4]

Vagus nerve stimulation (VNS) has emerged as a promising neuromodulation technique capable of promoting neuroplasticity through activation of the

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nucleus tractus solitarius and the release of neuromodulatory neurotransmitters such as norepinephrine and acetylcholine.[5] These neurochemical changes facilitate synaptic plasticity, cortical reorganization, and functional recovery after neurological injury.[6]

Although implanted VNS has demonstrated beneficial effects in improving upper limb motor recovery after stroke, its invasive nature limits widespread clinical use.[5] Consequently, non-invasive vagus nerve stimulation (nVNS), delivered transcutaneously without surgical implantation, has gained increasing attention as a safe, non-invasive, and cost-effective alternative.[7] Recent studies have reported that nVNS, when combined with rehabilitation therapy, enhances motor performance, functional recovery, and sleep quality in post-stroke patients.[4,6,8]

However, the effectiveness of non-invasive vagus nerve stimulation in improving upper limb sensory impairment remains inadequately investigated. Limited evidence is available regarding its role in sensory re-education during the acute phase of stroke rehabilitation. Therefore, the present study aimed to evaluate the effectiveness of non-invasive vagus nerve stimulation combined with conventional sensory re-education training in improving upper limb sensory function among acute stroke patients.

2. Materials and Methods

2.1 Study Design

This study was designed as a randomized controlled experimental trial to investigate the effectiveness of non-invasive vagus nerve stimulation (nVNS) combined with conventional sensory re-education training in improving upper limb sensory function among patients with acute stroke. The study was conducted in the Department of Physiotherapy at Swami Rama Himalyan University, Dehradun India. Ethical approval was obtained from the Institutional Ethics Committee prior to the commencement of the study, and written informed consent was obtained from all participants before enrollment. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

2.2 Participants

A total of 40 patients diagnosed with acute stroke and presenting with upper limb sensory impairment were recruited through convenience sampling. Participants were randomly allocated into two equal groups (n = 20 each) using a simple randomization method.

- **Experimental Group (n = 20):** Received non-invasive vagus nerve stimulation (nVNS) in combination with conventional sensory re-education training.
- **Control Group (n = 20):** Received sham vagus nerve stimulation together with the same conventional sensory re-education training.

The age of the participants ranged from **50 to 90 years**, irrespective of gender.

2.3 Eligibility Criteria

Inclusion Criteria

Participants were included in the study if they fulfilled the following criteria:

- Male or female patients aged between **50 and 90 years**.
- Clinically diagnosed with acute ischemic or hemorrhagic stroke confirmed by a neurologist.
- Presence of unilateral upper limb sensory impairment following stroke.
- Medically stable and able to participate in rehabilitation sessions.
- Able to understand and follow verbal instructions.
- Willing to participate and provide written informed consent.

Exclusion Criteria

Participants were excluded if they had:

- Implanted cardiac pacemakers or any electronic medical devices.
- History of epilepsy or recurrent seizures.
- Severe cognitive impairment or inability to cooperate during assessment.
- Skin infections, wounds, or lesions at the stimulation site.
- Other neurological disorders affecting upper limb sensation.
- Unstable cardiovascular or systemic medical conditions.

2.4 Sample Size

A total sample of **40 participants** was included in the study. Twenty participants were assigned to the experimental group, while the remaining twenty participants constituted the control group. The sample size was determined based on the availability of eligible participants during the study period and the feasibility of conducting the intervention within the available timeframe.

2.5 Randomization

Eligible participants were randomly assigned to either the experimental or control group using a simple random allocation method. Randomization was performed to minimize selection bias and ensure equal distribution of participants between both groups.

2.6 Intervention Protocol

Both groups received treatment for **30 minutes per session**, **once daily**, for **five consecutive days** under the supervision of an experienced physiotherapist.

Experimental Group

Participants in the experimental group received **non-invasive vagus nerve stimulation (nVNS)** followed by conventional sensory re-education training.

The non-invasive vagus nerve stimulation was administered using a transcutaneous vagus nerve stimulation device applied over the cervical branch of the vagus nerve according to the manufacturer's recommended protocol. Stimulation parameters were adjusted to produce a comfortable tingling sensation without causing pain or discomfort.

Following stimulation, participants underwent conventional sensory re-education exercises, which included:

- Light touch stimulation
- Texture discrimination training
- Proprioceptive exercises
- Localization of touch
- Object recognition (stereognosis)
- Position sense training
- Functional upper limb sensory activities

Each rehabilitation session lasted **30 minutes**.

Control Group

Participants assigned to the control group received **sham vagus nerve stimulation**, in which the stimulation device was applied in the same manner without delivering therapeutic electrical stimulation. This was followed by the same conventional sensory re-education training protocol administered to the experimental group.

The duration and frequency of treatment were identical to those of the experimental group to maintain consistency between groups.

2.7 Outcome Measures

Participants were evaluated at baseline (pre-intervention) and immediately after completion of the five-day intervention (post-intervention).

The following standardized assessment tools were used:

2.7.1 Sensory Component of the Fugl-Meyer Assessment for Upper Extremity (FMA-UE)

The sensory section of the Fugl-Meyer Assessment was used to evaluate upper limb sensory recovery, including assessment of light touch and proprioception. The FMA is a reliable and valid stroke-specific outcome measure widely used to assess sensorimotor impairment.

2.7.2 Nottingham Sensory Assessment (NSA)

The Nottingham Sensory Assessment was used to evaluate tactile sensation, proprioception, stereognosis, and cortical sensory function. It is a standardized clinical tool with good reliability and validity for assessing sensory impairment in individuals with stroke.

2.8 Statistical Analysis

All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 26.0

Descriptive statistics were calculated and presented as mean ± standard deviation (SD) for continuous variables and frequencies with percentages for categorical variables.

The normality of data distribution was assessed before inferential analysis.

- Paired t-test was used to compare pre- and post-intervention scores within each group.
- Independent t-test was used to compare post-intervention outcomes between the experimental and control groups.
- **A** p-value of <0.05 was considered statistically significant, while $p <0.001$ was considered highly statistically significant.

3. Results

A total of **40 participants** completed the study, with **20 participants in the experimental group** and **20 participants in the control group**. No participants withdrew from the study, and all completed the intervention protocol and post-intervention assessments.

3.1 Comparison of Pre- and Post-Intervention Sensory Outcomes

Table 1. Changes in sensory outcomes observed in both groups following the intervention. Significant improvements were observed in the Sensory Component of the Fugl-Meyer Assessment (FMA-UE**)** and the Nottingham Sensory Assessment (NSA) in both the experimental and control groups after completion of the treatment protocol (**$p < 0.001$**). However, participants receiving non-invasive vagus nerve stimulation (nVNS) combined with conventional sensory re-education demonstrated greater improvements in sensory function compared to those receiving sham stimulation with conventional therapy alone. These findings indicate that the addition of nVNS enhanced the effectiveness of conventional rehabilitation in promoting sensory recovery after acute stroke.

Table 1. Comparison of Pre- and Post-Intervention Sensory Outcomes

Outcome Measure	Experimental Group (n = 20)	Control Group (n = 20)	Within-Group p-value	Between-Group Interpretation
Sensory Component of Fugl-Meyer Assessment (FMA-UE)	Significant improvement after intervention	Significant improvement after intervention	**$p < 0.001$**	Experimental group demonstrated greater improvement than the control group

Nottingham Sensory Assessment (NSA)	Significant improvement after intervention	Significant improvement after intervention	**p < 0.001**	Experimental group demonstrated greater improvement than the control group

3.2 Changes in Upper Limb Sensory Function

Table 2. illustrates the overall trend in sensory function before and after intervention. Both groups had comparable baseline scores prior to treatment. Following five consecutive days of intervention, the experimental group exhibited a more pronounced increase in sensory function compared to the control group. The experimental group's score increased from **20 to 36**, whereas the control group's score improved from **20 to 29**, indicating superior recovery among participants receiving non-invasive vagus nerve stimulation.

Table 2 Changes in Upper Limb Sensory Function Following Intervention

Assessment	Experimental Group	Control Group
Pre-intervention	20	20
Post-intervention	36	29

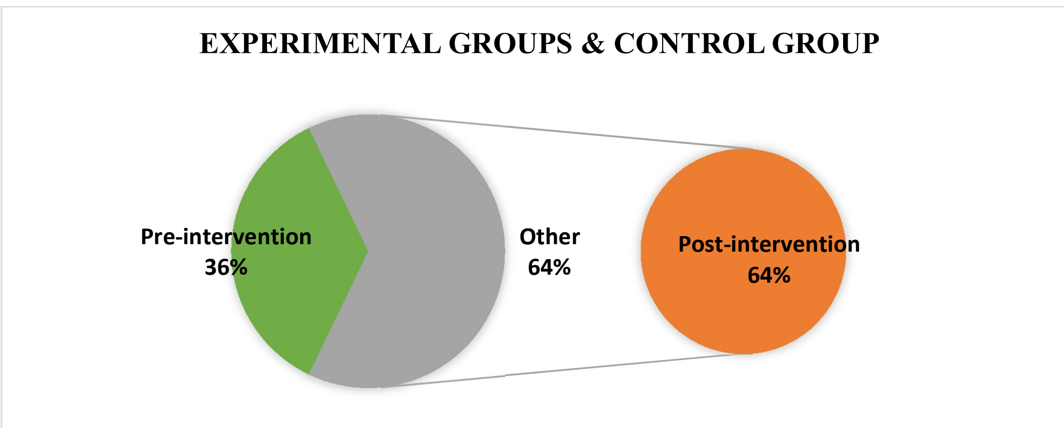

Fig : 1 -Experimental Groups & Control group

3.3 Summary of Statistical Findings

The statistical analysis demonstrated significant improvements in both outcome measures within each treatment group. The **FMA-UE Sensory Score** and the **Nottingham Sensory Assessment** showed statistically significant improvements following intervention (**p < 0.001**). Furthermore, comparison between groups revealed that the experimental group achieved greater overall sensory recovery than the control group, suggesting that non-invasive vagus nerve stimulation provided additional therapeutic benefits when combined with conventional sensory re-education.

Table 3. Summary of Statistical Findings

Variable	Experimental Group	Control Group	Statistical Significance
FMA-UE Sensory Score	Improved	Improved	**p < 0.001**
Nottingham Sensory Assessment	Improved	Improved	**p < 0.001**
Overall Sensory Recovery	Greater improvement	Moderate improvement	Experimental group superior

Overall Findings

The findings of the present study demonstrate that both intervention protocols resulted in improvements in upper limb sensory function among acute stroke patients. However, the combination of **non-invasive vagus nerve stimulation with conventional sensory re-education** produced greater improvements than conventional therapy with sham stimulation. These results suggest that non-invasive vagus nerve stimulation may serve as an effective adjunctive rehabilitation strategy for enhancing sensory recovery during the acute phase of stroke.

4. Discussion

The present randomized controlled study investigated the effectiveness of non-invasive vagus nerve stimulation (nVNS) combined with conventional sensory re-education training for improving upper limb sensory function in patients with acute stroke. The findings demonstrated that both the experimental and control groups showed significant improvements in sensory function following the intervention. However, participants who received nVNS in combination with conventional sensory rehabilitation exhibited significantly greater improvements than those receiving sham stimulation with conventional therapy alone. These findings suggest that nVNS is an effective adjunctive intervention for enhancing sensory recovery during the acute stage of stroke rehabilitation.

Sensory impairment is a common consequence of stroke, affecting approximately 50–80% of stroke survivors and substantially limiting motor performance, hand dexterity, balance, and independence in activities of daily living. Although conventional rehabilitation improves functional outcomes, sensory deficits often persist and hinder complete neurological recovery. The present study demonstrated that conventional sensory re-education alone resulted in measurable improvements, whereas the addition of non-invasive vagus nerve stimulation produced superior gains in both the Sensory Component of the Fugl-Meyer Assessment (FMA-UE) and the Nottingham Sensory Assessment (NSA). These findings indicate that combining neuromodulation with rehabilitation may enhance the effectiveness of sensory retraining.

The enhanced sensory recovery observed in the experimental group may be attributed to the ability of vagus nerve stimulation to facilitate activity-dependent neuroplasticity. Stimulation of the vagus nerve activates the nucleus tractus solitarius, which subsequently stimulates the locus coeruleus and basal forebrain, leading to increased release of norepinephrine and acetylcholine. These neurotransmitters play a critical role in strengthening synaptic connections, promoting cortical reorganization, and facilitating relearning of sensory pathways after neurological injury. When paired with task-specific sensory exercises, nVNS is believed to reinforce the neural circuits activated during rehabilitation, thereby accelerating functional recovery.

The present findings are consistent with previous investigations evaluating vagus nerve stimulation in stroke rehabilitation. Kimberley et al. reported that vagus nerve stimulation paired with upper limb rehabilitation significantly improved motor recovery compared with rehabilitation alone. Similarly, Dawson et al. demonstrated that transcutaneous vagus nerve stimulation combined with rehabilitation enhanced upper limb function and promoted greater functional gains in individuals with chronic ischemic stroke. Although these studies primarily focused on motor recovery, the present study extends their findings by demonstrating that non-invasive vagus nerve stimulation also has a positive effect on sensory rehabilitation, an area that has received comparatively less attention in stroke research.

Our findings also support the work of Engineer et al., who proposed that vagus nerve stimulation enhances experience-dependent cortical plasticity by pairing sensory input with neuromodulatory activation. This mechanism is particularly relevant during the acute phase of stroke, when spontaneous neuroplasticity is at its highest. Delivering nVNS concurrently with sensory re-education exercises may therefore maximize cortical reorganization and improve recovery of tactile sensation, proprioception, and higher cortical sensory functions.

The present study further demonstrated significant improvements in the Nottingham Sensory Assessment, suggesting enhanced recovery of tactile discrimination, proprioception, and stereognosis. Recovery of these sensory modalities is clinically important because improved sensory perception contributes to better motor control, object manipulation, coordination, and performance of daily functional activities. Consequently, improved sensory function may indirectly facilitate overall upper limb functional recovery and patient independence.

One of the major strengths of this study is its randomized controlled design, which minimized selection bias by allocating participants equally to experimental and control groups. Both groups received identical conventional sensory rehabilitation protocols, ensuring that the observed differences could be attributed primarily to the addition of non-invasive vagus nerve stimulation. Furthermore, the use of validated outcome measures, including the Fugl-Meyer Assessment and the Nottingham Sensory Assessment, enhanced the reliability and clinical relevance of the findings.

Despite these encouraging results, several limitations should be acknowledged. The study included a relatively small sample size (n = 40) recruited from a single rehabilitation center, which may limit the generalizability of the findings. The intervention period was limited to five consecutive days, and no long-term follow-up assessments were performed to determine whether the observed improvements were sustained over time. In addition, neurophysiological investigations such as functional magnetic resonance imaging (fMRI), electroencephalography (EEG), or somatosensory evoked potentials were not performed to objectively evaluate changes in cortical plasticity associated with vagus nerve stimulation.

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Future research should include larger multicenter randomized controlled trials with extended intervention periods and long-term follow-up assessments. Incorporating neuroimaging and electrophysiological techniques would further clarify the mechanisms underlying sensory recovery following non-invasive vagus nerve stimulation. Additionally, future studies should investigate optimal stimulation parameters, treatment duration, and the effectiveness of nVNS across different stages of stroke recovery.

Overall, the findings of the present study provide evidence that non-invasive vagus nerve stimulation combined with conventional sensory re-education is more effective than conventional therapy alone in improving upper limb sensory function among acute stroke patients. The results support the integration of nVNS as a safe, non-invasive, and promising adjunctive modality in comprehensive stroke rehabilitation programs aimed at enhancing sensory recovery and promoting functional independence.

5. Conclusion

The present study demonstrated that non-invasive vagus nerve stimulation (nVNS) combined with conventional sensory re-education is more effective than conventional therapy alone in improving upper limb sensory function in acute stroke patients. Significant improvements were observed in both the Fugl-Meyer Assessment (FMA-UE) and Nottingham Sensory Assessment (NSA), with greater sensory recovery in the experimental group. These findings suggest that nVNS is a safe and promising adjunctive rehabilitation technique for enhancing sensory recovery after acute stroke. Further large-scale studies with longer follow-up are recommended to validate these findings.

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