Combining Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) with Transcranial Magnetic Stimulation (TMS) to Enhance Cortical Excitability

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Background

- Transcranial Magnetic Stimulation (TMS) is becoming a widely used tool to augment cortical excitability in facilitating motor function post-stroke.
- The behavioral effects of TMS are transient and require multiple sessions to evoke reasonable changes.
- Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) has emerged as a promising facilitator of neuroplasticity when intricately paired with neuromodulation interventions.
- In this trial, we explore combining two forms of brain stimulation (TMS and taVNS) to boost cortical excitability.
- **Specific Aims:**
  1) Create a novel, dual-neuromodulation paradigm for boosting cortical excitability
  2) Conduct a mechanistic pilot exploring the use of paired taVNS/TMS to enhance motor cortex excitability in a 4 visit, single blind, sham controlled, counterbalanced study.

Hypothesis

- Pairing taVNS + TMS will increase motor cortex excitability compared to taVNS or TMS alone.

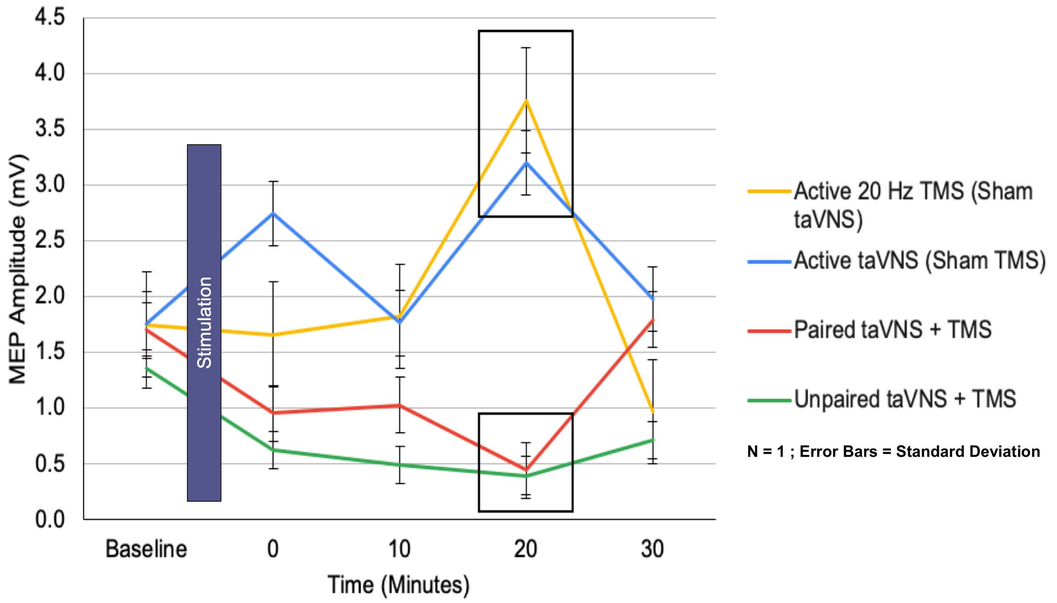
Results

Non-combinatory stimulation methods facilitate greater excitation than combined methods

- Active TMS alone *increases* motor evoked potential amplitude by +114.9% from Baseline at 20 minutes
- Active taVNS alone *increases* motor evoked potential amplitude by +82.4% from Baseline at 20 minutes
- Paired taVNS + TMS *decreases* motor evoked potential amplitude by -73.4% from Baseline at 20 minutes
- Unpaired taVNS + TMS *decreases* motor evoked potential amplitude by -70.4% from Baseline at 20 minutes

**** Please note that these results are preliminary from the first subject that completed all 5 randomized visits. We currently have 10 active participants that are being run through the randomized visits.**

Figure 3 – Changes in MEP Amplitude Over Time



N = 1 ; Error Bars = Standard Deviation

Methods

Figure 1 – Combining TMS and taVNS

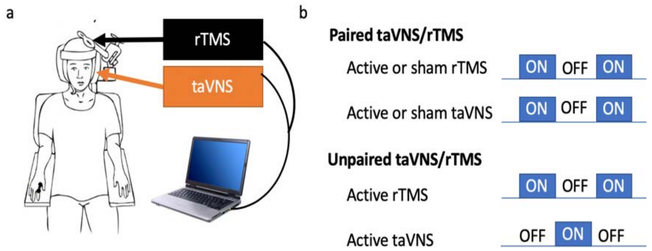
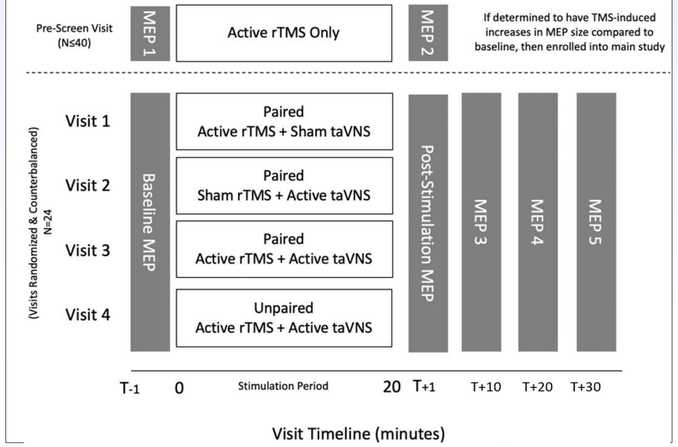


Figure 2 – Study Design with Visit Timelines



Overview

- We built a system to administer this dual neuromodulation technique and can adjusted to different stimulation settings
- To measure if these methods have an effect, we used a Motor Evoked Potential (MEP) paradigm to quantify cortical excitability through excitation of muscles in the hand muscle
- We will pre-screen 40 healthy individuals with no contraindication of taVNS or TMS and will select 24 individuals who had increases in average MEPs by 10% or more at the Pre-Screen visit (Figure 2)

Stimulation Parameters

TMS: 20 Hz TMS will be delivered to the motor hot spot of the left M1 region at 90% of rMT for 2.5 seconds ON and 10 seconds OFF with a total of 2000 pulses over the stimulation.
taVNS: 25 Hz taVNS will be delivered at the optimal stimulation parameters (500us pulse width, 2x perceptual threshold) targeting the left anterior wall of the ear canal.
Paired taVNS/TMS: We will synchronize taVNS with TMS using MATLAB written software. This software will deliver active taVNS concurrently with active TMS
Unpaired taVNS/TMS: In this condition, active TMS will be delivered with active taVNS in 2.5s trains during the rTMS using MATLAB software with a 6.25s offset

Conclusions

- It is feasible and safe to administer two forms of neuromodulation paired simultaneously
- Findings from the first completer suggest TMS and taVNS by themselves facilitate a transient increase in cortical excitability compared to baseline
- Both paired- and unpaired taVNS/TMS induce reductions in cortical excitability compared to baseline values
- These data suggest that combining two excitatory forms of brain stimulation may have a reciprocal inhibitory effect that is still unclear
- Further data will help untangle these counterintuitive findings and provide clarity for the trends in figure 3

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