Center for Lifespan Psychology

MAX PLANCK INSTITUTE FOR HUMAN DEVELOPMENT

Transcutaneous Vagus Nerve Stimulation Effects on Neuromodulatory BOLD-Activity and Sympathetic Arousal

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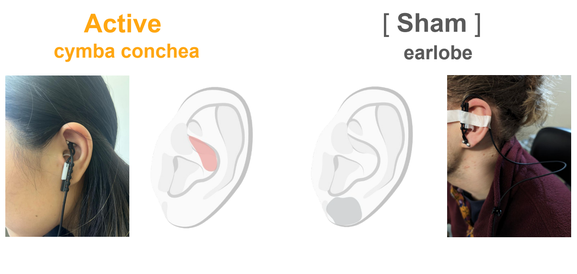
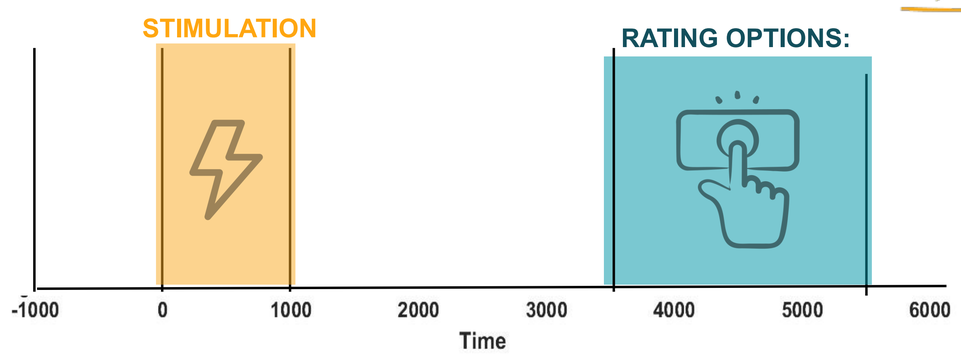
Background

- Neuromodulators, such as noradrenaline (NA) and dopamine (DA), regulate sympathetic arousal and higher-order cognitive functions [1 2 5].
- The vagus nerve is a key communication channel between the body and brain [3 4].
- Animal studies show that invasive electrical stimulation of the vagus nerve activates neuromodulatory brainstem centers like the locus coeruleus (LC) [6 8]. However, direct evidence from humans is scarce and inconsistent [7 9].
- This study examines how non-invasive transcutaneous auricular VNS (tVNS) influences vagal and brainstem neuromodulatory activity (target N=50).

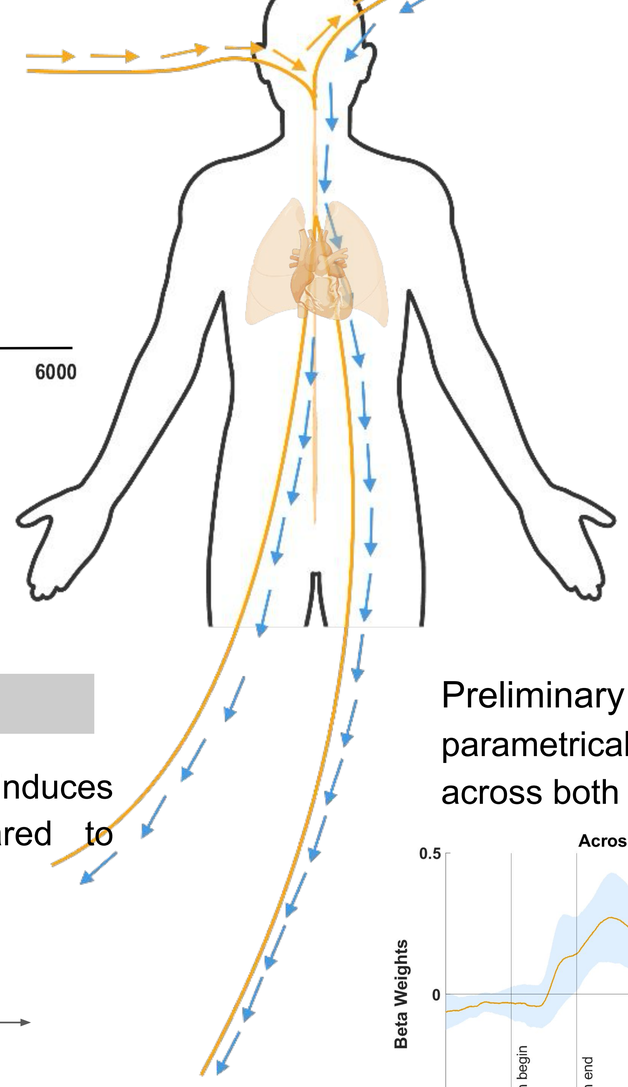
Experimental Setup





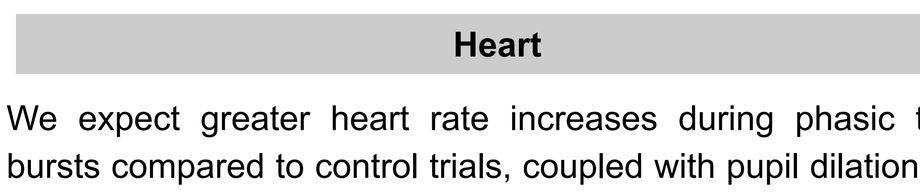
Freq: 25Hz
Width: 3
Amp: 40% cal mA
60% cal mA
80% cal mA

No sensation
Mild
Light
Moderate
Intense
Painful



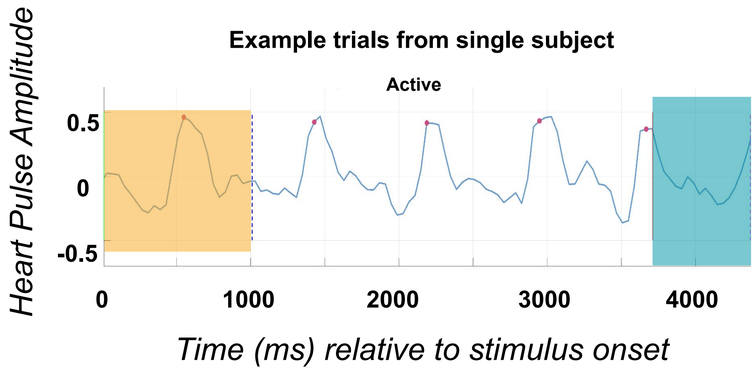
Breathing

Based on previous studies, it is hypothesised that tVNS induces higher brainstem activity during exhalation compared to inhalation.



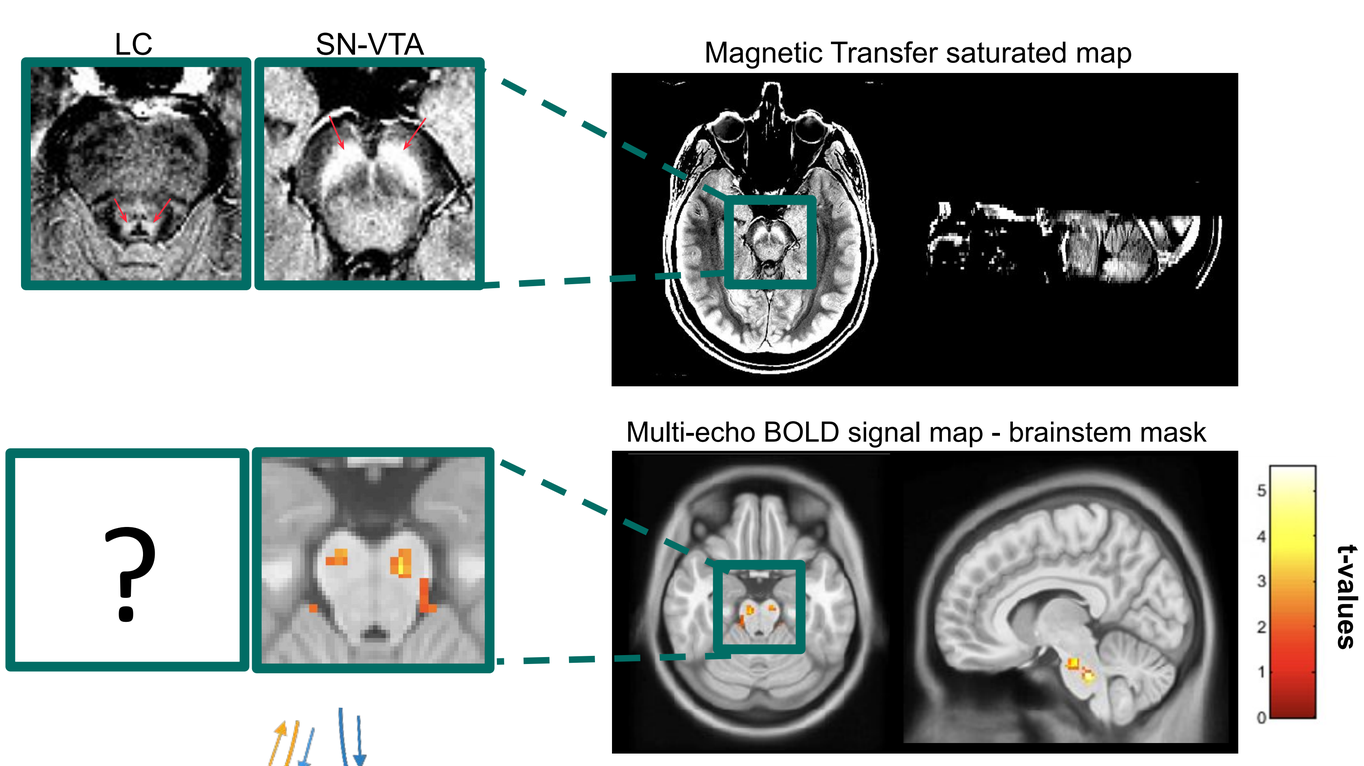
Heart

We expect greater heart rate increases during phasic tVNS bursts compared to control trials, coupled with pupil dilation as a marker of LC-driven sympathetic arousal.

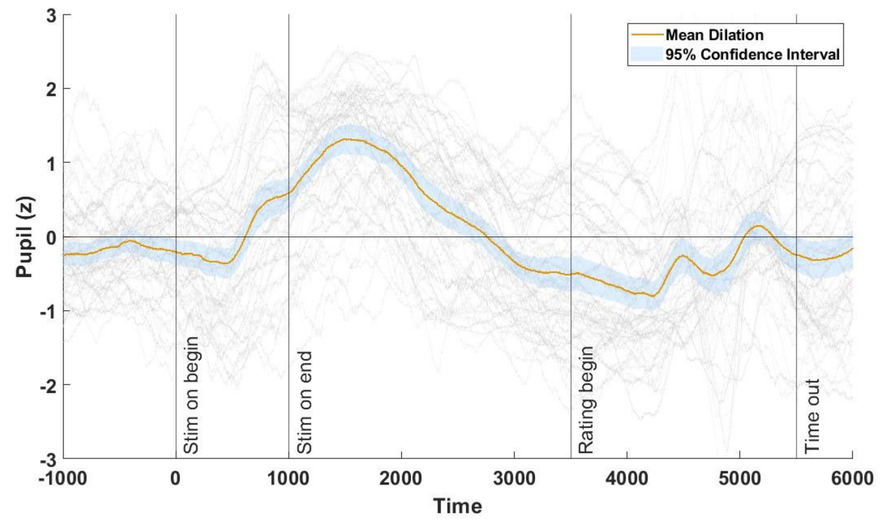


Quantitative MRI and Brainstem BOLD Activity (N=6)

Initial qMRI [10] results show successful visualization of neuromodulatory nuclei of interest, including the LC and substantia nigra (SN).

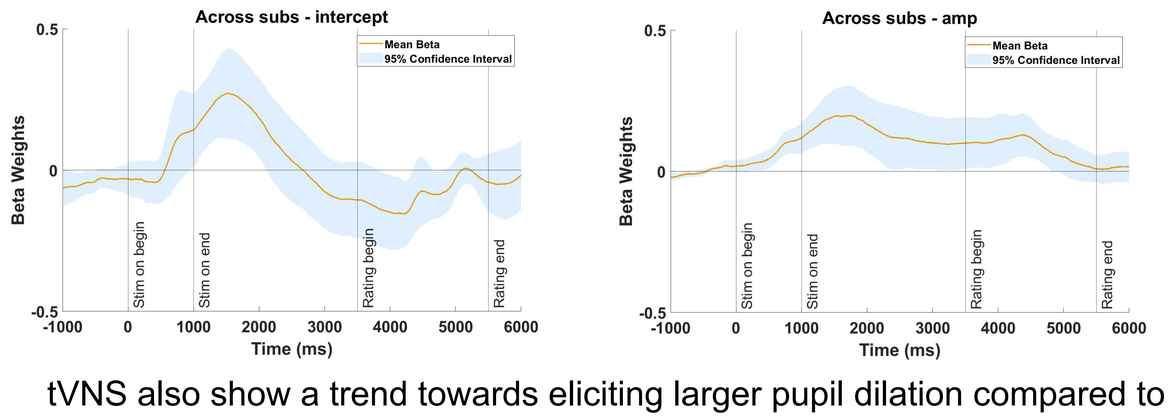


Average Pupil Traces (N=8)

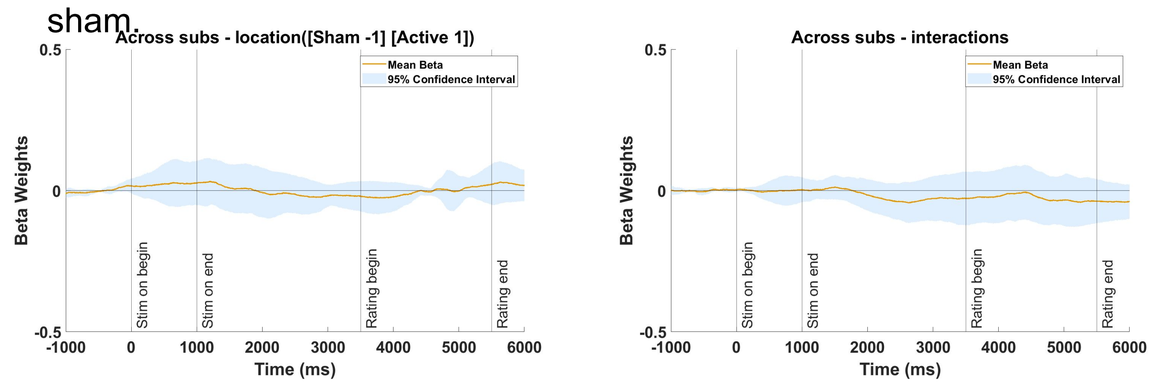


Pupil Regression Coefficients (N=8)

Preliminary pupil regression show that pupil dilation increases parametrically with stimulation intensity (in terms of amplitude level) across both locations.



tVNS also show a trend towards eliciting larger pupil dilation compared to sham.



References

[1] **Arnsten et al.** Catecholamine influences on prefrontal cortical function. *2011, Pharmacol Biochem Behav.*
[2] **Dahl et al.** Dopaminergic and noradrenergic integrity in late-life memory. *2023, Nat Aging.*
[3] **D'Agostini et al.** Short bursts of taVNS enhance evoked pupil dilation. *2023, Cortex.*
[4] **Farmer et al.** Minimum reporting standards for taVNS research. *2021, Front Hum Neurosci.*
[5] **Frank et al.** Computational models of DA and NA dysfunction in ADHD. *2007, Neuropsychopharmacology.*
[6] **Hulsey et al.** Neural activity in the LC in response to VNS. *2017, Exp Neurol.*
[7] **Ludwig et al.** Challenges in targeting the LC with taVNS. *2021, Auton Neurosci.*
[8] **Mridha et al.** Graded pupil-linked neuromodulation by VNS. *2021, Nat Commun.*
[9] **Sharon et al.** taVNS induces pupil dilation and attenuates alpha oscillations. *2021, J Neurosci.*
[10] **Weiskopf et al.** Quantitative MRI of brain anatomy and histology. *2021, Nat Rev Phys.*