SEX DIFFERENCES IN VAGUS NERVE STIMULATION INTENSITY AND RESPONSIVENESS

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BASELINE AUTONOMIC STATE AND CHILDHOOD LOW SES MAY INFLUENCE VNS RESPONSIVENESS, PARTICULARLY IN WOMEN.

INTRODUCTION

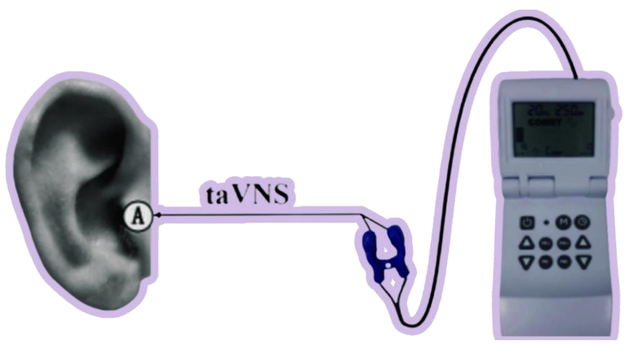
Vagus Nerve Stimulation (VNS) is a neuromodulation tool approved for treating epilepsy, depression, migraines, stroke recovery, and opioid withdrawal. However, VNS efficacy may vary due to person-based factors like vagal tone (Geng et al., 2022). Sex-based differences modulate vagal tone, with women showing higher vagal parasympathetic activity than men (Koenig & Thayer, 2016).

OBJECTIVE

This study examines how participant sex (male vs. female) affects:

- **VNS intensity** (i.e., tolerance to stimulation)
- **VNS responsiveness,** measured via heart rate variability (HRV)

Fig 1. Ear stimulation targets used of taVNS



Geng, D , 2022, PLoS ONE

METHODOLOGY

N = 87 eligible participants from the TCU SONA pool completed informed consent and a preliminary survey on a lab computer. Research assistants fitted participants with a Polar Strap connected to Kubios software to measure HRV. Trained graduate students administered Transcutaneous Vagus Nerve Stimulation (taVNS), a noninvasive form of VNS that applies electrical stimulation to the skin at the ear, stimulating the auricular branch of the vagus nerve.

N = 78 participants were included in the analyses. N = 9 participants were filtered out (e.g., failing attention checks, not following instructions).

Statistical analyses included t-tests to assess sex-based differences in VNS intensity and responsiveness and moderated regression analyses to examine the role of sex in the relationship between childhood variables and VNS outcomes.

RESULTS

- No sex-based differences were found in VNS intensity or responsiveness, *p*s > .134.
- Sex significantly moderated the relationship between baseline HRV and change in HRV, $R = .54$, $r2 = .29$, $F(3,65) = 8.75$, $p < .0001$. The association between baseline HRV and change in HRV was significant for females, $b = -1.79$, $SE = .36$, $t = -4.90$, $p < .001$. but not for males, $b = -.41$, $SE = .40$, $t = -1.03$, $p = .306$. .
- In a follow-up pristine analysis*, sex significantly moderated the relationship between childhood SES and change in HRV, $R = .423$, $r2 = .18$, $F(3,43) = 3.12$, $p = .036$. The association between childhood SES and change in HRV was significant for females, $b = .54$, $SE = .20$, $t = 2.71$, $p < .01$ but not significant for males, $b = -.22$, $SE = .17$, $t = -1.32$, $p = .192$.

*analysis excluding individuals with any kind of chronic conditions, or who took medication 24 hours before

DISCUSSION

Our conclusions support past literature's findings that participants with lower vagal tone are more responsive to VNS stimulation (Geng et al., 2022). We expanded upon these findings by demonstrating how some of the effects regarding VNS responsiveness were driven by female participants, including the association between (a) baseline LF/HF ratio and change in LF/HF ratio, and (b) childhood SES and change in LF/HF ratio. Results revealed that among females, higher sympathetic activity is associated with greater VNS responsiveness, and lower childhood SES is associated with more VNS responsiveness.

CONCLUSION

These findings have clinical implications for improving the therapeutic efficacy of VNS by providing insight into how sex-based differences relate to VNS intensity and responsiveness. Future research should measure the therapeutic efficacy of these results, specifically seeing if VNS is more successful in female individuals with higher sympathetic activity and individuals with lower childhood SES.

REFERENCES

Geng, D., Liu, X., Wang, Y., & Wang, J. (2022). The effect of transcutaneous auricular vagus nerve stimulation on HRV in healthy young people. Plos one, 17(2), e0263833.

Koenig, J., & Thayer, J. F. (2016). Sex differences in healthy human heart rate variability: A meta-analysis. Neuroscience & Biobehavioral Reviews, 64, 288-310.