

**Brief Title:** Leverage Noninvasive Transcutaneous Vagus Nerve Stimulation to Reduce Suicidal Behaviors in Vulnerable Adolescents

**Full Title:** Leveraging Noninvasive Transcutaneous Vagus Nerve Stimulation and Smartphone Technology to Reduce Suicidal Behaviors and Suicide Among Highly Vulnerable Adolescents

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For Aims 1 and 2:

The design is a 2 (tVNS: active vs. sham)  $\times$  2 (app: peer-support vs. control) factorial design. We will conduct separate analyses for each timepoint.

For the immediate post-intervention analysis, we will use ANCOVAs (Analysis of Covariance) with the following structure:

- Dependent variables: Each outcome measure (emotion dysregulation, social isolation, physiological reactivity, self-harm, depression, sleep, suicidal ideation, and suicidal behaviors)
- Independent variables:
  - tVNS condition (active vs. sham)
  - App condition (peer-support vs. control)
  - tVNS  $\times$  App interaction
- Covariates: Corresponding baseline measure for each outcome

This same analytical structure will be repeated separately for the one-year follow-up data, again using baseline measures as covariates.

Aim 3 (Moderation Effects): The analysis will use hierarchical multiple regression to examine individual differences in treatment response. Step 1 will include baseline scores and the hypothesized moderator (e.g., impulsivity, depression severity, maltreatment history). Step 2 will add main effects of both treatments (tVNS and app condition, coded -1/1). Step 3 will add all two-way interactions, and Step 4 will add the three-way interaction between both treatments and the moderator. Significant three-way interactions will be probed by examining the tVNS  $\times$  app condition interaction at different levels of the moderator ( $\pm 1$  SD for continuous moderators, or by category for categorical moderators). This process will be repeated for each hypothesized moderator. We will also examine whether early changes in mechanisms (emotion regulation, social connection) predict subsequent changes in outcomes using lagged analyses of the daily monitoring data.

Aim 4 (Treatment Adherence and Feasibility): For adherence, we will calculate descriptive statistics for tVNS usage (frequency, duration, intensity settings) and app engagement metrics (logins, interaction frequency, response rates to daily surveys). We will examine predictors of adherence using logistic regression. Acceptability will be assessed through quantitative ratings and qualitative feedback, with particular attention to side effects, burden, and perceived benefits. Feasibility metrics include recruitment rate, retention rate, data completeness, and rate of adverse events. We will also examine whether adherence levels mediate treatment outcomes using structural equation modeling and whether early engagement predicts subsequent adherence and outcomes.