Domain-Specific Benefits of Online Transcutaneous Auricular Vagus Nerve Stimulation in Subclinical ADHD

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Abstract

Subclinical ADHD is common in adults, marked by meaningful impairments, yet treatment options for this group remain limited. Transcutaneous auricular vagus nerve stimulation (taVNS) offers a scalable neuromodulatory approach, but its behavioral effects in subclinical ADHD are poorly understood. This study tested whether online (during-stimulation) taVNS yields domain-general or domain-specific cognitive benefits. Twenty adults with elevated inattention completed two single-blind, sham-controlled, and counterbalanced sessions. Stimulation was delivered at 25 Hz to the cymba concha (active) or at 1 Hz with identical montage and sensation (sham). Participants performed the Attention Network Task (ANT: alerting, orienting, executive control) and a 2-back working memory task. ANT reaction times were analyzed with generalized linear mixed models; 2-back accuracy with linear mixed models. Blinding was successful, and only mild transient side effects occurred. Results showed that active taVNS selectively reduced flanker interference, indicating enhanced attentional control, with no effects on alerting, orienting, or working memory. These findings demonstrate a domain-specific benefit of online taVNS in subclinical ADHD, selectively strengthening executive control rather than producing broad gains across attention and memory.

Keywords

Subclinical ADHD, taVNS, attention, executive control, domain-specific effect

1. Introduction

ADHD is best understood as a spectrum condition (Faraone et al., 2024). Many adults sit in a subclinical “grey zone”: their symptoms and day-to-day difficulties are substantial, yet they fall short of diagnostic thresholds and often receive no treatment or support (Balázs & Keresztény, 2014; Kirova et al., 2019). These subthreshold presentations carry meaningful functional costs in education, work, and wellbeing, underscoring an unmet clinical need in this population (Balázs & Keresztény, 2014; Kirova et al., 2019).

Transcutaneous auricular vagus nerve stimulation (taVNS) offers a mechanistically targeted and scalable option aligned to this need. taVNS activates auricular vagal afferents, which engage the nucleus tractus solitarius (NTS) and subsequently the locus coeruleus-noradrenergic (LC-NE) system (Badran et al., 2018; Frangos et al., 2015), a pathway in which tonic LC activity regulates arousal, while phasic LC activity conveyed through its projections to frontal and frontoparietal regions supports higher-order cognitive functions (Aston-Jones & Cohen, 2005). Importantly, both the subcortical regions and cortical networks are compromised in ADHD symptomatology (Bellato et al., 2020; Faraone et al., 2024). In humans, taVNS elicits activation in the NTS and LC-NE system as shown by fMRI (Badran et al., 2018; Frangos et al., 2015). Beyond autonomic effects, taVNS-induced activation is associated with broader behavioral benefits in humans. These gains appear particularly evident for high-order cognitive functions, with a meta-analysis showing more reliable advantages that concentrate on cognitive control (Ridgewell et al., 2021). Mechanistically, taVNS engages the NTC-LC pathway, increasing primarily central NE and secondarily GABA; this neuromodulatory shift is expected to strengthen cortical systems that subserve cognitive control, particularly conflict monitoring and response inhibition (Colzato & Beste, 2020). Importantly, these functions are core elements of executive control (Diamond, 2013) and are reliably compromised in ADHD (Boonstra et al., 2005; Willcutt et al., 2005; Pineda-Alhucema et al., 2018). taVNS also has a favorable safety profile, is portable and low-cost, and requires minimal training, enabling use beyond specialist clinics (Colzato & Beste, 2020). These practical features position taVNS as a pragmatic avenue for targeting ADHD-related behavioral difficulties, particularly those rooted in cognitive control (Zhang et al., 2023; Zhi et al., 2024).

We report, to our knowledge, the first evidence of behavioral consequences associated with taVNS in adults with subclinical ADHD. The study prioritized online (during-stimulation) effects as concurrent taVNS-fMRI has shown immediate engagement of vagal-brain circuits during stimulation (Badran et al., 2018). Behaviorally, this study examines whether online taVNS produces domain-general gains or domain-specific benefits. We paired the Attention Network with a 2-back task that differentially sample systems often compromised in ADHD. The ANT decomposes attention into (i) alerting, a tonic arousal signal linked to LC-NE modulation; (ii) orienting, a phasic spatial-selection signal supported by dorsal frontoparietal circuitry (intraparietal sulcus, superior parietal lobule, frontal eye fields); and (iii) executive control, a phasic conflict-resolution signal engaging cingulo-frontoparietal control regions (anterior cingulate/pre-SMA, dorsolateral prefrontal cortex) (Aston-Jones & Cohen, 2005; Corbetta & Shulman, 2002; Fan et al., 2002; Petersen & Posner, 2012). In contrast, the 2-back indexes working-memory maintenance and updating within a canonical frontoparietal network, with robust parietal contributions for short-term storage and serial monitoring (Owen et al., 2005; Wager & Smith, 2003), involving both tonic and phasic LC-NE modulation (Arnsten, 2011; D'Esposito & Postle, 2015). Under this design, a domain-general taVNS effect would manifest as parallel improvements across ANT components and 2-back accuracy; a domain-specific effect would appear as a selective change.

2. Methods

2.1 Participants

Subclinical ADHD was defined dimensionally using the ASRS Adult ADHD Self-Report (ASRS) 6-item screener (Kessler et al., 2005). An item was coded 'positive' if the response fell in the scale's shaded boxes. Participants with ⩾4/6 positive items and no prior ADHD diagnosis were classified as having elevated ADHD symptoms (Balázs & Keresztény, 2014). We initially estimated sample size under a conventional repeated-measures framework, yielding n = 18 for 80% power to detect a medium effect at $\alpha = .05$. Allowing ~10% attrition, we targeted n = 20. Our primary analyses instead used linear mixed-effects models, which are more efficient for within-subject data. Hence, the initial estimate remains valid as a conservative lower bound. The study was approved by the Monash University Human Research Ethics Committee (41941). All participants provided written informed consent.

We pre-screened 83 volunteers with the ASRS-6; 53 did not meet the subclinical threshold and 10 were excluded due to scheduling conflicts. The final sample comprised 20 adults (M_age = 21.65, SD = 2.32; 14 female, 3 male, 3 non-binary). Participants completed two single-blind and sham-controlled sessions in a counterbalanced within-subject design and were randomised to order (Active-first n = 10, Sham-first n = 10). Participant flow and screening outcomes are shown in Figure 1A.

2.2 Materials

taVNS was delivered with a consumer-grade device (Xinlepai, China) using earphone-style electrodes positioned at the cymba concha, a site innervated by the auricular branch of the vagus nerve. The device outputs biphasic, rectangular waveforms to minimize tissue polarization. Active stimulation was 25 Hz and sham was 1 Hz with identical montage, a preferred approach to elicit taVNS effects while maintaining an inert control (Kim et al., 2022). Current intensity was titrated in 0.1 mA increments to a strong-but-comfortable tingling sensation and then held constant for the session. See Figure 1B for the stimulation set-up.

Attention was assessed with the ANTI-VEA platform, a validated extension of the Attention Network Test that yields the standard network indices – alerting, orienting, and attentional control – within a single and interleaved task (Luna et al., 2018; Fan et al., 2002). Alerting contrasts reaction times (RTs) after an auditory tone versus no tone. Orienting compares RTs following valid versus invalid spatial cues. Attentional control contrasts incongruent versus congruent flanker arrays. To ensure reliability, participants completed extensive practice trials and achieved ≥ 90% accuracy in formal testing. Only correct trials with RTs between 200-1500 ms were analysed (Luna et al., 2018). Working memory was measured with a standard 2-back task, a widely used probe of updating and maintenance with well-characterized psychometrics and neural correlates (Heinzel et al., 2014; Owen et al., 2005). Digits were presented sequentially and participants judged whether the current digit matched the one two trials earlier. Practice blocks preceded formal testing to ensure instruction comprehension. The 2-back working memory task administered twice (before and after the attention task) to control for task-order effects.

Following Gerges et al. (2024), blinding and adverse events were assessed at session end: participants completed a brief condition-guess questionnaire (active vs sham), with guess accuracy compared against the assigned condition, and an Adverse Events Questionnaire listing commonly reported taVNS sensations (e.g., tingling, itching, manageable pain at the stimulation site).

2.3 Procedure

Participants completed two single-blind and sham-controlled sessions on separate days in counterbalanced order (active-first vs sham-first). After electrode placement and intensity titration, stimulation was initiated and maintained during a fixed sequence: 2-back (pre) → ANTI-VEA → 2-back (post), which controls for task-order effects. Practice preceded formal testing; blinding and adverse-event questionnaires were administered immediately after each session. See Fig. 1C for the experimental timeline.

2.4 Statistical analysis

To accommodate the skewed distribution of reaction times (RT), trial-level ANTI-VEA RTs were analyzed with generalized linear mixed models using a Gamma family and log link (Lo & Andrews, 2015). The random-effects structure was added sequentially (fixed effects only → + participant intercept → + trial/session intercepts → + by-participant slopes for task factors), retaining terms that improved fit by likelihood-ratio tests and AIC/BIC. Effect sizes were derived by exponentiating fixed-effect coefficients to obtain RT ratios and reporting percent change as (ratio - 1) × 100. 2-back accuracy (proportion correct) was analyzed with random-intercept linear mixed models, predicting accuracy from condition (active vs. sham) with participant as a random effect.

-INSERT FIGURE 1 HERE-

3. Results

3.1 Blinding and side effects

Blinding was successful: participants' ability to guess their assigned condition did not differ from chance ($p = .63$ for Session 1 and $p = .70$ for Session 2. Only minor side effects were reported. Some participants noted mild itching or prickling sensations in the ear during stimulation, but no serious adverse events occurred.

3.2 Attention

All three ANTI-VEA manipulations elicited the expected effects, confirming task validity: flanker effect ($b = 0.08$, $SE = 0.02$, $z = 4.46$, $p < .001$; ≈ +8.27%), alerting ($b = -0.04$, $SE = 0.01$, $z = -3.05$, $p = .002$; ≈ -4.08%), and orienting ($b = 0.06$, $SE = 0.02$, $z = 3.76$, $p < .001$; ≈ +6.60%). In the best-fitting GLMM, only the flanker component showed a session interaction. The congruency × session term was significant ($b = -0.04$, $SE = 0.02$, $z = -2.25$, $p = .025$; ≈ -4.13%), indicating a smaller incongruent–congruent RT difference under active taVNS than sham; the session main effect was not significant ($b = 0.03$, $SE = 0.02$, $z = 1.51$, $p = .131$). By contrast, interaction terms were not significant in the best-fitting models for alerting (tone × session: $b \approx -0.00$, $SE = 0.02$, $z = -0.13$, $p = .894$; ≈ -0.25%) or orienting (validity × session: $b = 0.02$, $SE = 0.02$, $z = 0.87$, $p = .386$; ≈ +2.05%), and session main effects were also nonsignificant (alerting: $b = 0.01$, $SE = 0.02$, $z = 0.58$, $p = .562$; orienting: $b = 0.01$, $SE = 0.02$, $z = 0.28$, $p = .776$).

3.3 Working memory

One participant was excluded from the analysis of working memory due to extremely low accuracy in one session. The session effect was not significant: $b = 1.55$, $SE = 1.33$, $t = 1.16$, $p = .26$.

4. Discussion

Using validated tasks that fractionate behavioral effect, we found that on-line taVNS selectively enhanced attentional control (i.e., reducing flanker interference) whereas alerting, orienting, and working memory showed no change in subclinical ADHD. The counterbalanced within-subject design with a montage- and sensation-matched sham limits expectancy and order confounds, supporting a causal link between taVNS and improved control – a domain-specific improvement.

Our findings offer deeper insight into how online taVNS influences behavior in subclinical ADHD by engaging the NTS → LC-NE → fronto-parietal pathway. This pathway involves multiple mechanisms, e.g., distinctions between tonic and phasic LC activity and differential recruitment of fronto-parietal networks (Aston-Jones & Cohen, 2005). Our experimental design separates: (i) attentional control, cingulo-frontoparietal circuits, preferentially modulated by phasic LC-NE signals; (ii) arousal, a tonic LC-NE process; (iii) orienting, implemented by dorsal frontoparietal orienting networks with phasic and stimulus-driven shifts; and (iv) 2-back working memory, maintenance/updating in frontoparietal systems, influenced by both tonic and phasic modulation. We observed a selective reduction in flanker interference with no concomitant change in ANT alerting/orienting or 2-back accuracy, evidence for a domain-specific enhancement of attentional control (i.e., phasic LC-NE activity underlying cingulo-frontoparietal circuits) rather than a domain-general benefit. This pattern is in line with LC adaptive-gain theory (Aston-Jones & Cohen, 2005), wherein phasic LC activity transiently raises cortical gain to improve signal-to-noise during conflict resolution (in other words, attentional control). The selective improvement is also in line with a meta-analysis that taVNS most reliably benefits tasks demanding cognitive control (Ridgewell et al., 2021).

Adults with subclinical ADHD often struggle with distractor resistance yet rarely access treatment, with downstream educational and occupational costs (Balázs & Keresztény, 2014; Kirova et al., 2019). Within this context, the current study suggests that concurrent taVNS may help sustain task focus when interference is high, offering a practical and low-burden option. More broadly, this supports a precision approach in which taVNS is paired with context-specific cognitive demands. Future work should refine timing and dose and test whether repeated sessions convert acute gains into durable, real-world benefits.

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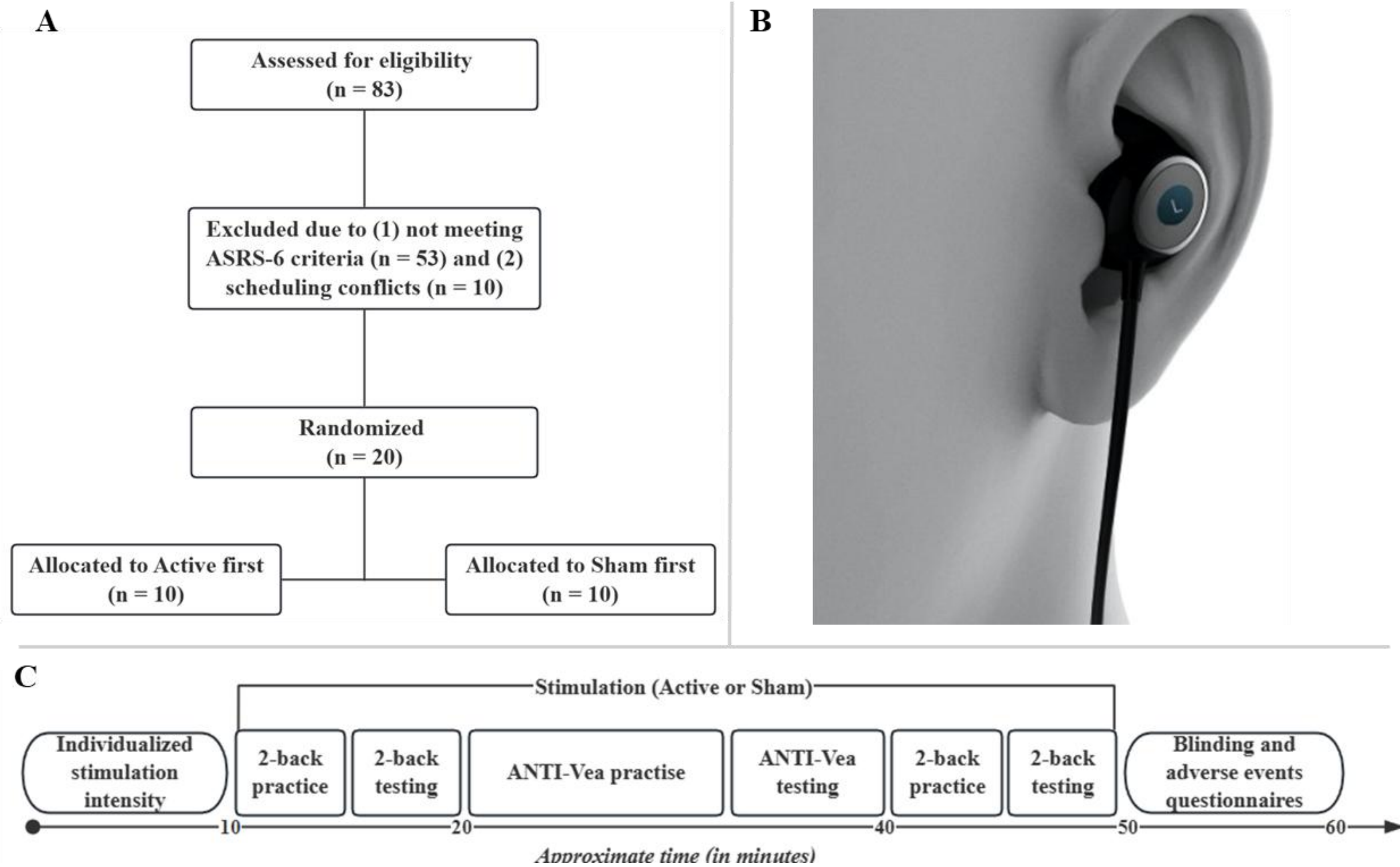

Figure 1. Study design and stimulation protocol. (A) Screening and allocation (ASRS-6 pre-screen; final n = 20; session order counterbalanced). (B) taVNS set-up at the cymba concha (earphone-style electrodes; biphasic rectangular waveform; 25 Hz active, 1 Hz sham; intensity titrated to comfortable tingling). (C) On-stimulation task sequence: 2-back (pre) → ANTI-VEA → 2-back (post); end-of-session blinding guess and adverse-events check.