PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

AURA: Direct Biological Response Evaluation of a Music-Envelope Transcutaneous Auricular Vagus Stimulation Platform

HUMAN SUBJECTS RESEARCH DOSSIER / IRB REVIEW SYNOPSIS

1. PROTOCOL PURPOSE

This study evaluates whether music-envelope modulation delivered through a noninvasive transcutaneous auricular stimulation platform produces measurable autonomic and biological responses beyond constant-carrier, matched non-musical envelope, and sham comparator conditions.

Existing noninvasive neuromodulation studies often rely on indirect autonomic measures without simultaneously verifying comparator separation, biological response, and tolerability. This protocol uses a controlled crossover design to isolate waveform condition and evaluate direct physiological signals during acute supervised use.

2. PRIMARY QUESTIONS

1. Does active AURA stimulation produce measurable autonomic response during the stimulation window relative to baseline?
2. Do responses differ from constant-carrier, matched non-musical envelope, and sham conditions?
3. Is the stimulation tolerable and safe under supervised acute-use conditions?
4. Do observed signals justify continued translational development?

3. STUDY THESIS

Active music-envelope stimulation will produce separable autonomic and physiological signatures compared with control conditions while remaining within predefined safety and tolerability limits.

A. PROTOCOL SYNOPSIS

Study class	Prospective, randomized, double-blind, within-subject human feasibility study
Population	Healthy adults, ages 21-50 years; N = 48 enrolled; target completers >= 40
Design	Randomized, double-blind, within-subject crossover
Study arms	Active AURA; Constant-carrier control; Matched non-musical envelope control; Sham
Session duration	Approximately 75 minutes per visit: 20 minutes baseline, 30 minutes stimulation, 25 minutes post-stimulation observation.
Primary endpoint family	Change in RMSSD during stimulation relative to baseline; Active versus sham/control separation in HRV window response
Risk level summary	Risks are expected to be no more than minimal to moderate transient discomfort under supervised, current-limited, noninvasive use. Direct benefit is not expected. The anticipated knowledge benefit is determination of whether the device produces interpretable biological signals under controlled conditions.
Analysis framework	Mixed-effects models will evaluate condition, time window, and condition-by-time interaction with participant as a random effect.

B. COMPARATOR / ARM LOGIC

Arm	Purpose
Active AURA	Tests music-shaped envelope effect.
Constant-carrier control	Isolates envelope modulation.
Matched non-musical envelope control	Controls for envelope dynamics without musical content.
Sham	Controls for placebo, attention, and expectancy.

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

IRB Approval Criteria and Submission Map

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

A. APPROVAL CRITERIA CROSSWALK

IRB Criterion	Protocol Location	Reviewer Evidence	Closure Test
Risks minimized	Risk closure matrix; procedures; device controls	Mitigations map to each participant exposure	No unmitigated exposure remains
Risk/benefit reasonable	Risk-benefit summary; endpoints	Knowledge value tied to defined outcomes	Risk level matches expected scientific yield
Equitable selection	Population and recruitment	Inclusion/exclusion criteria and recruitment sources	No unjustified targeting or exclusion
Informed consent adequate	Consent process and appendix language	Key information, risks, voluntariness, contacts	Consent covers actual procedures and risks
Data monitoring adequate	Safety monitoring; AE reporting	Monitoring roles, stopping criteria, reporting path	Action thresholds are explicit
Privacy and confidentiality protected	Data governance and HIPAA section	Identifiers, coding, access controls, sharing plan	Identifiable data are segregated and controlled
Vulnerable populations protected	Population exclusions and consent capacity	Special groups excluded or justified	Safeguards match enrolled population

B. REQUIRED PACKET ARTIFACTS

- Full protocol dossier
- Consent form or consent script
- Recruitment material
- Screening checklist
- Adverse event reporting plan
- Data security plan
- Delegation log and training plan

C. CONDITIONAL MODULES

- Device module: Enabled
- Biospecimen module: Enabled
- HIPAA module: If HIPAA applies, authorization or waiver documentation will be maintained according to institutional policy.
- Vulnerable population module: see population

D. SUBMISSION STATE

- Protocol version: 1.0
- Review body: Institutional Review Board
- Confidentiality: Investigator draft for IRB review. Not for clinical use.
- PI: [Principal Investigator Name]

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Study Design, Objectives, and Endpoint Logic

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

1. SCIENTIFIC PREMISE

- A time-varying envelope applied to a high-frequency carrier can be delivered reproducibly at the tissue interface under defined contact and safety limits.
- Music-derived envelope dynamics are treated as a programmable stimulus feature, not as assumed therapeutic content.
- Comparator conditions separate carrier presence, envelope variability, musical structure, and placebo or expectancy effects.

2. DESIGN TYPE

Randomized, double-blind, within-subject crossover. Washout: >= 72 hours between sessions. Session duration: Approximately 75 minutes per visit: 20 minutes baseline, 30 minutes stimulation, 25 minutes post-stimulation observation.

3. RANDOMIZATION AND BLINDING

Session order will be assigned by Latin-square counterbalancing. The randomization list will be generated and held by the biostatistician or unblinded technician.

Participants and outcome assessors will remain blinded to condition. Device logs and condition codes will be unavailable to blinded staff until the database lock unless unblinding is required for safety.

4. PARTICIPANT STOP RULE

Any participant may stop a session immediately for discomfort, anxiety, dizziness, pain, or request to stop.

A. ENDPOINT HIERARCHY

Tier	Endpoint(s)
Primary	**Change in RMSSD during stimulation relative to baseline** Primary autonomic index for within-subject comparison across conditions. **Active versus sham/control separation in HRV window response** Tests whether physiological response exceeds procedural and carrier controls.
Secondary	• Respiratory sinus arrhythmia • Skin conductance tonic level and phasic response frequency • Blood pressure and pulse wave amplitude • Pupil diameter and light reactivity • Tolerability rating and contact-site skin assessment
Exploratory	• Salivary alpha-amylase • Salivary cortisol • Inflammatory cytokine panel: IL-6, TNF-alpha, IL-1beta, IL-10, CRP

B. ARM PURPOSE MATRIX

Condition	Description	Purpose
Active AURA	Music-envelope modulation delivered on a 32 kHz carrier.	Tests music-shaped envelope effect.
Constant-carrier control	32 kHz carrier delivered without amplitude envelope modulation.	Isolates envelope modulation.
Matched non-musical envelope control	Amplitude envelope matched for RMS and modulation statistics but time-scrambled to remove musical structure.	Controls for envelope dynamics without musical content.
Sham	Identical setup with sub-threshold or disabled output according to validated sham procedure.	Controls for placebo, attention, and expectancy.

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Participants, Recruitment, and Consent

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

1. TARGET POPULATION

Healthy adults, ages 21-50 years. Sample size: N = 48 enrolled; target completers >= 40.

Recruitment will seek balanced representation by sex and will not preferentially include economically or educationally vulnerable groups.

2. RECRUITMENT SOURCES

- Institutional volunteer registry
- IRB-approved flyers and digital announcements
- Direct referral from research recruitment office

3. CONSENT PROCESS

Consent will be obtained prospectively in a private setting by trained study staff before any research procedures. Participants will receive the consent document, a verbal explanation of study purpose and procedures, time for questions, and confirmation that participation is voluntary.

4. COMPENSATION AND INJURY LANGUAGE

Compensation: $[amount] per completed session plus transportation reimbursement if applicable.

Research injury: Research-related injury procedures will follow institutional policy. Emergency care will be provided as clinically indicated.

A. INCLUSION / EXCLUSION HIGHLIGHTS

Inclusion	Exclusion
Age 21-50 years	History of seizure disorder or unexplained loss of consciousness
Able to provide informed consent	Implanted electronic, cardiac, or neurostimulation device
Normal external ear examination and suitable concha/cymba anatomy for device placement	Active ear infection, skin breakdown at contact site, tympanic membrane perforation, or chronic otitis
Able to attend four study sessions separated by washout intervals	Unstable cardiovascular disease, uncontrolled hypertension, clinically significant arrhythmia, or recent myocardial infarction
Willing to abstain from caffeine, alcohol, strenuous exercise, and new autonomic-active supplements before sessions	Current medication that substantially alters autonomic measures unless approved by study clinician
	Pregnancy or breastfeeding
	Current substance use disorder or condition impairing informed consent

B. KEY INFORMATION AND COMPREHENSION

KEY INFORMATION

- This is research and the device is investigational for this use.
- Participation involves four supervised sessions with noninvasive auricular stimulation or control conditions.
- The study is designed to evaluate physiology, safety, and tolerability; direct personal benefit is not expected.
- Participants can stop stimulation or withdraw at any time.

COMPREHENSION CHECKS

- Participant can describe study purpose in their own words.
- Participant can identify main discomforts and withdrawal rights.
- Participant understands that the active condition is blinded.

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Study Procedures and Schedule of Events

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

A. VISIT PROCEDURE MAP

Visit	Window	Activities
Screening	Day -14 to Day 0	• Consent • Medical history and medication review • Eligibility review • Ear/contact-site examination • Baseline questionnaires
Session 1	Randomized condition	• Pre-session restrictions confirmation • Baseline physiological recording • Stimulation or control condition • Post-session observation • Adverse event/tolerability assessment
Sessions 2-4	Crossover conditions	• Repeat session procedures with alternate condition • Washout compliance review • Safety check before and after session
Follow-up	+24 hours after each session	• Remote adverse event check • Delayed symptom assessment • Sleep and medication change query

B. SCHEDULE OF ASSESSMENTS

Assessment	Screening	Baseline	Stimulation	Post	+24 h
Informed consent / eligibility	X	-	-	-	-
Vitals and symptom screen	X	X	X	X	X
HRV / ECG	-	X	X	X	-
Skin conductance	-	X	X	X	-
Respiration	-	X	X	X	-
Blood pressure	X	X	X	X	-
Pupillometry	-	X	X	X	-
Saliva collection	-	X	-	X	X
Blood sample / biomarker panel	-	X	-	X	-
Adverse event review	X	X	X	X	X

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Participant Exposure and Risk Closure

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

1. RISK / BENEFIT POSITION

Risks are expected to be no more than minimal to moderate transient discomfort under supervised, current-limited, noninvasive use. Direct benefit is not expected. The anticipated knowledge benefit is determination of whether the device produces interpretable biological signals under controlled conditions.

2. ANTICIPATED ADVERSE EVENTS

- Ear discomfort or pressure
- Skin redness or irritation
- Headache
- Dizziness or lightheadedness
- Nausea
- Transient hearing change or tinnitus
- Fatigue
- Vasovagal symptoms related to blood draw

3. STOPPING CRITERIA

- Serious adverse event possibly related to study procedures
- Predefined physiological threshold exceeded
- Participant requests stimulation stop
- Device fault, overcurrent, overtemperature, or contact safety alarm
- Medical monitor or PI determines continuation is not appropriate

A. EXPOSURE-TO-MITIGATION MATRIX

Exposure	Risk	Mitigation	Monitoring
Auricular electrical stimulation	Ear discomfort, tingling, irritation, dizziness, headache	Conservative output limits, trained placement, real-time monitoring, stop-on-request	Tolerability scale, contact-site inspection, AE review
Physiological monitoring sensors	Skin irritation or inconvenience	Medical-grade sensors, limited duration, removal on discomfort	Skin check and participant report
Blood draw	Pain, bruising, vasovagal reaction, infection	Trained phlebotomist, sterile technique, limited volume	Post-draw observation and AE documentation
Collection of identifiable health data	Loss of confidentiality	Coded IDs, access controls, encrypted storage, limited data access	Audit trail and data incident reporting

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Privacy, Confidentiality, and Data Governance

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

1. IDENTIFIERS AND CODING

Participants will be assigned study IDs. Direct identifiers will be stored separately from research data in a restricted-access file.

- Name and contact information
- Age, sex, relevant medical history
- Physiological recordings and questionnaire responses
- Device session logs

2. STORAGE AND RETENTION

Storage: Study data will be stored on encrypted institutional systems with access restricted to approved study staff.

Retention: Data will be retained according to institutional policy and sponsor requirements, then archived or destroyed as approved.

3. SHARING AND HIPAA

De-identified aggregate results may be shared in publications, reports, or future grant applications. Identifiable data will not be shared outside the approved study team without authorization or IRB approval.

If HIPAA applies, authorization or waiver documentation will be maintained according to institutional policy.

A. DATA LIFECYCLE

B. ACCESS CONTROL TABLE

Direct identifiers	Stored separately; restricted to approved personnel
Research dataset	Coded participant ID; no direct identifiers in analysis file
Device/session logs	Linked by study ID; reviewed for safety and signal integrity
Publication outputs	Aggregate or de-identified results only

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Safety Monitoring and Adverse Event Reporting

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

1. MONITORING PLAN

A trained study clinician or PI-delegated staff member will review safety during each session and at follow-up. Adverse events will be graded for severity, relatedness, expectedness, and outcome.

2. UNANTICIPATED PROBLEMS

Unanticipated problems involving risks to participants or others will be reported to the IRB according to institutional reporting timelines.

3. MEDICAL MONITOR

An independent medical monitor will review any serious or unexpected events and may recommend pause, revision, or termination.

4. EMERGENCY PLAN

Stimulation will be stopped immediately for concerning symptoms. Standard clinical response procedures will be used for acute events. Emergency medical services will be activated when indicated.

A. REPORTING PATHWAY

Event Type	Immediate Action	Review / Report
Mild expected event	Document and monitor	Summarize at continuing review
Moderate or concerning event	Pause procedure; clinician review	PI and monitor review
Serious or unexpected related event	Stop study activity; clinical response	IRB report per institutional policy
Device malfunction or data incident	Quarantine / secure system	Deviation or incident report

B. SAFETY ROLE ACCOUNTABILITY

Role	Responsibility
Principal Investigator	Overall study conduct, participant safety, protocol compliance.
Study Clinician	Screening review, adverse event assessment, clinical escalation.
Unblinded Device Technician	Condition coding, device configuration, randomization implementation.
Blinded Outcome Assessor	Physiological data acquisition and participant assessments.
Biostatistician	Analysis plan, randomization list, statistical reporting.

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Statistical Analysis and Decision Rules

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

1. ANALYSIS POPULATION

Participants with at least one completed active and one comparator session will contribute to primary within-subject analyses.

2. PRIMARY ANALYSIS

Mixed-effects models will evaluate condition, time window, and condition-by-time interaction with participant as a random effect.

3. MULTIPLICITY AND MISSING DATA

Co-primary endpoints will be tested hierarchically. Secondary endpoints will be interpreted with false-discovery-rate control or clearly labeled exploratory.

Missing physiological data will be documented by reason. Mixed-model analyses will use available data under missing-at-random assumptions, with sensitivity analysis if missingness exceeds thresholds.

A. GO / REVISE / STOP MATRIX

Domain	Advance	Revise	Stop
Safety	No related serious adverse events; all hard safety thresholds maintained	Manageable non-serious events or nuisance shutdowns	Related serious adverse event or repeated threshold violation
Tolerability	>= 80% of sessions completed with mild discomfort or less	50-79% completed or moderate recurring discomfort	Intolerable discomfort or <50% completion
Signal integrity	>= 90% usable physiological data	70-89% usable data	<70% usable data
Comparator separation	Active condition separates from sham/control on primary endpoint	Directionally consistent but underpowered or noisy separation	No separation and no interpretable signal

B. INTERPRETABILITY STANDARD

The protocol advances only when safety remains acceptable and the primary signal is interpretable against the declared comparator structure. Otherwise the recommended output is revision, dose/procedure redesign, or study stop.

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Investigational Device / Product Module

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

1. DEVICE DESCRIPTION

AURA: A single-contact auricular stimulation platform that maps audio-derived envelope information onto a high-frequency carrier under zero-DC, current-limited output conditions.

2. SR / NSR RATIONALE

The sponsor will submit the device risk determination to the IRB. The protocol is written to support a nonsignificant-risk determination under supervised, noninvasive, limited-duration use, but the IRB determination controls study startup requirements.

3. ACCOUNTABILITY

Each device will be assigned a device ID, inspected before use, logged for session condition and fault status, and quarantined after any suspected malfunction.

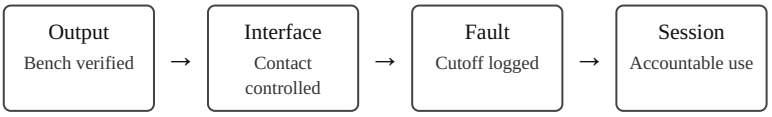
A. OUTPUT PARAMETERS

Parameter	Specification
Carrier frequency	32 kHz +/- 1%
Modulation bandwidth	0.1-25 Hz envelope domain
Nominal current range	0-2.0 mA RMS at tissue interface
Temperature cutoff	Warn at >= 40.0 C; cutoff at >= 42.0 C at contact site
Session cap	<= 30 minutes stimulation per session

B. SAFETY FUNCTIONS

- Series capacitive zero-DC blocking
- Current monitoring and hard cutoff
- Contact impedance monitoring
- Thermal supervision at contact interface
- Open/short/stuck-carrier detection
- Event log retained for each session

C. DEVICE EVIDENCE CHAIN



PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Biospecimen Collection and Handling Module

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

1. SPECIMEN TYPES AND TIMING

Types: Saliva, Peripheral blood

Baseline and post-session windows; selected +24 h saliva collection

2. VOLUME LIMITS

Blood volume will remain within institutional limits for healthy adult research participants.

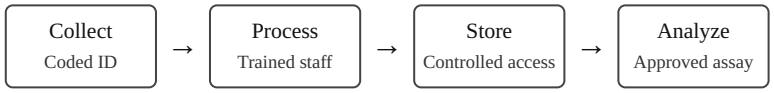
3. PROCESSING AND STORAGE

Specimens will be labeled with coded IDs, processed by trained staff, and stored in locked or access-controlled laboratory space or approved freezers.

A. FUTURE USE AND DISPOSITION

Future use	Future use will occur only if included in consent and approved by the IRB.
Destruction / de-identification	Residual specimens will be destroyed or de-identified according to consent and institutional policy.
Consent dependency	Specimen use must match the consent option selected by participant and approved by IRB.

B. CHAIN OF CUSTODY



PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Appendix A. Consent Form Core Language

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

A. PARTICIPANT-FACING LANGUAGE

Purpose	You are being asked to take part in a research study testing whether a noninvasive ear stimulation device changes short-term physiological signals.
Procedures	You will complete screening and up to four study sessions. During each session, sensors will measure physiology while the study device is active or inactive according to a blinded condition.
Risks	Possible risks include ear discomfort, skin irritation, headache, dizziness, nausea, temporary hearing changes, fatigue, and discomfort from blood draws if applicable.
Benefits	You are not expected to receive direct medical benefit. The study may help researchers understand whether the device produces measurable physiological responses.
Voluntary participation	Taking part is voluntary. You may stop stimulation or leave the study at any time.

B. RECRUITMENT COPY

Research volunteers are invited for a study evaluating physiology during noninvasive ear stimulation and control conditions. Participation includes screening and up to four study visits. Compensation is provided.

C. SCREENING CHECKLIST

- Age and consent capacity
- Neurological and cardiovascular history
- Medication and supplement review
- Implanted device screening
- Ear/contact-site examination
- Pregnancy screening if applicable

PROTOCOL NUMBER	VERSION	SUBMITTING UNIT	REVIEW BODY	DATE SUBMITTED
IRB-AURA-2026-001	1.0	Translational Neurotechnology Program	Institutional Review Board	June 10, 2026

Appendix B. Logs, Forms, and Closeout Artifacts

IRB REVIEW DOSSIER / FULL PROTOCOL COMPILER

A. REQUIRED LOGS

- Delegation of authority log
- Eligibility checklist
- Adverse event log
- Device accountability log
- Protocol deviation log
- Consent version log

B. DEVIATION CLASSIFICATION

Class	Example	Action
Minor	Administrative correction without risk impact	Document in deviation log
Major	Procedure outside approved protocol	PI review; report per policy
Safety-relevant	Exposure outside safety limits or consent failure	Immediate pause and IRB notification as required

C. REFERENCE BASIS

- 45 CFR 46 Subpart A - Federal Policy for the Protection of Human Subjects
- OHRP informed consent guidance and FAQs
- FDA guidance on significant risk and nonsignificant risk medical device studies, when applicable

D. FINAL READINESS CHECK

- All participant-facing language reconciled with protocol procedures.
- All exposures mapped to risks, mitigations, and monitoring.
- All endpoints mapped to study questions.
- All data flows mapped to privacy controls.
- All conditional modules either completed or marked not applicable.