CLINICAL RESEARCH PROTOCOL

Project Title:

Informational Perturbation Reverses Precision Collapse in a Metastable Proprioceptive Inference Regime

Protocol ID:	SAIM-PH3-20251214-FROZEN
Date of Protocol:	December 14, 2025
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Open Science Statement:
This protocol is made publicly available to ensure transparency and reproducibility of the research reported in the associated manuscript.

1. INTRODUCTION AND RATIONALE

Biological systems maintain adaptive stability by minimizing prediction error. However, under conditions of chronic uncertainty, systems may suppress sensory precision, leading to a maladaptive state termed "Proprioceptive Prediction Error Neglect" (PPEN). This study hypothesizes that this state acts as a metastable "frozen" attractor and can be resolved via Specific Informational Perturbation (SIP).

2. STUDY OBJECTIVES

- **Primary Objective:** To verify whether SIP triggers a phase transition from a frozen attractor to an adaptive state, quantified by the Free Energy Proxy (F).
- **Secondary Objectives:** To assess recovery in hemodynamic coupling (HEMO) and systemic integration (SII), and to validate the informational specificity of the intervention.

3. STUDY DESIGN

This research comprises three sub-studies conducted under a unified protocol:

1. **Study 1 (Randomized Controlled Trial):** A parallel-group, sham-controlled mechanistic trial ($N = 52$) to evaluate the causal effect of SIP.
2. **Study 2 (Specificity):** A **randomized crossover design** ($N = 24$) where each participant receives three conditions (SIP, Predictable, Mismatch) in a randomized order to assess informational specificity.
3. **Study 3 (Ecological Validation):** A **randomized crossover design** ($N = 30$) comparing Laboratory vs. Home settings. Participants are randomly assigned to the order of environments (Lab-first vs. Home-first) to confirm robustness across contexts.

4. PARTICIPANT SELECTION

Inclusion Criteria

- Healthy adults aged 18-65.
- Meeting the SAIM diagnostic criteria for "Frozen" state (Baseline $F > 0.8$ or Dynamic Fragility).
- Capacity to provide informed consent.

Exclusion Criteria

- History of cervical spine surgery or severe trauma.
- Current use of neuroactive (GABAergic) medications.
- Severe neurological deficits (e.g., Stroke, Parkinson's disease).
- Cognitive impairment precluding informed consent.

5. INTERVENTIONS

Experimental Group (SIP)

Application of a discrete, state-dependent tactile input to the craniocervical region. The stimulus is strictly information-based:

- **Force:** Sub-mechanical threshold (negligible work).
- **Vector:** Maximizing prediction error relative to the frozen prior.
- **Timing:** Aperiodic impulse (< 100 ms).

Control Group (Sham)

Application of a mimic touch with identical duration and location but lacking the specific vector directionality required to update the generative model (Zero-information placebo).

6. STUDY PROCEDURES (SEQUENCE)

Participants will undergo the following standardized sequence:

1. **Pre-Assessment:** Continuous monitoring during Rest (80s) $\rightarrow$ Stress Task (20s) $\rightarrow$ Recovery (80s).
2. **Intervention Phase:** Administration of SIP or Sham (or assigned crossover condition).
3. **Incubation Phase:** 15-minute supine rest to allow for metabolic stabilization and neural integration.
4. **Post-Assessment:** Repetition of the Pre-Assessment sequence.

7. OUTCOMES AND ANALYSIS

Primary Endpoint

Change in Free Energy Proxy (ΔF) between Pre- and Post-intervention baselines.

Data Acquisition

Data will be collected using the Muse S (Gen 2) Athena device (256 Hz EEG, PPG, Accelerometry). Raw data will be processed using the SAIM-v1.0 pipeline.

Statistical Analysis

Group differences in ΔF will be analyzed using independent t-tests (Study 1) and **Repeated Measures ANOVA (Study 2 and Study 3)**. Significance level is set at $\alpha = 0.05$.

8. ETHICS AND DATA SAFETY

This study is conducted in accordance with the Declaration of Helsinki. The protocol was approved by the Institutional Review Board (Protocol ID: SAIM-PH3-20251214-FROZEN). All participants provide written informed consent. Data will be anonymized and stored in a secure, encrypted repository.