

Designing a Sham-Controlled Study of Infra-Slow Neurofeedback: Learning Trajectories, Sleep Outcomes, and Neurophysiological Change

Arne Edvardsson¹, Sandra Weineland^{1,2}, Steinn Steingrímsson^{3,4}, Stefanie Enriquez-Geppert⁵, Michael G. Smith⁶

¹ Research and Development, Primary Health Care Region Västra Götaland, Borås, Sweden

² Department of Psychology, Faculty of Social Science, University of Gothenburg, Gothenburg, Sweden

³ Department of Psychiatry for Affective Disorders, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden

⁴ Section of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

⁵ Department of Clinical and Developmental Neuropsychology, Faculty of Behavioural and Social Sciences, University of Groningen, Groningen, the Netherlands

⁶ Department of Occupational and Environmental Medicine, School of Public Health and Community Medicine, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden

Introduction

Infra-slow oscillations (ISOs; <0.1 Hz) have been proposed to play a fundamental role in the temporal organization of large-scale brain networks and the coordination of neural activity across distributed systems. Research using electrophysiological and neuroimaging methods suggests that ultra-slow fluctuations may contribute to functional connectivity, network regulation, and transitions between brain states. Despite growing interest in these processes, their clinical relevance and suitability as neurofeedback targets remain incompletely understood.

Clinical applications of Infra-Slow Neurofeedback (ISF-NF) have expanded during the past decade, yet important questions remain regarding the neurophysiological mechanisms underlying observed clinical improvements. Previous work has proposed that ISF neurofeedback may influence large-scale regulatory networks and central brain hubs involved in self-regulation and arousal regulation. However, the relationship between clinical improvement, learning during training, and measurable neurophysiological change remains largely unexplored.

In a recent single-case experimental study of ISF neurofeedback for insomnia, several participants demonstrated gradual improvements in subjective sleep quality across repeated training sessions. In some cases, these trajectories appeared to coincide with improvements in wearable-derived indicators of sleep consolidation and sleep timing. These observations raise an important question: do such parallel trajectories reflect learning-related neurophysiological adaptation, non-specific treatment effects, placebo-related processes, or a combination of these factors?

The present proposal outlines a sham-controlled feasibility study designed to investigate clinical, behavioral, and neurophysiological trajectories during ISF neurofeedback and to obtain methodological feedback from the neurofeedback research community.

Methods

We present the design of a planned sham-controlled feasibility study intended to inform a future randomized clinical trial of ISF neurofeedback for sleep difficulties.

Participants will be randomized to active ISF neurofeedback or a sham condition. Potential sham approaches under consideration include simulation-based feedback designed to maintain treatment credibility while removing contingency between ongoing brain activity and reinforcement.

The proposed study will combine daily subjective sleep assessments, wearable-derived sleep metrics, treatment expectancy ratings, and repeated neurophysiological assessments. Particular emphasis will be placed on identifying and quantifying individual learning trajectories across the intervention period.

A central objective is to determine whether parallel trajectories can be observed across subjective sleep quality, wearable-derived indicators of sleep consolidation, and neurophysiological measures, and whether such trajectories differ between active and sham conditions.

Results

As this is a methodological proposal, no outcome data are available. Instead, feedback is sought on several key design questions:

- How can the role of infra-slow oscillations in large-scale brain regulation best be investigated within a neurofeedback framework?
- Which neurophysiological measures are most appropriate for assessing treatment-related changes in regulatory brain networks and central brain hubs?
- Can individual learning trajectories observed in subjective sleep ratings and wearable-derived sleep metrics be linked to measurable neurophysiological change?
- Can infra-slow activity be reliably measured using scalp EEG, and what are the major methodological limitations?
- What constitutes a credible sham condition in ISF neurofeedback research?
- Is double-blinding feasible in this context?
- How should learning during ISF neurofeedback training be operationalized and quantified?

Conclusions

The proposed study aims to address several important methodological challenges currently facing ISF neurofeedback research. Building upon observations from a previous insomnia study, the project seeks to investigate whether improvements in subjective sleep quality and wearable-derived sleep consolidation are accompanied by measurable neurophysiological change.

By combining placebo control, dense longitudinal outcome measurements, wearable monitoring, and repeated neurophysiological assessments, the study aims to move beyond simple pre-post comparisons and toward a mechanistic understanding of individual response trajectories during ISF neurofeedback.

Feedback from researchers working with neurofeedback, qEEG, real-time neuroimaging, sleep research, and placebo-controlled interventions is specifically sought to optimize study design prior to implementation.