Toward Precision Mechanistic Biomarkers of Acamprosate Response in Alcohol Use Disorder: Methodology of a Longitudinal EEG Trial

Submitter Parth Chholak

Affiliation National Institute on Alcohol Abuse & Alcoholism, National Institutes of Health

SUBMISSION DETAILS

I agree to provide poster pdf for attendee download. Yes

What is the Methodological Issue Being Addressed? Current pharmacologic treatment of Alcohol Use Disorder (AUD) is limited by substantial heterogeneity in treatment response and the absence of scalable mechanistic biomarkers capable of tracking neurophysiological recovery during treatment. Acamprosate is FDA-approved for AUD treatment, yet its neuronal mechanisms and predictors of response remain incompletely characterized. The EEGAcamp study addresses this gap through a randomized, double-blind, placebo-controlled longitudinal design integrating repeated electroencephalography (EEG), clinical phenotyping, and optional polysomnography (PSG).
The methodological innovation of this protocol lies in the longitudinal characterization of treatment-associated neural dynamics during early abstinence and recovery. The study combines resting-state EEG, event-related potentials (ERP), and clinical correlates to evaluate whether EEG markers can serve as biomarkers of acamprosate response and recovery trajectory.

Introduction AUD is associated with EEG abnormalities including elevated beta activity, reduced alpha and slow-wave power, and impaired P300 responses, reflecting cortical hyperexcitability and disrupted cognitive processing. Acamprosate is hypothesized to modulate glutamatergic and GABAergic signaling, potentially normalizing these abnormalities; however, longitudinal EEG studies of acamprosate in humans remain limited.
Traditional clinical trials in AUD frequently rely on behavioral endpoints alone and lack temporally-sensitive biomarkers capable of capturing dynamic neural recovery processes. EEG provides a scalable biomarker platform for repeated assessments during treatment and abstinence. The present study was designed to evaluate whether longitudinal EEG phenotyping can identify neural signatures of acamprosate response and support precision-treatment strategies.

Methods EEGAcamp is an ongoing Phase-IV randomized double-blind placebo-controlled longitudinal clinical trial conducted at the NIH Clinical Center. Forty inpatients aged 21-65 years with moderate-to-severe AUD are planned for enrollment, randomized 1:1 to receive either acamprosate calcium (1998 mg/day) or placebo for 21 days during inpatient treatment. Participants undergo repeated EEG assessments pre-treatment (Day-2), mid-treatment (Day-13; optional), post-treatment (Day-23), and optionally during follow-up visits at approximately 1-, 3-, and 6-months post-discharge. EEG sessions include resting-state and auditory/visual P300 paradigms targeting cortical hyperexcitability and cognitive control processes. Concurrent assessments include alcohol craving, anxiety, salivary cortisol, Alcohol Timeline Followback (during follow-ups), and optional PSG recordings.

Primary EEG endpoints include resting-state beta, alpha, delta, and theta spectral power; theta event-related synchronization; and P300 amplitude and latency measures. Linear mixed-effects models with fixed effects for treatment, time (Day-2 vs Day-23), and treatment-by-time interaction and participant-specific random intercepts will compare longitudinal EEG changes. The primary contrast will evaluate differential pre- to post-treatment change between groups. Bonferroni correction will be applied for independent EEG markers. Secondary analyses will evaluate associations between changes in EEG biomarkers and changes in craving, anxiety, cortisol, and PSG measures using Pearson/Spearman correlations. Exploratory analyses will investigate electrophysiological predictors of abstinence durability and treatment response trajectories.

Results Enrollment and data acquisition are ongoing. The target sample size is N=40 participants with an anticipated accrual rate of approximately one participant per month. By the time of presentation, N=12 participants are expected.
We hypothesize that acamprosate treatment will normalize electrophysiological markers associated with AUD beyond placebo, specifically through reductions in resting-state beta power, increases in alpha power, reductions in theta event-related synchronization, and amplification and hastening of P300 responses, while slow-band EEG changes may be less sensitive to short-term treatment. We further hypothesize that treatment-associated electrophysiological changes will correlate with reductions in alcohol craving, anxiety, and sleep-related hyperarousal measures.
Projected analyses will evaluate whether EEG phenotypes demonstrate sensitivity to treatment-related neurophysiological adaptation and whether baseline EEG characteristics predict sustained abstinence and treatment durability during follow-up assessments.

Conclusion The EEGAcamp study introduces a longitudinal multimodal electrophysiology framework for investigating mechanistic biomarkers of acamprosate response in AUD. By integrating repeated EEG, clinical phenotyping, and optional PSG assessments within a randomized placebo-controlled design, this study aims to establish neurophysiological markers supporting precision-treatment and objective response monitoring in AUD.

Co-Authors

Parth Chholak[1], Reza Momenan[1], Nadia Hejazi[2], Nancy Diazgranados[1], David Goldman[1]

[1] National Institute on Alcohol Abuse & Alcoholism, National Institutes of Health

[2] National Institute of Mental Health, National Institutes of Health

Keywords

Keywords
biomarker
precision medicine
translational psychiatry

mechanistic neuroscience
randomized controlled trial

Guidelines I have read and understand the Poster Guidelines

Disclosures <blank>

Related Tables and Supporting Materials <blank>