

Recalibrating Interoceptive Prediction in Substance Use Disorders: A Theoretical Framework for Second-Generation Interoceptive Exposure

*¹Syedehfatemeh Mirhosseiniamiri., ²Dr. Hita Claudia Rao

¹Student, DOS in Psychology, University of Mysore, Mysuru, Karnataka, India

²Faculty, DOS in Psychology, University of Mysore, Mysuru, Karnataka, India

*Corresponding Author

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ABSTRACT

Substance use disorders (SUDs) are increasingly conceptualized, in part, as disorders of deficient self-regulation associated with interoceptive dysregulation, an impaired ability to process internal bodily signals. During withdrawal or stress, addicted individuals often misinterpret physical sensations (like tachycardia) as urgent, dangerous, and intolerable signals that heighten cravings and reinforce substance use as a quick mechanism for relief. Predictive-coding and neurocognitive models suggest that learned expectations in the insula and anterior cingulate cortex drive these responses. Despite advancements in addiction treatments, high relapse rates indicate that standard therapies often miss the embodied aspects of craving; this article proposes a **second-generation interoceptive exposure framework** as a clinical adjunct. Adapted from panic disorder treatment, the method uses clinician-guided exposure to feared physical sensations to reshape patient expectations through individualized mapping, prediction-focused learning, and belief reclassification. Future research is needed to evaluate its safety, clinical feasibility, and underlying neurobiological mechanisms.

Keywords: Substance use disorder, addiction, interoceptive exposure, somatic distress, relapse-prevention.

INTRODUCTION

Reframing Addiction Beyond Behavior

Substance use disorders (SUDs) involve more than impaired decision-making or behavioral dyscontrol. Increasing evidence indicates that interoceptive processes—how internal bodily signals are detected, interpreted, and acted upon—are relevant to craving, affect regulation, and substance use behavior (May et al., 2022; Paulus & Feinstein, 2019). Predictive-processing and active-inference accounts provide one theoretical explanation for these patterns, proposing that learned expectations, or “priors,” can influence the meaning assigned to bodily sensations and the actions selected in response to them (Paulus & Feinstein, 2019; Smith et al., 2021). Building on these accounts, this article proposes that some individuals with substance use disorders may develop highly learned expectations that bodily distress is intolerable or is most effectively resolved through substance use. The proposition is not intended as a universal explanation of addiction; rather, it identifies a potentially modifiable mechanism that may be relevant for a subgroup of individuals whose craving and relapse are strongly linked to interoceptive distress.

The following sections use neurocognitive and predictive-processing accounts as conceptual tools rather than as definitive causal explanations of addiction. In particular, the insula and anterior cingulate cortex are commonly implicated in interoceptive, salience-related, and goal-directed processes relevant to substance use, but their specific roles in craving, relapse, and treatment response remain to be clarified (Noël et al., 2013; Paulus & Stewart, 2014).

The Problem of Interoceptive Distress in SUDs

Interoception refers to the sensing and interpretation of internal bodily states, including changes in heart rate, breathing, muscle tension, gastrointestinal discomfort, fatigue, and autonomic arousal. In substance use disorders, alterations in interoceptive processing have been associated with craving, stress reactivity, cue responding, and relapse vulnerability, although these relationships vary across substances and individuals (Paulus & Feinstein, 2019; Paulus, 2024; Sinha, 2024). For some individuals, bodily states associated with stress, withdrawal, or emotional arousal may be experienced not simply as unpleasant sensations, but as urgent signals requiring immediate action. In this context, substance use may become a learned strategy for reducing or escaping interoceptive distress. This does not imply that all substance use is caused by bodily discomfort; rather, it suggests that interoceptive distress may be a clinically relevant relapse pathway for a subgroup of individuals (Otto et al., 2005; Sinha, 2024). The proposed framework focuses on exposing this pathway, hypothesizing that relapse risk may increase when a person interprets bodily distress through a rigid expectation, such as: “I cannot tolerate this feeling,” or “Using a substance is the only way to make this stop.” Second-generation interoceptive exposure can therefore be the most effective method in examining and remedying these substance-linked interoceptive expectations under clinically appropriate post-stabilization conditions.

Aim and Contribution of the Article

Even though exposure-based approaches targeting internal and emotional cues have previously been proposed and evaluated in selected substance use disorder contexts, including opioid dependence treatment, the available evidence remains limited and mixed (Otto et al., 2005, 2014). For example, a randomized trial of interoceptive-cue cognitive behavioral therapy among methadone-maintained patients with opioid dependence did not demonstrate superiority over an active counseling comparison on toxicology outcomes (Otto et al., 2014). In light of this, the current paper arranges current exposure-based concepts into a framework tailored to addiction. It makes four contributions: (a) identifying bodily cues linked to craving, withdrawal, and relapse on an individual basis; (b) providing trauma-informed, staged care following clinical stabilization; (c) testing substance-linked interoceptive expectations explicitly; and (d) integrating this work with relapse-prevention planning. How this suggested framework expands on traditional interoceptive exposure is explained in the sections that follow.

Article Type and Scope

A theoretical, clinically focused framework for upcoming manual creation and empirical testing is presented in this article. Instead of determining or arguing about the effectiveness of therapy, the article incorporates previous research on interoception, exposure-based learning, and substance use disorders to identify a specific, testable relapse pathway.

From Conventional Interoceptive Exposure to the Proposed Second-Generation Framework

The development of conventional interoceptive exposure took place mostly in therapy situations connected to anxiety, especially panic disorder. To evaluate catastrophic expectations and lessen avoidance, these approaches used systematic, clinician-guided encounters with feared internal sensations. Inhibitory learning, i.e., the formation of a competing association that physical discomfort can be experienced without the anticipated event occurring, was the fundamental principle exploited by these conventional therapies. The outcome was not based on the belief that the initial fear-based association would vanish following treatment; rather, when distress reappears, the new learning must be readily accessible to address the signals so that the dysfunctional response patterns do not recur (Boettcher et al., 2016; Craske et al., 2014).

The current framework applies the same learning principle to previously introduced substance-linked interoceptive expectancies. In addition to relapse-prevention planning, it emphasizes tailored, post-stabilization dealing with physical states linked to appetite, withdrawal, and relapse risk. According to this approach, prediction updating specifies the particular expectation under investigation—that substance use is required to escape or control physical distress—while inhibitory learning defines the overall process of change.

Neurocognitive and Affective Features of Addiction

In this section, reflective-control, impulsive-reward, and interoceptive-salience processes are presented as a conceptual heuristic for understanding addiction-related decision-making. This distinction builds on triadic neurocognitive accounts of addiction, which describe interactions among executive-control processes, automatic reward- and habit-related processes, and interoceptive processes that shape urge, craving, and choice (Noël et al., 2013; Paulus & Stewart, 2014). These labels should not be interpreted as anatomically separate or exhaustive brain systems; rather, they provide a clinically useful framework for organizing the mechanisms discussed in the article.

A Multisystemic Dysregulation Model

Triadic accounts conceptualize addiction-related decision-making as arising from interactions among reward- and habit-related processes, executive-control processes, and interoceptive or salience-related processes (Noël et al., 2013; Paulus & Stewart, 2014). Planning, inhibition, and taking delayed repercussions into account are all supported by reflective-control processes. An individual may be more capable of pausing, assessing an urge, and choosing a response that is in line with longer-term recovery objectives when these processes are available.

Impulsive-reward systems work faster. Drug-related cues, situations, and expected consequences may gain motivational value with repeated substance use, automatically biasing behavior and attention toward usage. Therefore, this system may make substance use seem immediately gratifying or required in a high-risk situation before reflective appraisal has fully taken place.

How physical states are perceived and understood is influenced by interoceptive-salience processes. Stress-related arousal, withdrawal symptoms, cravings, or emotional discomfort might become particularly noticeable and be taken as urgent signals that need to be addressed right away. According to the current concept, this is the stage where physical suffering might increase the motivational pull of substance use and reinforce expectancies related to substance use.

These domains are not discrete brain processes working independently. Instead, they might interact dynamically: stress, hunger, or withdrawal may lessen the practical availability of reflective-control methods, while vivid bodily pain may increase reward-driven behavior. This interaction point is where the suggested interoceptive-exposure framework is situated. It does not attempt to erase reward learning or restore executive control directly; instead, it addresses the learned meaning attributed to relapse-relevant physical cues, with the objective of diminishing their automatic potential to activate substance-use desires.

Established Interventions and the Proposed Adjunct

Established psychosocial interventions for substance use disorders address craving, avoidance, emotion regulation, distress tolerance, relapse risk, and internal experience through different therapeutic pathways. Cognitive-behavioral and relapse-prevention approaches emphasize functional analysis, coping responses, and management of high-risk situations. Dialectical behavior therapy for substance use disorders (DBT-SUD) integrates behavioral change with distress tolerance, mindfulness, and emotion-regulation skills, whereas mindfulness-based approaches cultivate nonjudgmental awareness and altered responses to craving and internal cues (Korecki et al., 2020; Linehan et al., 1999; Stotts & Northrup, 2015).

The proposed framework is not intended to replace or portray these approaches as insufficient. Rather, it identifies a narrower and clinically testable target: substance-linked predictions that bodily distress is intolerable or can only be resolved through substance use. Conventional interoceptive exposure provides the relevant learning foundation through expectancy violation and inhibitory learning, while the proposed framework applies these principles to individualized bodily states associated with craving, withdrawal, and relapse vulnerability (Craske et al., 2014; Otto et al., 2005, 2014).

Table 1 presents a conceptual comparison, not an efficacy ranking. The proposed second-generation framework should be understood as a post-stabilization, clinician-guided adjunct whose feasibility, safety, mechanisms, and clinical outcomes require empirical evaluation.

Table 1 Conceptual Comparison of Established Substance Use Disorder Interventions, Conventional Interoceptive Exposure, and the Proposed Second-Generation Framework

Approach	Primary therapeutic emphasis	Relation to bodily experience	Distinct relationship to the proposed framework
CBT / relapse prevention	Cognitive coping, functional analysis, skills for high-risk situations, and behavior change	May address internal triggers and cravings through coping strategies	Provides essential relapse-prevention skills; the proposed model adds individualized exposure to bodily cues linked to craving and use
DBT-SUD	Emotion regulation, distress tolerance, mindfulness, and reduction of harmful behaviors	May strengthen awareness and tolerance of emotional and bodily distress	Provides stabilization and coping skills that may be needed before exposure; it does not typically organize treatment around testing substance-linked interoceptive predictions
Mindfulness-based relapse prevention	Nonjudgmental awareness, decentering, and altered responses to craving	Directly cultivates awareness of bodily sensations and urges	May improve observation of internal experience; the proposed model adds clinician-guided exposure and explicit prediction testing
Conventional interoceptive exposure	Reduction of avoidance of feared bodily sensations through expectancy violation and inhibitory learning	Commonly targets sensations associated with panic or anxiety	Provides the exposure-learning foundation; its central feared prediction is often that a sensation is dangerous or catastrophic
Proposed second-generation IE	Hypothesized updating of substance-linked interoceptive predictions and relapse-related avoidance	Targets individualized bodily states associated with craving, withdrawal, and relapse vulnerability	Extends conventional IE through addiction-specific mapping, post-stabilization delivery, trauma-informed safeguards, and relapse-prevention integration

Note. This table is a conceptual comparison, not an efficacy ranking. The proposed second-generation framework is a clinician-guided, post-stabilization adjunct; its safety, feasibility, mechanisms, and clinical outcomes require direct empirical evaluation.

Conceptual Mechanisms and Their Limits

Predictive-processing and active-inference accounts provide a useful conceptual language for describing how expectations about bodily states may shape interpretation and action, but they do not establish a single causal mechanism of addiction or relapse (Paulus & Feinstein, 2019).

Theoretical Status of the Proposed Mechanism

Predictive-coding accounts provide a mechanism for the core pathway outlined in Section 1. Bodily states are interpreted through learned expectations shaped by prior experience. When these expectations are strongly substance-linked, arousal, withdrawal, or stress-related sensations may be assigned the meaning that substance use is necessary for relief. The clinically relevant question is therefore not whether bodily distress occurs, but whether its interpretation can be updated through new experience (Paulus, 2024; Smith et al., 2021).

The proposed second-generation interoceptive exposure framework is designed to examine these predictions under clinician-guided, post-stabilization conditions. Its hypothesized learning sequence is: **bodily cue** → **substance-linked prediction** → **safe experience without substance use** → **revised prediction**. This sequence is compatible with inhibitory-learning models of exposure, in which expectancy violation supports new learning, but it specifies the addiction-relevant expectation being tested (Craske et al., 2014; Paulus & Feinstein, 2019). Whether changes in such predictions mediate reductions in craving or relapse remains an empirical question.

Physiological and Inflammatory Measures: Exploratory Considerations

Physiological measures may be useful for examining mechanisms relevant to substance use disorders, but their clinical interpretation remains limited. Heart-rate variability and respiratory sinus arrhythmia have been investigated as correlates of autonomic and self-regulatory functioning in substance-use research; however, their values are influenced by factors such as respiration, medication, physical health, and measurement procedures. They are not established biomarkers of interoceptive learning, relapse prevention, or treatment response (Cheng et al., 2019; Moon et al., 2024; Price & Crowell, 2016).

Similarly, the neutrophil-to-lymphocyte ratio is a nonspecific peripheral inflammatory index. It should not be interpreted as a direct measure of neuroinflammation, allostatic balance, or the therapeutic effects of interoceptive exposure. Accordingly, this article treats HRV, RSA, inflammatory markers, and neuroimaging measures as exploratory candidate outcomes for future mechanistic research rather than expected effects of the proposed framework. Vagal pathways contribute to the transmission of visceral information relevant to interoception; however, HRV and RSA are indirect, context-sensitive indices of cardiac autonomic regulation rather than direct measures of vagal tone. Their relevance to craving, relapse, or treatment response in substance use disorders remains exploratory (Moon et al., 2024; Price & Crowell, 2016).

Clinical Rationale for Targeting Interoceptive Distress

The suggested approach is particularly applicable when an evaluation reveals a recurrent pattern in which the expectation that substance use is required for relief follows physical indicators linked to stress, craving, withdrawal, or emotional arousal. The acquired connection between the experience, its urgent or frightening interpretation, and the ensuing desire to use is the clinical target in these situations rather than the physical discomfort itself. Clinicians can use this formulation to determine which internal cues are most strongly linked to a person's susceptibility to relapse (May et al., 2022; Paulus & Stewart, 2014).

One method of making these expectations transparent and testable in a controlled environment is suggested to be clinician-guided interoceptive exposure. The goal is to encourage fresh discoveries that certain physical states can be experienced without substance abuse and without the anticipated loss of control. By assisting people in applying revised interpretations and alternative responses in high-risk settings, this study aims to supplement rather than replace proven relapse-prevention treatments (Craske et al., 2014; Otto et al., 2005, 2014).

Proposal: Interoceptive Exposure as a Promising Tool

Interoceptive Exposure in the Substance Use Disorder Context

The suggested application of interoceptive exposure in the treatment of substance use disorders is most pertinent when internal cues consistently precede cravings or the danger of relapse. Evaluation would pinpoint the specific sequence that connects a physical condition, its expected meaning, and the desire to use—for instance, if withdrawal-related arousal, stress activation, or yearning is perceived as unbearable or as necessitating immediate substance use. This customized formulation serves as a foundation for choosing clinically suitable treatment targets and aids in differentiating relapse-relevant internal cues from more general discomfort (May et al., 2022; Otto et al., 2005; Paulus & Stewart, 2014).

The suggested intervention would be administered inside an established treatment program for substance use disorders, following stabilization. Exposure activities would be linked with coping and relapse-prevention plans after being chosen based on the individual's clinical presentation, health, and risk of relapse. The goal is to enhance alternate responses that can be applied outside of the therapeutic context while investigating if the

expected association between a bodily cue and substance use persists in practice. The safeguards and procedure elements required to convert this framework into a testable clinical model are described in the next section (Craske et al., 2014; Otto et al., 2014).

Clinical Scope, Sequencing, and Safeguards

The proposed second-generation interoceptive exposure framework is intended as an adjunct to established substance use disorder treatment, not as a standalone treatment or a substitute for withdrawal management, pharmacotherapy, trauma-focused care, or crisis intervention. Exposure-based work should be considered only after acute intoxication, clinically significant withdrawal, and other immediate medical or psychiatric safety concerns have been appropriately assessed and managed according to substance-specific clinical guidance (American Society of Addiction Medicine [ASAM], 2020).

As a theoretical framework, the present article does not prescribe a fixed eligibility algorithm or a self-guided exposure procedure. Rather, it proposes clinician-led, collaboratively paced intervention following individualized assessment of substance-use pattern, withdrawal risk, relevant medical factors, trauma-related symptoms, dissociation, and current treatment stability. The timing, intensity, and continuation of exposure work should remain subject to clinical judgment and ongoing monitoring.

The protocol stages described below are conceptual components for future treatment development and evaluation. They are not instructions for inducing bodily sensations outside supervised clinical care. Future studies should specify participant-selection criteria, clinician training, session-modification procedures, adverse-event monitoring, and referral pathways, consistent with standards for clear intervention description and replication (Hoffmann et al., 2014).

Proposed Second-Generation Interoceptive Exposure Framework

The previously mentioned reasoning is broken down into six interconnected elements in Table 2: evaluation and preparedness; interoceptive literacy; prediction mapping and hierarchy creation; clinician-guided experiential learning; meaning reclassification; and relapse-prevention integration. When combined, these elements offer a structured framework for locating clinically significant internal indicators and connecting them to customized relapse prevention efforts.

From conceptualization to experiential testing, the framework is intended to transition. Early components clarify specific physical sensations are associated with craving or return-to-use risk, whereas the later components focus on testing the person's substance-linked expectations and applying alternate reactions in relevant high-risk circumstances. This procedure keeps the separation between identifying distress and assessing the learned meaning attributed to it.

The six elements are not meant to serve as a set protocol for each session. Clinical presentation, treatment setting, and preparedness should all be taken into consideration when determining their order, intensity, and emphasis. For future manual creation, fidelity assessment, and empirical evaluation, Table 2 thus provides a suggested basis (Craske et al., 2014; Hoffmann et al., 2014; Otto et al., 2005, 2014).

Table 2 Proposed Components of the Second-Generation Interoceptive Exposure Framework

Component	Intended clinical function	Proposed clinician-led focus	Candidate proximal indicator
1. Assessment and readiness	Identify whether interoceptive distress is a relevant relapse pathway and whether exposure work is appropriate	Map the sequence from bodily cue to meaning, craving, urge, and substance-use behavior	Individualized interoceptive relapse signature identified

2. Interoceptive literacy	Distinguish bodily sensations from interpretations and urges	Psychoeducation and collaborative labeling of bodily states	Greater specificity in describing sensations, meanings, and urges
3. Prediction mapping and hierarchy development	Identify substance-linked expectations suitable for testing	Rank situations or bodily states by relevance, distress, and anticipated urge to use	Explicit statement of the prediction to be tested
4. Clinician-guided experiential learning	Test whether bodily distress necessarily requires substance use	Supervised contact with selected internal states, paced according to readiness and clinical judgment	Difference between expected and observed outcome; change in prediction strength
5. Meaning reclassification	Consolidate learning from expectancy violation	Compare the predicted consequence with the observed outcome and formulate an alternative interpretation	Reduced endorsement of beliefs such as “I must use to cope with this feeling”
6. Generalization and relapse-prevention integration	Transfer learning to naturally occurring high-risk contexts	Integrate individualized warning signs, coping responses, and existing relapse-prevention plans	Use of planned alternative responses during real-world interoceptive distress

Note. All components are theoretical and require empirical testing. The framework extends inhibitory-learning principles by specifying substance-linked interoceptive predictions as the proposed target of change (Craske et al., 2014; Otto et al., 2005, 2014). It is intended for clinician-guided, post-stabilization use alongside established substance use disorder care.

Testable Predictions and Research Agenda

The six elements listed in Table 2 directly inform the study plan. Early studies should address three linked questions: whether the framework can be delivered safely and consistently within routine substance use disorder care; whether it engages the intended target of substance-linked interoceptive expectations; and whether changes in that target are associated with meaningful clinical outcomes. Before conducting bigger efficacy studies, this phased strategy enables the examination of feasibility, treatment fidelity, and probable processes of change (Hoffmann et al., 2014; Onken et al., 2014).

Feasibility and acceptability. Among appropriately screened, post-stabilization patients, the framework is hypothesized to be feasible for clinician delivery and acceptable to participants when offered alongside established substance use disorder treatment. Early studies should assess recruitment, retention, completion, participant-reported acceptability, treatment fidelity, adverse events, and reasons for discontinuation.

Proposed mechanism. Whether the framework modifies the substance-linked prediction outlined in Section 1.4 is the main mechanistic question. Early investigations should therefore examine variations in the perceived necessity of substance use during specific bodily states, with interoceptive avoidance, detection of internal cues, and readiness to remain with distress without acting on the urge. These outcomes would clarify if the proposed intervention engages its targeted target before claims regarding broader therapeutic effect are investigated.

Clinical outcomes and heterogeneity. Changes in substance-linked predictions should be tested as possible mediators of changes in craving, urge-driven substance use, treatment retention, and relapse outcomes. Potential moderators include substance type, withdrawal history, trauma-related symptoms, co-occurring psychiatric conditions, and the consistency with which bodily distress precedes craving or substance use.

Exploratory mechanistic measures. Later research could utilize a tiered measurement method to examine how change occurs. Shifts in substance-linked expectations, interoceptive avoidance, and perceived tolerance of bodily distress may be evaluated by self-report measures; reactions to pertinent internal cues may be examined by behavioral tasks; and additional correlates may include psychophysiological or neuroimaging indices. When combined, these metrics may aid in identifying biological, behavioral, and subjective patterns of change. Until their clinical predictive usefulness, specificity, and reliability are established, these indicators should be considered experimental (May et al., 2022; Paulus & Stewart, 2014).

Limitations and Boundary Conditions

Two boundary criteria shape understanding of the proposed framework. First, different drugs, clinical groups, and techniques for evaluating interoceptive functioning are likely to have different significance. Second, because substance use is also influenced by social environment, mental symptoms, trauma exposure, substance availability, treatment access, and executive-control capability, the framework should not be viewed as a stand-alone explanation of relapse (May et al., 2022; Paulus & Stewart, 2014).

Participant selection and clinical formulation are also affected by these boundary circumstances. When assessment reveals a consistent, unique sequence in which physical discomfort, withdrawal-related feelings, or autonomic arousal come before substance-use cravings or recurrence, the suggested method might be most suitable. When environmental availability, social pressures, or other factors are the main causes of usage, it might not be as important. Therefore, rather than assuming a homogeneous target population, future research should record substance type, withdrawal history, trauma-related symptoms, psychiatric comorbidity, treatment setting, and the temporal relationship between internal cues and substance use (May et al., 2022; Paulus & Stewart, 2014; Sinha, 2024).

Measurement is another drawback. The field does not yet have an established measure that directly captures substance-linked interoceptive predictions or their change throughout therapy. Future research should measure the proposed target regularly, separate it from general decreases in craving or distress, and determine whether change in this target precedes improvements in substance-use outcomes.

Another study question is implementation. Clinician competences, supervision needs, pacing or cessation decision rules, and coordination with medicine, psychotherapy, and recovery supports should all be included in future manual development. According to Otto et al. (2014) and Onken et al. (2014), comparative studies can then ascertain whether and for whom adding this component enhances outcomes beyond standard substance use disorder care.

CONCLUSION

Substance use disorders are heterogeneous, and relapse cannot be reduced to a single cognitive, neural, social, or bodily mechanism. Nevertheless, interoceptive processes may be clinically relevant for a subgroup of individuals whose craving and return to substance use are closely linked to bodily distress, withdrawal-related sensations, or autonomic arousal (May et al., 2022; Paulus & Stewart, 2014).

This article has presented second-generation interoceptive exposure as a theoretical and clinically testable adjunct to established substance use disorder treatment. The framework retains inhibitory-learning principles from conventional exposure approaches while specifying an addiction-relevant target: learned predictions that bodily distress is intolerable or can only be resolved through substance use (Craske et al., 2014). Its proposed contribution is the integration of individualized interoceptive mapping, post-stabilization and clinician-guided delivery, trauma-informed safeguards, and relapse-prevention planning.

The framework should not be interpreted as an established treatment or as a replacement for pharmacotherapy, withdrawal management, trauma-focused care, or evidence-based psychosocial interventions. Existing evidence on interoceptive exposure in substance use disorder treatment remains limited; notably, a randomized trial in opioid-dependent outpatients did not show superiority over an active counseling comparison on toxicology outcomes (Otto et al., 2014).

The next task is therefore empirical. Research should first establish acceptability, safety, feasibility, and treatment fidelity, then test whether changes in substance-linked interoceptive predictions are associated with reduced craving and improved substance-use outcomes. The value of this framework lies not in claiming a completed intervention, but in offering a falsifiable model for investigating when and for whom interoceptive exposure may strengthen relapse prevention.

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