

Peer Review

# Review of: "The Scarred Circuitry of Fear: A Computational–Clinical Synthesis of PTSD Neurobiology"

Naeem Ur Rehman<sup>1</sup>

1. Pharmacology, Gomal University, Pakistan

## General assessment

This manuscript provides a rigorous, theory-driven synthesis of PTSD neurobiology, integrating fear circuitry, stress physiology, and computational formalization. The emphasis on heterogeneity, falsifiable predictions, and clinical relevance aligns well with the translational focus of *Biological Psychiatry*. The work is conceptually strong and carefully hedged.

## Major strengths

Clear integration of amygdala–vmPFC–hippocampal circuitry with neuromodulatory and endocrine systems.

Explicit rejection of biomarker determinism in favor of stratification and parameter-based heterogeneity.

Computational formalization that generates testable hypotheses rather than post hoc explanations.

## Minor comments

The abstract would benefit from explicitly stating that the computational model is conceptual and hypothesis-generating, rather than empirically fitted.

Repeated citation of Shin & Liberzon (2010) could be streamlined or complemented with more recent meta-analytic references.

The term “scarred circuitry” may be read as implying structural damage; a brief clarification emphasizing functional dysregulation would improve precision.

In the discussion of prazosin, the authors may briefly clarify whether null findings in large trials are interpreted as subgroup effects, contextual moderators, or outcome-measure specificity.

The equations in Section 6 are clearly written; adding a sentence noting that the model is phenomenological rather than neurally realistic would help manage expectations.

A schematic figure summarizing the three-layer framework would significantly enhance accessibility for non-computational readers.

### **Conclusion**

With minor clarifications and modest tightening of language, this manuscript would make a valuable contribution to the translational PTSD literature.

### **Declarations**

**Potential competing interests:** No potential competing interests to declare.