

Whole-brain network dynamics of arousal fluctuations in Insomnia: *Research protocol*

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Introduction

- **Insomnia Disorder (ID)** is a complex mental disorder often featuring **hyperarousal** throughout the day and impaired emotion regulation, in addition to sleep dysregulation [1].
- Different ID subtypes have been identified based on the overall negative affect and distress levels (**high vs low distress** [2]).
- The locus coeruleus (LC), a ~2 x 15 mm region in the pons, is the noradrenergic (NA) center of the brain and crucially involved in arousal regulation.
- **Main hypothesis:** Insomnia subtypes feature distinct dynamic brain network configurations driven by the LC.
- The present analysis demonstrates the feasibility of assessing the **role of LC in driving global brain connectivity states in healthy adults.**

Preliminary Results

- Healthy sleepers (N=19), aged=36.95 years (SD=19.34 years), 10 women, Insomnia Severity Index: mean=4.42 (SD=3.22, range=0-12) indicating absence or very mild insomnia symptoms.

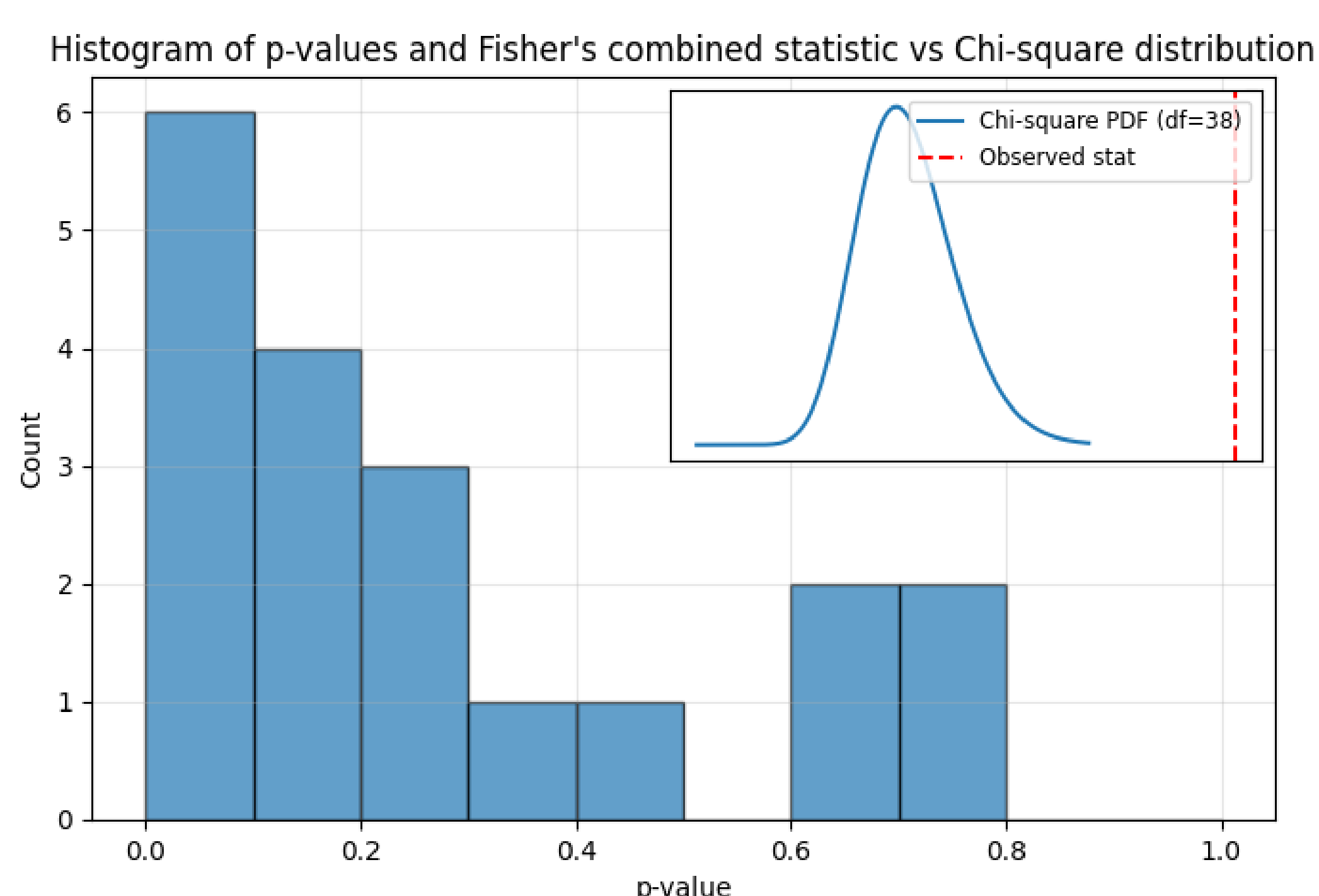


Figure: p-values for individual subject granger causality tests of LC BOLD activity causing global brain states

- Fisher's combined test: $\chi^2(38)=97.17$, $p=4.4 \times 10^{-7}$; Stouffer's $z=4.80$, $p=7.8 \times 10^{-7}$, indicating consistent effects across subjects

Discussion

By identifying hyperarousal signatures and their dynamic neural network associations, we aim to advance the understanding of ID mechanisms by addressing **subtype-specific characteristics**. Additionally, this work will represent a significant advancement in tracking **arousal via fMRI**, with broader applications in clinical research.

References

1. Van Someren. Brain mechanisms of insomnia: new perspectives on causes and consequences. *Physiological Reviews*. 2021
2. Blanken et al. Insomnia disorder subtypes derived from life history and traits of affect and personality. *The Lancet Psychiatry*. 2019
3. J. M. Shine et al. The Dynamics of Functional Brain Networks: Integrated Network States during Cognitive Task Performance. *Neuron*. 2016
4. Koshmanova et al. Locus coeruleus activity while awake is associated with REM sleep quality in older individuals. *JCI Insight*. 2023

Methods

- **Sixty** ID participants
- 20-50 years old
- **High distress (N=30), Low distress (N=30)**
- Healthy sleepers

