Depression and Inflammation in Acute HIV: An RDoC-Based PHQ-9 Factor Analysis

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INTRODUCTION

- Depression is common in HIV and may relate to neuroinflammation, but symptoms are heterogeneous.[1-9]
- The Research Domain Criteria (RDoC) supports dimensional phenotyping aligned with neurobiological systems.[10]
- We used an RDoC-based PHQ-9 factor model[11] to test inflammatory biomarker associations in acute HIV before initiation of antiretroviral therapy.

OBJECTIVE

To evaluate an RDoC-aligned PHQ-9 factor model in acute HIV and examine associations between symptom domains, HIV RNA, and plasma/CSF inflammatory biomarkers.

METHODS

- N=721 acute HIV participants from RV254 cohort (Thailand), PHQ-9 and biomarkers at enrollment prior to ART
- Confirmatory Factor Analysis (CFA) 4-Factor Model (RDoC-aligned) with PHQ-9 ≥5
  - Neg Valence Externalizing (Anhedonia, Depressed Mood)
  - Neg Valence Internalizing (Guilt, Suicidality)
  - Arousal/Regulatory (Sleep, Fatigue, Appetite)
  - Cognitive/Sensorimotor (Concentration/Psychomotor)
- Multivariable Regressions (Adjusted for Age and Fiebig Stage): Factor Scores with HIV RNA + 30 plasma/CSF biomarkers; Mann-Whitney comparisons by PHQ thresholds ≥5/10/15

STUDY SUMMARY

In people with early untreated HIV, different patterns of depressive symptoms were linked to inflammation and viral burden. TNFR1 was associated with all symptom domains, while HIV RNA levels were linked to specific domains involving mood, energy, and cognition.

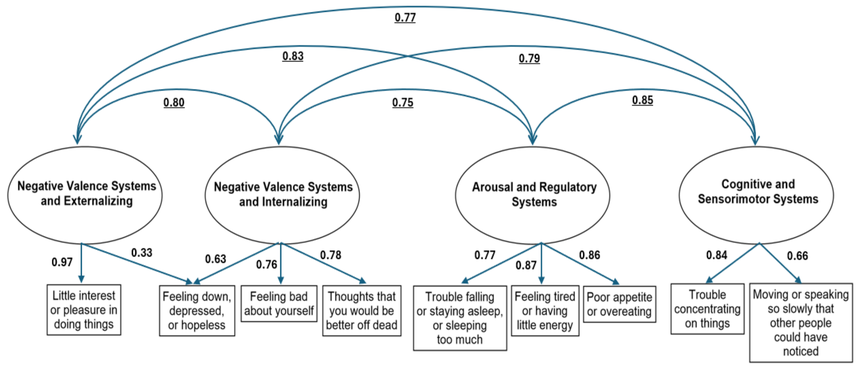


FIGURE 1. Confirmatory factor analysis model of PHQ-9 symptom domains mapped to RDoC-relevant systems.
Values shown are standardized CFA estimates: single-headed arrows indicate standardized factor loadings, and curved double-headed arrows indicate correlations between latent factors.

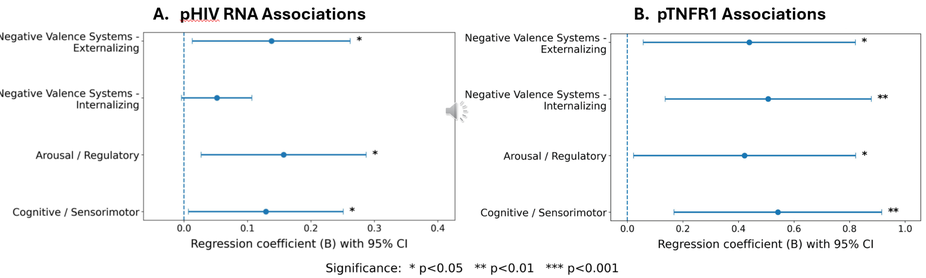


FIGURE 2. Multivariable regression coefficients (β) with 95% CI for plasma HIV RNA and TNFR1 across depressive symptom domains (PHQ-9 ≥5)

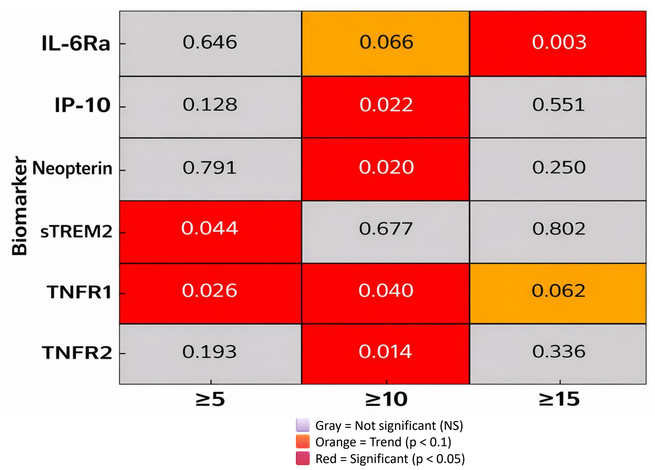


FIGURE 3. Inflammatory Biomarkers by PHQ-9 Severity Threshold

RESULTS

- Participants (N=721): Median age 26, 97.6% male, largest group Fiebig Stage III (45.6%), median HIV-1 RNA 5.99 log10 copies/mL (IQR 5.19–6.73), 79.8% with PHQ-9 ≥ 5
- CFA – Good Fit
  - Root Mean Square Error of Approximation 0.052, Comparative Fit Index 0.996, Tucker-Lewis Index 0.992
- Multivariable Regression Associations with RDoC Domains:
  - TNFR1 → all 4 domains (β 0.42–0.54, p<0.05)
  - HIV RNA → 3 domains (Externalizing, Arousal, Cognitive; β 0.13–0.16; p<0.05)
- PHQ-9 Severity and Inflammatory Biomarkers:
  - PHQ-9 ≥ 10: ↑ TNFR2, IP-10, neopterin
  - PHQ-9 ≥ 15: ↑ IL-6Ra
  - TNFR1 elevated at ≥5 and ≥10; trend at ≥15

CONCLUSION

- CFA supports a 4-factor PHQ-9 model aligned with RDoC domains in acute HIV.
- Depression symptom burden is associated with higher inflammatory biomarkers in acute untreated HIV. Plasma TNFR1 may function as a cross-RDoC domain inflammatory correlate, while plasma HIV RNA may only relate to externalizing, arousal, and cognitive symptom domains.
- Future studies needed to evaluate persistence beyond acute infection and RDoC/biomarker correlations with more severe PHQ-9 thresholds.

KEY REFERENCES

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Full list available upon request.

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