The Acker Model of Emotion: The CRP–Glucose Ratio as a Physiological Marker of Affective State Transitions

Abstract

The purpose of this manuscript is to articulate a biologically plausible and falsifiable hypothesis, not to report definitive clinical validation.

Background: Anxiety and depression are traditionally treated as distinct psychiatric disorders, yet both frequently co-occur and transition within individuals. Accumulating evidence suggests that inflammatory signaling and metabolic state jointly influence affective regulation.

Hypothesis: This paper proposes that affective state reflects the brain's internal perception of inflammatory threat relative to available metabolic energy. Specifically, the ratio of C-reactive protein (CRP) to circulating glucose functions as a physiological signal governing transitions between mobilized (anxiety-like) and collapse (depression-like) states.

Rationale: When inflammatory signaling rises in the context of adequate energy availability, threat is expressed as action-oriented arousal consistent with anxiety. When inflammatory signaling persists as energetic resources decline, the same threat signal produces behavioral inhibition and withdrawal consistent with depression. Clinical observations, prior psychoneuroimmunology research, and large critical-care datasets suggest this pattern recurs across conditions.

Implications: This framework predicts orderly transitions between affective states driven by immune–metabolic coupling rather than discrete psychiatric categories. It further predicts that interventions reducing inflammatory escalation or preserving metabolic capacity may prevent progression from anxiety to depressive collapse.

Testability: The hypothesis generates falsifiable predictions regarding temporal ordering of inflammatory and metabolic markers, differential symptom expression under energy-replete versus energy-depleted conditions, and selective response to anti-inflammatory or metabolic interventions.

Introduction

Affect has long been treated as a purely psychological phenomenon. Yet decades of research show that inflammatory markers and energy metabolism are deeply entwined with mood regulation. The Acker Model posits that emotion may reflect the body's internal readout of homeostatic state — specifically, the balance between inflammatory threat and energetic capacity.

These observations motivate the hypothesis described below.

Formal Hypothesis

Affective state transitions reflect immune–metabolic coupling rather than discrete psychiatric disease categories. Specifically, inflammatory signaling biases affective expression toward anxiety under conditions of preserved metabolic capacity and toward depressive withdrawal as metabolic capacity declines. The CRP–glucose ratio is proposed as a compact physiological representation of this coupling.

Observational Basis

The hypothesis described above is motivated by recurring patterns observed in large clinical datasets in which inflammatory markers and metabolic variables are measured longitudinally. Analyses of the MIMIC-IV critical care database suggest that relative changes in C-reactive protein (CRP) and circulating glucose often precede shifts in clinically coded affective or behavioral states.

In exploratory analyses, within-subject normalization and temporal interpolation were used to examine short-term transitions between baseline, mobilized (fight/flight–like), and withdrawal (collapse–like) states. A log-transformed CRP-to-glucose ratio was used as a compact representation of immune–metabolic coupling. These observations are not presented as definitive validation, but as empirical patterns that motivated formulation of the present hypothesis.

Supporting Patterns

Cohort: 16,597 observations across 14,616 subjects. Illustrative contrasts included: Fight/flight vs baseline OR = 1.13; Collapse vs fight/flight OR = 0.88. Temporal dynamics: Fight/flight preceded by CRP rise; collapse followed by CRP rise and glucose decline — a pattern consistent with sympathetic exhaustion.

Interpretation and Implications

These observations are consistent with the Acker Model of Emotion. Anxiety and depression

may reflect the same inflammatory signal, modulated by energetic context. When energy is plentiful, threat translates into action (anxiety). When energy wanes, the same threat triggers immobilization (depression). This mirrors the freeze response seen in animals as a conservation mechanism.

Conclusion

The CRP–glucose ratio is proposed as a measurable physiological substrate for affective transitions. The Acker Model integrates neuroscience, endocrinology, and immunology into a single explanatory framework for emotion.

This hypothesis would be falsified if affective state transitions do not covary with immune–metabolic coupling over time, or if inflammatory escalation fails to bias symptom expression under controlled metabolic conditions.

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