The Relationship Between the Immune System and Aggression

1. Introduction

A substantial body of research demonstrates a complex, bidirectional relationship between the **immune system** and **aggressive behavior**. Elevated levels of proinflammatory cytokines (such as IL-6, TNF-α, and CRP) are consistently associated with increased aggression in both clinical and non-clinical populations, including individuals with psychiatric disorders like schizophrenia and intermittent explosive disorder (Takahashi, 2024; Takahashi et al., 2018; Coccaro et al., 2023; Li et al., 2016; Coccaro et al., 2014; Yu et al., 2023; Morais et al., 2025; Barzilay et al., 2016; Han et al., 2026; Zhang et al., 2025; Wang et al., 2021; Aymen et al., 2019; Das et al., 2016; Tong et al., 2022; Coccaro et al., 2015; Marsland et al., 2008; Kachouchi et al., 2017). Experimental studies in animals reveal that immune activation can modulate aggression, with microglial activation and neuroinflammation influencing aggressive behaviors (Takahashi, 2024; Takahashi et al., 2021; Markova et al., 2024; Wang et al., 2025; Yu et al., 2023). Conversely, aggressive encounters themselves can acutely elevate inflammatory markers, suggesting a feedback loop between social stress, immune dysregulation, and behavioral outcomes (Takahashi et al., 2018; Takahashi et al., 2021; Campana et al., 2025). Mechanistic studies highlight the roles of specific cytokines (e.g., IL-1β, IL-33), microglia, and pathways such as the NLRP3 inflammasome in mediating these effects (Takahashi, 2024; Takahashi et al., 2021; Wang et al., 2025; Yu et al., 2023; Zhang et al., 2025). While most evidence points to a positive association between inflammation and aggression, some findings suggest context-dependent or cell-type-specific effects. This review synthesizes current knowledge on immune-aggression links across human and animal models, clinical populations, molecular mechanisms, and potential therapeutic implications.

Is there a positive association between immune system activation (inflammation) and aggressive behavior? N = 36

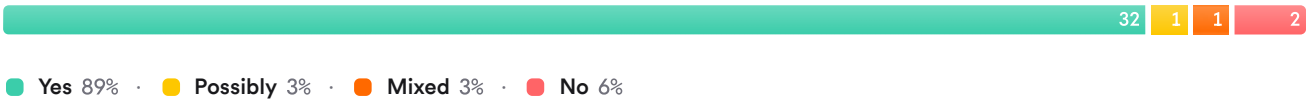

FIGURE 1 Consensus meter visualizing agreement on immune activation's link to aggression.

2. Methods

A comprehensive search was conducted across over 170 million research papers in Consensus—including Semantic Scholar, PubMed, and other sources—using targeted queries on foundational theories, mechanistic pathways (e.g., cytokines, microglia), clinical studies, animal models, contrasting perspectives, and interdisciplinary expansions. In total, 18663450 papers were identified; after multi-phase filtering for relevance and quality, 50 papers were included in this review.

Search Strategy

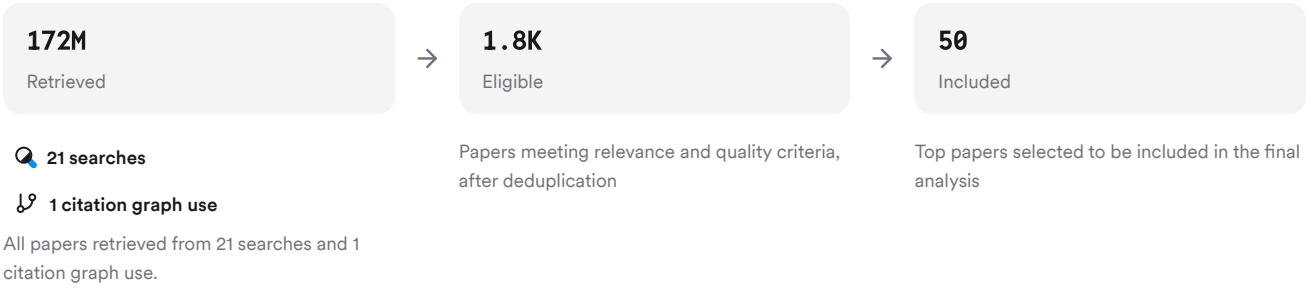

FIGURE 2 Flow diagram of paper selection for this review.

Six unique search strategies were used to capture foundational models, alternate terminology (e.g., neuroimmunology), mechanistic pathways (cytokines/microglia), critiques/null findings, interdisciplinary perspectives (evolutionary biology/psychoneuroimmunology), and clinical applications.

3. Results

3.1 Human Studies: Inflammation Markers & Aggression

Multiple studies report that individuals with high aggression traits or psychiatric diagnoses characterized by impulsive aggression exhibit elevated plasma levels of proinflammatory markers such as CRP and IL-6 (Takahashi et al., 2018; Coccaro et al., 2023; Li et al., 2016; Coccaro et al., 2014; Yu et al., 2023; Morais et al., 2025; Barzilay et al., 2016; Han et al., 2026; Zhang et al., 2025; Wang et al., 2021; Aymen et al., 2019; Das et al., 2016; Tong et al., 2022; Coccaro et al., 2015; Marsland et al., 2008). These associations persist after controlling for confounders like BMI or smoking (Marsland et al., 2008). In schizophrenia patients specifically, higher CRP levels correlate with more severe aggressive behavior (Li et al., 2016; Barzilay et al., 2016; Aymen et al., 2019; Kachouchi et al., 2017), while other markers such as IL-33 also show positive associations with aggression (Zhang et al., 2025).

3.2 Animal Models & Mechanistic Insights

Animal studies demonstrate that aggressive encounters acutely increase proinflammatory cytokines; conversely, peripheral immune activation (e.g., LPS administration) can reduce aggression as part of sickness behavior (Takahashi, 2024). Microglial activation is implicated in modulating intermale aggression in rodents (Takahashi, 2024), while manipulation of specific cytokine signaling (e.g., IL-1β in the dorsal raphe nucleus) alters individual differences in aggression via serotonergic circuits (Takahashi et al., 2021). The NLRP3 inflammasome pathway is shown to drive stress-induced aggressive behaviors through neuroinflammation (Yu et al., 2023).

3.3 Immune Modulation & Behavioral Interventions

Experimental transplantation of immune cells modulated by psychoactive substances (e.g., chlorpromazine) reduces aggressive behaviors in animal models by decreasing pro-inflammatory cytokines (IL-1β, IL-2, IL-6) and increasing anti-inflammatory cytokines (IL-4) within key brain regions (Markova et al., 2024; Markova et al., 2021; Markova et al., 2022). These interventions also promote neurogenesis and neuroplasticity while reducing microglial activation (Markova et al., 2024).

3.4 Evolutionary & Comparative Perspectives

Comparative studies in social insects like bees reveal that higher aggressiveness is associated with upregulated expression of innate immunity genes in brain tissues involved in defense behaviors (Campana et al., 2025). In humans and animals alike, social stressors leading to submission or defeat are linked to immunodepression or altered disease susceptibility (Azpiroz et al., 2003), while dominant/aggressive individuals may display enhanced cellular immunity (Granger et al., 2000).

Results Timeline

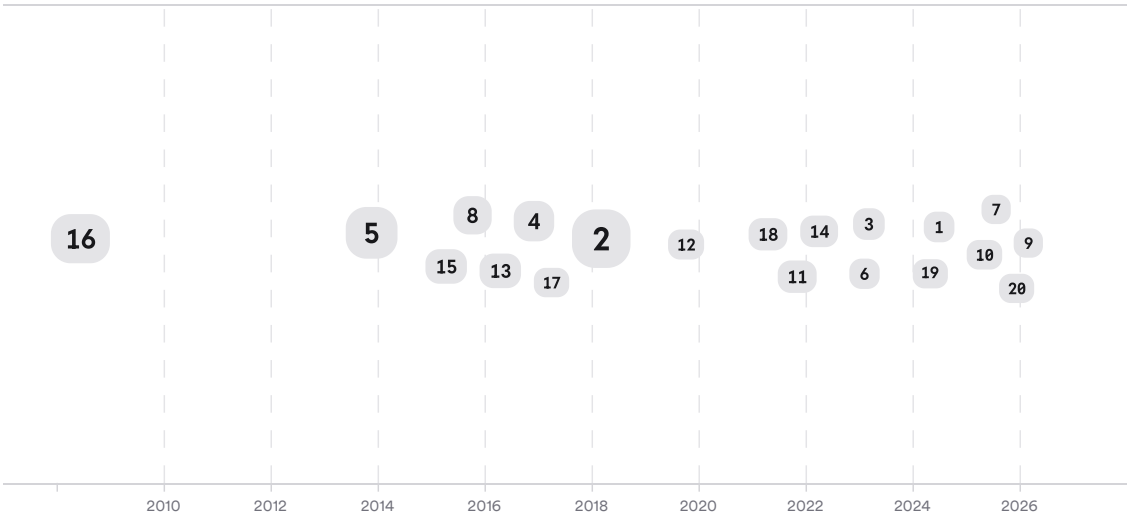

FIGURE 3 Timeline showing publication trends on immune-aggression research from foundational to recent mechanistic studies. Larger markers indicate more citations.

Top Contributors

Type	Name	Papers
Author	E. Coccaro	(Coccaro et al., 2023; Coccaro et al., 2014; Azpiroz et al., 2003; Hardy et al., 1990)
Author	Aki Takahashi	(Takahashi, 2024; Takahashi et al., 2018; Yu et al., 2023)
Author	E. Markova	(Zhang et al., 2025; Takahashi et al., 2021; Campana et al., 2025)
Journal	*Brain ` behavior ` and immunity*	(Tong et al., 2022; Alperina et al., 2019; Mahfoz, 2020; Pesce et al., 2011; Júnior et al., 2011)
Journal	*European Psychiatry*	(Zhang et al., 2025; Coccaro et al., 2015; Campana et al., 2025; Elmusrati et al., 2021)
Journal	*Neuropharmacology*	(Takahashi, 2024)

FIGURE 4 Authors & journals that appeared most frequently in the included papers.

4. Discussion

The literature robustly supports a **positive association between systemic inflammation/immune activation and aggressive behavior**, particularly through elevated cytokines such as CRP and IL-6 across diverse populations—including healthy individuals with high trait aggression as well as those with psychiatric disorders like schizophrenia or intermittent explosive disorder (Takahashi et al., 2018; Coccaro et al., 2023; Li et al., 2016; Coccaro et al., 2014; Yu et al., 2023; Morais et al., 2025; Barzilay et al., 2016). Mechanistically, both central (microglial/neuroinflammatory) and peripheral immune processes contribute to modulation of aggression; however, effects can be context-dependent—certain cytokines may suppress or facilitate aggression depending on brain region or dose (Takahashi, 2024; Takahashi et al., 2021).

Animal models provide causal evidence: manipulating microglial activity or specific cytokine signaling alters aggressive phenotypes (Takahashi, 2024; Takahashi et al., 2021), while interventions targeting neuroimmune interactions show promise for behavioral correction (Markova et al., 2024). Notably, some findings suggest that low social status/submission leads to immunodepression rather than heightened inflammation—a nuance highlighting the complexity of psychoneuroimmunological interactions (Azpiroz et al., 2003).

Despite strong correlations observed in cross-sectional human studies—and experimental support from animal work—causality remains difficult to establish definitively due to potential bidirectionality: aggressive acts themselves may provoke inflammatory responses via stress pathways (HPA axis/sympathetic nervous system), creating feedback loops between behavior and immunity (Takahashi et al., 2018).

Claims & Evidence Table

Claim	Evidence Strength	Reasoning	Papers
Elevated proinflammatory markers (CRP/IL-6) are associated with higher aggression	Strong	Multiple large-scale human studies consistently find this association across clinical/non-clinical samples	(Takahashi et al., 2018), (Coccaro et al., 2023), (Li et al., 2016), (Coccaro et al., 2014), (Yu et al., 2023), (Morais et al., 2025), (Barzilay et al., 2016), (Han et al., 2026), (Aymen et al., 2019), (Das et al., 2016), (Tong et al., 2022), (Coccaro et al., 2015), (Marsland et al., 2008)
Microglial activation/neuroinflammation modulates aggressive behavior	Strong	Animal models show causal links; human data suggest similar mechanisms but are less direct	(Takahashi, 2024), (Takahashi et al., 2021), (Wang et al., 2025), (Yu et al., 2023)
Immune cell-based interventions can reduce pathological aggression	Moderate	Experimental transplantation/modulation reduces aggression via anti-inflammatory shifts	(Markova et al., 2024), (Markova et al., 2021), (Markova et al., 2022)
Specific cytokines have region/dose-dependent effects on aggression	Moderate	Bidirectional effects observed depending on context; supported by animal/human data	(Takahashi, 2024), (Takahashi et al., 2021), (Zalcman & Siegel, 2006)
Social defeat/submission leads to immunodepression	Moderate	Observed mainly in animal models; less consistent evidence in humans	(Azpiroz et al., 2003)
Causality direction between inflammation/aggression remains unclear	Moderate	Cross-sectional designs limit inference; bidirectional feedback possible	(Takahashi et al., 2018), (Marsland et al., 2008)

FIGURE 5 Key claims and support evidence identified in these papers.

5. Conclusion

Current evidence strongly supports a **bidirectional relationship** between immune system activity—especially inflammation—and aggressive behavior across species. Proinflammatory states are linked to increased risk/severity of aggression; conversely, social stressors provoking aggression can further dysregulate immunity.

Research Gaps

Despite advances in understanding molecular mechanisms linking immunity to aggression—particularly via cytokine signaling/microglia—several gaps remain:

Topic/Outcome	Human Clinical Populations	Animal Models	Molecular Mechanisms	Intervention Studies
Cytokine biomarkers	12	8	7	5
Microglia involvement	2	7	8	4
Immune cell therapies	GAP	5	GAP	5
Longitudinal causality	2	GAP	GAP	GAP

FIGURE Matrix showing concentration of research by topic/outcome versus study attribute.

Open Research Questions

Future research should focus on clarifying causality using longitudinal/interventional designs; exploring sex differences; identifying precise molecular targets for therapy; and expanding beyond psychiatric populations.

Question	Why
Does reducing systemic inflammation decrease pathological aggression in humans?	Establishing causality could inform novel therapeutic strategies for managing impulsive/aggressive disorders.
What are the sex-specific mechanisms linking immunity to aggression?	Sex differences may influence both immune responses and behavioral outcomes but remain understudied.
How do early-life immune challenges shape adult aggressive phenotypes?	Early-life events may program long-term vulnerability/resilience but require more longitudinal investigation.

FIGURE Table summarizing open questions for future research directions.

In summary: mounting evidence indicates that **immune system activity—especially inflammation—is closely linked to the expression of aggressive behavior**, but further work is needed to clarify mechanisms and develop targeted interventions.

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