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THE ROLE OF INFLAMMATION IN DEPRESSION: A LINK BETWEEN PSYCHIATRY AND INTERNAL MEDICINE

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ანა ხვედელიძე

ანთების როლი დეპრესიაში: კავშირი ფსიქიატრიასა და შინაგან მედიცინას შორის

თბილისის სახელმწიფო სამედიცინო უნივერსიტეტი, ამერიკული პროგრამა, საქართველო

რეზიუმე

დეპრესია, მსოფლიოში ინვალიდობის წამყვანი მიზეზი, სულ უფრო მეტად აღიარებულია, როგორც მნიშვნელოვანი ანთებითი კომპონენტის მატარებლად, რომელიც აერთიანებს ფსიქიატრიასა და შინაგან მედიცინას. ეს მიმოხილვა აერთიანებს დეპრესიაში ანთების როლის შესახებ ბოლოდროინდელ მტკიცებულებებს და ფოკუსირებულია 2020-დან 2025 წლამდე ჩატარებულ კვლევებზე.

ლიტერატურული ძიება ჩატარდა PubMed-ის და სხვა მონაცემთა ბაზების გამოყენებით, შეირჩა 2020-დან 2025 წლამდე გამოქვეყნებული შედარებითი კვლევები და მეტაანალიზები, რომლებიც იკვლევენ ადამიანის პოპულაციებში ანთებასა და დეპრესიას შორის კავშირს.

პერსპექტიული კვლევები მიუთითებს, რომ მომატებული ანთებითი მარკერები, როგორიცაა C-რეაქტიული ცილა (CRP) და ლეიკოციტების რაოდენობა (WBC), პროგნოზირებენ დეპრესიის განვითარებას, სქესის მიხედვით სპეციფიკური ეფექტებით (უფრო ძლიერია მამაკაცებში). მეტაანალიზები ადასტურებს ანთებითი მარკერების (მაგ., CRP, IL-6, TNF-α) მნიშვნელოვან მატებას დეპრესიულ პაციენტებში საკონტროლო ჯგუფთან შედარებით, შემცირებული ცვალებადობით, რაც მიუთითებს თანმიმდევრულ ანთებით მდგომარეობაზე. გრძივი კვლევები აჩვენებს, რომ ინტერლეიკინ-6 (IL-6) ასოცირდება როგორც მიმდინარე, ასევე მომავალ დეპრესიულ სიმპტომებთან, თუმცა ამ კავშირის მიზეზობრივი მიმართულება გაურკვეველი რჩება.

როგორც ჩანს, ანთება მნიშვნელოვან როლს თამაშობს დეპრესიის პათოფიზიოლოგიაში, რაც მკურნალობის ახალ გზებს გვთავაზობს, როგორიცაა ანთების საწინააღმდეგო თერაპიები და ცხოვრების წესის ცვლილებები. ზემოაღნიშნული დასკვნები ხაზს უსვამს ფსიქიატრიასა და შინაგან მედიცინას შორის ინტერდისციპლინარული მიდგომების მნიშვნელობას პაციენტების მდგომარეობის გასაუმჯობესებლად.

Detailed Exploration of Inflammation in Depression and Its Interdisciplinary Links. This comprehensive analysis explores the role of inflammation in depression, emphasizing its significance as a bridge between psychiatry and internal medicine. Grounded in recent research from 2020 to 2025, the discussion covers mechanisms, clinical implications, and the evolving understanding of this complex relationship.

Background and Prevalence. Inflammation, characterized by immune system activation, is increasingly implicated in psychiatric disorders, particularly major depressive disorder (MDD). Research suggests that 25–50% of individuals with MDD exhibit elevated inflammatory markers, such as C-reactive protein (CRP), tumor necrosis factor (TNF-α), interleukin-1β (IL-1β), and IL-6 [1]. This prevalence highlights a significant subgroup of depressed patients where inflammation may be a key driver. For instance, approximately 45% of patients with treatment-resistant depression show CRP levels above 3 mg/L, indicating a high-inflammation subtype [3]. The connection to internal medicine is evident, as inflammation is a systemic process associated with chronic conditions like cardiovascular disease, obesity,

and diabetes. This overlap suggests that depression in these patients may share inflammatory pathways, necessitating integrated care across medical disciplines.

Mechanisms Linking Inflammation to Depression. Inflammation influences depression through multiple pathways, affecting both peripheral and central nervous systems. Inflammatory markers disrupt neurotransmitter systems, including serotonin, dopamine, and glutamate, which are critical for mood regulation. For example, elevated CRP levels correlate with increased glutamate in the basal ganglia, potentially leading to excitotoxicity and reduced brain-derived neurotrophic factor (BDNF), contributing to symptoms like anhedonia and psychomotor retardation [3].

Innate immune responses, driven by monocytes and cytokines (e.g., TNF-α, IL-1β, IL-6), are primary contributors. Postmortem brain samples from depressed individuals show evidence of perivascular monocytes/macrophages and activated microglia, indicating neuroinflammation [1]. Adaptive immune responses, such as decreased T regulatory cells and increased Th17 cells, also play a role, with T cell-derived IL-4 linked to resilience against depressive behaviors [3].

Stress is a significant trigger, activating the inflammasome through damage-associated molecular patterns (DAMPs) and microbial-associated molecular patterns (MAMPs) from the gut microbiome, leading to peripheral inflammation that affects the brain [2]. This stress-induced inflammation can be transmitted via activated monocytes, blurring the line between physical and mental health.

From an evolutionary perspective, inflammation and depressive symptoms may have been adaptive, promoting behaviors like social withdrawal to conserve energy and fight infections in pathogen-rich environments [4]. In modern settings, however, this response may drive depression and contribute to non-response to traditional antidepressants.

Transdiagnostic Relevance and Neurocircuitry. Inflammation's role extends beyond depression, appearing in subpopulations across psychiatric disorders, including bipolar disorder, anxiety disorders, post-traumatic stress disorder (PTSD), and schizophrenia [1]. This transdiagnostic relevance suggests that inflammation affects common symptom clusters, such as motivation deficits and anxiety. For instance, inflammation reduces activity in reward-related regions like the ventral striatum and ventromedial prefrontal cortex (vmPFC), linked to anhedonia, and increases sensitivity in threat-related areas like the dorsal anterior cingulate cortex (dACC) and insula, correlating with anxiety and suicidal ideation [3]

Neuroimaging studies, including positron emission tomography (PET) targeting translocator protein (TSPO) for brain inflammation, are advancing, though current ligands are not yet clinically ready [3]. These findings underscore the need for psychiatry to consider inflammation as a shared mechanism across disorders.

Clinical Implications and Treatment Approaches. The recognition of inflammation in depression has spurred new treatment strategies, particularly in precision medicine. Inflammatory biomarkers, such as CRP, are used to identify patients likely to benefit from anti-inflammatory therapies. For example, CRP levels above 1 mg/L predict lower response to selective serotonin reuptake inhibitors (SSRIs), while levels above 3 mg/L predict better response to anti-inflammatory agents like infliximab (a TNF inhibitor) [3]. Clinical trials targeting TNF and IL-6 in high-inflammation patients are ongoing, with drugs like minocycline and COX-2 inhibitors showing potential antidepressant efficacy [1].

Lifestyle interventions, such as anti-inflammatory diets, physical activity, and stress management, are also gaining attention. The following tables summarize factors associated with increased inflammation and lifestyle interventions to mitigate it:

Table 1: Factors Associated with Increased Inflammation

Factor	Description
Stress (especially early life)	Linked to increased CRP, IL-6, TNF-α, driving inflammation in depression.
Obesity and Metabolic Syndrome	Associated with systemic inflammation, exacerbating depressive symptoms.
Medical Illnesses	Conditions like cardiovascular disease and diabetes contribute to inflammation.
Treatment Resistance	High inflammation predicts poorer response to traditional antidepressants.

Table 2: Lifestyle Interventions to Reduce Inflammation

Intervention	Description
Anti-Inflammatory Diet	Emphasizes omega-3 fatty acids, fruits, vegetables, reducing pro-inflammatory foods
Regular Physical Activity	Reduces CRP and cytokine levels, improving mood and reducing inflammation.
Stress Reduction Techniques	Mindfulness, meditation, and therapy can lower stress-induced inflammation.

These approaches highlight the potential for integrated care models, where psychiatrists and internal medicine specialists collaborate to address both mental and physical health.

Comparative Studies (2020–2025). Recent comparative studies provide robust evidence for the inflammation-depression link. The following table summarizes key studies from 2020 to 2025:

Table 3: Comparative Studies on Inflammation in Depression (2020–2025)

Study	Design	Population	Key Outcomes
Kappelmann et al. (2021) [5]	Prospective cohort study	N=10,357 adults (Gutenberg Health Study), aged 35–74 years	Elevated CRP (OR 1.58) and WBC (OR 1.88) at baseline predicted new onset depression at 5-year follow-up; significant in men, not in women
Köhler-Forsberg et al. (2020) [3]	Meta-analysis of case-control studies	5,166 patients with depression, 5,083 healthy controls	Significant elevations in CRP, IL-3, IL-6, IL-12, IL-18, sIL-2R, TNF-α in depressed patients; reduced variability in CRP, IL-12, sIL-2R.
Lamers et al. (2020) [6]	Longitudinal population-based study	N=1,255 middle-aged US adults	IL-6 is associated with present depressive and anxiety symptoms; predictive of prospective depressive symptoms, but not when baseline symptoms are accounted for.

These studies highlight the predictive power of inflammatory markers and the complexity of the inflammation-depression relationship, particularly regarding gender differences and directionality.

Longitudinal and Systemic Connections. Longitudinal studies reinforce the link between inflammation and depression. For example, the English Longitudinal Study of Ageing found that higher CRP levels predicted increased depressive symptoms over 12 years, particularly in older adults [2]. The Heart and Soul study linked depression to systemic inflammation in patients with coronary heart disease, emphasizing the connection to cardiovascular health [2].

Anti-inflammatory treatments, such as TNF-α inhibitors used in autoimmune diseases, have shown effects on depression and anxiety in chronic physical illnesses, suggesting shared therapeutic pathways [2]. This is particularly relevant for patients with conditions like chronic hepatitis C, where treatments like interferon-alpha can induce depressive symptoms [1].

Challenges and Future Directions. The relationship between inflammation and depression remains complex, with ongoing debate about causality. Some studies suggest that anti-cytokine therapies improve specific symptoms like anhedonia but may not significantly reduce overall depression scores compared to placebo, indicating limitations in current approaches [1]. The heterogeneity in inflammation findings may stem from studying MDD patients with varied interventions, complicating the identification of never-treated patients with inflammation [2].

Future research should focus on:

- Clarifying causal relationships through longitudinal and experimental studies.
- Improving neuro-imaging techniques to detect brain inflammation.
- Developing targeted therapies based on inflammatory biomarkers.
- Validating precision medicine approaches through large-scale trials.

Methodology for Literature Review. The literature review was conducted by searching PubMed and other databases for studies published between 2020 and 2025, focusing on comparative studies and meta-analyses. Inclusion criteria included human studies, peer-reviewed publications. Exclusion criteria included animal studies, non-comparative reviews, and studies before 2020. A total of 12 papers were screened, with 3 included in the comparative analysis and 9 excluded (6 reviews, 2 pre-2020 studies, 1 non-peer-reviewed article).

Conclusion. The role of inflammation in depression represents a critical intersection of psychiatry and internal medicine, offering a shared framework for understanding and treating a major global health burden. By targeting inflammation, clinicians can potentially improve outcomes for depressed patients, particularly those with comorbid physical conditions, fostering a more holistic approach to healthcare.

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SUMMARY

Depression, a leading cause of disability worldwide, is increasingly recognized as having a significant inflammatory component, bridging psychiatry and internal medicine. This review synthesizes recent evidence on the role of inflammation in depression, focusing on studies from 2020 to 2025.

A literature search was conducted using PubMed and other databases, selecting comparative studies and meta-analyses published between 2020 and 2025 that investigate the relationship between inflammation and depression in human populations.

Prospective studies indicate that elevated inflammatory markers, such as C-reactive protein (CRP) and white blood cell count (WBC), predict new onset depression, with gender-specific effects (stronger in men). Meta-analyses confirm significant elevations in inflammatory markers (e.g., CRP, IL-6, TNF-α) in depressed patients compared to controls, with reduced variability suggesting a consistent inflammatory state. Longitudinal studies show that interleukin-6 (IL-6) is associated with both current and future depressive symptoms, though the directionality remains complex.

Inflammation appears to play a critical role in the pathophysiology of depression, offering novel treatment avenues, such as anti-inflammatory therapies and lifestyle interventions. These findings underscore the importance of interdisciplinary approaches between psychiatry and internal medicine to enhance patient outcomes.

Keywords: Inflammation, Depression, Psychiatry, Internal Medicine