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Mental health is the health of the whole body: How psychoneuroimmunology & health psychology can inform & improve treatment

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Abstract

Background: Converging and accumulating evidence for the cross-communication among the nervous, immune, and endocrine systems, a field of study known as psychoneuroimmunology, implicates immunological dysfunction as a shared and common mechanism of both mental and physical illness. For example, psychiatric disorders like schizophrenia, bipolar disorder, major depression, and anxiety disorders have higher prevalence rates across a spectrum of autoimmune conditions compared to the general population. Additionally, subclinical immunological abnormalities are observed in a variety of psychiatric conditions, with chronic inflammation most extensively studied in the pathophysiology of depression. These observations blur the historical distinctions between mental and physical illness, yet clinical practice remains fragmented and primarily focused on differentially treating individual symptoms.

Proposed thesis: Therapeutically targeting inflammation offers translational opportunities for integrating mental and physical healthcare, a key niche of the interdisciplinary field of health psychology.

Conclusion: Utilizing a psychoneuroimmunological lens, health psychologists and clinicians can reconceptualize healthcare through integrative treatment approaches and advocacy for comprehensive policy-level reform at both the individual-level of care as well as community-wide prevention approaches.

KEYWORDS

health psychology, immune health, mental health, psychoneuroimmunology

Mental and physical disorders are often conceptualized and treated as distinct diagnoses with unique etiologies, stemming from the mind-body dualism that underlies much of modern medical biology.[1] The emergence of psychoneuroimmunology, or study of the cross-communication between the nervous, immune, and endocrine systems, is increasingly blurring the historical distinctions between mental and physical illness as converging and accumulating evidence suggests immune dysfunction and systemic inflammation are commonly observed across many psychiatric conditions.[2-4] Despite this growing body of scientific knowledge, clinical practice remains fragmented and primarily focused on differentially treating disparate symptoms. Psychoneuroimmunology provides a framework for integrating mental and physical healthcare, a key niche of the growing interdisciplinary field of health psychology. This paper describes some of the existing literature documenting the overlap between immune function and mental health and suggests potential clinical implications of a psychoneuroimmunological lens for both individual-level of care as well as community-wide approaches.

1 | IMMUNE ACTIVATION & PSYCHOSIS: A BRIEF HISTORICAL OVERVIEW

As early as the late 1800s, clinicians observed apparent links between immune activation and psychosis. Emil Kraepelin, the father of modern psychiatry, first documented cases of psychosis and other mental disturbances following the contraction of influenza.[5] Today, prenatal exposure to a viral infection during pregnancy is a well-established risk factor for developing schizophrenia.[6] Infections of the central nervous system during childhood are also associated with an increased risk of schizophrenia,[7,8] and population-based Danish studies show that any history of hospitalization due to infection is associated with a 60% increased risk of schizophrenia relative to no infection (30-year incidence rate ratio = 1.60; absolute risk difference = 9%).[9] Furthermore, the incidence risk ratio for schizophrenia appears to increase in a linear dose-response relationship as number of infections increase.[9]

Psychotic disorders are also associated with an increased prevalence of autoimmune illnesses, a heterogeneous group of over 70 diseases characterized by impaired tolerance to self-antigens and subsequent tissue damage and destruction.[10] Higher prevalence rates between schizophrenia and celiac disease have been reported since the 1950s, and contemporary clinical studies estimate a 2.1% to 2.6% prevalence of celiac disease in schizophrenic patients compared to 0.2% to 1% in the general population.[11] Population-based studies show that prior history of any autoimmune disorder diagnosis increases the risk of developing schizophrenia by 29% (30 year incidence risk ratio = 1.29; absolute risk difference not provided).[9] Notably, a history of both hospitalization due to infection and autoimmune disorder diagnosis is associated with over a 2-fold (incidence risk ratio = 2.25; absolute risk difference not provided) increased risk of schizophrenia, suggesting a synergistic effect of multiple exposures.[12] Though psychotic disorders like schizophrenia are diagnosed and treated as disorders of the brain, these well-known associations between immunity and psychosis demonstrate the integral role of immune function in mental health.

2 | AUTOIMMUNITY & MENTAL DISORDERS: EVIDENCE FOR SHARED BIOLOGICAL MECHANISMS

Autoimmune disorders commonly co-occur with a broad array of other psychiatric symptoms and conditions. In addition to its links with schizophrenia, celiac disease is associated with higher lifetime prevalence rates of major depressive disorder and panic disorder, compared to individuals without a personal or family history of celiac disease.[13] Depressive symptoms are highly common in systemic lupus erythematosus, with an estimated prevalence up to 40% to 75%.[14] Psychiatric symptoms are also prevalent in inflammatory bowel diseases (IBD), which include Crohn's disease and ulcerative colitis. An estimated 40% of patients with an IBD exhibit clinically significant anxiety,[15] and 14% of IBD patients meet diagnostic criteria for at least one anxiety disorder compared to 5.7% in the general population.[16] In a recent case-control study of over 292 572 children, those with autism spectrum disorder (ASD; n = 48 762) were 1.5-times more likely to be diagnosed with Crohn's (0.13% ASD vs 0.09% controls) and nearly twice as likely to be diagnosed with ulcerative colitis compared to controls (0.11% ASD vs 0.06% controls).[17] These associations demonstrate the high co-morbidity between autoimmune and a diverse array mental disorder diagnoses.

Common assumptions surrounding illness experience may suggest that this co-morbidity is a function of increased psychosocial stress in the context of coping with a chronic physical illness. After all, it is depressing to confront mortality and stressful to worry about painful and embarrassing symptom flare-ups. Yet, comorbidity rates of psychiatric and autoimmune diseases vary; not all autoimmune diseases are independently associated with an increased risk of a mental disorder, suggesting that these associations are not simply due to general distress common to chronic illness management. For example, while autoimmune hepatitis is associated with a 2.75-fold increased risk of schizophrenia,[9] schizophrenia has an apparent protective effect against rheumatoid arthritis, hypothesized to be due to differential genetic influences.[18] Depressive symptoms are prevalent in over 50% of rheumatoid arthritis patients but just 28% in osteoarthritis patients.[19] Similarly, in women, multiple sclerosis is associated with up to a 30-fold increased risk of bipolar disorder incidence (0.3% BP vs 0.001% general population) while lupus is associated with a 6-fold increase (5.8% BP vs 1.0% general population).[2] Furthermore, the children of bipolar disorder patients are at an increased risk of developing inflammatory disorders such as autoimmune thyroiditis, suggesting shared biological pathways may underlie the development of both autoimmune and mental disorders.[2]

3 | IMMUNE DYSREGULATION IN DEPRESSION

Accumulating evidence for subclinical immunologic dysfunction across a variety of psychiatric conditions further implicates the importance of immune function in the context of mental illness.[2,4] In particular, low-grade chronic inflammation appears to play a role in the development of neuropsychiatric symptoms. Chronic inflammation has been most extensively studied in the pathophysiology of depression, in a theory known as the "cytokine hypothesis".[20,21]

A causal role for inflammation in depression was first evidenced by observations that proinflammatory cytokine treatment (eg, interferon alpha [IFNα]) for Hepatitis C reliably induced a major depressive episode in up to half of patients.[22] Cytokines, the chemical messengers of the immune system, are responsible for the experience of "sickness behaviors" such as lethargy and loss of appetite that commonly co-occur with inflammation and acute illness adaptation.[23] Almost all patients receiving cytokine treatment first develop the neurovegetative symptoms typically associated with sickness behavior, while a subset of patients (30%-50%) further develop mood and cognitive symptoms characteristic of major clinical depression, likely due to additional vulnerability factors.[24]

Follow-up studies in both animals and humans demonstrate that exogenous administration of cytokines or cytokine inducers (eg, endotoxins) leads to depressive symptoms, which can be prevented by prior anti-depressant treatment.[25,26] In multiple clinical studies, cytokines (eg, interleukin [IL]-6 and IL-1β) and other markers of inflammation (eg, C-Reactive Protein [CRP]) are elevated in medically healthy depressed patients.[3] Moreover, elevated inflammatory markers predict onset of depressive symptoms in longitudinal studies.[27,28] Additional immune alterations observed in major depressive disorder include reduction of natural killer (NK) cell activity and decreased number of lymphocytes such as B cells, indicating that immune dysfunction in major depression is associated with aspects of both immunosuppression as well as activation.[29]

4 | IMMUNE DYSREGULATION IN OTHER MENTAL DISORDERS

While neuroinflammatory hypotheses have been primarily investigated in major depression,[30] emerging evidence broadly implicates immunological dysfunction in other mental disorders. Altered cytokine profiles are observed in anxiety disorders, bipolar disorder, schizophrenia, and autism, as well as neurodegenerative diseases.[24] Higher levels of peripheral cytokines, particularly interferon-gamma (IFN-γ) and IL-1β, are associated with greater severity of behavioral impairments in autism,[31] and higher levels of IL-6 are also observed in clinically anxious participants compared to healthy controls.[32] In schizophrenia, elevated circulating levels of IL-6 are most consistently reported, and higher levels of IL-1β have also been found in the cerebrospinal fluid of schizophrenic patients.[4]

Bipolar disorder, a condition where individuals can vacillate among maniac, depressive, and euthymic states, appears linked to changes in immune functioning. One meta-analysis of 30 studies investigating inflammation in 1351 patients with bipolar disorder reported higher concentrations of cytokines IL-6 and tumour necrosis factor-alpha (TNFα) as well as IL-2 soluble receptors during manic phases.[33] Furthermore, acute psychosis and mania may be accompanied with changes in cell-mediated immune responses, including reductions in NK cell count and increased number of macrophages.[4,34,35] First-episode psychosis as well as psychotic relapse are associated with a proinflammatory shift in systemic inflammation, indexed by increased pro-inflammatory IL-6 and TNFα and decreased anti-inflammatory IL-10.[4] These findings highlight the relevance of subclinical immune dysregulation and inflammation in mental disorders.

5 | THE NERVOUS SYSTEM, THE IMMUNE SYSTEM, & STRESS: A UNIFYING FRAMEWORK

Psychoneuroimmunology provides a framework for understanding the shared associations between immune dysfunction and mental illness. The study of the psychological modulation of the immune system began in the 1970s with the discovery that the immune system could be classically conditioned in animal models as well as humans.[36] It is now well-established that the brain and the immune system communicate bidirectionally, connected primarily through the autonomic nervous system and neuroendocrine signalling of the hypothalamic-pituitary-adrenal (HPA) axis.[37] Peripheral cytokines affect the central nervous system by modulating neurotransmitter metabolism, activating the HPA axis and afferent vagal nerves, or directly crossing the blood-brain-barrier where it is highly permeable (eg, circumventricular organs).[14]

HPA axis dysregulation is observed in many psychiatric conditions as well as autoimmune disorders,[38] implicating the role of dysregulated stress systems in immune and mental health. Cortisol, the hormone product of the HPA axis, is considered anti-inflammatory and typically suppresses the elevated immune response that occurs under conditions of acute stress.[39] However, when repeatedly activated by chronic stress, the body's stress response systems are thought to become dysregulated and desensitized to their own feedback mechanisms, contributing to a low-grade inflammatory response.[37] Thus, chronic stress and increased stress reactivity can directly contribute to systemic inflammation and immune dysfunction.

In animal models, stress induces depressive behaviors as well as subsequent increases in cytokine levels,[40] while in humans, psychological stress often precipitates mood disorder episodes.[41] An estimated 80% of the first-onset major depressive episodes are preceded by a major life stressor, making stress a significant risk factor for developing depression.[42]

Stress has also long been recognized as playing a key role in the etiology and course of autoimmune diseases such as multiple sclerosis (MS).[43] Higher environmental stress is positively associated with MS onset as well as course with exacerbations preceded by increased anxiety and depressive symptoms.[44] Relapse in ulcerative colitis, once considered a classic psychosomatic disorder,[45] is also associated with precipitating stress exposure.[46] These findings suggest a shared causal role of stress in the cause and course of both autoimmune and mental disorders. Considering the body as a complex and integrated system, co-occurring immune disruptions and psychiatric symptoms may therefore exemplify shared underlying etiologies manifested within distinct yet interconnected systems.[47]

5.1 | Gut microbiome

The relationships among psychological stress, the nervous system, and the immune system further implicate the relevance of the microbiome and gut health in mental disorders. In addition to fighting acute illness and infection, a major role of the immune system involves proactively regulating the body's bacterial ecosystems.[48] Maintenance of the gastrointestinal (GI) tract's microbiome is especially important, as many microbes aid in digestive processes and curtail the proliferation of more dangerous pathogens like *C. difficile*.[48] The central nervous system also communicates bidirectionally with the GI tract, commonly

referred to as the "brain-gut axis". Microbes are known to affect neurotransmitter modulation and synthesis, including serotonin metabolism, and can activate the central nervous system via neuroimmune and neuroendocrine pathways.[49]

Both animal and human studies demonstrate that psychological stress can disrupt microbiota composition.[50,51] Germ-free mice raised in sterile conditions display exaggerated HPA activity, suggesting colonization of the gut microbiota is critical for normal development of the body's stress response systems.[48] While this research is still in its infancy, altered composition and reduced diversity of gut microflora are found in autism, depression, anxiety disorders, bipolar disorder, and schizophrenia.[49,52] Clinical depression as well as other psychiatric conditions also display evidence of disruption in the mucus and endothelial cell barrier that line the GI tract.[53] This increased permeability of the intestines can allow bacteria in the gut to enter the bloodstream, resulting in an inflammatory response. Microbiome and gut health are therefore critical and interrelated components of both immune and mental health.

6 | THERAPEUTICALLY TARGETING INFLAMMATION

The cross-communication between the nervous and immune systems and their relationships with stress and gut health highlight the central role of inflammation as a common mechanism of disease. Inflammation is a universal response mechanism to pain and stress, whether psychological or physiological, and systemic inflammation may be viewed as a general marker of chronic mental as well as physical illness.[37] Therapeutically targeting inflammation offers translational implications for integrating mental and physical healthcare at both the individual and community-level.

6.1 | Pharmacological interventions

Growing recognition of the shared pathways between the brain and immune system has initiated investigation into potential novel uses of existing pharmacological treatments, such as nonsteroidal anti-inflammatory drugs (NSAIDs) as mono- and adjunct immunomodulation therapies. In animal models, the NSAID celecoxib prevents HPA axis dysregulation, reduces cytokine levels in the hypothalamus, and induces behavioral changes.[54,55] Multiple randomized controlled trails (RCTs) investigating celecoxib in conjunction with an anti-psychotic for treatment of schizophrenia demonstrate that the anti-inflammatory drug is more effective for improving cognitive symptoms and reducing overall symptomatology compared to treatment as usual, though the efficacy appears most beneficial in the first stages of illness onset.[56,57]

For treatment of major depression, NSAIDs reduce depressive symptoms more than placebo[58] and celecoxib adjunctive to antidepressants is more effective than anti-depressant treatment alone.[59] One 6-week, double-blind RCT investigating the efficacy of celecoxib plus sertraline demonstrated greater reductions in both depressive symptoms and circulating IL-6 levels, as well as greater remission rates, compared to placebo.[60] Other studies investigating the use of cytokine inhibitors to directly suppress inflammation demonstrate reduction of depressive symptoms in chronic inflammatory illness.[61] These studies support the application of pharmacotherapies to treat psychiatric symptoms by targeting inflammation. However, the use of immunomodulating medications has known limitations, including low treatment adherence due to adverse side-effects like gastrointestinal bleeding and potential harm from long-term usage.[62,63] Moreover, pharmacological treatments do not offer solutions for the prevention of chronic mental and physical illnesses before they develop into diagnosable disorders.

6.2 | Dietary interventions

Lifestyle changes and behavioral interventions can offer safer, sustainable, and more cost-effective approaches for therapeutically targeting inflammation to both prevent and treat chronic mental and physical illness. Diet may be targeted to reduce systemic inflammation, as poor diet can both directly and indirectly affect inflammation via microbiota disruptions and nutritional deficits. Highly processed diets with refined carbohydrates and added sugars are associated with higher inflammatory markers like CRP, while dietary interventions that increase consumptions of fruits and vegetables decrease inflammation.[22] Shifting diet composition from processed to whole food may help reduce systemic inflammation, thereby improving immune and mental health. Beyond dietary modifications, additional evidence suggests that interventions affecting the timing of food consumption (ie, intermittent fasting) may also reduce inflammation.[27]

Both single-nutrient and broad-based supplementation may improve mental health by targeting inflammation. For example, supplementation with vitamin D, a major modulator of the immune system that is widely deficient in Westernized diets, reduces depressive symptoms as well as markers of inflammation in patients with cystic fibrosis.[22] While supplementation with single nutrients may be efficacious for some symptom reduction, multi-nutrient interventions may be more likely to optimally support brain and immune functioning. Several RCTs, conducted primarily in nonclinical and elderly populations, demonstrate sustained improvements in antisocial behavior, major depression, anxiety disorders, and bipolar disorder symptoms following supplementation with broad-based micronutrient formulas (ie, multivitamin; see Rucklidge & Kaplan, 2013 for a complete list of micronutrient formulas used in existing RCTs).[53,64]

A multitude of RCTs have investigated the immunomodulation benefits of omega-3 fatty acid (FA) supplementation as adjunctive treatment for psychiatric conditions.[65] In addition to their essential role in cell membrane integrity and fluidity, omega-3 FAs are generally considered anti-inflammatory. Rigorous RCT trials investigating omega-3 FA supplementation in major depression and schizophrenia generally show mixed findings, with both positive and negative trials reported.[66,67] While this remains an open question of study, evidence suggests that omega-3 FAs may have a protective effect against the development of mental illness.[4]

Probiotic supplementation to target gut dysbiosis may also reduce inflammation and improve psychiatric symptoms. At least one RCT to date investigating the effects of probiotics on depression and inflammation has documented reduced depressive symptoms and lower CRP levels compared to placebo.[68] The use of probiotics as an adjunctive treatment for mental disorders is still a nascent area of study, and which strains of probiotics may be most beneficial for which populations remains unknown.

While there is overall insufficient evidence to recommend specific diets as treatment for mental disorders, some individuals may benefit from self-experimenting with short-term elimination diets followed by reintroduction of specific foods to assess their perceived impact on psychiatric and other symptoms.[69,70] As diet, microbiome composition, and potential dietary sensitivities are highly variable between individuals and thus more difficult to empirically study in group analyses, this case-by-case approach to treating psychiatric symptoms with dietary modifications may be viewed as a form of personalized medicine.

6.3 | Psychological interventions

Given the relationship between inflammation and stress, inflammation may also be indirectly targeted by modifying the perceptions and appraisals that initiate physiological stress responses. By altering cognitive interpretations of stress and facilitating stress recovery, these approaches could plausibly reduce overall inflammatory levels by affecting chronic HPA axis activation and increasing recovery time between stressors.[71] Though relatively few studies have examined the mediating role of reduced inflammation in psychotherapy efficacy, one recent review of the anti-inflammatory effects of cognitive-behavioral therapy (CBT) in depressed patients found preliminary evidence that CBT treatment is associated with reductions in inflammation corresponding to improvements in depressive symptoms.[72]

Other psychological interventions that may alter inflammation include mindfulness and acceptance-based approaches. A recent review of RCTs investigating the efficacy of mindfulness interventions concluded that tentative evidence exists for mindfulness-related changes in various immune biomarkers, with at least three trials demonstrating dosage-dependent or trending effects on reductions in circulating inflammatory markers like CRP.[73] These trials provide preliminary support for the integration of psychological therapies to target inflammation and psychiatric symptoms in both mental and physical illness.

7 | AN INTEGRAL ROLE FOR HEALTH PSYCHOLOGISTS

Therapeutically targeting inflammation as a common mechanism of chronic illness will necessitate an integrative approach to mental and physical healthcare. With its roots in psychosomatic medicine, medical sociology, and epidemiology, health psychology is an emerging field that offers a deeply interdisciplinary perspective of the biopsychosocial influences on health.[1] See Figure 1 for key takeaways. Health psychologists, whether in the clinic or through research, can play a key role in providing psychoeducation for both patients and medical professionals about brain-immune system interactions and their implications for mental and physical chronic illnesses. More specifically, psychiatric services must increase their awareness of underlying immune dysfunction as a possible causal influence of mental symptoms,[74] while physicians primarily treating somatic illness need to recognize the potential for psychosocial influences to exacerbate if not cause physical symptoms.[75]

For example, an estimated 2/3 of patients with autoimmune encephalitis, a rare inflammatory disorder of the brain, initially present to psychiatric services for acute psychosis.[76] Symptoms of this condition are virtually indistinguishable from classic psychiatric disorders like schizophrenia, with patients often receiving multiple misdiagnoses and subsequent delays in treatment. Likewise, depression and anxiety symptoms are highly common in inflammatory bowel disease patients[46]; yet, these symptoms often go undetected due to lack of physician awareness and training.[15] More integrated screening and treatment within both psychiatric and physical health treatment settings is therefore critical to providing adequate and comprehensive care across a broad range of disorders. Greater awareness and recognition of brain-immune system interactions are needed at both the individual-level of care as well as more systemic policy-level changes to cohesively integrate screening measures and procedures. Congruent with this approach, lifestyle and psychological interventions should be components of multi-pronged treatment protocols for mental and physical chronic illnesses. Ideally, health psychologists would work within transdisciplinary treatment teams as part of this integrated healthcare.

Beyond individual-level determinants of health, another key area to influence for health psychologists is the recognition of the social and ecological influences on health and illness.[77] While rigorous RCTs may demonstrate the efficacy of a particular intervention to reduce inflammation, implementing and integrating clinical research findings into applied practice require consideration of the larger environmental context in which health behaviors are shaped and reinforced. From micro-level interactions with family members to macro-level structural barriers to change, the social and physical environment is a powerful driver of individual health behaviors and subsequent illness risk, of which up to 70% is estimated to be outside an individual's control.[78] In order to effectively utilize lifestyle interventions to target inflammation in mental and physical illness, the highly contextualized environmental influences that can help or hinder behavioral change must be incorporated into treatment decision-making as well as policy-level changes.

In recognizing the integral role that stress plays in immune and mental health as well as the ecological influences that drive health behaviors, health psychologists and medical professionals also have a responsibility to advocate for broader policy proposals that are more effective in improving population health than individual treatments alone. Socioeconomic influences have a greater impact on all-cause mortality than individual risk behaviors like smoking or physical

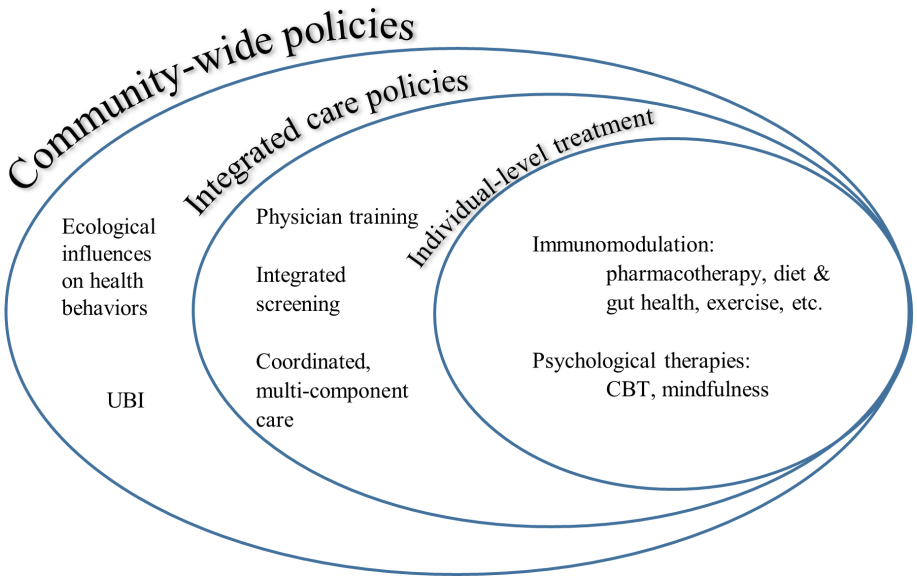

FIGURE 1 Key takeaways. Utilizing a psychoneuroimmunological lens, health psychologists and clinicians can reconceptualize healthcare through integrative treatment approaches and advocacy for comprehensive policy-level reform at both the individual-level of care as well as community-wide prevention approaches. CBT, cognitive behavioral therapy; UBI, universal basic income

inactivity and are key drivers of health disparities.[79,80] Poverty is one of the most significant chronic stressors and subsequently a primary driver of mental and physical chronic illness.[81] Congruent with a psychoneuroimmunological lens of health, poverty is also associated with higher circulating inflammatory markers.[82] Targeting inflammation at this systemic level, however, requires directly addressing the primary source of stress for many: the stressor of being poor.

One policy proposal with significant potential to reduce this stress and thereby improve mental and physical health is universal basic income (UBI), a direct form of income transfer.[83] While no studies have examined the effect of UBI on inflammatory markers per se, multiple field experiments conducted over the past several decades document both immediate and sustained improvements in various measures of health, including birth outcomes, well-being, prevalence of mental disorder diagnoses, and healthcare utilization.[83] Advocating for public policies such as UBI that can reduce or eliminate significant sources of stress should be a key objective supported by health psychologists and other medical professionals to systematically improve community-level mental and physical health.

8 | CONCLUSION

The cross-communication among the nervous, immune, and endocrine systems suggests that chronic inflammation may be a common response mechanism underlying both psychological and physiological chronic illness. This framework blurs existing distinctions between mental and physical disorders, implicating new and integrative treatment targets for preventing and treating chronic disease. In contrast to traditional treatment approaches and their focus on individual symptom management, targeting inflammation offers a plausible mechanistic framework to integrate mental and physical healthcare.

Notably, therapeutically targeting inflammation is likely not a one-size-fits-all approach. The stress of early childhood adversity and particularly trauma appears most strongly linked to systemic inflammation later in life.[84] While not all severely depressed individuals exhibit higher circulating inflammatory markers, elevated inflammation is observed in both depressed and non-depressed patients with histories of childhood maltreatment.[85] This finding suggests increased inflammation may be a "biological scar" from early stress exposure that sensitizes and dysregulates stress response systems, thereby contributing to poorer mental as well as physical health outcomes.[84] Anti-inflammatory treatments therefore may be most beneficial for a subset of patients.

Conceptualizing mental and physical health through the lens of psychoneuroimmunology implicates inflammation as a common mechanism of chronic illness, reinforcing the notion that "mental health is the health of the whole body".[84] Through psychoeducation, integrative treatment approaches, and advocacy within local clinical settings as well as more comprehensive community- and policy-level reform, clinicians and health psychologists in particular can play a key role in integrating mental and physical healthcare.

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