*Special Article*

# SYNERGISTIC RELATIONSHIPS AMONG STRESS, DEPRESSION, AND TROUBLED RELATIONSHIPS: INSIGHTS FROM PSYCHONEUROIMMUNOLOGY

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***Stress and depression consistently elevate inflammation and are often experienced simultaneously, which is exemplified by people in troubled relationships. Troubled relationships also elevate inflammation, which may be partially explained by their ability to engender high levels of stress and depression. People who are stressed, depressed, or in troubled relationships are also at greater risk for health problems than their less distressed counterparts. Inflammation, a risk factor for a variety of age-related diseases including cardiovascular disease, Type II diabetes, metabolic syndrome, and frailty, may be one key mechanistic pathway linking distress to poor health. Obesity may further broaden the health implications of stress and depression; people who are stressed or depressed are often overweight, and adipose tissue is a major source of proinflammatory cytokines. Stress, depression, and troubled relationships may have synergistic inflammatory effects: loneliness, subclinical depression, and major depression enhance inflammatory responses to an acute stressful event. The relationship between distress and inflammation is bidirectional; depression enhances inflammation and inflammation promotes depression. Interesting questions emerge from this literature. For instance, some stressors may be more potent than others and thus may be more strongly linked to inflammation. In addition, it is possible that psychological and interpersonal resources may buffer the negative inflammatory effects of stress. Understanding the links among stress, depression, troubled relationships, and inflammation is an exciting area of research that may provide mechanistic insight into the links between distress and poor health. Depression and Anxiety 30:288–296, 2013.***



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People who are stressed, depressed, or in troubled relationships are at greater risk for health problems than their less distressed counterparts.[1] For example, major depression enhances risk for osteoporosis, metabolic syndrome, coronary heart disease, myocardial infarction, and premature all-cause mortality.[2–6] Similarly,

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compared to their less stressed counterparts, chronically stressed people were more vulnerable to the common cold and had higher cardiovascular disease and myocardial infarction incidence rates.[7–9] Troubled interpersonal relationships are also linked to multiple health problems including coronary heart disease, delayed wound healing, metabolic syndrome, and premature all-cause mortality.[10–13] Importantly, the links among stress, depression, troubled relationships, and health remain after controlling for important sociodemographic and health-relevant risk factors.

Growing evidence suggests that inflammation, a key component of the immune system's response to injury or infection, may be one potential pathway linking stress, depression, and troubled relationships to poor health. Chronic inflammation increases risk for premature all-cause mortality and age-related diseases such as cardiovascular disease, Type II diabetes, metabolic syndrome, neurodegenerative disorders, and frailty.[14–17]

In this review, we first discuss evidence that stress, depression, and troubled relationships elevate inflammation and briefly describe potential mechanistic pathways. Next, we examine the synergistic relationships among stress, depression, and troubled relationships and evaluate the clinical implications of distress-related inflammation. We also discuss evidence supporting the bidirectional relationship between distress and inflammation. We conclude by suggesting areas for future research. Throughout this review, we focus on the empirical adult human literature and common inflammatory mediators such as C-reactive protein (CRP), interleukin-1 beta (IL-1$\beta$), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-$\alpha$).

## INFLAMMATION: A BIOLOGICAL CORRELATE OF STRESS, DEPRESSION, AND TROUBLED RELATIONSHIPS

Both major depression and depressive symptoms elevate inflammation.[18] For example, data from a meta-analysis demonstrated that people with major depression had higher IL-6 and TNF-$\alpha$ than those who were not depressed.[19] In addition, a series of epidemiological studies demonstrated that older adults with more depressive symptoms had higher IL-6 than those with fewer symptoms.[20–23] Similarly, older adults with higher levels of depressive symptoms had larger IL-6 responses to an influenza vaccine immune challenge than less depressed older adults.[24] The links among inflammation and clinical and subclinical depression have been replicated in chronically ill populations including cancer survivors and acute coronary syndrome (ACS) patients.[25–28]

Stress reliably enhances inflammation in naturalist and laboratory contexts.[29–32] For example, students had higher inflammation levels, including stimulated IL-6 and IL-1$\beta$ production, immediately after a stressful exam compared with a lower stress baseline period.[33–36] In addition, IL-6, interferon (IFN) gamma, and other inflammatory markers were higher after a laboratory stressor (delivering an evaluated and timed speech) than before the stressor.[37–39]

Lower socioeconomic status (SES), a chronic stressor, is also associated with elevated inflammation. Lower SES people are more stressed than their higher SES counterparts.[40] In addition, chronic stresses such as restricted access to medical care, poor environmental conditions, and limited income are more commonly experienced by people with lower rather than higher SES.[41] Lower SES, whether measured by personal or household income, social class, work position, financial assets, or education level, is linked to elevated inflammation.[42–52]

Stress and depression are often experienced simultaneously,[53] which is exemplified by people in troubled relationships. For example, troubled relationships are a reliable risk factor for both clinical and subclinical depression,[54–56] and people in unsupportive relationships are less resilient to stress than those with more supportive relationships.[57–59] Indeed, troubled relationships are often conceptualized as one form of chronic stress that also engenders major depression or depressive symptomology.[56] Troubled relationships elevate inflammation, which may be partially explained by their ability to engender high levels of stress and depression.[54,55]

Observational studies of marital conflict discussions provide a unique window into the effects of troubled relationships on inflammation; behavioral coding systems assess actual relationship behaviors and thus do not rely on self-reported relationship quality. A provocative study using this paradigm demonstrated that wound healing, an inflammation-mediated event, was slower after a marital disagreement than a socially supportive discussion.[11] In addition, production of inflammatory cytokines at the wound site was lower following the conflict than the support discussion. In contrast to systemic inflammation, which is linked to a variety of age-related diseases,[14–17] local inflammation at the wound site is adaptive and critical to effective wound healing. These results show that marital conflict produces maladaptive immunological responses, as evidenced by differences in wound repair and cytokine production at the wound site.

Negative and hostile behaviors during a conflict discussion, such as blaming or interrupting the partner, appear to be particularly detrimental. A conflict discussion led to slower wound healing among couples displaying more hostile behaviors compared to those with fewer hostile behaviors.[11] Furthermore, while hostile couples had higher systemic inflammation following a conflict discussion compared to a social support discussion, low-hostile couples had similar levels of inflammation across both discussions.[11]

Loneliness, a state of perceived social isolation and interpersonal distress, also elevates inflammation. For instance, compared with people who felt more socially connected counterparts, those who felt lonelier had higher

inflammation, upregulated proinflammatory genes, and downregulated anti-inflammatory genes.[60–62] A preliminary mindfulness-based stress intervention concurrently reduced loneliness and downregulated proinflammatory gene transcription.[61] Taken together, these studies provide further support that troubled and distressed relationships, in this case as experienced by lonely people, have negative inflammatory effects.

Family members providing care for a loved one with Alzheimer's disease or a related dementia are, on average, more stressed, depressed, and lonely than noncaregivers.[63,64] Thus, it is not surprising that multiple studies show elevated inflammation among caregivers. For example, dementia family caregivers had higher IL-6 and TNF-$\alpha$ than noncaregivers.[65–67]

Stress, depression, and troubled relationships may also fuel longitudinal changes in inflammation over time, particularly among older adults. Indeed, more depressed older adults had larger IL-6 increases over 6 years than their less depressed counterparts.[68] Similarly, IL-6 increases over a 6-year period were about four times as large among spousal dementia caregivers than noncaregivers.[64] Furthermore, the IL-6 increases did not differ between current caregivers and former caregivers even several years after the death of the dementia patient. However, perceived stress and loneliness also did not differ between current and former caregivers, suggesting that psychological recovery from a stressor may be critical to reducing inflammation over time. Consistent with this possibility, people who recovered from an episode of major depression within the prior year continued to show higher levels of CRP compared with nondepressed controls.[69,70] Major depression is often followed by subclinical depressive symptoms, which may partially account for elevated inflammation after a depressive episode ends.

Stress, depression, and troubled relationships can influence inflammation through a variety of pathways. One common mechanism linking stress and depression to inflammation is health behaviors; people who are stressed or depressed often have poor health behaviors such as inactivity or smoking,[71,72] and these health choices can elevate inflammation.[48] Stress, depression, and troubled relationships also influence inflammation via the sympathetic and parasympathetic nervous systems. For example, stress activates the sympathetic nervous system, which causes the release of epinephrine and norepinephrine. In turn, these stress hormones stimulate the release of proinflammatory cytokines. A full review of mechanistic pathways is outside of the scope of this chapter; more detailed explanations are available elsewhere for the interested reader.[73–75]

In sum, there is a large body of evidence demonstrating that stress, depression, and troubled relationships elevate inflammation. In addition, initial evidence suggests that stress and depression may fuel longitudinal increases in inflammation over time, especially among older adults. Inflammation is a risk factor for age-related diseases,[14–17] suggesting one mechanistic pathway linking stress, depression, and troubled relationships to poor health.

## SYNERGISTIC RELATIONSHIPS AMONG STRESS, DEPRESSION, AND TROUBLED RELATIONSHIPS

Stress, depression, and troubled relationships often occur simultaneously and may have synergistic effects on inflammatory responses.[53,76] Initial evidence suggests that people who are highly distressed about a task may have an exaggerated inflammatory reaction to that task.[35,77] For instance, people who were more anxious about an upcoming speech had higher postspeech IL-6 than those who were less anxious.[78] In addition, students who perceived an exam as very stressful had higher levels of the soluble interleukin-6 receptor (sIL-6r) than those who perceived it as less stressful.[79] Because sIL-6r potentiates the effects of IL-6 by increasing its inflammatory capabilities,[80] the sIL-6r data suggest that stress may exacerbate inflammatory activity.

Depression and loneliness may also prime the immune system's response to stressful events. For example, the stress of giving birth led to greater IL-6 increases among women with a history of major depression than those without a history of major depression.[81] In addition, healthy adults with higher levels of depressive symptoms produced more IL-6 in response to an acute laboratory stressor than those with lower levels of depressive symptoms.[82] Among healthy adults and posttreatment breast cancer survivors, inflammation was elevated after an acute laboratory stressor for those experiencing greater loneliness compared with those who were less lonely.[62,83]

In sum, stress, depression, and troubled relationships often occur simultaneously and mutually influence each other. The studies described above suggest that the combination of stressful events, depression, and troubled relationships may fuel immune dysregulation, and thus may further elevate risk for health problems.[84]

## CLINICAL IMPLICATIONS OF DISTRESS-RELATED INFLAMMATION

Inflammation is related to both the incidence and prognosis for a number of chronic medical conditions, including cancer, metabolic syndrome, rheumatoid arthritis, neurodegenerative disorders, asthma, gingivitis, and cardiovascular disease.[85–89] In addition, stress and depression are highly prevalent among people with chronic medical conditions.[90] Accordingly, stress- and depression-related inflammation have clear clinical implications for the management of these chronic conditions. The broad literature addressing stress and depression among medical populations is beyond the scope of

this review; we provide brief exemplars using two very different inflammatory conditions, gingivitis, and cardiovascular disease. We also discuss how obesity may exacerbate the links among stress, depression, inflammation, and inflammatory diseases.

Stress and depression enhance risk for gingivitis, a mild periodontal disease characterized by inflamed gums.[91–94] For example, spousal dementia caregivers had more gingival symptoms than noncaregivers, which was explained, in part, by caregivers' elevated stress and depressive symptoms.[95] A series of studies further demonstrated that stress elevated specific inflammatory markers that promoted gingival symptoms, suggesting one pathway through which stress affected gingivitis. Interleukin-8 (IL-8), which initiates degradation of connective tissue at inflamed gingival sites, was higher in students' gingival crevicular fluid (GCF) after delivering a videotaped and timed speech than after a control task.[96] Similarly, adults who reported more socially oriented stressful life events had higher IL-8 in their GCF than those who reported fewer events.[97] IL-1$\beta$, a cytokine that hampers bone formation and fosters periodontal tissue destruction, was elevated in the GCF of students who took a stressful exam compared with those who did not take an exam.[98] Furthermore, GCF IL-1$\beta$ concentrations remained elevated 2 weeks after the exam ended,[99] suggesting that stressful events may have longer lasting prognostic potential for gingival symptoms.

There is a vast literature demonstrating that people who are highly stressed or depressed are more likely to develop cardiovascular disease and have worse disease-related outcomes than their less stressed or depressed counterparts.[2,100,101] Furthermore, numerous studies have demonstrated that stress and depression elevate CRP and IL-6, two inflammatory markers that promote cardiovascular disease, suggesting one mechanism linking cardiovascular disease, stress, and depression.[15,102] For instance, among women with suspected coronary ischemia, those with current depressive symptoms and a history of major depression had higher CRP and IL-6 and were more likely to develop cardiovascular disease than those who had neither.[103] In addition, men with ACS who had more depressive symptoms and higher levels of CRP experienced more adverse cardiac events than men with ACS who were less depressed and had lower levels of CRP.[101]

Obesity, a worldwide epidemic,[104] may further broaden the clinical implications of stress and depression. People who are highly stressed or depressed are more likely to be overweight than their less stressed or depressed counterparts.[105,106] Highly depressed people also experience greater increases in abdominal fat over time than those who are less depressed.[107] In addition, abdominal adiposity (i.e., belly fat) is a major source of proinflammatory cytokines including IL-6, TNF-$\alpha$, and IL-1$\beta$,[108,109] and is an important risk factor for a variety of diseases such as metabolic syndrome, Type II diabetes, and cardiovascular disease.[110,111] Importantly, stress, depression, and obesity independently elevate inflammation.[18,42] Thus, among people who are stressed or depressed, those who are also overweight are particularly at risk for elevated inflammation and inflammatory diseases.

Taken together, the gingivitis and cardiovascular disease findings suggest that stress and depression may exacerbate inflammatory diseases by elevating inflammatory markers that are implicated in risk of those diseases. Furthermore, the inflammatory effects of stress and depression are both local (as in the gingivitis studies) and systemic (as evidenced by the cardiovascular studies). Obesity may further exacerbate the relationships among stress, depression, and inflammation. Accordingly, distress-related inflammation has clinical implications for the management of inflammatory diseases.

## THE BIDIRECTIONAL RELATIONSHIP BETWEEN DISTRESS AND INFLAMMATION

The relationship between depression and inflammation is bidirectional; depression enhances inflammation and inflammation promotes depression.[112] Proinflammatory cytokine administration induces "sickness behaviors," behavioral changes that resemble the somatic symptoms evident in depression, such as anhedonia and lethargy.[113] For example, both IL-6 and negative affect increased following a typhoid vaccine.[114,115] In addition, depressed mood increased following an injection of endotoxin, bacterial toxins that provoke an inflammatory response.[116,117] IFN-alpha (IFN-$\alpha$) treatment results in symptoms consistent with major depression for a subset of people.[118,119] Additional evidence suggests that IFN-$\alpha$ treatment-related depression produced more somatic depressive symptoms than traditional major depression,[120] at least during the initial phase of treatment. Cognitive-affective symptoms appear to develop shortly thereafter and may be more responsive to antidepressant treatment.[121,122] On the other hand, a TNF-$\alpha$ inhibiting medication improved psoriasis patients' depressive symptoms, independent of disease improvement.[123] Accordingly, research suggests that cytokine administration can promote depression, and anti-inflammatory medications may decrease depressive symptoms. Furthermore, immune-challenge paradigms are most clearly linked to depression-related somatic symptoms (e.g., sickness behaviors); the effects of immune-challenge paradigms on the core cognitive-affective symptoms of depression, such as suicidal ideation and guilt, requires further examination.[124]

If stress and depression elevate inflammation, then treatments designed to reduce stress and depression should reduce inflammation. Consistent with this possibility, CRP decreased following antidepressant medication for a subset of people with major depressive disorder, and the anti-inflammatory effects of the medication were most reliable for those who benefited

psychologically from treatment.[125,126] People who do not benefit from antidepressants often have persistently higher IL-6 than those who do benefit, suggesting one potential way to identify people who will respond to antidepressants.[114,125] Nonprescription pharmacological treatments may also improve depression and thus reduce inflammation. For example, growing evidence suggests that omega-3 fatty acids may have antidepressant effects.[127,128] In addition, omega-3 supplementation reduces inflammation.[129,130]

Behavioral data further suggest that lowering distress reduces inflammation. For instance, a compassion meditation intervention reduced emotional distress and IL-6 for people who practiced more frequently than less frequently.[131] In addition, the regular practice of yoga was related to lower baseline and stress-induced inflammation.[132] Exercise also has well-documented anti-inflammatory and antidepressant effects.[133,134] Some evidence even suggests that exercise interventions may be as effective as antidepressive medications in alleviating major depression for some individuals.[135]

In sum, the relationship between distress and inflammation is bidirectional. Cytokine administration and other immune-challenge studies suggest that inflammation induces sickness behaviors such as anhedonia and lethargy. Studies demonstrating that depression interventions reduce inflammation support the argument that depression enhances inflammation.

## FUTURE DIRECTIONS

Stress, depression, and troubled relationships reliably increase inflammation. However, it is possible that some stressors are more potent than others and are thus more strongly linked to inflammation. For example, loneliness threatens the need to belong, a fundamental need that is at the core of human nature, and thus should impact immune function across cultures and demographic groups.[136,137] On the other hand, threats to social harmony are particularly relevant in Eastern cultures[138] and thus may be more strongly related to inflammation among Eastern compared to Western cultures.

Stress and depressive symptoms often remain elevated after a stressful event ends.[64,139] In addition, psychological recovery may be impacted by the length and intensity of the stressor, depressive episode, or troubled relationship. Accordingly, another intriguing question is how long inflammation remains elevated after a stressor ends and how this relates to psychological recovery. Furthermore, it is possible that older adults may be particularly influenced by the long-lasting inflammatory consequences of stress and depression.[140]

Depression and loneliness exacerbate stress-induced inflammation.[82,83] However, some people may be more resilient in the face of stress than others. Indeed, psychological resources (e.g., self-esteem) and interpersonal resources (e.g., social support) may buffer the negative impacts of stress.[141] For example, people with higher self-esteem perceived a timed and evaluated performance task as less stressful than those with lower self-esteem.[142] In response to being told that a potential dating partner left the study early, higher self-esteem participants explained the other person's behavior with more benign (e.g., the other participant was sick) than malevolent (e.g., the other participant did not like me) attributions.[143] These studies suggest that, compared to their lower self-esteem counterparts, people with higher self-esteem may experience less stress in response to an objective stressor and may interpret ambiguous situations as less threatening. A novel new direction is to explore whether self-esteem differences in stress perceptions translate into altered stress-related inflammatory responses.

Researchers are beginning to understand the relationships between stress-induced health behaviors and inflammation. For example, people often eat poorly and stop exercising when they are stressed or depressed;[71,144] both food and exercise influence inflammation.[133,145] Researchers in these areas can investigate multiple hypotheses about the relationships among distress, health behaviors, and inflammation. For instance, stress and depression may affect inflammation because they cause poor health behaviors. Another possibility is that poor health behaviors exacerbate stress-induced inflammation.

Understanding the relationships between inflammation and interventions to reduce stress and depression is a burgeoning area of research.[125,126,146] Because some people respond to behavioral and pharmacological treatments differently than others,[125] exploring the relationship between psychological symptom improvement and decreased inflammation is important. Furthermore, the strongest evidence demonstrating that inflammation causes depression has focused on somatic symptoms (e.g., "sickness behaviors" such as lethargy). Mechanistic insight may be gained if researchers can determine whether depression-related inflammatory changes are related to reduced "sickness behaviors," cognitive-affective symptoms such as suicidal ideation and guilt, or a combination of these factors.

In sum, research reliably demonstrates that inflammation is linked to stress, depression, and troubled relationships. Because elevated inflammation is a risk factor for poor health,[14–17,85,86,89] these studies may provide mechanistic insight into the ways that stress, depression, and troubled relationships affect health.

## REFERENCES

1. Kiecolt-Glaser JK, McGuire L, Robles TF, Glaser R. Emotions, morbidity, and mortality: new perspectives from psychoneuroimmunology. Annu Rev Psychol 2002;53: 83–107.
2. Joynt KE, Whellan DJ, O'Connor CM. Depression and cardiovascular disease: mechanisms of interaction. Biol Psychiatry 2003;54(3):248–261.

3. Michelson D, Stratakis C, Hill L, et al. Bone mineral density in women with depression. N Engl J Med 1996;335(16):1176–1181.
4. Pan A, Keum N, Okereke OI, et al. Bidirectional association between depression and metabolic syndrome: a systematic review and meta-analysis of epidemiological studies. Diabetes Care 2012;35(5):1171–1180.
5. Pratt LA, Ford DE, Crum RM, Armenian HK, Gallo JJ, Eaton WW. Depression, psychotropic medication, and risk of myocardial infarction. Prospective data from the Baltimore ECA follow-up. Circulation 1996;94(12):3123–3129.
6. Schulz R, Beach SR, Ives DG, Martire LM, Ariyo AA, Kop WJ. Association between depression and mortality in older adults: the Cardiovascular Health Study. Arch Intern Med 2000;160(12):1761–1768.
7. Cohen S, Tyrrell DA, Smith AP. Psychological stress and susceptibility to the common cold. N Engl J Med 1991;325(9):606–612.
8. Kuper H, Marmot M. Job strain, job demands, decision latitude, and risk of coronary heart disease within the Whitehall II study. J Epidemiol Community Health 2003;57(2):147–153.
9. Theorell T, Tsutsumi A, Hallquist J, et al. Decision latitude, job strain, and myocardial infarction: a study of working men in Stockholm. The SHEEP Study Group. Stockholm Heart Epidemiology Program. Am J Public Health 1998;88(3):382–388.
10. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. PLoS Med 2010;7(7):e1000316.
11. Kiecolt-Glaser JK, Loving TJ, Stowell JR, et al. Hostile marital interactions, proinflammatory cytokine production, and wound healing. Arch Gen Psychiatry 2005;62(12):1377–1384.
12. Orth-Gomér K, Wamala SP, Horsten M, Schenck-Gustafsson K, Schneiderman N, Mittleman MA. Marital stress worsens prognosis in women with coronary heart disease: the Stockholm Female Coronary Risk Study. JAMA 2000;284(23):3008–3014.
13. Whisman MA. Loneliness and the metabolic syndrome in a population-based sample of middle-aged and older adults. Health Psychol 2010;29(5):550–554.
14. Ershler WB, Keller ET. Age-associated increased Interleukin-6 gene expression, late-life diseases, and frailty. Annu Rev Med 2000;51(1):245–270.
15. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 2005;352(16):1685–1695.
16. Harris TB, Ferrucci L, Tracy RP, et al. Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. Am J Med 1999;106(5):506–512.
17. Hotamisligil GS. Inflammation and metabolic disorders. Nature 2006;444(7121):860–867.
18. Howren MB, Lamkin DM, Suls J. Associations of depression with c-reactive protein, IL-1, and IL-6: a meta-analysis. Psychosom Med 2009;71(2):171–186.
19. Dowlati Y, Herrmann N, Swardfager W, et al. A meta-analysis of cytokines in major depression. Biol Psychiatry 2010;67(5):446–457.
20. Bremmer MA, Beekman ATF, Deeg DJH, et al. Inflammatory markers in late-life depression: results from a population-based study. J Affect Disord 2008;106(3):249–255.
21. Dentino AN, Pieper CF, Rao KMK, et al. Association of interleukin-6 and other biologic variables with depression in older people living in the community. J Am Geriatr Soc 1999;47(1):6–11.
22. Penninx B, Kritchevsky SB, Yaffe K, et al. Inflammatory markers and depressed mood in older persons: results from the Health, Aging and Body Composition study. Biol Psychiatry 2003;54(5):566–572.
23. Tiemeier H, Hofman A, Van Tuijl HR, Kiliaan AJ, Meijer J, Breteler MMB. Inflammatory proteins and depression in the elderly. Epidemiology 2003;14(1):103–107.
24. Glaser R, Robles TF, Sheridan J, Malarkey WB, Kiecolt-Glaser JK. Mild depressive symptoms are associated with amplified and prolonged inflammatory responses after influenza virus vaccination in older adults. Arch Gen Psychiatry 2003;60(10):1009–1014.
25. Jehn CF, Kuehnhardt D, Bartholomae A, et al. Biomarkers of depression in cancer patients. Cancer 2006;107(11):2723–2729.
26. Miller GE, Freedland KE, Duntley S, Carney RM. Relation of depressive symptoms to C-reactive protein and pathogen burden (cytomegalovirus, herpes simplex virus, Epstein-Barr virus) in patients with earlier acute coronary syndromes. Am J Cardiol 2005;95(3):317–321.
27. Musselman DL. Higher than normal plasma interleukin-6 concentrations in cancer patients with depression: preliminary findings. Am J Psychiat 2001;158(8):1252–1257.
28. Shimbo D, Rieckmann N, Paulino R, Davidson KW. Relation between C reactive protein and depression remission status in patients presenting with acute coronary syndrome. Heart 2006;92(9):1316–1318.
29. Altemus M, Rao B, Dhabhar FS, Ding W, Granstein RD. Stress-induced changes in skin barrier function in healthy women. J Invest Dermatol 2001;117(2):309–317.
30. Brydon L, Edwards S, Jia H, et al. Psychological stress activates interleukin-1beta gene expression in human mononuclear cells. Brain Behav Immun 2005;19(6):540–546.
31. Steptoe A, Willemsen G, Owen N, Flower L, Mohamed-Ali V. Acute mental stress elicits delayed increases in circulating inflammatory cytokine levels. Clin Sci 2001;101(2):185–192.
32. Von Känel R, Kudielka BM, Preckel D, Hanebuth D, Fischer JE. Delayed response and lack of habituation in plasma interleukin-6 to acute mental stress in men. Brain Behav Immun 2006;20(1):40–48.
33. Dobbin JP, Harth M, McCain GA, Martin RA, Cousin K. Cytokine production and lymphocyte transformation during stress. Brain Behav Immun 1991;5(4):339–348.
34. Dugué B, Leppänen E, Gräsbeck R, Benoit D, Esa L, Ralph G. The driving license examination as a stress model: effects on blood picture, serum cortisol and the production of interleukins in man. Life Sci 2001;68(14):1641–1647.
35. Maes M, Song C, Lin A, et al. The effects of psychological stress on humans: increased production of pro-inflammatory cytokines and a Th1-like response in stress-induced anxiety. Cytokine 1998;10(4):313–318.
36. Paik IH, Toh KY, Lee C, Kim JJ, Lee SJ. Psychological stress may induce increased humoral and decreased cellular immunity. Behav Med 2000;26(3):139–141.
37. Bierhaus A, Wolf J, Andrassy M, et al. A mechanism converting psychosocial stress into mononuclear cell activation. Proc Natl Acad Sci USA 2003;100(4):1920–1925.
38. Buske-Kirschbaum A, Kern S, Ebrecht M, Hellhammer DH. Altered distribution of leukocyte subsets and cytokine production in response to acute psychosocial stress in patients with psoriasis vulgaris. Brain Behav Immun 2007;21(1):92–99.
39. Goebel MU, Mills PJ, Irwin MR, Ziegler MG. Interleukin-6 and tumor necrosis factor-$\alpha$ production after acute psychological stress, exercise, and infused isoproterenol: differential effects and pathways. Psychosom Med 2000;62(4):591–598.

40. Cohen S, Doyle WJ, Baum A. Socioeconomic status is associated with stress hormones. Psychosom Med 2006;68(3):414–420.
41. Baum A, Garofalo JP, Yali AM. Socioeconomic status and chronic stress: does stress account for SES effects on health? Ann N Y Acad Sci 1999;896(1):131–144.
42. Alley DE, Seeman TE, Ki Kim J, Karlamangla A, Hu P, Crimmins EM. Socioeconomic status and C-reactive protein levels in the US population: NHANES IV. Brain Behav Immun 2006;20(5):498–504.
43. Gruenewald TL, Cohen S, Matthews KA, Tracy R, Seeman TE. Association of socioeconomic status with inflammation markers in black and white men and women in the Coronary Artery Risk Development in Young Adults (CARDIA) study. Soc Sci Med 2009;69(3):451–459.
44. Hemingway H, Shipley M, Mullen MJ, et al. Social and psychosocial influences on inflammatory markers and vascular function in civil servants (the Whitehall II study). Am J Cardiol 2003;92(8):984–987.
45. Jousilahti P, Salomaa V, Rasi V, Vahtera E, Palosuo T. Association of markers of systemic inflammation, C reactive protein, serum amyloid A, and fibrinogen, with socioeconomic status. J Epidemiol Community Health 2003;57(9):730–733.
46. Koster A, Bosma H, Penninx BWJH, et al. Association of inflammatory markers with socioeconomic status. J Gerontol A Biol Sci Med Sci 2006;61(3):284–290.
47. Loucks EB, Sullivan LM, Hayes LJ, et al. Association of educational level with inflammatory markers in the Framingham Offspring Study. Am J Epidemiol 2006;163(7):622–628.
48. McDade TW, Hawkley LC, Cacioppo JT. Psychosocial and behavioral predictors of inflammation in middle-aged and older adults: the Chicago Health, Aging, and Social Relations Study. Psychosom Med 2006;68(3):376–381.
49. Owen N, Poulton T, Hay FC, Mohamed-Ali V, Steptoe A. Socioeconomic status, C-reactive protein, immune factors, and responses to acute mental stress. Brain Behav Immun 2003;17(4):286–295.
50. Pollitt RA, Kaufman JS, Rose KM, Diez-Roux AV, Zeng D, Heiss G. Cumulative life course and adult socioeconomic status and markers of inflammation in adulthood. J Epidemiol Community Health 2008;62(6):484–491.
51. Ranjit N, Diez-Roux AV, Shea S, Cushman M, Ni H, Seeman T. Socioeconomic position, race/ethnicity, and inflammation in the Multi-Ethnic Study of Atherosclerosis. Circulation 2007;116(21):2383–2390.
52. Steptoe A, Owen N, Kunz-Ebrecht S, Mohamed-Ali V. Inflammatory cytokines, socioeconomic status, and acute stress responsivity. Brain Behav Immun 2002;16(6):774–784.
53. Hammen C. Stress and Depression. Annual Review of Clinical Psychology. 2005;1(1):293–319.
54. Beach SRH, Fincham FD, Katz J. Marital therapy in the treatment of depression: toward a third generation of therapy and research. Clin Psychol Rev 1998;18(6):635–661.
55. Cacioppo JT, Hawkley LC, Thisted RA. Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. Psychol Aging 2010;25(2):453–463.
56. Kiecolt-Glaser JK, Newton TL. Marriage and health: his and hers. Psychol Bull 2001;127(4):472–503.
57. Cohen S, Hoberman HM. Positive events and social supports as buffers of life change stress. J Appl Soc Psychol 1983;13(2):99–125.
58. Ozbay F, Fitterling H, Charney D, Southwick S. Social support and resilience to stress across the life span: a neurobiologic framework. Curr Psychiatry Rep 2008;10(4):304–310.
59. Heffner KL, Kiecolt-Glaser JK, Loving TJ, Glaser R, Malarkey WB. Spousal support satisfaction as a modifier of physiological responses to marital conflict in younger and older couples. J Behav Med 2004;27(3):233–254.
60. Cole SW, Hawkley LC, Arevalo JM, Sung CY, Rose RM, Cacioppo JT. Social regulation of gene expression in human leukocytes. Genome Biol 2007;8.
61. Creswell JD, Irwin MR, Burklund LJ, et al. Mindfulness-Based Stress Reduction training reduces loneliness and pro-inflammatory gene expression in older adults: A small randomized controlled trial. Brain Behav Immun. 2012;26(7):1095–1101.
62. Hackett RA, Hamer M, Endrighi R, Brydon L, Steptoe A. Loneliness and stress-related inflammatory and neuroendocrine responses in older men and women. Psychoneuroendocrinology 2012;37(11):1801–1809.
63. Kiecolt-Glaser JK, Dura JR, Speicher CE, Trask OJ, Glaser R. Spousal caregivers of dementia victims: longitudinal changes in immunity and health. Psychosom Med 1991;53(4):345–362.
64. Kiecolt-Glaser JK, Preacher KJ, MacCallum RC, Atkinson C, Malarkey WB, Glaser R. Chronic stress and age-related increases in the proinflammatory cytokine IL-6. Proc Natl Acad Sci USA 2003;100(15):9090–9095.
65. Damjanovic AK, Yang Y, Glaser R, et al. Accelerated telomere erosion is associated with a declining immune function of caregivers of Alzheimer's disease patients. J Immunol 2007;179(6):4249–4254.
66. Lutgendorf SK, Garand L, Buckwalter KC, Reimer TT, Hong SY, Lubaroff DM. Life stress, mood disturbance, and elevated interleukin-6 in healthy older women. J Gerontol A Biol Sci Med Sci 1999;54(9):M434–M439.
67. Von Känel R, Dimsdale JE, Ancoli-Israel S, et al. Poor sleep is associated with higher plasma proinflammatory cytokine interleukin-6 and procoagulant marker fibrin D-dimer in older caregivers of people with Alzheimer's disease. J Am Geriatr Soc 2006;54(3):431–437.
68. Stewart JC, Rand KL, Muldoon MF, Kamarck TW. A prospective evaluation of the directionality of the depression-inflammation relationship. Brain Behav Immun 2009;23(7):936–944.
69. Danner M, Kasl SV, Abramson JL, Vaccarino V. Association between depression and elevated C-reactive protein. Psychosom Med 2003;65(3):347–356.
70. Kling MA, Alesci S, Csako G, et al. Sustained low-grade pro-inflammatory state in unmedicated, remitted women with major depressive disorder as evidenced by elevated serum levels of the acute phase proteins c-reactive protein and serum amyloid. Biol Psychiatry 2007;62(4):309–313.
71. Steptoe A, Wardle J, Pollard TM, Canaan L, Davies GJ. Stress, social support and health-related behavior: a study of smoking, alcohol consumption and physical exercise. J Psychosom Res 1996;41(2):171–180.
72. Vitaliano PP, Scanlan JM, Zhang J, Savage MV, Hirsch IB, Siegler IC. A path model of chronic stress, the metabolic syndrome, and coronary heart disease. Psychosom Med 2002;64(3):418–435.
73. Miller AH. Depression and immunity: a role for T cells? Brain Behav Immun 2010;24(1):1–8.
74. Irwin MR. Human psychoneuroimmunology: 20 years of discovery. Brain Behav Immun 2008;22(2):129–139.
75. Irwin MR, Miller AH. Depressive disorders and immunity: 20 years of progress and discovery. Brain Behav Immun 2007;21(4):374–383.

76. Whisman MA, Uebelacker LA. Comorbidity of relationships distress and mental and physical health problems. In: Snyder DK, Whisman MA, editors. Treating Difficult Couples: Helping Clients with Coexisting Mental and Relationship Disorders. New York, NY: Guilford Press; 2003:3–26.
77. Wirtz PH, Von Knel R, Emini L, Suter T, Fontana A, Ehlert U. Variations in anticipatory cognitive stress appraisal and differential proinflammatory cytokine expression in response to acute stress. Brain Behav Immun 2007;21(6):851–859.
78. Carroll JE, Low CA, Prather AA, et al. Negative affective responses to a speech task predict changes in interleukin (IL)-6. Brain Behav Immun 2011;25(2):232–238.
79. Song C, Kenis G, Van Gastel A, et al. Influence of psychological stress on immune-inflammatory variables in normal humans. Part II. Altered serum concentrations of natural anti-inflammatory agents and soluble membrane antigens of monocytes and T lymphocytes. Psychiatry Res 1999;85(3):293–303.
80. Jones SA, Horiuchi S, Topley N, Yamamoto N, Fuller GM. The soluble interleukin 6 receptor: mechanisms of production and implications in disease. FASEB J 2001;15(1):43–58.
81. Maes M, Ombelet W, Verkerk R, Bosmans E, Scharpé S. Effects of pregnancy and delivery on the availability of plasma tryptophan to the brain: relationships to delivery-induced immune activation and early post-partum anxiety and depression. Psychol Med 2001;31(05):847–858.
82. Fagundes CP, Glaser R, Hwang BS, Malarkey WB, Kiecolt-Glaser JK. Depressive symptoms enhance stress-induced inflammatory responses. Brain Behav Immun; in press.
83. Jaremka LM, Fagundes CP, Peng J, et al. Loneliness promotes inflammation during acute stress. Psychol Sci; in press.
84. Kiecolt-Glaser JK, Gouin J-P, Hantsoo L. Close relationships, inflammation, and health. Neurosci Biobehav Rev 2010;35(1):33–38.
85. Aggarwal BB, Shishodia S, Sandur SK, Pandey MK, Sethi G. Inflammation and cancer: how hot is the link? Biochem Pharmacol 2006;72(11):1605–1621.
86. Corren J. Anti-interleukin-5 antibody therapy in asthma and allerges. Curr Opin Allergy Clin Immunol 2011;11(6):565–570.
87. Fitzgerald JE, Kreutzer DL. Localization of interleukin-8 in human gingival tissues. Oral Microbiol Immunol 1995;10(5):297–303.
88. Foster PS, Hogan SP, Ramsay AJ, Matthaei KI, Young IG. Interleukin 5 deficiency abolishes eosinophilia, airways hyperreactivity, and lung damage in a mouse asthma model. J Exp Med 1996;183(1):195–201.
89. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342(12):836–843.
90. Kiecolt-Glaser JK, Glaser R. Depression and immune function: central pathways to morbidity and mortality. J Psychosom Res 2002;53(4):873–876.
91. Hugo FN, Hilgert JB, Bozzetti MC, et al. Chronic stress, depression, and cortisol levels as risk indicators of elevated plaque and gingivitis levels in individuals aged 50 years and older. J Periodontol 2006;77(6):1008–1014.
92. Johannsen A, Rydmark I, Söder B, Åsberg M. Gingival inflammation, increased periodontal pocket depth and elevated interleukin-6 in gingival crevicular fluid of depressed women on long-term sick leave. J Periodontal Res 2007;42(6):546–552.
93. Johannsen A, Rylander G, Söder B, Asberg M. Dental plaque, gingival inflammation, and elevated levels of interleukin-6 and cortisol in gingival crevicular fluid from women with stress-related depression and exhaustion. J Periodontol 2006;77(8):1403–1409.
94. LeResche L, Dworkin SF. The role of stress in inflammatory disease, including periodontal disease: review of concepts and current findings. Periodontology 2002;30(1):91–103.
95. Vitaliano PP, Persson R, Kiyak A, Saini H, Echeverria D. Caregiving and gingival symptom reports: psychophysiologic mediators. Psychosom Med 2005;67(6):930–938.
96. Weik U, Herforth A, Kolb-Bachofen V, Deinzer R. Acute stress induces proinflammatory signaling at chronic inflammation sites. Psychosom Med 2008;70(8):906–912.
97. Giannopoulou C, Kamma JJ, Mombelli A. Effect of inflammation, smoking and stress on gingival crevicular fluid cytokine level. J Clin Periodontol 2003;30(2):145–153.
98. Deinzer R, Förster P, Fuck L, Herforth A, Stiller-Winkler R, Idel H. Increase of crevicular interleukin 1beta under academic stress at experimental gingivitis sites and at sites of perfect oral hygiene. J Clin Periodontol 1999;26(1):1–8.
99. Deinzer R, Kottmann W, Förster P, Herforth A, Stiller-Winkler R, Idel H. After-effects of stress on crevicular interleukin-1ß. J Clin Periodontol 2000;27(1):74–77.
100. Chandola T, Britton A, Brunner E, et al. Work stress and coronary heart disease: what are the mechanisms? Eur Heart J 2008;29(5):640–648.
101. Frasure-Smith N, Lespérance F, Irwin MR, Sauvé C, Lespérance J, Théroux P. Depression, C-reactive protein and two-year major adverse cardiac events in men after acute coronary syndromes. Biol Psychiatry 2007;62(4):302–308.
102. Kaptoge S, Di Angelantonio E, Lowe G, et al. C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis. Lancet 2010;375(9709):132–140.
103. Vaccarino V, Johnson BD, Sheps DS, et al. Depression, inflammation and incident cardiovascular disease in women with suspected coronary ischemia—the National Heart, Lung, and Blood Institute-sponsored WISE study. J Am Coll Cardiol 2007;50(21):2044–2050.
104. World Health Organization. Fact Sheet: Obesity and Overweight. World Health Organization; 2012. Available at: http://www.who.int/mediacentre/factsheets/fs311/en /index.html.
105. Björntorp P. Do stress reactions cause abdominal obesity and comorbidities? Obes Rev 2001;2(2):73–86.
106. Luppino FS, De Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry 2010;67(3):220–229.
107. Vogelzangs N, Kritchevsky SB, Beekman ATF, et al. Depressive symptoms and change in abdominal obesity in older persons. Arch Gen Psychiatry 2008;65(12):1386–1393.
108. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol 2006;6(10):772–783.
109. Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. Br J Nutr 2004;92(03):347–355.
110. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health 2009;9.
111. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. J Am Coll Cardiol 2009;53(21):1925–1932.

112. Miller AH, Maletic V, Raison CL. Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. Biol Psychiatry 2009;65(9):732–741.
113. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. Nat Rev Neurosci 2008;9(1):46–56.
114. Strike PC, Wardle J, Steptoe A. Mild acute inflammatory stimulation induces transient negative mood. J Psychosom Res 2004;57(2):189–194.
115. Wright CE, Strike PC, Brydon L, Steptoe A. Acute inflammation and negative mood: mediation by cytokine activation. Brain Behav Immun 2005;19(4):345–350.
116. Eisenberger NI, Inagaki TK, Mashal NM, Irvin MR. Inflammation and social experience: an inflammatory challenge induces feelings of social disconnection in addition to depressed mood. Brain Behav Immun 2010;24(4):558–563.
117. Reichenberg A, Yirmiya R, Schuld A, et al. Cytokine-associated emotional and cognitive disturbances in humans. Arch Gen Psychiatry 2001;58(5):445–452.
118. Capuron L, Miller AH. Cytokines and psychopathology: lessons from interferon-alpha. Biol Psychiatry 2004;56(11):819–824.
119. Musselman DL, Lawson DH, Gumnick JF, et al. Paroxetine for the prevention of depression induced by high-dose interferon alfa. N Engl J Med 2001;344(13):961–966.
120. Capuron L, Fornwalt FB, Knight BT, Harvey PD, Ninan PT, Miller AH. Does cytokine-induced depression differ from idiopathic major depression in medically healthy individuals? J Affect Disord 2009;119(1–3):181–185.
121. Capuron L, Gumnick JF, Musselman DL, et al. Neurobehavioral effects of interferon-alpha in cancer patients: phenomenology and paroxetine responsiveness of symptom dimensions. Neuropsychopharmacology 2002;26(5):643–652.
122. McNutt MD, Liu S, Manatunga A, et al. Neurobehavioral effects of interferon-$\alpha$ in patients with hepatitis-C: symptom dimensions and responsiveness to paroxetine. Neuropsychopharmacology 2012;37(6):1444–1454.
123. Tyring S, Gottlieb A, Papp K, et al. Etanercept and clinical outcomes, fatigue, and depression in psoriasis: double-blind placebo-controlled randomised phase III trial. Lancet 2006;367(9504):29–35.
124. DellaGioia N, Hannestad J. A critical review of human endotoxin administration as an experimental paradigm of depression. Neurosci Biobehav Rev 2010;34(1):130–143.
125. Lanquillon S, Krieg J-C, Bening-Abu-Shach U, Vedder H. Cytokine production and treatment response in major depressive disorder. Neuropsychopharmacology 2000;22(4):370–379.
126. O'Brien SM, Scott LV, Dinan TG. Antidepressant therapy and C-reactive protein levels. Br J Psychiatry 2006;188:449–452.
127. Appleton KM, Rogers PJ, Ness AR. Updated systematic review and meta-analysis of the effects of n-3 long-chain polyunsaturated fatty acids on depressed mood. Am J Clin Nutr 2010;91(3):757–770.
128. Lin P-Y, Su K-P. A meta-analytic review of double-blind, placebo-controlled trials of antidepressant efficacy of omega-3 fatty acids. J Clin Psychiatry 2007;68(7):1056–1061.
129. Kiecolt-Glaser JK, Belury MA, Andridge R, Malarkey WB, Hwang BS, Glaser R. Omega-3 supplementation lowers inflammation in healthy middle-aged and older adults: a randomized controlled trial. Brain Behav Immun 2012;26(6):988–995.
130. Kiecolt-Glaser JK, Belury MA, Andridge R, Malarkey WB, Glaser R. Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial. Brain Behav Immun 2011;25(8):1725–1734.
131. Pace TWW, Negi LT, Adame DD, et al. Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress. Psychoneuroendocrinology 2009;34(1):87–98.
132. Kiecolt-Glaser JK, Christian L, Preston H, et al. Stress, inflammation, and yoga practice. Psychosom Med 2010;72(2):113–121.
133. Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol 2011;11(9):607–615.
134. Herring MP, Puetz TW, O'Connor PJ, Dishman RK. Effect of exercise training on depressive symptoms among patients with a chronic illness: a systematic review and meta-analysis of randomized controlled trials. Arch Intern Med 2012;172(2):101–111.
135. Hoffman BM, Babyak MA, Craighead WE, et al. Exercise and pharmacotherapy in patients with major depression: one-year follow-up of the SMILE study. Psychosom Med 2011;73(2):127–133.
136. Baumeister RF, Leary MR. The need to belong: desire for interpersonal attachments as a fundamental human motivation. Psychol Bull 1995;117(3):497–529.
137. Hawkley LC, Cacioppo JT. Loneliness matters: a theoretical and empirical review of consequences and mechanisms. Ann Behav Med 2010;40(2):218–227.
138. Markus HR, Kitayama S. Culture and the self: implications for cognition, emotion, and motivation. Psychol Rev 1991;98(2):224–253.
139. Bodnar JC, Kiecolt-Glaser JK. Caregiver depression after bereavement: chronic stress isn't over when it's over. Psychol Aging 1994;9(3):372–380.
140. Kiecolt-Glaser JK, Glaser R. Stress and immunity: age enhances the risks. Curr Dir Psychol Sci 2001;10(1):18–21.
141. Uchino BN, Cacioppo JT, Kiecolt-Glaser JK. The relationship between social support and physiological processes: a review with emphasis on underlying mechanisms and implications for health. Psychol Bull 1996;119(3):488–531.
142. Rector NA, Roger D. The stress buffering effects of self-esteem. Pers Individual Diff 1997;23(5):799–808.
143. Ford MB, Collins NL. Self-esteem moderates neuroendocrine and psychological responses to interpersonal rejection. J Pers Soc Psychol 2010;98(3):405–419.
144. Appelhans BM, Whited MC, Schneider KL, et al. Depression severity, diet quality, and physical activity in women with obesity and depression. J Acad Nutr Diet 2012;112(5):693–698.
145. Kiecolt-Glaser JK. Stress, food, and inflammation: psychoneuroimmunology and nutrition at the cutting edge. Psychosom Med 2010;72(4):365–369.
146. Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress, and immune parameters in breast and prostate cancer outpatients. Psychosom Med 2003;65(4):571–581.