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Special points of interest:

- Trauma survivors have higher than average rates of heart disease, diabetes and other serious illnesses.
- These illnesses are most likely caused by trauma-related alterations to the immune system that increase inflammation.
- Treatments that lower inflammation can ease both physical and mental health effects of trauma.

Why Trauma Makes People Sick

Inflammation, Heart Disease and Diabetes in Trauma Survivors

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Trauma survivors have higher than average rates of serious illness including heart disease, diabetes and metabolic syndrome, the precursor to type 2 diabetes (Batten et al., 2004; Felitti et al., 2001; Kendall-Tackett & Marshall, 1999). The intriguing question is why this is so. One possible explanation is the connection between inflammation and disease--specifically, elevated levels of proinflammatory cytokines. Cytokines are proteins that regulate immune response and proinflammatory cytokines help the body heal wounds and fight infection by stimulating an inflammatory response. But there can be too much of a good thing; chronic inflammation is a likely cause of a wide range of illnesses including heart disease, diabetes, Alzheimer's disease, and even cancer (Batten et al., 2004; Robles et al., 2005; Suarez, 2006).

So why would proinflammatory cytokines to be elevated in trauma survivors? Low levels of cortisol, which are common in trauma survivors, can allow inflammation to go unchecked since cortisol generally regulates the inflammatory response. Another possibility is that cytokines increase in the wake of two common trauma sequelae--depression and hostility. Depression and hostility act as stressors, and increase inflammation and subsequent risk of disease. These can affect survivors' health long after the trauma has ended.

Depression, Inflammation and Health

Depression is one of the most commonly occurring sequelae of trauma (Kendall-Tackett, 2003). But it's one we tend to think of it as an outcome--an endpoint we measure in the wake of traumatic events. Yet depression can also be a mechanism that leads to poor health. The negative impact of depression is well known in the cardiovascular literature. Patients who become depressed after a heart attack are two to three times more likely to have another one and are three to four times more likely to die (deJong et al., 2006; Lesperance & Frasure-Smith, 2000). And inflammation is the likely culprit (Kiecolt-Glaser et al., 2007).

In depressed people, there are several biomarkers of increased inflammation including acute-phase proteins, such as C-reactive protein (CRP; Kop & Gottdiener, 2005; Robles, Glaser, & Kiecolt-Glaser, 2005), and proinflammatory cytokines. The proinflammatory cytokines that have been most consistently identified in studies of depressed people are abnormal levels of the normally present biochemicals interleukin-1 β (IL-1 β), interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α) and interferon- γ (IFN- γ ; Kiecolt-Glaser et al., 2007; Robles et al., 2005). Researchers hypothesize that chronic inflammation increases the risk of heart disease by damaging blood vessels, reducing the stability of plaque, and increasing the risk of acute episodes (e.g., Kop & Gottdiener, 2005).



In summary, depression raises inflammation and is generally bad for people's health. It alone could explain many of the health effects of trauma. But unfortunately, depression is not the only mental state that increases the risk of disease. Hostility is another common sequela of trauma that leads to poor health. Its effects are described below.

Hostility and Trauma

For people with a hostile world view, life is not benign. People high in trait hostility don't trust others, are suspicious and cynical about human nature, and tend to interpret the actions of others as aggressive (Smith, 1992). And hostility is a common response among trauma survivors. In a sample from primary care, 52% of female sexual abuse survivors indicated that they could not trust others compared with 17% of the non-abused women (Hulme, 2000). In a community sample, approximately half of sexual abuse survivors indicated that their views of themselves and others were very negative. And in a sample of 90 women veterans (Butterfield, Forneris, Feldman, & Beckham, 2000), women with PTSD reported significantly higher levels of hostility and had poorer health than women without PTSD.

The Health Effects of Hostility

Hostility is a reaction that may have been adaptive at one point, and served to protect the survivor from further danger. However, hostility has a well-documented negative impact on health. Hostility increases physiological arousal because of the way hostile people interpret the world (Kiecolt-Glaser & Newton, 2001). This reaction increases both the risk of cardiovascular disease and diabetes. In their review, Smith and Ruiz (2002) noted that people who are high in trait hostility are more prone to ischemia and constriction of the coronary arteries during mental stress. Trait hostility predicts new coronary events in previously healthy people. And for patients who already have coronary heart disease, hostility speeds-up the progression of the disease.

Hostility also increased levels of proinflammatory cytokines (IL-1 α , IL-1 β , IL-8 and TNF- α) in a study 44 healthy, non-smoking, premenopausal women (Suarez et al., 2004). The combination of depression and hostility was especially deleterious, and there was a dose-responsive effect: the more severe the depression and hostility, the greater the production of cytokines. A study with men had similar results (Suarez, 2003). The author noted that increased levels of IL-6 predicted both future risk of cardiac events and all-cause mortality, and hypothesized that IL-6 may mediate the relationship between hostility and these health problems.

Hostility also increases the risk of metabolic syndrome. In a three-year follow-up of 134 white and African American teens, hostility at Time 1 predicted risk factors for metabolic syndrome at Time 2 (Raikkonen, Matthews, & Salomon, 2003). These risk factors were at the 75th percentile for age, gender and race and included BMI, insulin resistance, ratio of triglycerides to HDL cholesterol, and mean arterial blood pressure.

More recently, Suarez (2006) studied 135 healthy patients (75 men, 60 women) with no symptoms of diabetes. He found that women with higher levels of depression and hostility, and who had a propensity to express anger, had higher levels of fasting insulin, glucose, and insulin resistance. These findings were not true for men and they were independent of other risk factors for metabolic syndrome including BMI, age, fasting triglycerides, exercise regularity, or ethnicity. The author indicated that these findings were significant since pre-study glucose levels were in the non-diabetic range. The author noted that inflammation, particularly elevated IL-6 and C-reactive protein, may mediate the relationship between depression and hostility, and risk of type 2 diabetes and cardiovascular disease, possibly because they increase insulin resistance. This would be in addition to our common use of eating to self-treat depres-



“Trauma sequelae, such as depression and hostility, can raise inflammation levels and impair health.”



sion and anger, with consequent obesity, and the predisposition of obesity to insulin resistance and diabetes.

Anti-Inflammatory Treatment Approaches

The studies cited above indicate that two common trauma sequelae—depression and hostility—appear to increase inflammation and impair health. The inflammation-health connection raises at least the possibility that reducing inflammation may help lessen the severity of symptoms. The depression literature already indicates that many of the effective treatments for depression are also anti-inflammatory, and this may be another mechanism for their efficacy. For example, the selective serotonin reuptake inhibitor (SSRI) class of antidepressants have been found to lower levels of C-reactive protein in cardiac patients with major depression (O'Brien et al., 2006). This anti-inflammatory effect was independent of whether depression resolved in these patients.

Even cognitive therapy, a treatment with well-established efficacy, is arguably anti-inflammatory (Rupke et al., 2006). Two recent studies have demonstrated that negative beliefs, such as hostility, can increase the levels of proinflammatory cytokines—especially IL-6 (Kiecolt-Glaser et al., 2005; Suarez et al., 2004). The primary goal of cognitive therapy is to reduce negative cognitions. Since negative cognitions increase inflammation, reducing their occurrence should reduce inflammation.

Omega-3 Fatty Acids, Inflammation and Health

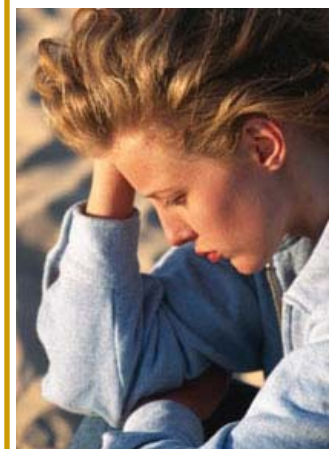
In my view, some of the more promising work, with potential application to trauma survivors, is research on the health effects of the long-chain Omega-3 fatty acids: EPA and DHA. EPA and DHA are anti-inflammatory and lower levels of proinflammatory cytokines. A recent large population study found that people with high blood levels EPA and DHA had low levels of IL-6, IL-1, TNF- α and lower levels of C-reactive protein. The opposite was true for people with low EPA/DHA in their blood (Ferrucci et al., 2006). Another study of older adults found that the combination of depressive symptoms and low blood levels of Omega-3s had enhanced production of IL-6 and TNF- α (Kiecolt-Glaser et al., 2007). These are the same cytokines that are high in depression and hostility and that likely have a relation to heart disease and diabetes.

EPA and DHA may also protect mental health. High levels of EPA and DHA increased resilience to laboratory-induced psychological stressors in college students and attenuated the proinflammatory response (Maes et al., 2000). In population studies, populations with higher levels of EPA and DHA in their diets (usually from eating fatty fish) had lower levels of major depression (Tanskanen et al., 2001), postpartum depression (Hibbeln, 2002), bipolar disorder (Noaghiul & Hibbeln, 2003), and even future suicide risk (Sublette et al., 2006).

Similar findings have been noted in randomized clinical trials, where researchers have given either EPA/DHA supplements or a placebo to people currently receiving treatment for unipolar or bipolar depression. Two recent studies added EPA to patients' normal regimen of antidepressants and found that EPA made the antidepressants more effective in treating depression than the placebo (Nemets et al., 2002; Peet & Horrobin, 2002). Similarly, in a study of childhood depression, children who received EPA and DHA in addition to their medications had significantly improved depression compared with children who received their meds and a placebo (Nemets et al., 2006). And EPA also helped stabilize symptoms of bipolar disorder in a 12-week double-blind trial (Frangou et al., 2006).



“Omega-3 fatty acids show promise as adjunctive treatments for trauma survivors.”



Although these findings are preliminary, treatments that are anti-inflammatory show promise as primary or adjunct treatments in trauma survivors. Although cognitive therapy and antidepressants have been used successfully with trauma survivors (Kendall-Tackett, 2003), to my knowledge, EPA and DHA have not been tried. But this may prove to be an effective addition to our treatment regimens and would be a fruitful avenue to explore.

Conclusions

Depression and hostility are common sequelae of trauma and violence. In addition to their negative impact on day-to-day functioning, they can also act as chronic stressors in trauma survivors. Both of these can have a profound impact on health, in part, by raising levels of proinflammatory cytokines. Treatments that reduce inflammation show promise in alleviating depressive and trauma symptoms, and also in decreasing the risk of subsequent health problems.

This paper is part of a Division 56 Symposium that will be presented at the 2007 APA Convention: Traumatic Stress, Cardiovascular Disease, Metabolic Syndrome and Neurodegenerative Disease. Session co-presenters include Kathleen Kendall-Tackett, Ph.D., Jeff Kibler, Ph.D., Mary Meagher, Ph.D., James Flatt, Ph.D., and Robert Geffner, Ph.D.

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