Physical Health and Post-traumatic Stress Disorder: Review and Synthesis

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This article reviews the empirical evidence on post-traumatic stress disorder (PTSD) and physical health and considers this evidence in light of the physical health outcomes associated with other psychiatric disorders. The existing data show that PTSD is associated with poor self-reported health and increased utilization of medical services. To a lesser extent, the data also show an association between PTSD and increased morbidity. Possible psychological, behavioral, and biological mechanisms are discussed, and a model integrating these mechanisms is presented.
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Psychological stress is associated with poor physical health outcomes. These outcomes include not just self-reports and illness behavior, but also disorders across a wide range of bodily systems.[1-3] Although most of the research on the physical health consequences of stress has focused on significant, but nontraumatic, stressors such as marital and occupational disruption, a subset of studies have focused on traumatic stressors such as military combat, physical and sexual assault, and natural disasters. These studies have found that traumatic exposure is consistently associated with poor health outcomes (Table 1).[4] Although most of the evidence is based on health perceptions or utilization, traumatic exposure also is associated with physician-diagnosed morbidity and even mortality. For example, in one recent study, reports of adverse childhood experiences among adult members of a large health maintenance organization were related to increased risk of serious medical conditions, including cancer, ischemic heart disease, and chronic lung disease.[5]

To understand the relationship between stress and physical health, one must address the question of how stressor exposure relates to physical outcomes. Models of the relationship between nontraumatic stress and health have posited (or assume) a distress reaction as a crucial and initial part of the pathway. Analogously, Friedman and Schnurr[4] argued that post-traumatic stress disorder (PTSD) should be considered the primary mediator of the relationship between traumatic exposure and physical health outcomes. This article reviews the empirical evidence on PTSD and physical health and considers this evidence in light of the physical health outcomes associated with other psychiatric disorders. Psychological, behavioral, and biological mechanisms are discussed, and a model integrating these mechanisms is presented.

PTSD and Physical Health

Self Report

The vast majority of research that has examined PTSD and physical health outcomes has used self-reported physical health as an outcome, measured in one of three ways. The first is self-report of physical health conditions, as distinguished from physical symptoms. Subjects typically are asked whether they have any of a given list of medical disorders; or, for example, Boscarino[6] asked subjects whether they ever had been told by a physician that they had any of a given list of illnesses. The second type of self-report measure is perceived health status. This usually is assessed with an instrument such as the SF-36,[7] a self-report measure of general health functioning, or with a single 5-point scale that ranges from poor to excellent. The third type of self-report is a measure of somatic symptoms in which subjects report current symptoms from a list provided. Measures of self-reported health can be valid indicators of actual morbidity,[6,7] but should be interpreted cautiously because they may be influenced by psychological processes as well.

Physical health conditions. There are consistent findings across studies to show an association between PTSD and self-reported physical health conditions. These studies primarily have been with veteran populations, but two studies have reported similar findings in civilian populations.[8,9] In the two largest studies, Vietnam combat veterans with PTSD were compared to those without PTSD on number of chronic health problems[10] and on specific chronic disease categories.[6] In the original analyses from the National Vietnam Veterans Readjustment Study (NVVRS), Kulka et al[10] found that both men and women with PTSD reported a greater number of chronic health problems than those without PTSD. In a reanalysis of the NVVRS data, Zatzick et al[11,12] found that the association between number of chronic health problems and PTSD remained after controlling for comorbid psychiatric and other medical conditions for male, but not for female, Vietnam veterans. In the

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Table 1. Summary of Results Concerning the Relationship Between Traumatic Exposure and Adverse Health Outcomes

	Outcome			
Trauma	*Self-Report*	*Utilization*	*Morbidity*	*Mortality*
Military	++	+	+/−	+
Sexual	++	++	+/−	NA
Disaster	+	+	+	+/−
Other[a]	++	NA	+	+

[a]Includes war refugees, hostages, and motor vehicle accident survivors.
++, clear association; +, probable association; +/−, inconsistent information; NA, information not available.
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most sophisticated analysis of the NVVRS data, Taft et al[13] conducted separate path analyses for men and women to model how war zone exposure, PTSD, and the personal resources of hardiness and perceived social support relate to physical health problems. For both men and women, PTSD mediated the relationship between war zone exposure and physical health. These findings are consistent with Wolfe et al[14] and Friedman and Schnurr,[4] who found that PTSD was a more robust predictor of physical health outcome than war zone exposure, and that PTSD at least partially mediated the effects of war zone exposure on physical health conditions, in a sample of female Vietnam veterans. Taft et al[13] also found that the effects of hardiness and perceived social support on reported physical conditions were mediated through PTSD.

Boscarino,[6] using a sample of male Vietnam veterans from the Centers for Disease Control and Prevention's Vietnam Experiences Study, found an association between PTSD and chronic disease, including circulatory, digestive, musculoskeletal, nervous, respiratory, and non-sexually transmitted infectious disease. This study is particularly important because it controlled not only for demographics and selection bias, but also for factors such as behavioral risk factors, including smoking and substance abuse. Moreover, it controlled for hypochondriasis, thereby decreasing any reporting bias due to psychosomatic factors. The question of whether PTSD is uniquely associated with chronic physical diseases was partially addressed by also examining the effects of depression and other anxiety disorders on chronic physical conditions. Although PTSD was found to be most strongly related to chronic physical disease, comorbidity between PTSD, anxiety, and depression was not accounted for.

Beckham et al,[15] in a sample of Vietnam veterans, found that PTSD was associated with a greater number of both lifetime and current physical conditions, and that PTSD severity was positively related to self-report of physical conditions. Depression was not predictive of physical conditions. PTSD also is related to reports of physical conditions in Vietnam veterans from New Zealand[16] and from Canada,[17] and in Dutch World War II (WWII) resistance veterans.[18] Only one study has failed to find an increased report of physical health conditions among male veterans with PTSD.[19]

Two studies have examined the relationship between PTSD and physical health conditions among nonveterans. Breslau and Davis[8] found that young adults with PTSD lasting at least one year reported more physical health conditions than young adults with PTSD that lasted less than one year. In a study of Israeli immigrants who originated around the site of the 1986 Chernobyl nuclear accident, Cwikel et al[9] found that the number of chronic physical conditions was related to PTSD, but no individual physical condition was strongly associated with PTSD.

Perceived health status. A handful of studies have assessed PTSD in relation to self-reported physical health status or health functioning. The aforementioned NVVRS data also were analyzed according to health functioning, and PTSD was associated with poorer perceived health status[10] for both men and women. Additional analyses, controlling for comorbid psychiatric and other medical disorders, found that among male veterans, PTSD was associated with diminished well-being, increased report of fair or poor physical health, and physical limitations[12]; among female veterans, PTSD was associated with increased report of fair or poor physical health and one or more bed days for a physical health problem within the prior 3 months.[11] Similarly, Taft et al[13] found substantial effects of PTSD on functional health status for both men and women, but particularly for men. This same relationship has been found for Vietnam veterans from New Zealand.[16] Schnurr and Spiro[20] also found a strong association between PTSD symptoms and perceived health status, adjusting for mental health status, using data from WWII and Korean conflict veterans in the Normative Aging Study. The behavioral risk factors of smoking and alcohol use were assessed as potential mediators and, although PTSD symptoms were positively related to both smoking and alcohol use, neither mediated the effects of PTSD on health status.

PTSD and perceived health status has been studied in selective psychiatric populations. One study found an association between PTSD and poor self-reported medical status among cocaine-dependent patients.[21] Among a sample of treatment-seeking adults with other anxiety disorders, those with comorbid PTSD, or who had experienced a traumatic event but who did not have PTSD, reported poorer perceived health status, as compared to adults with anxiety but without PTSD or trauma.[22]

Recently, Jacobsen et al[23] examined PTSD symptoms in a sample of women with breast cancer who had previously undergone autologous bone marrow trans-

plantation. They found that PTSD symptoms were associated with poorer self-reported health-related functioning and with stage of illness, such that PTSD was more severe among women who had more extensive disease.

Physical symptoms. The majority of studies that have examined PTSD and physical health outcomes have used self-reported physical symptoms as an outcome. Taken together, this literature overwhelmingly indicates an association between PTSD and greater somatic complaints. Populations studied primarily have been male veterans, but there also have been studies of male firefighters,[24,25] and of community-residing young adults[26] and adolescents.[27] Beckham et al[15] found results similar to that which they observed for self-reported chronic health problems: PTSD was associated with a greater number of physical symptoms as well. In contrast, whereas Litz et al[19] found no relationship between PTSD and self-reported physician-diagnosed disorders, PTSD was related to an overall increased number of physical symptoms. Ohry et al[28] found a signifiant association between PTSD symptoms and somatic complaints in Israeli former prisoners of war. Also in an Israeli veteran population, Solomon[29] and Shalev et al[30] found greater physical symptoms among those with PTSD. Specific symptoms related to PTSD were cardiovascular, gastrointestinal, neurological, low back pain, and headaches.[30] Schnurr et al,[31] using longitudinal data from the Normative Aging Study, found that PTSD symptoms were positively related to number of physical symptoms, such that those men with the greatest number of physical health symptoms between ages 30 and 75 also reported the greatest amount of PTSD symptoms.

Other studies of American veteran and military populations, including older veterans seeking outpatient medical treatment,[32] Persian Gulf War veterans,[33] and army personnel deployed to the Persian Gulf,[34] have consistently found PTSD to be related to physical symptoms. In a sample of Dutch WWII survivors, composed of both veterans and civilians, PTSD was found to be related to somatic complaints, even after statistical control for anxiety, depression, anger, and optimism, factors that presumably could inflate the reporting of somatic symptoms.[35]

Among the studies that used nonmilitary and nonveteran populations, two studies have investigated PTSD and physical health complaints among professional firefighters. In both studies, those with PTSD endorsed a greater number of total symptoms overall, and specifically more cardiovascular symptoms.[24,25] McFarlane et al[24] also found more musculoskeletal and neurological symptoms among those with PTSD. Moreover, firefighters with PTSD who endorsed physical symptoms were compared with firefighters with PTSD who did not endorse physical symptoms. Those with physical symptoms were more likely to be comorbid for depression and to have greater overall PTSD severity, and in particular, greater intrusive symptoms.[24] In a community sample of young adults, PTSD was associated with greater symptoms overall and with cardiopulmonary, gastrointestinal, conversion, and sexual symptoms in particular.[26] Moreover, PTSD, as compared to all other psychiatric disorders combined, was associated with a greater number of somatic symptoms across the abovementioned categories. In the only study of adolescents identified,[27] PTSD was related to a greater number of self-reported physical health symptoms. Among adolescents, depression also was related to endorsement of physical symptoms, and no differences were found between PTSD and depression in their association with physical health symptoms.

Medical Utilization

As compared to the association of PTSD and self-reported physical health outcomes, the association of PTSD and medical service utilization has been surprisingly understudied. The NVVRS, as reported by Kulka et al,[10] found that both male and female Vietnam veterans with PTSD were more likely than veterans without PTSD to have used services for physical health problems. Similarly, MacDonald et al,[16] in a sample of Vietnam veterans from New Zealand, found that veterans with PTSD reported greater utilization of health care services. Finally, Australian firefighters with PTSD were more likely to seek medical help and to consult a doctor for medical problems than were firefighters without PTSD.[24]

Morbidity and Mortality

Despite the importance of examining PTSD and morbidity, as opposed to relying solely on self-report of physical health problems, considerably less research has been conducted using morbidity as an outcome measure. Recently, two studies have investigated PTSD in relation to physician diagnosed medical disorders. Beckham et al[15] compared male Vietnam combat veterans with and without PTSD while controlling for smoking and alcohol abuse and found that men with PTSD had more physician-diagnosed medical disorders. Schnurr et al[36] examined the association between PTSD symptoms and 12 chronic disease categories, using a community sample of male combat veterans of WWII and the Korean conflict. Even with control for age, smoking, alcohol consumption, and body mass index (BMI), survival analysis found that PTSD symptoms were associated with increased onset of medical disorder in four categories: arterial, lower gastrointestinal, dermatological, and musculoskeletal. The findings from this study may underestimate the association between PTSD and morbidity because the sample was composed of relatively healthy older men and only a few men had clinically elevated PTSD scores, suggesting the possibility of a greater association between PTSD and the onset of

chronic medical disorders among a less healthy population.

Several studies have examined cardiovascular morbidity in relation to PTSD. Falger et al[37] compared male Dutch resistance WWII veterans with and without PTSD and found that men with PTSD had a higher likelihood of angina than those without PTSD. (It is unclear, however, whether this cardiovascular risk variable was a physician-rated diagnosis or based on a self-report of a physician diagnosis.) Shalev et al[30] examined the association between PTSD and cardiovascular risk factors based on medical exam and laboratory test findings in a sample of male Israeli combat veterans. Even when controlling for smoking, they found that veterans with PTSD did not perform as well as their non-PTSD counterparts on a laboratory stress test that measured effort tolerance. No differences were reported, however, with regard to heart rate or blood pressure. Boscarino and Chang,[38] in a sample of male Vietnam veterans, also examined PTSD in relation to cardiovascular disease by comparing veterans with and without PTSD on electrocardiogram (ECG) findings. While controlling for risk factors such as alcohol consumption, BMI, current substance abuse, and smoking, in addition to current cardiovascular and central nervous system medication use, the investigators found that PTSD was associated with having a nonspecific ECG abnormality, atrioventricular conduction defects, and infarctions. For comparison purposes, anxiety and depression were also assessed in relation to ECG findings. Although anxiety and depression also were associated with nonspecific ECG abnormality, and depression additionally with arrhythmias, these findings must be interpreted with caution due to the high comorbidity between PTSD, anxiety, and depression that was not controlled for in the study.

One study examined PTSD in relation to risk of stroke among WWII prisoners of war and found a slightly increased risk that was not statistically significant.[39] Another study assessed PTSD within a clinical population of men and women with irritable bowel syndrome (IBS). Irwin et al[40] found that 36% met criteria for lifetime PTSD; on average, PTSD symptoms preceded onset of IBS symptoms by 9 years.

Only one study has examined mortality and PTSD.[41] In a sample of male Vietnam veterans from the Agent Orange Registry, those with PTSD, relative to those without PTSD, had elevated all-cause mortality; regarding specific causes, only mortality due to external factors such as suicide and accidents was elevated. Standardized mortality ratios for veterans with PTSD, which provide a comparison to men of similar age and ethnicity, also were elevated for all causes and seemed to be accounted for primarily by external causes; however, the ratio also was elevated for diseases of the digestive system, most of which were cases of cirrhosis of the liver. In comparison, standardized mortality ratios for veterans without PTSD showed decreased risk of mortality due to circulatory disease.

Summary

There is a consistent association between PTSD and physical health, regardless of whether physical health is measured as morbidity or self-report. Although research examining PTSD and specific disorders primarily has been based on self-report, there is some converging evidence from these studies to suggest that PTSD is related to cardiovascular, gastrointestinal, and musculoskeletal disorders. It is noted also that the one morbidity study that has examined PTSD in relation to specific disorders found similar results.[36] PTSD appears to be related to increased utilization of medical services. The association of PTSD with poor health holds across both veteran and civilian populations, and remains after control for behavioral risk variables such as smoking and alcohol use. There also is some evidence that the relationship between PTSD and physical health remains after controlling for comorbid psychiatric disorders.

Motor vehicle accident and other trauma survivors may be injured as a result of their traumatic experience. Prisoners of war and political prisoners may not only experience injury through beatings and torture, but also may experience starvation and disease-promoting conditions. Increases in health problems might be expected in such cases, at least for a period of time following traumatic exposure. However, the observed relationships between PTSD and poor health outcomes are unlikely to result from traumatic injury or illness alone. Most trauma survivors are not injured or exposed to disease; for example, a study of combat veterans with PTSD found that 60% had a serious medical problem, but only 6% had a problem related to injury in combat.[42]

Caution is warranted in making a causal interpretation of the findings relating PTSD to poor health. Most of the existing literature is based on cross-sectional designs, and even longitudinal designs are subject to threats to internal validity from unmeasured "third variables," thus raising the question: Is it PTSD that causes poor health, or some correlate of PTSD, such as smoking or depression, that is the actual cause? It is our view that many of these correlates are actually potential mechanisms, rather than confounds, and below we present a model that elaborates this view.

Mechanisms

Our multidimensional perspective on the possible mechanisms through which PTSD could lead to poor health is presented in Fig 1. As indicated in the figure, the biological and psychological correlates of PTSD could independently and jointly combine, directly, and indirectly, through behavioral pathways, to promote disease.

Psychological Factors

Most of the findings on PTSD and physical health are based on self-reports of health, which may be substantially influenced by psychological factors such as somati-

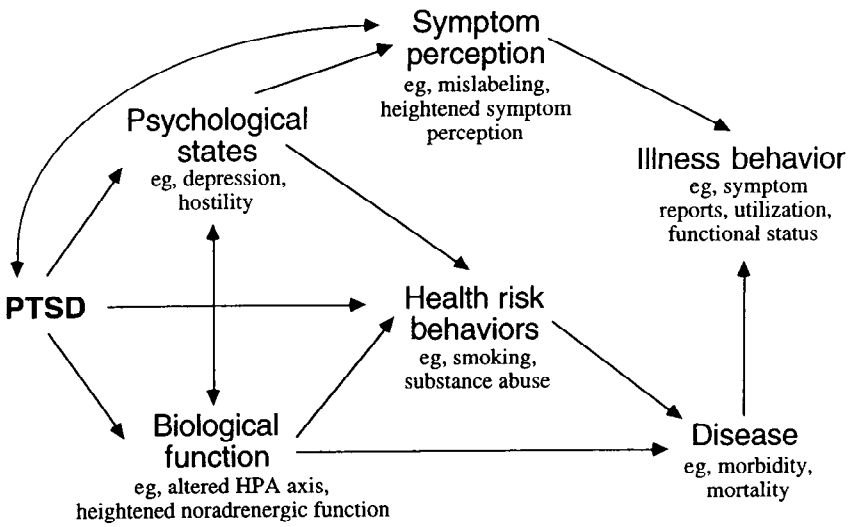

Figure 1. A model of possible mechanisms underlying the relationship between PTSD and physical health.

zation and neuroticism.[43] A related issue is that physical symptom inventories may include symptoms of depression and anxiety, such as low energy, rapid heartbeat, and shortness of breath. Thus, increased attention to physical symptoms, as well as mislabeling of depressive and anxious symptoms, is likely to explain at least part of the association between poor health and PTSD. There are several lines of evidence, however, that strongly indicate that this association is not solely due to attentional and mislabeling processes. Psychiatric disorders other than PTSD are associated with increased physical morbidity, which demonstrates that psychiatric disorder can be associated with poor health.[44,45] Also, neuroticism is linked to self-reports of physical symptoms and general health, but less so to utilization, and not at all with morbidity and mortality.[43] In addition, self-reported health status is predictive of both morbidity and mortality.[7,46] Finally, although self-reports may be only moderately accurate, PTSD patients and controls do not differ with respect to accuracy.[15]

PTSD may be related to poor health outcomes through comorbid depression. Depressed individuals report more physical symptoms and use more medical treatment than do nondepressed individuals.[47] As discussed above for PTSD, it is possible that these relationships reflect somatization or overlap between physical symptom measures and some symptoms of depression. However, depression has been linked to morbidity from cardiovascular disease in previously healthy populations and to additional morbidity and mortality among patients with serious medical illness.[48-50] Furthermore, depression is related to decreased immune function.[51]

PTSD also may be related to poor health outcomes through more general symptoms of comorbid anxiety or panic. Overall, the evidence linking anxiety to cardiovascular morbidity and mortality is quite strong,[44] although most studies have not controlled for cardiovascular risk factors and the mechanisms are largely unknown. Panic disorder is especially interesting because many of the symptoms of a panic attack are cardiovascular in nature. A recent review[52] concluded that although panic disorder is linked to poor health outcomes and increased utilization, that these relationships are unlikely to be due to biological consequences of panic, and instead are most likely due to increased sensitivity to symptoms and to behavioral factors.

Hostility, or anger, is a common correlate of PTSD. Decades of research on the health risks associated with the Type A behavior pattern have isolated hostility as a crucial factor in cardiovascular disease.[53] The mechanism is presumed to be the propensity of hostile individuals to show increased sympathetically mediated cardiovascular responses to provocation, as well as decreased parasympathetic responses to this activation, although behavioral factors such as smoking also are involved.[3] Thus, hostility could mediate a relationship between PTSD and cardiovascular illness.

Little is known about how coping and social support relate to health in PTSD. One longitudinal study found that initial levels of PTSD and low social support, but not poor coping, predicted subsequent physical symptoms.[54] No evidence of mediating or moderating roles for coping and social support were found, although ultimately such roles may be important in understanding the relationship between PTSD and physical health (eg, use of alcohol as an avoidant coping strategy for reducing hyperarousal).

Biological Factors

As indicated elsewhere in this issue of *Seminars in Clinical Neuropsychiatry* (see articles by Southwick and Yehuda), PTSD involves alterations in two of the major systems that mediate the body's response to stress, the adrenergic and hypothalamic-pituitary-adrenal (HPA) systems. In addition to the direct relationship between adrenergic and HPA function and normal

physiological activity, both systems influence other key neurobiologic mechanisms that are involved in the relationship between stress and physical health.[1,55]

To evaluate the possible health consequences of these changes in PTSD, it is important to consider the increasing evidence of interactions among the immune, nervous, and endocrine systems.[2,56] For example, the immune system is mediated by the autonomic nervous system and the HPA axis, as well as regulatory peptides and pituitary hormones; the immune system, in turn, releases chemical messengers that affect the nervous system, with the "trafficking" of immune cells being an important part of this process.[2] Also, these interactions may be far-ranging; for example, glucocorticoids affect the reproductive axis by influencing luteinizing hormone-releasing hormone, luteinizing hormone and follicle stimulating hormone; testosterone and estradiol; and affect the growth and thyroid axes by influencing growth hormone, thyroid-stimulating hormone, and triiodothyronine (T_3).[1]

Altered HPA axis function. The central role of glucocorticoids in interactions with the immune system suggests that the altered HPA axis function in PTSD could be a key mechanism leading to poor health. What to expect is unclear, however. Because cortisol has immunosuppressive effects, the low levels of cortisol in PTSD would imply that PTSD might lead to disorders involving increased immune system activity. Chrousos[57] included PTSD in a list of disorders potentially associated with activation of immune-mediated inflammation through decreased HPA-axis activity (eg, rheumatoid arthritis). However, the enhanced receptor sensitivity and periodically high levels of cortisol in PTSD imply that PTSD might, like depression, lead to disorders involving decreased immune function and suppression of immune-mediated inflammation.

Studies of the immune system in PTSD are inconclusive, although they suggest that the former scenario may be somewhat more likely. Two of three studies have found that PTSD is associated with elevated numbers of leukocytes.[58,59] Lymphocyte numbers appear unrelated to PTSD,[59,60] except in one study with a very large sample size, which found PTSD associated with increased numbers of total lymphocytes, total T cells, and CD4 cells.[58] PTSD is unrelated to the number of natural killer (NK) cells.[59,60] In one study, NK cell activity was found to be increased in PTSD,[60] whereas in another, it was decreased.[59] A further study failed to find any relationship between PTSD and NK cell activity;[61] however, this study also administered an in vitro challenge with methionine-enkephalin and found that PTSD patients showed decreases in NK activity, which was not observed in normal or substance-abusing controls.

Additional evidence of immune system activation in PTSD comes from findings on responses to a standard antigen battery. One study failed to find any differences in responsiveness between PTSD and no PTSD groups,[58] but another found that combat veterans with PTSD had increased responsiveness relative to both military and non-veteran control groups.[62] Further evidence of an immune profile that is consistent with a pattern of increased activation is the elevation of interleukin-1-beta (IL-1β) levels in PTSD, an inflammatory cytokine which can increase cortisol by stimulating the HPA axis.[63] Note that levels of IL-1β (and other cytokines) are elevated in depression, despite the elevated levels of cortisol that typically are observed—a coexistence that has been described as a paradox with implications for the etiology of depression.[51] Note also that investigations have failed to find a relationship between levels of cortisol and immune measures in PTSD,[60,63] which suggests a dysregulation of how these systems interact. It will be important for future research to examine possible influences from the noradrenergic and endogenous opioid systems in order to clarify the nature of immune functioning in PTSD as well as overlaps with depression and other disorders.

Other biological correlates. One of the hallmark symptoms of PTSD is physiological reactivity to traumatic reminders, a response demonstrated many times in the laboratory (see article by Pitman et al in this issue). Over 10 years ago, Rosen and Fields[64] proposed that autonomic hyperreactivity in PTSD could lead to increased medical morbidity. Because sympathetically mediated reactivity is associated with the development of cardiovascular disorder,[65] individuals with PTSD might be especially likely to develop cardiovascular disorder. As indicated above, emerging evidence is consistent with this possibility.

The mechanisms that might operate in mediating the effects of PTSD on cardiovascular disorder are likely to be those that have been suggested for depression, hostility, and stress, and include sympathoadrenal hyperactivity, diminished heart rate variability, and platelet aggregation.[3,48,49] These mediators involve complex interactions among systems. For example, individuals who exhibit the largest sympathetically mediated increases in cardiovascular reactivity to brief experimental stressors also show the largest catecholaminergic increases and immune changes.[66]

Blood pressure reactivity to laboratory stressors has been hypothesized to be related to the development of hypertension, although data are inconsistent and suggest that laboratory reactivity predicts hypertension only among individuals with a family history of the disorder.[67] A number of studies have investigated laboratory reactivity to traumatic and nontraumatic stressors among individuals with PTSD. The largest, by Keane et al,[68] studied over 1,400 male Vietnam veterans and found that those with current PTSD had a greater reactivity than those who never had PTSD to traumatic stressors. Although the PTSD group has less blood pressure reactivity than the never-PTSD group and a past-PTSD group to a nontraumatic stressor, is it possible

that chronic PTSD may confer additional risk of hypertension among those already at risk due to family history. This subgroup may be relatively small because Keane et al found no differences in mean resting levels of systolic and diastolic blood pressure among current-, past-, and never-PTSD groups. However, more specific investigations that control for known risk factors for hypertension are needed before any firm conclusions can be drawn.

Another biological correlate of PTSD—sleep dysregulation—recently has been linked to decreased NK cell activity. In one study of disaster survivors,[59] self-reported sleep problems partially mediated the relationship between PTSD symptoms and NK cell activity. In a study of PTSD symptoms among bereaved individuals, which was conducted in a sleep laboratory, time awake during non-rapid eye movement (NREM) sleep substantially mediated the relationship between PTSD symptoms and NK activity.[69]

Behavioral Factors

Our review of the literature found that PTSD is correlated with poor physical health even when behavioral factors such as smoking are controlled, and one study found only small evidence of mediation.[20] Nevertheless, the relationship between PTSD and poor health is likely to be mediated in part by behavioral factors that are known risk factors for disease, such as smoking, substance abuse, diet, and lack of exercise. The increased likelihood of substance abuse in PTSD has been well documented.[10,70] Less research has been done establishing a connection between PTSD and smoking, but it is clear that PTSD is related to smoking as well.[58] PTSD is related to amount smoked,[71] and a longitudinal study found that increases in PTSD were associated with increases in alcohol consumption and smoking.[72] These behavioral factors may interact with one another and with psychological and biological correlates of PTSD; for example, smoking is related to excessive drinking, and both are related to depression.[73]

Allostatic Load: An Integrative Mechanism

A helpful approach to understanding how PTSD could lead to poor health is provided by McEwan and Stellar's[2,74] psychobiological model of how a potential stressor can lead to physical disease. Central to their model is the concept of allostatic load, which is defined as: "The strain on the body produced by repeated up and downs of physiologic response, as well as the elevated activity of physiologic systems under challenge, and the changes in metabolism and wear and tear on a number of organs and tissues." In the model, psychological factors and genetic and acquired predispositions combine to determine appraisal and behavioral processes. The behavioral response is seen as affecting the biological response, which also is affected by genetic and developmental factors. The biological response, in turn, is seen as initiated by the brain, the autonomic nervous system, and neuroendocrine mediators, which influence effectors (immune system, cardiovascular system, adipose tissue, and muscle) that ultimately influence disease outcomes. The chronic or repeated stimulation of the effectors may lead to allostatic load, which over time causes "wear and tear," according to the authors—and thereby increases the risk for pathology and disease. Specific types of load mentioned are repeated stressor exposure, lack of adaptation, a prolonged stress response that fails to return to normal, and an inadequate response to stressor exposure.

McEwan and Stellar[2] offer an example of how interactions among systems can lead to disease: Elevated glucocorticoids can cause insulin hypersecretion and insulin resistance, which together promote obesity and facilitate atherosclerotic plaque formation. According to our model, an example might be that an individual with PTSD uses smoking and excessive alcohol consumption to manage intrusive symptoms, which themselves lead to the biological consequences of excessive, repeated sympathetic activation; both the smoking and alcohol would have biological consequences, and the alcohol consumption in particular also might have negative psychosocial consequences that could be a further source of stress.

Key aspects of McEwan and Stellar's[2,74] model are its multivariate, longitudinal perspective and an emphasis on the cumulative and interactive effects of factors that alone, or in a short time frame, may have only minimal or transient effects that would be insufficient for promoting disease. We believe that these elements make allostatic load a likely mechanism though which the various correlates of PTSD could combine, over time, to increase the likelihood of disease, and perhaps to a greater extent than in other psychiatric disorders. PTSD and other disorders share a great deal in common, both biologically and psychologically, as well as behaviorally, but it may be the sheer number and chronicity of disease-enhancing elements in PTSD that produce more "wear and tear" than is typical in other disorders.

Conclusions and Future Directions

The existing data show that PTSD is associated with poor self-reported health and increased utilization of medical services. To a lesser extent, the data also show an association between PTSD and increased morbidity. However, it is premature to draw definitive causal conclusions about the effect of PTSD on physical health.

The suggestive nature of the data, along with the increasing information about the effects of psychological stress on biological systems, indicates that research on the health consequences associated with PTSD would be both promising and important. As an agenda for this research, we suggest that the highest priority is to determine the nature of the association between PTSD and poor health; before trying to understand how

PTSD might cause poor health, we need to know more precisely the kinds of medical conditions that are associated with PTSD. The focus needs to be on morbidity, and not on assessments based solely on self-reported health or documentation of utilization. Also, investigations into mechanisms can and should proceed simultaneously with investigations into the correlates of PTSD; for example, studies of HPA axis function or smoking in PTSD should include assessments of cardiovascular function whenever possible.

An important next step in the suggested program of research is to determine the uniqueness of the association between PTSD and physical health, relative to that observed for other psychiatric disorders, particularly, depression, panic, and substance abuse. As indicated above, disorders other than PTSD also are associated with serious medical illness,[44,45] and there is only limited evidence indicating that PTSD may be especially likely to lead to poor health.[25,38] We consider the comorbidity of PTSD with other psychiatric disorders as part of the mechanism underlying the association of PTSD with poor health. We also have proposed allostatic load as a possible framework for understanding how PTSD might be different from other psychiatric disorders, but this hypothesis needs to be tested.

A related issue is that of life-threatening medical illness, such as cancer or cardiovascular disorder, as trauma.[23] Here, the PTSD-illness relationship is reversed, with the illness as cause. The question of whether PTSD might lead to poorer disease outcomes in such cases has not been addressed, although this is possible given findings showing that depression predicts increased morbidity and mortality.[48-50]

The existing data also suggest an agenda for clinical practice that involves increased collaboration with primary and specialty medical care professionals. Because PTSD, like other psychiatric disorders,[47] is associated with higher levels of medical service utilization, increased attention should be paid to the role of screening for PTSD in medical settings—as is now being done for depression and substance abuse. If PTSD, like depression, turns out to predict poor recovery from serious illness, integration of PTSD treatment services with medical care services is warranted. Finally, if PTSD does indeed cause poor health, attempts should be made to address and prevent these health consequences from occurring.

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