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IMMUNE-SPECTRUM DISEASE AMONG FEMALE VETERANS: RELATIONS WITH POSTTRAUMATIC STRESS DISORDER AND MALADAPTIVE REPETITIVE THOUGHT

by

Elizabeth Ann Mullen-Houser

An Abstract

Of a thesis submitted in partial fulfillment
of the requirements for the Doctor of Philosophy
degree in Psychology (Clinical Psychology)
in the Graduate College of
The University of Iowa

May 2013

Thesis Supervisor: Professor Susan K. Lutgendorf

ABSTRACT

BACKGROUND: Female veterans are at risk for stress-related physical disorders given unique environmental stress factors, high rates of trauma exposure and a heightened physiologic stress response. There is a need to identify modifiable risk factors which may help minimize the emergence and impact of veteran illness. RESEARCH QUESTION: The present study investigated the contributions of posttraumatic stress symptoms, maladaptive repetitive thought (MRT), depression, childhood trauma and health behaviors (sleep, alcohol use and smoking) to physical disease as operationalized by immune-mediated inflammatory disease occurrence and related functional disability. METHOD: Female Reserve or National Guard veterans (*N* = 643) enrolled in a parent study conducted through the Iowa City Veteran's Affairs Hospital completed a one-time computer-assisted telephone interview. The current study examined self-report measures of posttraumatic stress symptoms, MRT, depression, childhood trauma, smoking, alcohol use, sleep, inflammatory disease incidence and physical functioning. RESULTS: Proposed models of primary hypotheses were tested using structural equation modeling. Results indicated that both physical disease and functional decline were greater in veterans reporting a history of trauma. Physical disease was associated with greater depression and childhood trauma but lower levels of alcohol use after accounting for covariates. Unexpectedly, greater MRT was associated with less physical disease, although it was only related to disease when depression was included as a covariate. Reduced sleep was linked with greater disease but only when depression was not included in the model, and depression was found to fully mediate the relationship between sleep and physical disease. Smoking and the interaction between posttraumatic stress symptoms and MRT were generally unrelated to physical disease in this sample. CONCLUSIONS: Results of this study are consistent with the hypothesis that physical disorders and related functional decline are greater in trauma-exposed individuals and that depression, childhood trauma, repetitive thought and

alcohol use have independent associations with physical disease. This study offers support for further research and interventions which address these relationships to protect female veteran health.

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Graduate College
The University of Iowa
Iowa City, Iowa

CERTIFICATE OF APPROVAL

PH. D. THESIS

This is to certify that the Ph. D. thesis of

Elizabeth Ann Mullen-Houser

has been approved by the Examining Committee for the thesis requirement for the Doctor of Philosophy degree in Psychology (Clinical Psychology) at the May 2013 graduation.

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To Jeff (CFFP) and Noah (SP).

ACKNOWLEDGEMENTS

I would like to acknowledge my advisor and dissertation committee chair, Dr. Susan Lutgendorf, for invaluable mentoring as a researcher and clinician. She has taught me how to approach psychological questions as a scientist and has also given me great freedom to pursue independent work. I have found inspiration in her wisdom, knowledge and commitment to the highest standards.

I am also grateful to my dissertation committee members, Drs. Erika Lawrence, James Marchman, Anne Sadler, Lisa Segre and Mark Vander Weg, for helpful feedback on the study design, implementation and interpretation of results. Dr. Anne Sadler is the principle investigator of this project's parent study through the Iowa City Veteran's Affairs Hospital. She has generously provided me with scientific and clinical opportunities throughout my graduate career. I would like to acknowledge Carrie Franciscus and Drs. Michelle Mengeling, Brenda Booth and Jim Torner with the Iowa City Veteran's Affairs Hospital for their time and assistance with implementation of this study. I thank Dr. Kristian Markon of the University of Iowa and Dr. Sherwin Toribio of the University of Wisconsin - La Crosse for statistical advice. Finally, I am grateful to all of the women who participated in this study.

On a personal level, I would like to extend heartfelt appreciation to my friends and family for their lifelong support in my career and otherwise, including my siblings Karen, Mary and Mike. I am grateful to my parents, Jan and Tom, who taught me the value of intellectual curiosity and always supported my goals. I especially thank my husband Jeff and son Noah for their continued support and encouragement. You all have been my rock through this process.

The parent study for this dissertation was funded by VA HSR&D Grant DHI 05-059 to Dr. Sadler. The writing of this dissertation was funded by a research fellowship from the University of Iowa Graduate College.

ABSTRACT

BACKGROUND: Female veterans are at risk for stress-related physical disorders given unique environmental stress factors, high rates of trauma exposure and a heightened physiologic stress response. There is a need to identify modifiable risk factors which may help minimize the emergence and impact of veteran illness. RESEARCH QUESTION: The present study investigated the contributions of posttraumatic stress symptoms, maladaptive repetitive thought (MRT), depression, childhood trauma and health behaviors (sleep, alcohol use and smoking) to physical disease as operationalized by immune-mediated inflammatory disease occurrence and related functional disability. METHOD: Female Reserve or National Guard veterans (*N* = 643) enrolled in a parent study conducted through the Iowa City Veteran's Affairs Hospital completed a one-time computer-assisted telephone interview. The current study examined self-report measures of posttraumatic stress symptoms, MRT, depression, childhood trauma, smoking, alcohol use, sleep, inflammatory disease incidence and physical functioning. RESULTS: Proposed models of primary hypotheses were tested using structural equation modeling. Results indicated that both physical disease and functional decline were greater in veterans reporting a history of trauma. Physical disease was associated with greater depression and childhood trauma but lower levels of alcohol use after accounting for covariates. Unexpectedly, greater MRT was associated with less physical disease, although it was only related to disease when depression was included as a covariate. Reduced sleep was linked with greater disease but only when depression was not included in the model, and depression was found to fully mediate the relationship between sleep and physical disease. Smoking and the interaction between posttraumatic stress symptoms and MRT were generally unrelated to physical disease in this sample. CONCLUSIONS: Results of this study are consistent with the hypothesis that physical disorders and related functional decline are greater in trauma-exposed individuals and that depression, childhood trauma, repetitive thought and

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INTRODUCTION

> Stress-related disease emerges, predominantly, out of the fact that we so often activate a physiological system that has evolved for responding to acute physical emergencies, but we turn it on for months on end, worrying about mortgages, relationships, and promotions. (Sapolsky, 2004, p. 6)

The role of the mind in both health and disease is not new, with references dating back to the medical philosophy of the ancient Greeks (Lipowski, 1984). Modern understanding of the effect of the mind on our biological systems emerged in the 1920s with the work of Walter Cannon (Lovallo, 2005). Cannon recognized that mental, as well as physical challenge could disrupt the body's physiological functioning and coined the term "stress" in reference to such demands placed on the body. Building on the work of Cannon, Lazarus and Folkman (1984a, 1984b) described in their transactional theory of stress that appraisal of an event plays a fundamental role in determining the magnitude of the stress reaction. Thus not only the event, but also our *interpretations* of the event are associated with a disruption of physical functioning.

The reactions these stressors provoke in our bodies are called the stress *response*, entailing both our body's initial defensive reaction to the stressor and homeostasis, a compensatory return to the normal pre-stressor physical state in order to maintain internal stability. Such stressors and stress responses are encountered many times a day, often of short duration and with little long-lasting effect. However, when the stressor is prolonged, the stress response is also prolonged.

Chronic stress has been defined as a threat in which "the eliciting stimulus remains in the environment for an extended period of time…or, alternatively, that the threat a stimulus poses to the self looms for an extended period of time (e.g. the sense of danger that follows a sexual assault), even if the stimulus itself does not" (Miller, Chen & Zhou, 2007, p. 28). A plethora of studies in the last ten years have provided evidence that chronic stress negatively impacts health, including impaired wound healing (Kiecolt-

Glaser, 1995), disease onset (Leserman,1999) and disease-related immune dysregulation (Kiecolt-Glaser, McGuire, Robles & Glaser, 2002). In addition, stress-related diseases are associated with increased disability (Sareen et al., 2006).

Between 7 and 9 billion dollars are projected to be spent on Iraq and Afghanistan veteran health costs in the U.S. over the next 10 years (Goldberg, 2007). This enormous financial and functional burden to our soldiers and society indicates the importance of identifying factors which may help minimize the emergence and impact of veteran illness. Trauma exposure and associated posttraumatic stress symptoms adversely impact both health and functioning (Benyamini, Ein-Dor, Ginzburg & Solomon, 2009). Approximately 83% of female veterans have a lifetime history of trauma exposure (Escalona, Achilles, Waitzkin & Yager, 2004). Accordingly, our soldiers may be at risk for not only increased stress and stress-related disorders, but also a greater burden of those disorders. Research is needed to improve our understanding of the mechanisms of the stress-disease relationship and identify modifiable disease and disability risk factors. The need is particularly true for female veterans because of their high rate of trauma exposure.

The present study proposes the concurrent assessment of posttraumatic stress symptoms, maladaptive repetitive thought (MRT), childhood trauma, depression, health behaviors and both physical disease occurrence and related functional disability, with the aim of detailing the links between these constructs more fully. The following review of the literature provides the theoretical context for the current study. First, the concept of posttraumatic stress, and a maladaptive response to that stress in the form of posttraumatic stress disorder (PTSD) and posttraumatic stress symptoms, will be considered. Second, a discussion will follow of the relationship of stress and posttraumatic stress symptoms to physical health disorders, including inflammatory disease and physiological disease indicators, with consideration of the role of childhood trauma and female veteran's particular vulnerability in these relationships. Third, the role

of repetitive thought in the stress-disease relationship will be explored, including an overview of the construct of repetitive thought and a specifically maladaptive form of repetitive thought. The conceptual overlap between MRT and both intrusive thoughts within posttraumatic stress disorder and avoidance will be reviewed. Third, the relationship of MRT to both posttraumatic stress symptoms and inflammatory diseases are discussed. Fourth, consideration will be given to the contribution of health behaviors to the association between trauma exposure, posttraumatic stress symptoms, MRT and both disease and functional disability. Finally, conclusions drawing from all fields are offered and the current study is proposed.

Posttraumatic Stress Disorder, Posttraumatic Stress Symptoms and General Health

War Stress and Health

The relationship between stress and health has been widely studied within the active-duty military environment, since threats to both physical and psychological integrity are constant and prolonged. As early as the U.S. Civil War, war-related trauma was observed to be positively associated with incidence of cardiac and gastrointestinal disorders (Pizarro, Silver & Prause, 2006). Among Gulf War veterans, greater combat exposure was correlated with an elevation in report of somatic symptoms such as joint stiffness, muscle tension and fatigue (Noyes et al., 2004). Moreover, combat involvement was unrelated to hypochondriacal worry, suggesting that this type of MRT did not contribute to the relationship between combat exposure and physical discomfort. Although findings are correlational, such studies suggest that the chronic stress of combat may result in the physical decline observed in other persistently stressed populations.

Stressors associated with the most recent wars in Iraq and Afghanistan may leave veterans uniquely at risk for stress-related physical disorders. Hoge et al. (2004) interviewed over 7,000 Army and Marine Corps members both before and after deployment to either Iraq or Afghanistan and reported that several aspects of these wars

are particularly strenuous. First, the guerilla warfare environment of these conflicts puts soldiers at constant risk of violence, resulting in a need for more constant vigilance than other recent military actions. Hypervigilance, in turn, may prolong their emotional and physiological stress reactions. In these conflicts it is also much more difficult to ascertain the difference between innocent civilians and dangerous combatants. Thus the ambiguity of the situation leaves soldiers both feeling they are unable to appropriately defend themselves, and at a heightened risk for feeling shame and guilt when they do. Additionally, they found that veterans are also reluctant to seek help for emotional stress; over 70% of veterans who reported a mental disorder did not seek mental health care post-deployment, often due to the fear of stigmatization. Soldiers expressed fears about how they would be perceived by both peers and leaders after seeking mental health services; importantly, the soldier relies on these coworkers for not only a paycheck, but also protection. In addition, fear of stigmatization was greatest among those needing mental health services.

The stressors of the most recent conflicts have left veterans at risk for psychopathology associated with the stress and also inhibit their ability to seek care for their psychological needs. These factors leave veterans at risk for prolonged stress responses, associated psychopathology and potentially physical health difficulties. Consequently both the NIMH and representatives of our armed forces have emphasized the importance of identifying factors which may help minimize the emergence of veteran illness (Department of Veterans Affairs Office of Research and Development, National Institute of Mental Health & United States Army Medical Research and Material Command, 2006). One such factor, a maladaptive response to trauma in the form of posttraumatic stress disorder, will be considered next.

Posttraumatic Stress Disorder and Posttraumatic Stress Symptoms Overview

Seventeen percent of currently deployed soldiers have been diagnosed with one type of chronic stress, posttraumatic stress disorder (PTSD; Mental Health Advisory Team [MHAT] IV, 2006). PTSD is defined by the DSM-IV-TR (American Psychiatric Association [*DSM-IV-TR*], 2000) as an anxiety disorder which involves feelings of intense fear, helplessness or horror in reaction to an extreme traumatic stressor. The trauma must involve either threat of death, actual death, serious injury, or threat to the physical integrity of the self, witnessing such a threat to others, or learning of a similar event involving a loved one.

A diagnosis of PTSD involves three clusters of symptoms: a) re-experiencing of the event (e.g. nightmares, intrusive thoughts), b) avoidance of phenomena that stimulate recollections of the trauma (e.g. thoughts, feelings, behaviors or situations) or emotional numbing (e.g. restricted affect), and c) hyperarousal symptoms (e.g. hypervigilance, exaggerated startle response) (*DSM-IV-TR*, 2000). In addition, these symptoms must persist for at least 1 month and be accompanied by significantly impaired functioning.

In a further examination of the structure of PTSD, Simms, Watson & Doebbeling (2002) performed a confirmatory factor analysis of PTSD symptoms and found four primary factors; intrusions, avoidance, hyperarousal and dysphoria. They suggest that while the avoidance, hyperarousal and dysphoria dimensions may represent nonspecific distress common to anxiety and mood disorders, the intrusion factor is specific to PTSD. These findings help illuminate the inclusion of PTSD as a chronic, as opposed to acute, stressor. The traumatic event, although itself short-lived, may be in effect maintained in the patient's environment through the recurrent intrusive images and thoughts prominent in those diagnosed with PTSD.

PTSD is one of the most common mental disorders, with a lifetime prevalence rate of 6.8% in the United States (Kessler et al., 2005), over 20 million people. While this

number represents only a fraction of the 50% of the population that will experience at least one traumatic event (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995), 30% of those who experienced high-impact trauma were diagnosed with PTSD, including both Vietnam veterans (NCPTSD, n.d.) and sexual assault victims (Resnick, Kilpatrick, Dansky, Saunders & Best, 1993). PTSD is also a persistent disorder. Data from the National Comorbidity Study revealed that 40% of PTSD cases fail to resolve after ten years, even in those who obtained treatment (Kessler, et al., 1995). In a longitudinal study of Vietnam Veterans almost 30 years after return from deployment, 10% of veterans reported severe PTSD symptoms (Koenen, Stellman, Sommer & Stellman, 2008). Moreover, within these veterans a PTSD diagnosis predicted worsening functioning 10 years later.

While the field of psychology cannot prevent our soldiers from being exposed to the trauma of war, the disability associated with trauma may be mitigated through a better understanding of the etiology of posttraumatic stress symptom-related functional decrements. Consideration will turn next to the particular impact of PTSD and posttraumatic stress symptom-related functional decline in the form of physical illness.

Posttraumatic Stress Disorder, Posttraumatic Stress Symptoms and General Health

Across DSM-IV anxiety disorders, post-traumatic stress disorder (PTSD) has the strongest relationship with chronic physical disorders (Sareen et al., 2005). Although trauma exposure is associated with increased disease risk, post-trauma health decline is more strongly related to a maladaptive response to trauma than to the traumatic experience itself (Spitzer et al., 2009). For example, Weisberg et al. (2002) cross-sectionally examined 502 primary care patients and found that PTSD was a stronger predictor than trauma history of medical conditions including arthritis and diabetes. Similarly, in a sample of over 1500 victims of a man-made disaster, van den Berg et al. (2008) reported that reactions to the trauma such as intrusions and avoidance, not

necessarily a PTSD diagnosis, mediated the relationship between trauma exposure and medically unexplained physical symptoms including fatigue and headache. The relationship between either PTSD or posttraumatic stress symptoms and physical disorder has been found in a number of other studies as well, including diseases such as fibromyalgia, anemia, arthritis, asthma, back pain, diabetes, eczema, kidney disease, lung disease and ulcers (Ciccone, Elliot, Chandler, Nayak & Raphael, 2005; Sareen, Jacobi & Cox et al., 2006; Weisberg et al., 2002). In a recent meta-analysis, among trauma survivors both PTSD and subthreshold posttraumatic stress symptoms were found to be associated with elevated general health symptoms, medical conditions and poorer health-related quality of life (Pacella, Hruska & Delahanty, 2012).

Health decrements in PTSD and posttraumatic stress symptoms have also been reported in an exclusively female veteran population (Frayne et al., 2004). In a cross-sectional survey of over 30,000 women enrolled with the U.S. Veteran Health Administration, PTSD with or without comorbid depression was associated with a greater number of serious medical conditions (e.g. arthritis, chronic pain) and worse physical functioning than those with a history of depression but not PTSD or neither disorder. Moreover among female veterans one year after return from combat in Iraq, a diagnosis of PTSD was related was related to not only worse general health and illness symptom severity, but also greater sick call visits and missed workdays, even after controlling for physical injury (Hoge, Terhakopian, Castro, Messer & Engel, 2007).

Importantly, subthreshold posttraumatic stress symptoms, rather than a full PTSD diagnosis, are also associated with significant functional and physical morbidity (Benyamini, Ein-Dor, Ginzburg & Solomon, 2009; Eadie, Runtz & Spencer-Rodgers, 2008; Marshall & Schell, 2002; Pacella, Hruska & Delahanty, 2012), including dysregulated biological stress markers (Thomas et al., 2012) and inflammatory activity (von Känel et al., 2007). For example, subthreshold posttraumatic stress symptoms have been associated with reduced functioning (Breslau, Lucia & Davis, 2004) and the

impairment associated with subthreshold posttraumatic stress symptoms has been observed to be long-standing (Cukor, Wyka, Jayasinghe & Difede, 2010). Furthermore, a PTSD-related adjustment disorder is proposed for the DSM-V (Friedman, Resick, Bryant & Brewin, 2011), indicating a move toward greater use of subthreshold PTSD symptoms both in research and clinical arenas. Recent research also suggests that the morbidity associated with potentially traumatic events is independent of the DSM-IV PTSD A2 criteria that an event be experienced with fear, helplessness or horror (Anders, Frazier & Frankfurt, 2011). It is thus important to consider the impact of the full spectrum of potentially traumatic events and related posttraumatic stress symptoms rather than just a PTSD diagnosis on physical disease and related physical functioning difficulties.

Thus a growing number of studies suggest that both a diagnosis of PTSD and subthreshold posttraumatic stress symptoms are related to not only greater physical disorders, but a high burden of those illnesses. The physical health morbidity associated with posttraumatic stress symptoms may be particularly salient to recently returned Iraq and Afghanistan veterans. Since seventeen percent of currently deployed soldiers assessed in 2006 met criteria for PTSD (MHAT IV, 2006), a significant number of future veterans may be at risk for the chronic illnesses associated with this disorder. To better understand this relationship, attention will next turn to a review of chronic illness in the form of inflammatory disorders and related physiological mechanisms, as well as the contribution of posttraumatic stress symptoms and trauma to both physical disease and functioning decline.

Immune Mediated Inflammatory Disease and Stress

Immune Mediated Inflammatory Disease Overview

The term immune-mediated inflammatory disease (IMID) encompasses a diverse set of disorders affecting a range of organs with inflammatory dysregulation central to their pathogenesis. These diseases have traditionally been labeled autoimmune disease, and over 80 such diseases have been identified, including rheumatoid arthritis, lupus,

Crohn's Disease and ulcerative colitis (National Institute of Health [NIH], 2005). However there is a growing recognition that there are more inflammatory-related diseases than has been encompassed in the autoimmune disease literature, thus the term IMID has been proposed as a new, broader and potentially more accurate category of such diseases (Williams & Meyers, 2002). For example, while chronic fatigue syndrome often co-exists with autoimmune diseases, only recently has research found a relationship between levels of proinflammatory cytokines and cortisol dysregulation within symptoms of chronic fatigue (Nater et al., 2008). Other disorders which might be considered based in part on identification of inflammatory etiology include interstitial cystitis (Lamale, Lutgendorf, Zimmerman & Kreder, 2006), fibromyalgia (Buskila & Sarzi-Puttini, 2008) and cardiovascular disease (van Bussel, Schouten, Henry & Schalkwijk, 2011).

The incidence and prevalence of IMIDs is widespread and growing, with up to eight percent, or 23 million people, living with IMIDs in the United States alone (NIH, 2005). IMIDs are the third leading cause of morbidity and mortality among industrialized nations (Notkins, Lernmark & Leslie, 2004). For example up to 80% of rheumatoid arthritis patients are disabled by the disease (Choy & Panayi, 2001). Moreover IMIDs are the eighth leading cause of mortality in young and middle-aged women in the United States (Walsh & Rau, 2000). These diseases account for a significant portion of the rising U.S. health care costs (NIH, 2005), including at least 6% of total employer healthcare spending (Williams & Meyers, 2002). These disorders also disproportionately affect women. Approximately 75 percent of IMIDs occur in women, often during childbearing years (NIH, 2005). No cure has been found for these disorders, and treatments often involve toxicity risks (Shoenfeld & Gershwin, 2006), underscoring the need to find avenues of prevention. Addressing the role of trauma and posttraumatic stress symptoms in IMID etiology may represent one such approach.

Posttraumatic Stress Disorder, Posttraumatic Stress Symptoms and Immune-Mediated Inflammatory Disease

While both trauma and PTSD are associated with greater incidence of disease, IMIDs seem to be more specifically related to a prolonged maladaptive response to the trauma in the form of PTSD (O'Toole & Catts, 2008). For example, in a study by Boscarino (2004), Vietnam veterans with chronic PTSD were more likely to have IMIDs such as rheumatoid arthritis, psoriasis, diabetes and hypothyroidism. Similarly, researchers have reported that both civilian and veteran patients with PTSD present with greater prevalence of IMIDs such as arthritis (Weisberg et al., 2002), asthma and eczema (Davidson et al., 1991; Dobie et al., 2004) and Type 1 diabetes (Sepa & Ludvigsson, 2006). Spitzer et al. (2009) also found increased risk for cardiovascular disease in members of the general population with a history of trauma, with the risk higher for those with a PTSD reaction to the trauma. Strikingly, Frayne (2004) found that 60% of female veterans with PTSD reported being diagnosed with arthritis.

Seng, Clark, McCarthy and Ronis (2006) examined epidemiological data on women with PTSD and found that among reproductive-aged women, chronic PTSD was associated with an elevated risk for physical morbidity beyond variance contributed by depression or victimization itself, and with a dose-response pattern increasing with PTSD severity. Patients with PTSD uncomplicated by depression were more likely to have IMIDs such as chronic fatigue (OR=3.1) and fibromyalgia (OR=1.9). These rates were generally higher among women with complex PTSD, with an odds ratio of 6.7 for chronic fatigue within the PTSD group. In addition, the PTSD group had significantly more chronic physical conditions, such as being 11 times more likely to have four such diagnoses. Similarly, in the O'Toole and Catts (2008) study of PTSD and physical morbidity, the pattern of diseases specifically related to PTSD were those known to be associated with an altered inflammatory response.

Hence, across multiple studies, evidence is accumulating for an increased incidence of IMIDs within patients diagnosed with PTSD, and these diseases seem to be more strongly related to a prolonged reaction to trauma than to the exposure to the trauma itself In addition, it is crucial to address such vulnerabilities early in the stress-disease pathway, before a positive feedback system of stress and disease is entrenched. The relationship between stress and disease can become a vicious cycle, with chronic disorders such as IMIDs amplifying psychological stress, further increasing vulnerability to disease progression (Stojanovich & Marisavljevich, 2008). The particular vulnerability of women to the effects of stress on health will be considered next.

Posttraumatic Stress Disorder, Posttraumatic Stress Symptoms and Disease in Women

In both civilian and veteran populations, women have been found to have a greater incidence of PTSD (Kessler et al., 2005), including female veterans of the recent OIF / OEF conflicts (MHAT IV, 2006). In addition, Breslau and Davis (1992) found that women were four times as likely to have a chronic course of PTSD, defined as PTSD symptoms sustained for at least one year. Consistent with other studies, those with chronic PTSD reported a greater number of medical conditions, including arthritis.

Female veterans are also at risk for particularly devastating non-combat trauma exposure while serving in the military. Sadler, Booth, Cook, Torner & Doebbeling (2001) interviewed 537 female veterans who served during the Vietnam War, post-Vietnam or Persian Gulf War. When asked about exposure to non-fatal assaults during their military service, 79% reported sexual harassment, 54% reported unwanted sexual contact, 36% experienced threatened or completed physical assault, with 30% of all participants acknowledging completed physical assaults. In addition, these assaults were most often perpetrated by the coworkers they not only worked but also lived with. The unique nature of military service may amplify the distress and associated pathology of

such assault since victim and assailant live and work together, the victim is not at liberty to leave, and weapons are readily available to assailants (Frayne et al., 1999).

Furthermore, barriers to reporting such assault exist. Within sexually victimized female veterans, 75% did not file a report of the incident, with 25% reporting that the ranking officer was their attacker and the majority stating a belief that such a report would make the situation worse and harm their military career (Sadler, Booth, Cook & Doebbeling, 2003). These factors associated with the military environment may inhibit the normal stress recovery process and predispose female soldiers to a maladaptive stress response. In fact, whereas PTSD is diagnosed in approximately 30% of civilian rape survivors (Resnick et al., 1993), it is diagnosed in 60% of female military sexual trauma victims (Yaeger et al., 2006).

Young returning female veterans may be particularly vulnerable to the health sequelae of deployment-related stress. While similar rates of PTSD have been found in women and men deployed to Iraq (MHAT-IV, 2006), the effects of PTSD on health may be intensified in young female veterans due to a heightened physiologic stress response (Becker, Monteggia, Perrot-Sinal et al., 2007) and unique environmental stress factors such as sexual assault perpetrated by coworkers (Frayne et al., 1999; Street, Vogt & Dutra, 2009). In a review of risk for PTSD in female combat veterans, Hoge, Clark & Castro (2007) describe the need to understand gender differences in long-term post-deployment PTSD course. These authors found that veteran PTSD was measured relatively soon after return from active duty. Since civilian women tend to have a prolonged course of PTSD (Breslau & Davis, 1992), female veterans may be more likely than their male counterparts to maintain debilitating high levels of PTSD-related biological dysregulation with an associated increased risk for mental and physical morbidity.

In fact, in female veterans both trauma and a maladaptive response to trauma are associated with increased rates of physical disorders, including diseases with

inflammatory mechanisms. Increased reports by female soldiers of rheumatoid arthritis, chronic fatigue, pelvic pain and fibromyalgia are associated with both assault during military service (Frayne et al., 1999) and a PTSD diagnosis (Dobie et al., 2004; Frayne, 2004). Decreased physical functioning is also associated with history of sexual trauma and current PTSD in female veterans (Booth et al., 2012). Furthermore, compromised health status is still robustly related to female veteran assault after controlling for age and pre- and post-military violence exposure (Sadler, Booth, & Doebbeling, 2005). These studies reflect the fact that inflammatory-related diseases disproportionately affect women; approximately 75% of inflammatory diseases occur in women, often during childbearing years (NIH, 2005). Moreover, the biological dysregulation found in both PTSD and inflammatory disorders may affect not only the female veteran but future generations, since such stress-related physiological disruption changes the interuterine environment, producing long-lasting health consequences for the unborn child (Yehuda, Blair, Labinsky, & Bierer, 2007).

The number of women in the military is increasing. The U. S. Department of Veteran Affairs (DVA; 2007) reported that the last 30 years have evidenced an almost four-fold increase in the percent of active duty military women, from 2.5 percent in 1975 to nearly 14 percent in 2005, representing an additional 150,000 females in the military. The rise in female veterans represents related increases in VA healthcare usage by women. Since PTSD is the top diagnostic category for female veterans treated by the VA (DVA, 2007) and both IMIDs and the biological dysregulation associated with them are greater in women, a more accurate understanding is needed of the relationship between PTSD and female veteran health outcomes. IMIDs, in particular, have been associated with PTSD (O'Toole & Catts, 2008; for a review see Boscarino, 2004), with stress being implicated in the disease pathogenesis (Calcagni & Elenkov, 2006; Cutolo & Straub, 2006). In order to better understand the way that stress can influence disease initiation

and progression, physiological mechanisms of the stress response will next be considered.

Biological Mechanisms of the Stress Response

Recent research has begun to elucidate the biological mechanisms by which traumatic stress can "get inside the body" to increase susceptibility to chronic disease (see reviews by Ironson, Cruess & Kumar, 2007; Lovallo, 2005; Stam, 2007). Moreover, posttraumatic stress symptoms and PTSD are increasingly implicated in these pathways, as discussed in several recent reviews (Stam, 2007; Wessa & Rohleder, 2007). During a stressful event, sensory intake of the situation is accompanied by cognitive and emotional processing, investing the information with meaning. Interpretations of the situation as threatening trigger the sympathetic nervous system to release catecholamines such as norepinepherine and epinephrine, activating the individual's fight or flight defense. In addition, immune cells have catecholamine receptors, allowing activation of immune defenses in response to signals of perceived physical danger. One component of this immune response is the cytokine family, protein messengers which promote the cellular inflammatory response. Examples of pro-inflammatory cytokines are IL-1, IL-6 and TNF-α.

Parallel to increased catecholamine and pro-inflammatory cytokine production, the body initiates a protective dampening of this physiological response, since prolonged defensive activation is in itself harmful (McEwen, 1998). The hormone cortisol is released by the hypothalamus-pituitary-adrenal system in response to perceived threat. Similar to catecholamines, cortisol helps prepare the body for defensive action. In addition, however, high levels of cortisol trigger a negative feedback loop, tempering the production of both catecholamines and pro-inflammatory cytokines. Thus cortisol-related systems, when functioning properly, help bring the body back to biological homeostasis (Lovallo, 2005). The change in this sequence under conditions of chronic stress will be considered next.

Biological Mechanisms of Posttraumatic Stress Disorder
and Immune-Mediated Inflammatory Disease

The cycle described above, of proinflammatory upregulation followed by compensatory cortisol-driven down-regulation, is accurate in the face of acute stressors. However the clinical significance of acute stressors on inflammatory diseases may be minimal, in part because the stressors, or the perceptions of the stressors, do not persist long enough to influence disease vulnerability (Segerstrom & Miller, 2004). In contrast, in the face of chronic stressors, such as PTSD, the body is in a constant state of high alert. Maintenance of the cortisol/proinflammatory cytokine homeostasis during prolonged stressors can eventually impair health, including damage from persisting high levels of cortisol (McEwen, 1998).

Consequently during long-term stressors, the body sometimes adjusts to chronically high cortisol levels by decreasing cortisol production or cortisol receptor sensitivity on other cells, blocking the effects of cortisol regardless of actual cortisol level. For example, Miller, Chen and Zhou (2007) conducted a meta-analysis of chronic stress and HPA activity. They found that, as expected, acute laboratory stressors resulted in cortisol increases. In contrast, within individuals exposed to a traumatic stressor, only those diagnosed with PTSD evidenced blunted levels of cortisol. Thus once again the prolonged negative response to trauma rather than trauma itself was associated with physical disruption in the form of cortisol downregulation.

Not all studies have reported low cortisol levels among individuals with PTSD (reviewed in Ironson et al, 2007). However, in a review of neuroendocrine function in stress disorders, Raison and Miller (2003) found that PTSD patients reliably demonstrated either hypercortisolism or reduced cellular *responsiveness* to cortisol, indicating that regardless of cortisol levels, glucocorticoid signaling was reliably reduced. With chronically elevated stress, the body may be protecting itself from the damage produced by protracted high levels of cortisol either by reducing overall cortisol levels

(Miller et al., 2007) or by reducing cellular responsiveness to cortisol regardless of level (Butts & Sternberg, 2008; Tait, Butts & Sternberg, 2008).

Reduced cortisol signaling, however, means that cortisol does not regulate the stress-induced immune upregulation, resulting in chronically elevated levels of inflammation. For instance, Raison and Miller (2003) found that chronic stress was related to not only insufficient glucocorticoids signaling, but also elevations in inflammatory activity. Similarly, de Kloet et al. (2007) examined trauma survivors both with and without PTSD. They report that while glucocorticoid receptor activity was reduced in both groups, immune regulation was reduced in PTSD survivors only. Without cortisol-driven regulation, the overactive immune system begins to attack its own tissues.

For example, IMIDs such as rheumatoid arthritis, diabetes and lupus are associated with both abnormal cortisol levels or signaling and elevated levels of the proinflammatory cytokines IL-6, IL-1 and TNF-α as well as inflammatory markers such as leukocytes (Calcagni & Elenkov, 2006; Ford, 2002; Sanchez et al., 2008; Tarrant & Patel, 2006). Likewise, Boscarino (2008) found that veteran PTSD diagnosis predicted elevations in inflammatory markers such as higher erythrocyte sedimentation rate and a trend toward higher white blood cell count. Sala et al. (2008) note that within individuals diagnosed with PTSD, studies have found both blunted and dysregulated cortisol, higher catecholamine levels, and increased circulating T-lymphocytes, all potential precursors to inflammatory-related diseases. PTSD-related epigenetic changes to immune regulation have also been reported (Uddin et al., 2011). In addition, relationships have been found between specific aspects of the PTSD response and IMID-related pathology. A positive relationship has been noted between PTSD-related intrusive re-experiencing and IL6 receptors, which both function as IL-6 agonists and have proinflammatory actions of their own (Miller et al., 2001). Thus both PTSD diagnosis and symptoms are related to both a high rate of IMIDs and the biological dysregulation implicated in these inflammatory

disorders. Furthermore, PTSD-related biological responses may be particularly frequent in women, and may help account for the greater number of IMIDs found in women (Butts & Sternberg, 2008; Meewisse, Reitsma, Vries, Gersons & Olff, 2007). Attention will next turn to the role of childhood trauma in IMID development, especially among female veterans.

Childhood Trauma, Disease and Biological Mechanisms

Childhood trauma exposure is another factor which is important to consider in the relationship between stress and health in veterans. Childhood trauma and a generally greater length of time since trauma exposure are related to both IMID incidence and greater disease-related physiological dysregulation. For example, in the Adverse Childhood Experiences Study survey of more than 16,000 adults, childhood trauma exposure was related to increased incidence of chronic disease, including diabetes and cardiac disease (Felitti et al., 1998). Similarly a history of childhood adversity was found to be related to chronic physical disease independent of the effects of psychopathology (Scott et al., 2011). Recently greater depression and inflammatory dysregulation have been reported for females with a history of childhood trauma, potential precursors for medical difficulties (Miller & Cole, 2012).

Moreover a history of childhood trauma may result in trauma-related physiological disruption by adulthood. In fact, studies have found a positive relationship between length of time since trauma and disease-related biological dysregulation. For example, von Känel et al. (2007) reported a positive correlation between PTSD re-experiencing symptoms and the proinflammatory cytokine TNF-α. However this relationship was moderated by the length of time since the trauma, with an increased length of time since trauma related to higher levels of TNF-α. This study suggests that when trauma occurs early in life greater wear and tear on the body's systems may occur, such as dysregulated cortisol and elevated inflammatory markers such as TNF-α. Thus when a PTSD response to trauma is not resolved, the associated prolonged biological

dysregulation may result in development of inflammatory-related disorders. The effect of childhood trauma exposure on disease is especially important to consider in female veterans as a history of childhood trauma exposure is frequent in that population (Rosen & Martin, 1996).

Summary of Posttraumatic Stress Disorder, Posttraumatic Stress Symptoms and Immune-Mediated Inflammatory Disease Associations

Thus research has revealed that the elevated and sustained physiologic arousal associated with PTSD can increase physical morbidity. PTSD and early trauma exposure are related to both an increased risk of IMIDs and the physiological dysregulation associated with immune-related disorders. Moreover these relationships have been observed particularly in war veterans, women and individuals with a history of childhood trauma. However the psychological mechanisms of this relationship are still poorly understood and require further investigation (Sareen et al., 2006). It has been proposed that psychological stressors or the perception of stressors do not, on their own, confer physiologic dysregulation great enough to result in disease. Brosschot, Pieper & Thayer (2005) suggest that a protracted cognitive representation of these stressors is necessary to prolong the physiological effects of the stressors. A similar viewpoint was expressed in a 2006 joint meeting between the VA, NIMH and US Army convened to examine the physical and mental health needs of veterans post-deployment (Department of Veterans Affairs Office of Research and Development, National Institute of Mental Health & United States Army Medical Research and Material Command, 2006). They recommended the identification of the cognitive mechanisms involved in the pathogenesis of PTSD and physical morbidity. The report also underscored the clinical significance of such pathways as they would inform targets for prevention and medical management of PTSD. As such, one potential cognitive mechanism by which stress can adversely impact health will be considered.

Maladaptive Repetitive Thought

One psychological process increasingly associated with prolonged and elevated physiological arousal as well as poor psychological stress recovery is maladaptive repetitive thought (MRT) such as rumination, worry and anticipatory stress (see Watkins, 2008 for a review). In their review of perseverative cognition and health, Brosschot, Gerin and Thayer (2006) describe that while this cognitive coping style is associated with both physiological arousal and immunological dysregulation, the role of perseverative cognition in the etiology of somatic disease is largely unexamined. Moreover, MRT in the form of rumination is predictive of both incidence and course of PTSD (Ehring, Frank & Ehlers, 2008; Michael, Halligan, Clark & Ehlers, 2007; Nolen-Hoeksema & Morrow, 1991). Thus there is support for consideration of repetitive thought patterns such as rumination as a partial mechanism of the PTSD and IMID relationship. The following review of MRT will examine first a general non-valenced repetitive thought construct. Next, aspects of specifically harmful repetitive thought will be considered, including a review of avoidance and negative affect as possible mechanisms of the relationship between MRT and psychopathology.

Repetitive Thought Overview

Repetitive thought has been described as “the process of thinking attentively, repetitively or frequently about oneself and one’s world” (Segerstrom, Stanton, Alden & Shortridge, 2003, p. 909). Models of repetitive thought have been extensively studied within the field of psychology, as summarized in a number of recent reviews (Clark, 2005; Nolen-Hoeksema, Wisco & Lyubormirsky, 2008; Segerstrom et al., 2003; Stroebe et al., 2007; Watkins, 2008). Many separate conceptualizations of repetitive thought have emerged in diverse research domains, such as rumination, worry, perseverative cognition, cognitive and emotional processing, counterfactual thinking, reflection and habitual negative self-thinking. repetitive thought models overlap in theoretical conceptualization, sharing a focus on cognitions that are either prolonged or recurrent and

with content involving a focus on the self, one's emotions, or life events, either past or future (Segerstrom et al., 2003).

Repetitive thought is reported as a common psychological phenomenon in both clinical and nonclinical populations. For example, Segerstrom et al. (2003) examined repetitive thought in healthy individuals and reported that on average healthy participants report experiencing moderately frequent and prolonged repetitive thought. In addition, independent raters judged the valence of the thought content as either positive or negative, and a balance of both positive and negative thoughts were found in this healthy sample. Brewin, Christodoulides and Hutchinson (1996) also found that healthy individuals report a high frequency of repetitive thought, specifically intrusive thoughts, over the course of two weeks, providing further evidence of repetitive thought in non-clinical samples. Similarly, worry has been found to be a common experience in psychologically healthy individuals (Borkovec, Ray & Stober, 1998).

Although repetitive thought is reported by healthy participants, it has been found to be greater in those with clinical disorders. Elevated levels of repetitive thought are found in almost all Axis I disorders, including both anxiety and depressive disorders (for reviews, see Ehring & Watkins, 2008; Nolen-Hoeksema, 2008). There is thus evidence of a relationship between repetitive thought and psychopathology; however the fact that it is a commonly experienced phenomena suggests that it is related to psychopathology in only a portion of those who experience it. Repetitive thought also seems to be reflective of the self-absorption paradox proposed by Trapnell and Campbell (1999), in which private self-consciousness is associated with both factors of psychological growth such as increased self knowledge *and* increased psychological distress and psychopathology. For example, repetitive thought about traumatic experiences has been suggested as necessary to come to terms with the event (Pennebaker, 1997) and is associated with finding meaning in the experience (Ullrich & Lutgendorf, 2002). Conversely, post-trauma

repetitive thought has been found to predict future depression and overall poor recovery (Nolen-Hoeksema & Morrow, 1991).

The seemingly opposing effects of repetitive thought on health appear to be due to the existence of both adaptive and maladaptive forms of repetitive thought. Researchers and theorists in a number of domains have identified features distinguishing adaptive versus maladaptive repetitive thought. These conceptualizations of repetitive thought include (1) Segerstrom and colleagues who have found repetitive thought to vary on two dimensions, valence and purpose (Segerstrom, Roach, Evans, Schipper & Darville, 2010; Segerstrom, Stanton, Alden & Shortridge, 2003). They report that while adaptive repetitive thought is associated with positively-valenced content with a solving, planning and/or certain purpose, MRT contains negatively- valenced content with a purpose that is searching, questioning and/or uncertain; (2) Treynor, Gonzales and Nolen-Hoeksema (2003), in their examination of rumination, posit a form of adaptive repetitive thought they call reflective pondering, which represents active ruminative repetitive thought aimed at understanding and solving problems, versus MRT in the form of brooding rumination, passively thinking about problems and their related consequences; (3) Coarocco, Vohs & Baumeister (2010) describe adaptive repetitive thought as active, with content which is goal-oriented, task-relevant and focused on error-correction, and MRT which contains thoughts that are brooding about implications of mistakes; (4) Watkins and Teasdale (Teasdale, 1999; Watkins & Teasdale, 2004) note that among conscious cognitions about distressing events, adaptive repetitive thought is non-evaluative and involves directly experiencing distress, while MRT is conceptual-evaluative, with thoughts that are vague and abstract about the causes and consequences of distressing events. Thus across conceptualizations, adaptive repetitive thought and MRT differ by function and context, with adaptive repetitive thought representing active, goal-oriented problem solving cognitions while MRT involves passively thinking about the implications of problems and more often contains negatively-valenced content.

Clinical Differences Between Adaptive and Maladaptive Repetitive Thought

Empirical studies of repetitive thought provide evidence of the differing effects of adaptive versus maladaptive repetitive thought on psychological health. For instance, rumination has been found to contain repetitive thought about both negative and positive content (Martin & Tesser, 1996). Treynor, Gonzalez & Nolen-Hoeksema (2003) explored the possibility of such different aspects of rumination within the Ruminative Response Scale (RRS) of the Response Styles Questionnaire (RSQ; Nolen-Hoeksema & Morrow, 1991). After removing Ruminative Response Scale items confounded with depression content, factor analysis revealed two separate aspects of ruminative self-focus. One was labeled brooding and involves focusing on the negative consequences of life events (e.g. "Think 'Why do I have problems that other people don't have?'"). The second factor, called reflective pondering, involves neutrally-valenced attempts to understand the reasons for current problems (e.g. "Go away by yourself and think about why you feel this way"). They examined the relationship of each rumination subscale on depression in a secondary analysis of data collected by Nolen-Hoeksema et al. (1999). Results indicated that the reflection subscale was related to more depression concurrently but less depression longitudinally. They hypothesized that self-reflection may arouse negative affect in the short-term but may be adaptive in the long term, potentially reducing negative affect through effective problem-solving. In contrast the brooding rumination subscale was both concurrently and predicatively related to elevations in depression, even after controlling for baseline depression.

Intriguing support for the relationship between negative, brooding self-thought and psychopathology was reported in a depression intervention study. Gortner, Rude and Pennebaker (2006) found that an expressive writing intervention led to decreases in both depressive symptoms and RRS brooding subscale scores. Analyses revealed that brooding, but not reflective rumination mediated the effect of the writing intervention on

the benefits of treatment. Moreover, in a different repetitive thought domain, a meta-analysis of studies of self-focus negatively-valenced self-focus was related to elevated negative affect, while positively valenced self-focus was associated with less negative affect (Mor & Winquist, 2002).

These studies demonstrate a positive relationship between MRT and psychological morbidity across diverse repetitive thought definitions. In fact MRT has been proposed to be a transdiagnostic process in the maintenance of emotional problems, such as generalized anxiety disorder, PTSD and depression (Ehring & Watkins, 2008), and interventions aimed at MRT reductions are proposed as treatment strategies for both anxiety and mood disorders. Ciesla and Roberts (2007) examined the relationship of rumination and depression in undergraduate students. They found that rumination was associated with depression only following a significant number of stressful life events. Thus while people may have stable tendencies in the amount of repetitive thought they experience, the consequences of repetitive thought may be more dire following an increase in life stressors.

Maladaptive Repetitive Thought and Avoidance

A recent development in the repetitive thought field is to dismantle the construct of repetitive thought to specify the maladaptive aspects of prolonged cognition. The relationship of repetitive thought to avoidance has been proposed as one such mechanism of poor adjustment. Borkovec et al.'s (1998) avoidance theory of worry posits that the verbal nature of worry is used to avoid distressing imagery, thus limiting physiological arousal to aversive stimuli. Accordingly, recent studies have found that although MRT focuses on negative content, it is paradoxically used to avoid other painful emotions and sensations. For example, a study by Laguna et al. (2004) found that high trait worriers avoided distressing images despite specific instructions to attend to the images. Similarly, among rape survivors diagnosed with chronic PTSD, intrusive symptoms were

related to avoidance but not numbing, suggesting the use of effortful avoidance to cope with reminders of the trauma (Feuer, Nishith & Resick, 2005).

Avoidance has been found to have a paradoxical effect on internal states, however, as described by Walser and Hayes (2006): “Current research suggests that attempting to avoid or suppress unwanted negative thoughts, emotions and memories as a means to create psychological health may actually contribute to a magnification of the negative emotional responses and thoughts, and to a longer period of experiencing those events” (p. 150). Empirical evidence of this phenomenon was described in the classic white bear experiments conducted by Wegner, Schneider, Carter and White (1987). They found that participants who were instructed not to think of a white bear reported significantly more thoughts about the bear than participants who were told to think about the bear.

A study by Trinder and Salkovskis (1994) found that not only do participants in a thought suppression condition experience more of these thoughts; they also experience more distress with the thoughts. Similarly, excessive attempts to control emotional experiences have been found to increase the very emotions the individual is attempting to regulate (Craske, Miller, Rotunda & Barlow, 1990). Finally, in a prospective study 78 adolescents reported levels of MRT in the form of rumination and worry, behavioral and cognitive avoidance, and sad and anxious affect for 7 days (Dickson, Ciesla & Reilly, 2012). Cognitive but not behavioral avoidance was found to predict increased rumination and worry, and rumination was found to mediate the relationship between cognitive avoidance and both sadness and anxiety.

Thus studies suggest that MRT is associated with emotional and behavioral avoidance of distressing internal phenomena. However such avoidance has been found to instead increase both the intensity and duration of psychological distress. In addition, avoidance of such private events has been noted in PTSD patients, preventing healthy forms of exposure and strengthening problematic responses such as avoidance of

intimacy (Walser & Hayes, 2006). Thus MRT can be seen as a feed-forward mechanism of emotional distress, both sustaining and amplifying the effects of suffering on both the psychological and biological systems of the individual. This review will next consider the role of negative affect in the process by which MRT impacts physical health.

Maladaptive Repetitive Thought and Negative Affect

The possibility of a third variable, negative affect, mediating the effect of MRT on poor adjustment must be considered, however. Both rumination and worry have demonstrated a strong relationship with negative affectivity, or the predisposition to experience negative mood states (Thomsen, 2006; Watson & Clark, 1984). Thus the relationship between MRT and both psychological and physical health may be spurious, due to shared variance with negative affect instead of mechanisms unique to MRT.

However a number of studies have demonstrated an effect of MRT on psychopathology independent of indices of negative affect. A structural equation modeling examination of the contributions of rumination and negative affect to health anxiety found that rumination and health anxiety were indirectly related through the pathway of negative affect operationalized as depression (Marcus, Hughes and Arnau, 2008). However the model also suggested a direct path between rumination and health anxiety independent of depression. Thus rumination was found to contribute independent variance to health anxiety, above variability contributed by negative affect. Moreover, in student nurses undergoing examination, trait rumination has been found to predict cortisol dysregulation more strongly than neuroticism, implying that MRT contributes to physiologic dysregulation independent of negative affect (Roger & Najarian, 1998).

Experimental evidence of the relationship between negative affect and rumination was explored in an examination of the relative contributions of rumination and negative affect to induced distress (Feldner, Leen-Feldner, Zvolensky & Lejuez, 2006). Ninety healthy individuals completed a cognitive challenge test, the paced serial auditory addition task (PASAT), known to elicit elevations in state frustration and irritation, as

well as measures of rumination through the Response Style Questionnaire (Nolen-Hoeksema et al., 1991) and trait negative affect by the Multidimensional Personality Questionnaire – negative affectivity superfactor (MPQ-NA; Tellegen et al., 1988). They found that while negative affect moderated the effect of rumination on the valence of the emotional response, rumination was related to the level of emotional arousal independent of negative affect.

An experience sampling study by Moberly and Watkins (2008) provided further clarification of the relationship between MRT and negative affect on state mood. Ninety-three adults completed measures of depression and rumination at baseline. Participants then completed measures of depression and rumination 8 times daily for 1 week in response to randomly timed beeps on an electronic watch. Analyses revealed that controlling for baseline depression, rumination predicted depression at subsequent recording, indicating an independent effect of rumination on state negative affect. However depression also independently predicted rumination controlling for baseline rumination. The results of these studies indicate that MRT has independent predictive power in emotional adjustment, and this relationship is not simply an artifact of associations with negative affect. However the relationship between MRT and negative affect is complex. For example elevations in negative affect make high ruminators more at risk for psychopathology (Feldner et al, 2006), and conversely associations between negative affect intensity and PTSD were only found in the presence of MRT in the form of negative evaluation of emotional responses (Tull, Jakupcak, McFadden & Roemer, 2007). These studies also suggest that while MRT is independently related to morbidity, MRT and negative affect are reciprocally related in their impact on psychopathology.

Maladaptive Repetitive Thought Summary

Thus strong evidence has emerged for a role of MRT in the etiology of PTSD-related biological dysregulation and inflammatory disease. Repetitive thought has been found to be common phenomena in both clinical and nonclinical populations (Segerstrom

et al., 2003). However evidence suggests that psychopathology is primarily associated with repetitive thought which has negatively valenced content, frequent or prolonged duration, and reduced feelings of control (Wisco & Lyubormirsky, 2008). In addition, worry and rumination are suggested as methods of operationalizing MRT. They have been found to have similar long-term, detrimental effects on both psychological and physical adjustment, and these effects were found to be due to a shared latent factor of MRT (Segerstrom et al., 2000). However there is also some evidence that rumination may be more potent in its effects on psychopathology, especially anxiety (Hughes et al., 2008).

Possible mechanisms of MRT considered above include avoidance and its association with negative affect. Avoidance of internal sensations has been found to paradoxically increase magnify and prolong the same states (Wegner et al., 1987). MRT is associated with avoidance of distressing interoceptive states, and may not only prevent therapeutic exposure within PTSD patients but also increase their distress (Walser & Hayes, 2006). In contrast, the relationship between MRT and negative affect is more complex. Evidence suggests a reciprocal relationship between these constructs. Events that elicit negative affect are found to put those high in MRT at greater risk for psychopathology, thus MRT may be especially dangerous after distressing events. However PTSD risk in those high in trait negative affect was only found with comorbid trait MRT; negative affect on its own did not confer risk. In addition, analyses suggest that MRT contributes to variance in psychopathology independent of a trait negative affect. Thus since MRT is implicated in development of psychopathology and its effects are independent of but reciprocally related to negative affect, its specific relationship with PTSD and PTSD-related disease will now be considered.

Maladaptive Repetitive Thought and Posttraumatic Stress Disorder Etiology

As discussed previously, efforts to avoid trauma-related thoughts and material are a core diagnostic feature of PTSD. Experiential avoidance is also a key feature of many of the problematic coping patterns that develop in response to exposure to a traumatic event, such as self-harm, substance use and both cognitive and behavioral avoidance of trauma-related stimuli (Polusny & Follette, 1995). In turn, these maladaptive coping patterns serve to minimize the experience of painful trauma-related affect and cognitions. The white bear studies of Wegner et al. (1987) confirmed that avoidance of emotional distress intensifies this distress over time. Batten, Orsillo and Walser (2005) suggest that this phenomenon is true within PTSD as well.

> Although such [avoidant] regulatory processes may be negatively reinforced in the short term because they result in reduced immediate distress, they are likely to cause increased symptoms and behavioral problems over time. Thus, experiential avoidance can be seen as a contributory factor in the development and maintenance of PTSD (p. 247).

Empirical support for this theory was provided in a study of male veterans seeking PTSD treatment (Plumb, Orsillo & Luterek, 2004). Participants completed self-report measures tapping the constructs of experiential avoidance through the Acceptance and Action Questionnaire (AAQ; Hayes et al, 2004), degree of combat experienced with the Combat Exposures Scale (CES; Lund, Foy, Sipprelle & Strachnan, 1984), and depression with the Beck Depression Inventory (BDI; Beck, Ward, Mendelsohn, Mock & Erbaugh, 1961). Results indicated that experiential avoidance was positively associated with PTSD severity, and accounted for 13% of the unique variance in PTSD symptoms after controlling for combat exposure.

Thus there is evidence that avoidance of interoceptive distress is related to a maladaptive reaction to traumatic stress. Since multiple lines of research have demonstrated the association between MRT and avoidance, it follows that individuals

high in trait MRT, and thus avoidance, would be more adversely impacted by traumatic events. A recent prospective study of road traffic accident survivors by Ehring et al. (2008) supports this hypothesis. The authors report that controlling for baseline PTSD and depression, both rumination and rumination frequency predicted both PTSD and depression 6 months post-accident. Holeva, Tarrier and Wells (2001) similarly demonstrated that worry immediately following trauma predicted the presence of PTSD three months post-trauma.

Murray and colleagues speculate on the mechanisms by which rumination may maintain PTSD (Murray, Ehlers & Mayou, 2002). First, they propose that MRT may prevent trauma survivors from accepting the trauma as an event from the past, and instead cognitively maintain it as an ongoing event. Second, MRT may also interfere with the formation of complete trauma memories by focusing on the "what if" questions of the trauma, rather than memories of the experience as it actually happened. Third, through these mechanisms MRT may actually cue intrusive memories of the event. Thus there is evidence that premorbid MRT is a factor which confers vulnerability to a maladaptive response to trauma. In addition, researchers have posited that MRT may increase likelihood of the intrusive memories central to a PTSD reaction to trauma. The similarities and difference between MRT and intrusions will next be considered in more detail.

Maladaptive Repetitive Thought and Intrusions in Posttraumatic Stress Disorder

The validity of MRT as an etiological mechanism of PTSD may be questioned in light of its potential overlap with the PTSD diagnostic criteria of intrusive re-experiencing, another form of repetitive cognition in trauma survivors. Similar to MRT, trauma-related intrusions positively correlate with the severity of trauma exposure, and in a factor analysis of PTSD diagnostic criteria was found to be the only factor unique to PTSD (Simms, Watson & Doebbeling, 2002). In addition, intrusions have been found to

mediate the relationship between trauma and maladjustment, including unexplained physical symptoms (van den Berg et al., 2008).

However important conceptual differences have been suggested to exist between MRT and intrusive thoughts (reviewed in Watkins, 2008). As described by Clark and Rhyno (2005),

> Rumination represents a much longer train of thought that is recurrent, repetitive, cyclical, highly ego-systonic, past-oriented, and directed. Unwanted intrusions, on the other hand, are brief, sudden, and somewhat unexpected thoughts or images, of relatively short duration, often ego-dystonic, and undirected by the individual (pp. 16-17).

Similar distinctions have been proposed between MRT and PTSD-related intrusive reexperiencing, including within the domains of content, type of cognition and duration (Ehring et al., 2008). Support for such phenomenological differences was found in a study involving 31 trauma survivors referred for PTSD treatment (Speckens, Ehlers, Hackmann, Ruths & Clark, 2007). Characteristics of the patient's most salient ruminations and intrusions were explored through semi-structured interview. Similar to the description by Clark and Rhyno (2005), ruminations were of significantly longer duration and though-based, while intrusions were significantly more sensory-oriented. In addition, feelings of shame were significantly related to ruminations, but not intrusions.

Empirical investigations of MRT and intrusions in PTSD have demonstrated MRT as an independent risk factor for maladaptive responses to trauma. In a 6-month prospective study of assault survivors, Michael, Ehlers, Halligan & Clark (2005) found that both baseline intrusions and rumination significantly predicted 6 month PTSD severity. In addition, in regression analyses, responses to the intrusions, including rumination, distress and suppression, predicted PTSD severity after controlling for baseline intrusion frequency. Thus this study provides evidence of not only the role of both intrusions and rumination in PTSD, but also of the independent role of MRT in PTSD maintenance.

These studies provide support for an earlier observation that it is distress caused by particularly obsession intrusions, not their occurrence per se, which distinguishes clinical from nonclinical populations (Rachman & de Silva, 1978). While posttraumatic intrusions are common, not all survivors find such intrusions distressing (Shalev, Schreiber & Galai, 1993) and thus poor post-trauma adjustment may be caused by maladaptive responses to the intrusions, such as perseverative thinking and distress, not the intrusions themselves. For example, the effect of intrusions on depression was found to be fully mediated by cognitive coping style, including rumination (Kraaij et al. 2006), and rumination, but not intrusions, was found to be significantly related to post-trauma emotional reactions such as shame (Speckens et al., 2007). Moreover, trauma survivors with PTSD are more likely than those without to report that ruminations about PTSD serve to trigger intrusive memories (Michael, Halligan, Clark & Ehlers, 2007).

Similarly, Watkins (2004) had 69 healthy participants undergo an induced failure IQ test stressor, then write 2 essays about the event over the course of 24 hours. Participants were randomly assigned to write their essays with a focus that was either ruminative and conceptual-evaluative (e.g. “Why did you feel this way?”) or a control condition of writing directly about their feelings about the event (e.g. “How did you feel moment-by-moment?”). The Impact of Events Scale (IES) was completed after essay 2 to measure post-writing intrusions and avoidance. Results indicated that participants in the conceptual-evaluative writing condition reported significantly more intrusions, avoidance and a higher overall IES score than participants in the control condition. This study provides evidence that MRT may play a causal role in the relationship between trauma-related intrusions and psychological morbidity. Thus although both intrusive memories and MRT are perseverative cognitions, there is support for considering MRT as an independent predictor of the morbidity associated with traumatic exposure.

Maladaptive Repetitive Thought and Immune-Mediated Inflammatory Diseases

As Sapolsky (2004) suggests, physiologic arousal is a healthy and necessary alarm reaction to short-term stressors. However he also warns that when negative thought prolongs the psychological and thus physical reactions to stress, the protracted biological arousal can result in physical disease. Brosschot et al. (2006) elaborate this concept in their perseverative cognition hypothesis of stress-related disease. If follows, then, that since MRT is associated with increases in both the intensity and duration of PTSD, MRT may also be associated with the increased IMID incidence found in PTSD patients (Boscarino, 2004), as well as the biological mechanisms associated with those disorders. However Brosschot et al. (2004) note that MRT has been largely neglected in the literature on stress, coping and disease, with the majority of studies focusing on cardiac-related illness. For example, rumination has been found to contribute to hypertension by prolonging stress-related cardiovascular activation (Key, Campbell, Bacon & Gerin, 2008).

Maladaptive Repetitive Thought and Immune-Mediated Inflammatory Disease Incidence

Some evidence does also exist for a role of MRT in the development of physical disorders and health perceptions, including IMIDs. For example, the prevalence of rumination was examined in a cross-sectional study of adults diagnosed with lupus, depressed but otherwise healthy adults, and healthy undergraduates (Siegle, Moore & Thase, 2004). Rumination was found to be significantly more prevalent in the adults with lupus than the healthy controls, although the depressed participants reported the greatest rumination elevations. In addition, while the overall Ruminative Style Questionnaire was more strongly related to depression than the other rumination measures, the brooding subscale was not uniquely associated with depressive symptomatology, providing divergent validity of its use to measure rumination uncontaminated by negative affect.

Since psychological stress is both strongly associated with lupus and hypothesized to intensify lupus symptoms (Elenkov & Chrousos, 2002), it is possible that rumination is also involved in the pathogenesis of lupus. Siegle et al. provide a cautionary note in interpreting their results since both rumination and depression were elevated in the lupus participants. However, as discussed above, MRT has been found to account for unique variance in stress-related morbidity controlling for depression, thus their study does not rule out a unique role for MRT in lupus etiology or progression. Rather, it indicates the importance of controlling for depression when examining MRT and disease outcomes.

Prospective studies have also indicated a relationship between MRT and IMID pathology. The relationship between worry and rheumatoid arthritis functional status was assessed in 91 rheumatoid arthritis patients both shortly after diagnosis and at a one-year follow-up visit (Evers, Kraaimaat, Geenen & Bijlsma, 1998). Regression analyses revealed that baseline worry predicted objective measures of functional status (mobility and grip strength) one year later after controlling for baseline reports of demographic variables, laboratory measures of disease activity and reported levels of pain. Hence this study suggests a causal role for MRT in functional status declines associated with one IMID, rheumatoid arthritis.

An examination of psoriasis patients provides evidence of an etiological role of MRT in biological manifestations of IMID disease progression (Fortune et al., 2003). Among patient being treated for psoriasis, an elevated worry score at pre-treatment was found to be the only significant predictor of the treatment-related time to clearance of disease symptoms. Patients with high levels of worry were 1.8 times slower to clear psoriasis than those with low levels of worry. As elevated inflammation is implicated in the etiology of psoriasis (Späh, 2008), this study suggests a causal role of MRT in IMID progression.

Maladaptive Repetitive Thought and Biological Indicators
of Immune-Mediated Inflammatory Disorder Pathology

While MRT has been found to predict both the biological and functional course of IMIDs, the putative biological mechanisms of this relationship are less clear. Similar to the literature on disease course, exploration of physiological disease parameters has focused primarily on concomitants of cardiovascular disease such as blood pressure recovery (Gerin et al., 2006). As described previously, an overactive proinflammatory cytokine response and dysregulated hypothalamic-adrenal-pituitary axis, including cortisol, is at the heart of current theories of IMID prevalence. Relationships between MRT and these biological parameters, such as IL-1, IL-6 and TNF-α, have been largely neglected. One correlational study conducted by Segerstrom et al. (2008) examined the relationship between immune response to vaccination and MRT in caregivers of Alzheimer's disease patients and controls. They reported a trend for MRT to be positively related to pre and post vaccination IL-6, but that it did not reach significance. Interestingly, they also found that among caregivers elevated levels of neutral repetitive thought were associated with significantly higher post-vaccination IL-6 levels.

The relationship between MRT and biological dysregulation was also examined in an experimental paradigm. Relationships between both trait and state rumination and cortisol were measured in response to an experimentally manipulated stressor among healthy adults (Zoccola, Dickerson & Zaldivar, 2008). Trait rumination (Response Style Questionnaire) was assessed pre-task, while post-task state rumination was operationalized as the self-rated frequency of negative thoughts contained in the Thoughts Questionnaire (Edwards, Rapee & Franklin, 2003). The stressor task consisted of performed a speech and contained two conditions, either in front of an evaluative panel or without being evaluated. Cortisol was collected both pre and post-task, then 10, 25 and 40 minutes post-task. Study results indicated that high post-task state rumination was associated with elevated cortisol levels both post-task and through the 40 minute recovery

period. However a different cortisol pattern emerged for trait rumination, with greater trait rumination predicting a blunted cortisol response to the social evaluative stressor and in fact not differing from participants in the control task. Bivariate correlations suggested that both state and trait measures had independent effects on cortisol response after adjusting for the other measure. These results indicate that although acutely elevated cognitive responses are associated with normative elevations in cortisol in response to a stressor, more long-standing patterns of MRT are associated with blunted cortisol reactions regardless of acute stress reactions, indicating a more dysregulated hypothalamic-adrenal-pituitary axis stress response. In addition, trait rumination was unrelated to cortisol responses in the control task. Since IMIDs are associated with hypothalamic-pituitary-adrenal axis dysregulation, this study may indicate a relationship between MRT and the types of biological changes found in inflammatory disorders.

Maladaptive Repetitive Thought, Posttraumatic Stress Disorder and Immune-Mediated Inflammatory Disorders

Thus while examination of MRT and immune-mediated diseases and disease processes are still relatively rare, data is emerging that both rumination and worry are related to incidence and progression of IMIDs. In addition, there is evidence that MRT is related to the biological dysregulation associated with IMIDs, such as elevated immune parameters and a less flexible hypothalamic-pituitary-adrenal axis response to stress.

However the relationship between MRT and IMIDs may be particularly strong when accompanied by stress. As discussed previously, MRT and negative affect are synergistically related to psychopathology. Each contributes independent variance to psychopathology, but the effect of each is also magnified when accompanied by the other. Thus while trait MRT may be related to IMID development or progression, this relationship may be particularly strong in the wake of the elevated distress associated with a PTSD reaction to trauma.

This interactive effect of stress and trait MRT can be seen in the above study of trait rumination and cortisol response to stress (Zoccola, Dickerson & Zaldivar, 2008). High trait rumination was related to a blunted cortisol response to the acute stressor, similar to the hypocortisolism reported in both PTSD and IMIDs. Moreover, those low in trait rumination mounted the expected rise in cortisol in response to the stressor task. Hence the stressful event itself wasn't necessarily related to an unhealthy biological response; those with low trait rumination demonstrated a healthy cortisol rise, which would regulate any stress response-induced inflammatory elevation. The stressful event was only associated with blunted cortisol in high trait ruminators, impairing their ability to regulate stress-induced cytokine elevations. Thus the biological implications of stress occurred only in the presence of trait rumination. Conversely, trait ruminators may be especially vulnerable to IMIDs in the face of chronic stressors; their blunted cortisol may leave them unable to regulate stress-induced cytokine elevations, but may not matter as much when stress is low, and cytokine levels are normal.

Thus the chronic stress of PTSD may only be associated with the development of inflammatory diseases in the face of trait rumination, when rumination prolongs both the emotional and biological stress response, leading to disease (Brosschot et al, 2006). However trait rumination may only activate IMID development in the face of stressors such as PTSD, as the heightened stress fuels the need for coping, prompting a spiral of avoidant coping through rumination and paradoxical increases in stress, with associated increases in inflammatory activity. So although trait rumination may predate a traumatic event, its relationship to IMID development may only start after a PTSD reaction to trauma. In turn, MRT may prolong and intensify the distress and physiological dysregulation related to PTSD and lead to eventual development of inflammatory disorders.

The Role of Health Behaviors in the Relationship Between Posttraumatic Stress Disorder, Maladaptive Repetitive Thought and Immune-Mediated Inflammatory Disorders

Although converging evidence suggests a causal role of MRT in the biological dysregulation associated with both PTSD maintenance and IMID development, it is important to examine health behaviors in a model of the impact of PTSD on disease (Boscarino, 2008; Freedland, Miller & Sheps, 2006). Maladaptive behavioral coping patterns are well-known to adversely affect the impact of traumatic stress on both physiology and autoimmune disease outcomes (for a review see Olff, Langeland & Gersons, 2005). For example, smoking has been linked to inflammatory dysregulation, and smoking cessation with reduced peripheral inflammation (reviewed in Goncalves et al., 2011). It follows that risky health behaviors are associated with poorer IMID outcomes and functioning (Karlson et al., 1999; reviewed in Stojanovich & Marisavljevich, 2008). Individuals with PTSD are more likely to have such risky health habits, such as a greater propensity for alcohol and drug abuse and less exercise (reviewed in Rheingold, Acierno & Resnick, 2004). For example, among 921 male veterans, PTSD symptom level was found to positively predict both smoking and alcohol use (Schnurr & Spiro, 1999). A PTSD diagnosis among veterans was also found to predict alcohol abuse and dependence twenty years later (Boscarino, 2008). Moreover, male veterans with comorbid diabetes, PTSD and depression were found to have higher total cholesterol, body mass index, weight and rate of substance use disorders than those with depression alone, suggesting that PTSD impacts behaviors that are risk factors for this IMID (Trief, Ouimette, Wade, Shanahan & Weinstock, 2006).

Conclusions and the Current Study

Literature Summary

We know that chronic stress can negatively impact health (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002). Seventeen percent of currently deployed soldiers

have been diagnosed with one type of chronic stress, posttraumatic stress disorder (PTSD; U.S. Army Surgeon General, 2006). PTSD is associated with a significant functional burden to our soldiers (Hoge, Terhakopian, Castro, Messer & Engel, 2007) as well as a financial burden to both the soldiers and society (Goldberg, 2007). PTSD is strongly related to chronic physical illnesses (Sareen et al., 2005) and functional impairment, indicating the importance of identifying factors which may help minimize the emergence of veteran illness.

IMIDs, in particular, have been associated with PTSD within both the general population (O'Toole & Catts, 2008) and veterans in particular (Boscarino, 2004). In addition, PTSD has been associated both with the presence of individual IMIDs such as arthritis (O'Toole & Catts, 2008) and the overall number of IMIDs diagnosed (Boscarino, 2004). Seng and colleagues (2006) demonstrated a dose-response relationship of PTSD symptoms and IMID risk. PTSD is also associated with dysregulation of biological stress correlates such as proinflammatory cytokines and cortisol being implicated in the disease pathogenesis (Cutolo & Straub, 2006). IMIDs, such as Type 1 diabetes, rheumatoid arthritis and Crohn's disease, occurs when the body's immune system attacks its own tissues, causing damage to organs, tissues and cells (National Institute of Health [NIH], 2005). Moreover, subthreshold posttraumatic stress symptoms, rather than a full PTSD diagnosis, are also associated with significant functional and physical morbidity and associated physiological dysregulation (Benyamini, Ein-Dor, Ginzburg & Solomon, 2009; Eadie, Runtz & Spencer-Rodgers, 2008; Marshall & Schell, 2002; Pacella, Hruska & Delahanty, 2012; Thomas et al., 2012). There is also evidence that traumatic events are associated with functional decline regardless of whether fear, helplessness or horror are experienced in conjunction with the event (Anders, Frazier & Frankfurt, 2011). It is thus important to consider the impact of the full spectrum of potentially traumatic events and related posttraumatic stress symptoms rather than just a PTSD diagnosis on physical disease and related physical functioning difficulties.

The incidence and prevalence of IMIDs is widespread and growing, with 23 million people living with these diseases in the United States alone. In addition, IMIDs are the third leading cause of morbidity and mortality among industrialized nations (Notkins, Lernmark & Leslie, 2004), and account for a significant portion of the rising U.S. health care costs (NIH, 2005). No cure has been found for IMIDs, and treatments often involve toxicity risks (Shoenfeld & Gershwin, 2006), underscoring the need to find avenues of prevention. In addition, the relationship between stress and disease can become a vicious cycle, with chronic disorders such as autoimmune disease amplifying psychological stress, further increasing vulnerability to disease progression (Stojanovich & Marisavljevich, 2008). However the mechanisms of this relationship are still poorly understood and require further investigation (Sareen et al., 2006).

There is a growing consensus among psychopathology researchers that a protracted cognitive representation of stressors may be necessary to produce emotional or physical morbidity (Brosschot et al., 2006; Watkins, 2008). MRT, which figures strongly in the development of PTSD, may be particularly important to advance our understanding of the effects of chronic stress on IMIDs (Brosschot, Pieper & Thayer, 2005). The physiological and emotional effects of MRT are similar to both IMIDs and PTSD. Experimental MRT inductions result in dysregulation of the specific immune and stress hormone parameters implicated in both IMID etiology (Zoccola et al., 2008) and PTSD (Ironson et al., 2007). MRT is also positively related to and predictive of PTSD (Murray et al., 2002). MRT is associated with emotional and behavioral avoidance of distressing internal phenomena, serving to paradoxically increase both the intensity and duration of psychological distress, and this relationship has been noted in patients with PTSD (Walser & Hayes, 2006).

The contribution of MRT to PTSD morbidity is independent of the effect of general negative affect on adjustment (Tull, Jakupcak, McFadden & Roemer, 2007) as well as empirically distinct (Speckens et al., 2007) and predictive of the intrusive

memories found in PTSD (Michael et al., 2005; Watkins, 2004). In addition, while both worry and rumination are used to operationalize MRT (Segerstrom et al., 2008), rumination may be a more potent form of MRT (Hughes et al., 2008) and is more frequently used in literature examining the relationship of MRT to PTSD.

A closer examination of MRT within PTSD is also needed to refine psychological treatment approaches. Although MRT is a prominent feature of prolonged PTSD, it may not be addressed adequately in the most commonly used PTSD psychotherapies (Walser & Hayes, 2006). Unaddressed MRT may disrupt the therapeutic effects of the most effective PTSD psychological treatment, imaginal exposure, or may even lead to worse symptoms (Lee, Scragg & Turner, 2001). Neglect of protracted cognitions may be increasing veteran vulnerability to future physical and emotional pathology. In fact recent studies suggest that rates of neuro-immune dysregulation are positively related to the amount of time since the stressor onset. Finally, studies have found that an increased duration of time since stressor onset is related to greater neuro-immune disruption (Miller et al., 2007; von Känel et al., 2007), suggesting that these maladaptive cognitive and physiological reactions to trauma may incubate within the body, possibly resulting in disorders such as inflammatory disease. In addition, maladaptive health behaviors both predict IMID course and are overrepresented in those with PTSD (Karlson, 1999; Schnurr & Spiro, 1999), suggesting that they may account for additional variance in the impact of PTSD on IMIDs.

Specific Aims and Hypotheses

The goal of the current study was to expand this literature in five key ways. In sum, it appears that MRT may increase the duration and intensity of posttraumatic stress symptoms. It has also been reported to result in neuro-immune dysregulation, both in laboratory manipulations and longitudinal studies. Similar biological dysregulation has been found in PTSD, and is implicated in the pathogenesis of IMIDs (both individual diseases and total disease number); in fact, there is emerging evidence of elevated MRT

predicting IMID development. This relationship may be especially true for individuals with a history of childhood trauma and thus longer durations since stressor onset. It is crucial to consider this disease pathway in female veterans of the current conflicts since they may be particularly vulnerable to the development of both PTSD and IMIDs. Researchers have not yet, however, investigated the role of MRT in the relationship between posttraumatic stress symptoms and IMIDs. In addition, it is important to consider the separate role that maladaptive lifestyle factors will play in this model. A more complete understanding of the role of MRT and harmful health behaviors in both posttraumatic stress symptoms and physical disease will allow us to increase the specificity and efficacy of our current diagnoses, psychological interventions and disease prevention within the female veteran population.

In the current study, brooding rumination was used to operationalize MRT based on its prevalence in the PTSD literature and evidence that it is a more potent form of repetitive thought than worry among anxiety disorders (Hughes et al., 2008). In addition, the brooding rumination subscale of the Ruminative Response Style questionnaire has been noted as an adequate representative of rumination in studies examining health outcomes (Segerstrom, 2008) and found to be related to health independent of depression (Siegle et al., 2004).

This study was designed to examine the following hypotheses:

1. Consistent with previous research, IMID prevalence and related functional decline will be greater in participants who have experienced a trauma than among those without a trauma history.
2. Among participants who have experienced a trauma, there will be a positive relationship between posttraumatic stress symptoms and both IMID incidence and functional decline. Specifically, greater posttraumatic stress symptom severity will be related to increased overall number of IMIDs and increased functional

decline. These relationships will be found after controlling for demographic factors significantly related to outcome variables.

3. Among participants with a history of trauma, an interaction between MRT and posttraumatic stress symptoms will predict overall number of IMIDs and functional decline. Specifically, the interaction of high levels of both posttraumatic stress symptoms and MRT will be related to elevations in IMID diagnoses and poorer physical functioning. This relationship will be significant after including in models, and thus controlling for, depression and childhood trauma and health behaviors including smoking, alcohol use and sleep. MRT and posttraumatic stress symptoms are each also hypothesized to be independently, positively related to physical disease.
4. Among participants with a history of trauma, health behaviors such as smoking, alcohol use and sleep will mediate the relationship between the posttraumatic stress symptom-MRT interaction and elevations in IMID prevalence and physical function status. In other words, the cross product of posttraumatic stress symptoms and MRT will be calculated and the relationship of that cross-product to IMID prevalence and functioning will be estimated. Health behaviors are predicted to mediate the relationship between the posttraumatic stress symptom-MRT interaction (cross-product) and IMID prevalence and function.

In addition, the following exploratory analysis will also be conducted:

5. The impact of individual symptom clusters of posttraumatic stress symptoms (re-experiencing, avoidance and hyperarousal), rather than a posttraumatic stress symptom latent variable, on hypotheses 2 through 4.

METHOD

Participants

The sample for the current study were drawn from a cross-sectional Veteran's Affairs funded study being initiated by Dr. Anne Sadler, P.I. at the Iowa City Veteran's Hospital entitled *Physical and sexual assault in deployed women: Risk, outcomes and services*. Participants identified for the Veteran's Affairs study were 643 female Reserve or National Guard veterans who were either deployed to the combat-related regions of Iraq or Afghanistan, or were not deployed. These women were selected from a 5-state region, including Iowa, Illinois, Kansas, Missouri and Nebraska.

Procedure

Qualifying female veterans were mailed a summary of the study and asked to take part in a study examining the deployment health of military women. Consenting participants completed a one-time computer-assisted telephone interview assessing variables including socio-demographic status, trauma exposures, history and current physical and emotional health, military environmental factors, both military and Department of Veteran Affairs health care and usage, as well as barriers to such care. Participant involvement was voluntary. Consent was implied by their participation in the study and participants were paid $50.00 for their participation. Phone interviews were conducted by trained employees of the Iowa City Veteran's Hospital. Phone interviews were conducted from 3/11/2010 to 9/26/2010.

Objectives of the larger VA study included 1) Identifying and describing risk factors for both physical and sexual assault among female veterans; 2) Determining the relationship between such assault and both physical and mental health, as well as health risk behaviors; and 3) Identifying internal and external barriers to health services with regard to deployment and assault status. The current study involved only a portion of the phone interview measures included in the larger study, including those measuring PTSD,

rumination, demographics, health behaviors, inflammatory related disorders and related physical and emotional functioning.

Measures

All measures being used in the current investigation are included in Appendix B. Predictor, mediator and outcome variables are presented and summarized in Table A1. All measures were administered orally due to the phone interview format of the study. Cronbach alpha of measures for the current study can be found in Table A4.

Demographic Information

Participants were asked to report basic demographic data, including age, ethnicity, education level, partner status, employment status and family income.

Posttraumatic Stress

PTSD Checklist (PCL; Blanchard, Jones-Alexander, Buckley & Forneris, 1996). The PCL is a 17-item questionnaire that assesses Criteria B, C, and D of the DSM-IV PTSD symptoms. Participants rated how much they were bothered in the past month by each symptom on a 5-point scale, ranging from 1 (not at all) to 5 (extremely). The Cronbach alpha of the PCL-C was found to be high for the total score (0.94) as well as for the reexperiencing (0.94), avoidance (0.82) and hyperarousal (0.84) subscales (Blanchard et al., 1996). This same study reported convergent validity of correlation with the gold-standard Clinician Administered PTSD Interview (CAPS; Blake, Weathers, Nagy, Kaloupek, Klauminzer, Charney & Keane, 1990) of .93. A value of 38 for female veterans (Dobie et al., 2002) was used as a cutoff score to provide descriptive information about the sample regarding the proportion who screened positive for a likely diagnosis of PTSD. Based on the example of von Känel and colleagues (2007), who found a dose-response relationship between PTSD symptoms and inflammatory activity in even sub-threshold PTSD, PTSD total and symptom cluster scores were used as continuous variables in analyses to represent the posttraumatic stress symptom variable.

Traumatic Experiences. Participants were asked whether they experienced any of 27 discrete potentially traumatizing events. These questions came from a number of sources, including the Diagnostic Interview Schedule for the DSM-IV - Criterion A for PTSD (Robins, Cottler, Buckoltz & Compton, 1995; serious accident, fire etc, natural disaster, non-sexual assault, imprisonment, life threatening illness, witnessed someone seriously injured, witnessed someone killed, seen dead body, experienced sudden death of close friend, cared for wounded soldier), the Deployment Risk and Resilience Inventory - Post Battle Experiences (King, King & Vogt, 2003; exposed to sight sound smell of dying, interaction with enemy POWs), the Millenium Cohort Study Questionnaire (Smith et al., 2007; IED explode near you, feeling great danger of being killed), as well as questions original to studies by Kilpatrick and Ruggiero (2004; lifetime history of attempted sexual assault and lifetime history of completed rape) and Hoge and colleagues (2004; receiving incoming artillery, discharge weapon at enemy, responsible for death of enemy combatant, seeing dead bodies, seeing ill civilians, being wounded, clearing homes or buildings) as well as questions original to the parent study of this project (responsible for body searches, left by unit during mission, observed children run over, any other traumatic event).

The participant was classified as having experienced a trauma if one or more of these events were positively endorsed. Participants were given this designation regardless of whether or not they reported the DSM-IV PTSD A2 criteria of experiencing fear, helplessness or horror with the event since recent research suggests that the morbidity associated with potentially traumatic events is independent of the A2 criteria (Anders et al., 2011).

Rumination

Ruminative Response Subscale of the Response Styles Questionnaire (RSQ; Nolen-Hoeksema & Morrow, 1991). The RSQ is a 22-item self-report instrument which assesses a characteristic tendency to engage in ruminative behavior when depressed.

Treynor, Gonzalez and Nolen-Hoeksema (2003) derived a 5-item Brooding Rumination subscale from the RSQ which is free of depression content and is proposed to be maladaptive, assessing a tendency to passively compare one's current situation with an unattained standard. This Brooding subscale will be used to assess negative ruminative thought. All five items identified by Treynor et al. as belonging to the Brooding Scale were summed to compute Brooding rumination scores. Items appear to have minimal overlap with depressive symptoms and read: "What am I doing to deserve this?", "Why can't I get going?", "Think about a recent situation, wishing it had gone better", "Why do I have problems other people don't have?", "Why can't I handle things better?" Coefficient alpha of the Brooding subscale has been reported as acceptable (α=.77-.78; Fresco et al., 2007; Treynor et al., 2003). Divergent validity with depression was explored among lupus patients and the Brooding subscale was found to be unrelated to depressive symptomatology (Siegle et al., 2004).

Depression

Patient Health Questionnaire-9 (PHQ-9; Kroenke, Spitzer, & Williams, 2001). The PHQ-9 is a self-report measure of depressive symptoms that is comprised of 9 items that map onto the 9 DSM-IV and asks about the presence of symptoms in the past 2 weeks. Items are scored from 0 to 3 with response options "not at all" (score 0), "several days" (score 1), "more than half the days" (score 2) and "nearly every day" (score 3). The maximum total score is 27. Higher scores represent increased severity of depressive symptoms, and the standard cutoff score to identify possible depression is 10 (Kroenke et al., 2001; Manea, Gilbody & McMillan, 2012). Of note, there is little conceptual overlap among the PHQ-9 items and rumination. Coefficient alpha was found to be 0.89 in a sample of primary care patients (Kroenke et al., 2001).

Self-Reported Health

Millenium Cohort Study Questionnaire (MCSQ; Smith et al., 2007). This instrument is an 83-item questionnaire being used for a 21-year longitudinal study of

more than 100,000 U.S. veterans. The questionnaire assesses a range of symptom domains and experiences, including current chronic health condition diagnoses given by a medical professional within the past 3 years (rheumatoid arthritis, lupus, Crohn's Disease, chronic fatigue syndrome and fibromyalgia), and health behaviors (smoking and alcohol use). The MCSQ study was launched in 2000 and preliminary results of this study have been published. Although internal consistency was not computed for these scales, test-retest reliability is reported as moderate to excellent for all (kappa: demographics=.87; smoking=.82; alcohol use=.54; physical conditions=.48), and reliability was generally greater among female respondents. Participants in the current VA study were asked a portion of the MCSQ items.

There is also additional support for the validity of measuring health in a self-report format in both national studies of traumatized individuals (Boscarino, 1997; Schnurr et al., 1998) and examinations of biological mediators. For example, Lekander et al. (2004) found that among female participants, lower ratings of health as measured by a single health item was related to elevations in proinflammatory cytokines, including IL-1β, IL-1ra, and TNF-α. Undén et al. (2007) replicated this result in female participants. Moreover, self-reported health but not depression was found to be related to levels of inflammation (Janszky, Lekander, Blom, Georgiades & Ahnve, 2005). Thus while objective validation of health status would be ideal, there is support for a relationship between self-rated health and inflammatory dysregulation.

Medical Outcomes Study Short Form-12 (SF-12; Ware, Kosinski & Keller, 1996). The SF-12 is a 12-item self-report shortened version of the SF-36, a measure of functional disability. Two summary scores can be derived, the physical component score (PCS) and mental component score (MCS). The 12 items were scored and transformed according to the standard procedure in the manual (Ware et al., 1995). Briefly, each item score is weighted by a factor derived from regressing response category scores of each of the SF-12 items on PCS-36 and MCS-36 scores in a general

US sample (Ware et al., 1996). The resulting scores are then transformed to a mean of 50 and a standard deviation of 10 in the general US population, with higher scores reflecting better health. The SF-12 norm-based scoring allows interpretation of scores by comparing them to a reference population, and final scores are interpreted as departures from the standard. This shortened version is reported to have strong predictive validity with the 36-item version (physical functioning subscale r^2=.91; mental functioning subscale r^2=.92) and test-retest reliability is reported as acceptable (r^2=.86; Ware et al., 1996). Internal consistency has been examined, with reported alpha coefficients of .80 for physical functioning and .78 for emotional functioning (Larson, Schlundt, Patel, Beard & Hargreaves, 2008). The SF-12 has been found to be a useful measure of disability in inflammatory rheumatic diseases (Maurischat, Ehlebracht-König, Kühn & Bullinger, 2006). The PCS was used in this study to estimate the outcome variable of general physical impairment. For SEM analyses the PCS was multiplied by negative one so that higher scores indicate worse functioning, to match the directionality of the other indicator of the physical disease latent variable, IMID diagnoses. For preliminary analyses, including correlations, ANOVAs and ANCOVAs, the untransformed PCS was used for ease of interpretation (thus high scores indicate better functioning).

Childhood Trauma

Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003). The CTQ is a 28-item adult self-report retrospective measure of child maltreatment. Items are rated on a 5-point Likert scale with higher scores indicating a higher degree of childhood maltreatment. Items assess childhood histories of trauma including emotional, sexual, and physical abuse and emotional and physical neglect. This study utilized a shortened 8-item version of the full measure with items representing each type of childhood maltreatment.

Statistical Plan

IBM SPSS Statistics for Windows, Version 19.0.0 (Armonk, NY) was used for preliminary data analyses. AMOS, Version 17.0 (Arbuckle, 2008) was used for SEM analyses with covariance matrix data as input.

Preliminary Analyses

Four sets of preliminary analyses were conducted. First, all variables were tested for non-normal distributions and transformed if found to be non-normal.

Second, bivariate correlations and univariate ANOVAs were performed to examine the possibility of significant associations between demographic characteristics and outcome variables (reported IMID diagnoses and associated physical functioning decline). Independent variables were regressed on all demographic characteristics with significant associations to outcome variables and the residuals were saved and used as the independent variables in further analyses.

Third, with respect to the first study hypothesis, an ANCOVA was conducted to determine whether the prevalence of IMID and physical functioning were greater in female veterans who have experienced a trauma than in those who have not, controlling for demographic characteristics, including age, income, ethnicity, partner status, educational attainment and employment status. Specifically, a trauma variable (0=no, 1=yes) was indicated for each veteran, and the groups were compared on the mean number of IMIDs diagnosed and physical functioning score.

Fourth, a correlation between the PCL and the RRS-brooding subscale was conducted to examine whether PTSD and rumination represent unique constructs in this population.

Primary Analysis

Structural equation modeling was used for the remaining analyses. Structural equation modeling (SEM) is a two-step statistical technique that is an extension of the general linear model, thus is in the same family as multiple regression. However, SEM

has a number of advantages over multiple regression, including the ability to test multiple predictor and dependent variables and overall models rather than individual coefficients, interpretation with multicollinearity among predictors, as well as modeling both mediating variables (rather than additive models) and error terms. SEM models allow for exploration of multiple construct relationships in one analysis, thus examining relationships while accounting for multiple other sources of variability. Thus two primary purposes of SEM include first, understanding patterns of correlations among *a priori* specified variables and second, explaining as much of the variance among these variables as possible through the model specified by the researcher.

Within SEM, the data collected are referred to as observed variables, or indicators, and are said to represent the underlying constructs of interest, or latent variables (MacCallum & Austin, 2000). According to SEM convention, in graphical models observed variables are represented by rectangles and latent variables by ovals. In this study the latent variable of PTSD was hypothesized to be comprised of three observed variables, the individual PTSD symptom cluster scores (intrusions, avoidance and arousal) and the latent variable of physical disease was represented by two observed variables, the number of reported IMID diagnoses and physical functioning. Additional observed independent variables not encompassed by latent variables included the health behaviors of smoking, alcohol consumption and sleep, depression, childhood trauma, and post-deployment health change.

SEM allows assessment of the effectiveness of measurement of latent variables as well as estimation of the relationship both between independent variables (both latent and observed) and between independent and dependent variables. Thus it is a two-step process involving both validation of the measurement model of the data through factor analysis and fitting of the structural model through path analysis (Weston & Gore, 2006).

Five sets of model analyses were planned and/or conducted. First, the measurement model, depicted in Figure B3, was tested first. The measurement model

delineates how the latent variables in the model will be measured, thus the observed variables were tested in a model with their respective latent variables. Specifically, the observed indicators of the PTSD and physical disease latent variables were subject to confirmatory factor analysis to examine the degree of relatedness between the observed indicators within latent variables, since strongly related indicators define the latent variable most accurately. The next step involved determining how the independent latent variables and additional independent observed variables were related to the outcome variables of interest as well as to each other. SEM is a more direct way than regression analyses of testing direct and indirect paths from independent to dependent variables.

Second, upon establishing that the measurement model was an adequate fit for the data, the full structural model was tested. The structural model, also shown in Figure B3, contained the physical disease latent variable as the dependent variable and as independent variables the posttraumatic stress symptom latent variable, MRT, a posttraumatic stress symptom-MRT interaction, depression, childhood trauma, smoking, alcohol use and sleep duration.

Third, analysis of the potential mediating effect of health behaviors on the posttraumatic stress symptom-MRT interaction was also planned. Four conditions have been considered necessary for mediation (Baron & Kenny, 1986; Judd & Kenny, 1981a, 1981b). In the following description of these four conditions, X represents the posttraumatic stress symptom-MRT interaction, Y represents the physical disease latent variable, and M represents the mediating health variable. The four conditions for mediation are as follows (Baron & Kenny, 1986; Fritz & MacKinnon, 2007):

1. The total effect of X on Y is significant.
2. The effect of X on M is significant.
3. The effect of M on Y controlling for X is significant.
4. The direct effect of X on Y controlling for M must be nonsignificant for full mediation (Judd & Kenny, 1981a, 1981b) or smaller than the total effect of X on

Y for partial mediation (Baron & Kenny, 1986).

These four conditions can be established by examining two SEM models (Hopwood, 2007). The first, the full model described above, examines the first condition, whether the effect of the posttraumatic stress symptom-MRT interaction term on physical health is significant. The second through fourth conditions were planned to be examined in a second mediator relationship model. There is some evidence that SEM is as adequate or superior to regression in examining a mediated relationship as SEM explicitly models both error and multiple indicators for Y, the outcome variable (Iacobuci, Saldanha & Deng, 2007).

Fourth, the relationship of individual PTSD subscales to outcome variables was examined by substituting the PTSD subscales (reexperiencing, avoidance and arousal) for the posttraumatic stress symptom latent variable in the full structural model.

Fifth, based on initial results the following exploratory analyses were conducted: 1) depression mediating the relationship between MRT and physical disease; 2) depression mediating the relationship between posttraumatic stress symptoms and physical disease; 3) depression mediating the relationship between sleep and physical disease; and 4) a parsed version of the full structural model which excluded depression.

Power Analysis

For the ANCOVA test of group differences between veterans with and without trauma, an *a priori* sample size was estimated based on guidelines indicated in Cohen (1992). Previous studies have indicated odds ratios of 2.6 (Boscarino, 2004) and 2.12 (Dominick, Golightly & Jackson, 2006) for IMID disease occurrence in traumatized versus non-traumatized populations. As specified by Chinn (2000), these odds ratios can be compared to effect sizes of .53 and .41, respectively, a medium effect. According to Cohen (1992) and MacCallum, Browne & Sugawara (1996), a sample size of 64 per group provides power of .80 to detect medium effects at the $\alpha = .05$ level in tests of

differences between means. Therefore, the present sample size of 643 participants reporting a history of trauma was more than sufficient for detecting medium effects.

For the SEM analyses, power analysis for the data-model fit was conducted using guidelines recommended by MacCallum, Browne, and Sugawara (1996) and Hancock (2006). These analyses estimated the sample size that would provide sufficient power (π=0.80) for testing null hypotheses of unacceptable overall data-model fit (in structural equation models the role of the null hypothesis is reversed, so that significant results provide strong support for a good data-model fit). This approach allows for a direct estimation of power, where effect sizes are defined in terms of fit indices such as the root-mean-square error of approximation (*RMSEA*). According to Hancock, the minimum sample size for testing a "close" data-model fit, in order to achieve π = 0.80 with *df*=25 (rounded up from the actual degrees of freedom of 24) is *N*=368; in order to achieve π = 0.50 with *df*=25 the required *N*=218. Thus, with the study sample size of 643 women reporting a history of trauma, this study has sufficient power to examine fit of the proposed model to the data. Moreover, according to the *t*-rule of necessary condition of identification (Bollen, 1989), the model was able to be estimated and was identified, since the number of observed variables (78) was greater than the number of known parameters (54).

RESULTS

Participant Characteristics

Out of the 1,682 women contacted by the Iowa City VA Medical Center for study participation, 350 refused and 832 agreed to participate. When the target goal of 665 complete interviews was reached, recruitment was suspended on 436 potential participants and 167 participant interviews partially completed or not completed. Of the 665 participants who completed full interviews, 643 women (96.69%) reported a history of trauma exposure, including both early and current traumatic experiences. Further analyses were restricted to participants who reported a history of trauma. Demographic characteristics of the sample are presented in Table A2.

With respect to clinical characteristics, as can be seen in Table A3, 14.8% met criteria for a PTSD diagnosis and 16.7% for a diagnosis of depression. Physical functioning (PCL M = 50.03) was higher than has been previously reported in female veterans within a similar age range (PCL M = 37.1; Frayne et al., 2006). Self-reported inflammatory disease incidence (4.4% IMID, 14.0% cardiovascular) was commensurate with previously reported rates for IMIDs in the general population (4%; Robinson et al., 2006) but lower than reported rates for IMIDs in similar-aged female veterans (9.8% for just one IMID, fibromyalgia; Booth et al., 2012), male veterans (6.3%; Boscarino, 2004) or cardiovascular disease in women (35%; Roger et al., 2012). Specific inflammatory diseases assessed in the current study included fibromyalgia (2%), rheumatoid arthritis (2.7%), Crohn's disease (0.2%), Chronic Fatigue Syndrome (.5%) and cardiovascular disease (14%). No participant reported a diagnosis of lupus.

Preliminary Analyses

Data were first examined for potential violations of statistical assumptions. Departures from univariate normality were determined by skewness > 3 and kurtosis > 10 (Kline, 2010), and for non-normal variables Blom's transformation ([r-3/8] / [w+1/4]; Blom, 1958) was applied to the raw scores. All variables that required a transformation

fell within the limits of skewness and kurtosis after transformations were applied. The distribution of each variable was also examined for outliers. Potential outliers were all determined to represent reasonable variance within the variables of interest. Multicollinearity was not detected among the variables of interest (cutoff $r = .85$; Kline, 2010). Multivariate normality is an assumption of the most commonly used estimator, maximum likelihood (ML; Bollen, 1989). Multivariate outliers were determined by a Cook's distance score > 1 (Ullman, 2007) and no outliers were detected (all values $\leq$ .10). As a precaution, one general model was run using ML and then bootstrapped Bollen-Stine as the estimator, which has been found to produce robust estimates with non-normal data (Bollen, 1989). There was found to be a negligible difference in the fit indices. Thus, all models were estimated using the ML estimator with Blom transformed variables as needed. Zero-order correlations among variables as well as means, standard deviations and alpha reliabilities of measures can be found in Table A4—n's ranged from 633-643.

Analyses were conducted to determine whether participant demographic characteristics were significantly associated with the *raw* scores of either the number of IMIDs reported or physical functioning. Correlations were calculated using the demographic characteristics of age and annual household income. One-way ANOVAs were performed using the demographic characteristics of education, ethnicity, employment status and partner status. Planned comparisons were conducted using paired sample t-tests. To reduce the risk of Type I error, *p*-values were adjusted using Bonferroni's method to account for the number of tests performed.

Correlation analyses indicated a greater number of IMIDs reported among those who were older age ($r = .28$, $p < .01$) and reported higher annual household income ($r = .19$, $p = .02$). Physical functioning was worse in older participants ($r = -.21$, $p < .01$) but was unrelated to annual household income ($r < -.01$, $p = .97$). Results of one-way ANOVAs indicated that for IMIDs, significant differences were found among

participants for the characteristics of employment status and ethnicity. Specifically, more IMID diagnoses were reported by participants currently looking for work (M = 0.42, SD= 0.89) and those who were unable to work for an undisclosed reason (M =0.43, SD=0.81), $p < .01$ than for participants working part time (M = 0.09, SD= 0.29) , $F(7,631) = 3.45$. For the characteristic of ethnicity, participants reporting an ethnicity of Native American (M = 1.50, SD=0.71) reported significantly more IMID diagnoses than those reporting ethnicities of Asian (M = 0.11, SD= 0.33), Black (M = 0.26, SD= 0.64), White (M = 0.19, SD= 0.47), Multi-race (M = 0.00, SD= 0.00) or Other (M = .25, SD= .46), $F(6,635) = 2.88$, $p = .01$. This result is similar to previously reported elevated incidence of IMIDs in individuals of Native American heritage (Del Puente, Knowler, Pettitt & Bennett, 1989). Physical functioning was significantly different for the characteristics of education and marital status. Specifically, participants who indicated educational attainment of less than a high school degree (M = 48.38, SD= 10.04) reported worse physical functioning than participants with either a high school degree (M = 51.47, SD= 8.62) or some college or technical training (M = 50.76, SD= 8.79), $F(3,631) = 3.83$, $p = .01$. There were no significant differences between the outcome variable of IMIDs reported and levels of educational attainment or partner status or between physical functioning and levels of either employment status or ethnicity (all p's < .05). Due to these significant associations between outcome and demographic variables, predictor variables (MRT, re-experiencing, avoidance, hyperarousal, posttraumatic stress symptoms-MRT interaction, depression, childhood trauma, alcohol consumption, smoking and sleep) were regressed on demographic variables with a significant association with either outcome variable (significant indicator variables were age, annual household income, education, ethnicity, employment status and partner status) and the residuals were saved and used as the indicator variables in SEM analyses.

ANCOVA models demonstrated significant associations between *raw* outcome variables and a history of early and/or current trauma. For IMID prevalence, participants

with a history of current trauma exposure (M = 0.21, SD = 0.50) reported more IMID diagnoses than participants without a history of trauma (M = 0.00, SD = 0.00), $F(7, 636) = 9.70$, $p < 0.01$. Similarly, participants with a history of trauma exposure (M = 49.89, SD = 9.29) reported worse physical functioning than participants without a history of trauma (M = 52.87, SD = 4.19), $F(7, 639) = 7.17$, $p < 0.01$.

The zero-order correlation matrix among the raw variables can be seen in Table A4. Across the raw variables, relationships were generally in the expected direction. Correlations between MRT and the PTSD subscales of re-experiencing (r = 0.36, $p < 0.01$), avoidance (r =0.39, $p < 0.01$) and arousal (r = 0.41, $p < 0.01$) were moderate in strength with greater MRT related to elevated PTSD symptoms. Consistent with previous research (Michael et al., 2005), these patterns provide support for discriminant validity between MRT and PTSD, suggesting that in this sample these constructs are related but independent. Relationships between physical functioning and predictor variables were small but significant with the exception of a moderate negative relationship with depression (r = 0.45) with greater depression associated with worse physical functioning. The correlations between predictor variables and the number of IMIDs diagnosed were small, except for a lack of significant relationship between IMIDs diagnosed and either cigarettes smoked per day (r = -0.01) and alcohol drinks per day (r = -0.01). Strong relationships were seen between depression and the PTSD subscales of re-experiencing (r = 0.53), avoidance (r = 0.66) and hyperarousal (r = 0.69), as has been previously reported (Kessler, Berglund, et al., 2005; Posta, Zoellner, Youngstrom, & Feeny, 2011).

Model Analyses

Measurement Model

The measurement model was estimated first to explore the effectiveness of latent variable measurement before testing the structural model (Anderson & Gerbing, 1988; Kline, 2010). Model fit for both the measurement and structural models was judged on

the fit indexes of chi-square, relative chi-square, Root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI) and Standardized Root Mean Square Residual (SRMR). The chi-square statistic, also called "deviance," reflects the difference between the observed covariance matrix and the matrix predicted by the model. The lower the chi-square statistic and the higher the *p* value, the more closely the researcher's model reproduces the covariances observed in the data. Thus a non-significant chi-square is suggestive of good model fit. However chi-square is sensitive to sample size and with large sample sizes (over 200 participants) can be inflated, incorrectly implying a poor data-to-model fit and resulting in Type II error (Schumacker & Lomax, 2004). Thus while chi-square will be reported, four other statistics will be examined to draw the most accurate conclusions. Relative chi-square is the chi-square divided by degrees of freedom (χ^2/df; Wheaton, Muthen, Alwin, & Summers, 1977). This norming is designed to reduce the influence of sample size on chi-square. Relative chi-square of 2 or less is generally considered good fit (Ullman, 2007). CFI is an incremental fit index that compares the improvement in model fit over a baseline model in which the indicator variables in the model are uncorrelated. A result of 1 indicates a perfect fit and greater than or equal to .95 indicates good fit (Bentler, 1990). RMSEA is a measure of overall fit which, unlike CFI, does not require comparison to a null model but instead assess the model on its own merit. RMSEA less than .05 is considered good fit (MacCallem, Browne, & Sugawara, 1996). CFI and RMSEA are considered the fit indices least affected by sample size. SRMR is the average difference between the predicted and observed model covariances based on standardized residuals. The closer SRMR is to zero, the less discrepancy between these matrices. SRMR less than .05 is considered to indicate a model with good fit (Kline, 2010).

The estimated measurement model is shown in Figure B3 as a part of the first structural model. In all models physical functioning scores were multiplied by negative one so that directionality of physical disease indicators were similar, with higher scores

reflecting worse functioning and greater disease incidence. In addition, the observed reexperiencing and avoidance error terms were correlated based on past research finding these PTSD subscales to load on a single factor (Buckley, Blanchard & Hickling, 1998; Elhai, Gray, Cocherty, Kashdan & Kose, 2007; Taylor, Kuch, Koch, Crockett & Passey, 1998).

Overall fit of the measurement model was strong, $\chi^2(3) = 0.07$, $p = 0.99$, $\chi^2/df = 0.02$, CFI = 1.00, RMSEA = 0.00, SRMR = 0.00. The standardized loadings were all significant ($p \leq .004$) and in the expected direction (loadings = .40-.89), suggesting that all indicators were adequate markers for their hypothesized construct. On the physical disease latent variable, physical functioning loaded more strongly than IMID diagnosis. A model was tested with correlated error terms for all three PTSD indicators (reexperiencing, avoidance and arousal). However as model fit declined (AIC original model = 24.06; correlated error terms on all three indicators AIC = 26.05) and there is less empirical support for conceptual overlap between arousal and the remaining two PTSD factors, the original model was retained.

Structural Models

Next the first general model (including both the measurement and structural or causal model) was estimated. Once again, this model is depicted in Figure B3. In this model physical disease is influenced by the latent posttraumatic stress symptoms variable and the observed variables of MRT, the posttraumatic stress symptom-MRT interaction term, depression, childhood trauma, alcohol use, smoking and sleep. All exogenous predictor variables, both observed and latent, were allowed to covary. This model evidenced adequate fit: $\chi^2(24) = 39.48$, $p = 0.02$, $\chi^2/df = 1.65$, CFI = 0.99, RMSEA = 0.03, SRMR = 0.02. Although the chi-square statistic is significant, the model was retained as other fit indices less influenced by sample size were within accepted ranges. Figure B3 shows the standardized parameter estimates for the relationships among the constructs in the model. Within this model, MRT, depression, childhood trauma and

alcohol use were significantly associated with physical disease, with higher levels of depression and childhood trauma associated with higher levels of physical disease, but contrary to expectations, lower levels of MRT and alcohol use related to higher levels of physical disease. For instance, the standardized coefficient of physical disease on MRT (-.16) indicates that a one standard deviation (SD) increase in MRT results in a .16 SD decrease in physical disease. Posttraumatic stress symptoms, sleep, smoking and the posttraumatic stress symptom-MRT interaction term were unrelated to physical disease. These variables were retained in the model despite being unrelated to physical disease as the constructs have been found to be related to health decline in previous studies. When eliminating variables based on model indicators rather than theory there is a danger of "overfitting" the model to the data and reducing model generalizability to other populations (McCallum, Roznowski & Necowitz, 1992). The R^2 value for physical disease is 0.20, indicating that the model explains 20% of the variance in physical disease.

Relationships among variables in the primary structural model were examined to determine the appropriateness of estimating a mediation model depicting the impact of health behaviors on the relationship between the posttraumatic stress symptoms x MRT variable and physical health. As the posttraumatic stress symptoms x MRT variable was not found to be significantly associated with physical health, this mediation model was not estimated.

To explore the relationship of individual posttraumatic stress symptoms subscales with physical disease, three similar models were run, each including all of the variables depicted in Figure B3, but substituting a posttraumatic stress symptoms subscale (reexperiencing, avoidance or arousal) for the posttraumatic stress symptoms latent variable. Fit for all three models was adequate (reexperiencing: $\chi^2(7) = 15.31$, $p = 0.03$, $\chi^2/df = 2.17$, CFI = 0.99, RMSEA = 0.04, SRMR = 0.02; avoidance: $\chi^2(7) = 15.31$, $p = 0.03$, $\chi^2/df = 2.17$, CFI = 0.99, RMSEA = 0.04, SRMR = 0.02; arousal: $\chi^2(7) = 15.16$, $p =$

0.03, χ^2/df = 2.19, CFI = 0.99, RMSEA = 0.04, SRMR = 0.02), but none of the posttraumatic stress symptoms subscales were significantly related to physical disease (*p*s > 0.10). These results indicate that while some variables in this exploratory model were significantly related to physical disease, such as depression, childhood trauma and alcohol use, the posttraumatic stress symptoms subscales were not related to disease.

To further explore the finding that decreased MRT was related to greater physical disease, depression was modeled as a mediator of the relationship between MRT and physical disease; however this model was a not a good fit for the data: $\chi^2(30) = 331.86$, $p < 0.001$, χ^2/df = 11.06, CFI = 0.83, RMSEA = 0.13, SRMR = 0.10. Next a parsed model was tested which excluded depression, as seen in Figure B4. Depression was taken out to allow exploration of the relationship of MRT with physical disease when the general factor of negative affectivity was not explicitly modeled. This parsed model did evidence good fit: $\chi^2(21) = 26.04$, $p = 0.205$, χ^2/df = 1.24, CFI = 1.00, RMSEA = 0.02, SRMR = 0.02. Within this model worse physical health was related to greater posttraumatic stress symptoms and childhood trauma as well as fewer sleep hours but related to less alcohol use. MRT, smoking and the posttraumatic stress symptoms-MRT interaction were unrelated to physical health.

Finally, to explore the relationship of posttraumatic stress symptoms to physical health, depression was modeled as a mediator of the posttraumatic stress symptoms-physical health relationship in the full model. This model, however, did not evidence good fit: $\chi^2(21) = 31.92$, $p = 0.03$, χ^2/df = 0.32, CFI = 0.83, RMSEA = 0.04, SRMR = 0.05. Next a reduced model was fit to the data which examined depression as a mediator of the relationship between posttraumatic stress symptoms and physical disease without covariates included in the model. This model is depicted in Figure B5. This model was a good fit to the data: $\chi^2(6) = 1.92$, $p = 0.93$, χ^2/df = 0.32, CFI = 1.00, RMSEA = 0.00, SRMR = 0.001. In this model the posttraumatic stress symptoms variable is significantly related to depression and depression is significantly related to physical

disease, but the relationship between posttraumatic stress symptoms and physical disease is not significant. In addition, as shown in Figure B4, posttraumatic stress symptoms were significantly related to physical disease when depression was not included in the model. Thus this model provides support for a mediating role of depression in the relationship between posttraumatic stress symptoms and physical disease. The R^2 value for physical disease is 0.18, indicating that the model explains 18% of the variance in physical disease.

Finally, to better understand the relationship between sleep and physical disease in the presence of an indicator of depression, depression was modeled as a mediator of the relationship between sleep and physical disease, as can be seen in Figure B6. This model was a good fit to the data: $\chi^2(1) = 1.25$, $p = 0.26$, $\chi^2/\text{df} = 1.25$, CFI = 0.99, RMSEA = 0.02, SRMR = 0.003. In this model sleep was significantly related to depression and depression is significantly related to physical disease, but the relationship between sleep and physical disease is not significant. This model provides support for depression fully mediating the relationship between sleep and physical disease in this population of female veterans. The R^2 value for physical disease is 0.19, indicating that the model explains 19% of the variance in physical disease.

DISCUSSION

The objectives of the current cross-sectional study were five-fold. First, a preliminary goal was to explore both the rate of lifetime potentially traumatizing events and the relationship of physical disease and trauma in female veterans. This is in contrast to previous studies which have primarily examined the trauma-disease relationship in male veterans. Specifically, the present study examined the prevalence of self-reported immune-mediated inflammatory diseases (IMIDs) and physical functioning in female veterans who report a history of at least one potentially traumatizing event versus those who do not report a history of trauma, controlling for significantly related demographic factors. A second, related goal was to examine the relationship of posttraumatic stress symptoms to both IMID diagnosis and related functional disability within those women who report a history of trauma. It was hypothesized that greater posttraumatic stress symptoms would be related to an increased number of IMIDs and worse physical functioning.

A third objective was to examine the relationships between posttraumatic stress symptoms, maladaptive repetitive thought (MRT) and physical disease as defined by IMID prevalence and associated physical dysfunction. Specifically, an interaction between posttraumatic stress symptoms and MRT was hypothesized to be associated with elevated physical disease. The present study examined this prediction controlling for negative affect, childhood trauma and health behaviors by including depression, childhood trauma, alcohol use, smoking and sleep variables as model covariates. In addition, demographic factors were accounted for by residualizing predictor variables for variance due to age, annual household income, education, ethnicity, employment status and partner status. A fourth objective was to explore the relationships between both MRT and posttraumatic stress symptoms with physical disease when controlling for model covariates. A related objective involved exploratory analyses to examine the relationship of individual PTSD symptom clusters with physical disease in a model which

included, thus controlled for, negative affect in the form of depression, childhood trauma and health behaviors.

A fifth goal of this study was to examine the role of harmful health behaviors as a mediator in the relationship between posttraumatic stress symptoms, MRT and physical disease. It was hypothesized that health behaviors would mediate the relationship between the posttraumatic stress symptom-MRT interaction and physical disease.

In the current investigation, 643 female veterans completed a one-time interview to examine the relationships between MRT, PTSD, depression, childhood trauma and health behaviors with physical disease. Nearly 97% of participants in the study reported a lifetime history of at least one potentially traumatizing event, including both civilian and military traumas, which is higher than previous reports of female civilians (40% to 70%; Hidalgo & Davidson, 2000) and lifetime trauma history in female veterans (83%; Escalona, et al., 2004). PTSD diagnosis was 14.8% in this study, similar to other reports in female veterans (10-19%; Bean-Mayberry et al., 2011). Depression diagnosis criteria were met by 16.7% of participants, which is higher than one-year occurrence rates described for the U.S. population (9%; Kessler, Chiu, Demler, Merikangas & Walters, 2005) but lower than the incidence among trauma survivors of the Oklahoma City bombing (25%; North et al., 1999).

The remaining analyses were conducted only on those participants who experienced at least one potentially traumatizing event. As expected, in correlation analyses a greater number of IMIDs reported and / or worse physical functioning was associated with elevated posttraumatic stress symptoms, brooding MRT, depression, childhood trauma and smoking but reduced alcohol use and sleep.

In structural equation modeling analyses, a history of trauma, including both childhood and adult civilian and service-related trauma, and elevated depression were associated with greater physical disease. Contrary to hypotheses, greater MRT and alcohol use were associated with lower reported physical disease. However MRT was

only related to physical disease when modeled with depression. Also contrary to hypotheses, posttraumatic stress symptoms and smoking were unrelated to physical disease when depression was included in the model. Thus the construct of depression in these models appears to represent an important aspect of the variance between the latent outcome variable of physical disease and the predictor variables of MRT, posttraumatic stress symptoms and smoking behavior. The possible meaning of depression to these relationships will be discussed more fully below. The posttraumatic stress symptom - MRT interaction was unrelated to physical disease in all models. Previous literature has suggested that the concurrent experience of posttraumatic stress symptoms and MRT may initiate a spiral of avoidant coping through rumination and paradoxical increases in stress, resulting in heightened vulnerability to inflammatory disorders and related physical functioning decline. However the lack of relationship between physical disease and the posttraumatic stress symptom-MRT interaction term in the current study implies that the interplay of MRT and posttraumatic stress symptoms did not affect physical disease in this sample. Several structural equation models were tested and, taken together, fail to support the central hypothesis that an interaction between posttraumatic stress symptoms and MRT is related to impaired health as measured here by IMID incidence and impaired physical functioning.

Trauma – Disease Associations

In examining the results in more detail, several important points emerge. There was support for the first hypothesis; consistent with previous research, participants who reported at least one potentially traumatizing event were also more likely to report both a greater number of IMIDs and worse physical functioning as compared to participants who did not report a history of trauma. Previous research has demonstrated greater inflammatory disease in male veterans with trauma (Boscarino, 2004), and the current investigation extends the literature by demonstrating that this relationship exists for female veterans as well. Furthermore, the relationship between trauma and inflammatory

disease is potentially of greater clinical significance to female versus male veterans since IMIDs are more prevalent in women (NIH, 2005). Greater childhood trauma, specifically, was also significantly associated with elevated physical disease in SEM analyses after parceling out variance due to the demographic variables of age, annual household income, education, ethnicity, employment status and partner status and when the model included as covariates, and thus controlled for, posttraumatic stress symptoms, depression, MRT and health behaviors.

These findings are similar to a substantial body of literature documenting the relationship between trauma exposure and health decline. For example, in female veterans a history of rape has been associated with poorer physical functioning (Booth et al., 2012). Similarly, Ullman and Siegel (1996) found that both acute and chronic trauma exposure were associated with poor health perception and limited physical functioning due to health decline. In accordance with the current study, these patterns remained after controlling for psychiatric diagnoses and demographic variables. Studies have also reported negative health outcomes specific to childhood trauma (Dube et al., 2003; Goodwin & Stein, 2004), including cardiac disease (Dong, Giles, Felidti, Dube et al., 2004). Recently childhood adversity, specifically, has been shown to be related to greater disease risk after controlling for current psychiatric disorders, with associations found for heart disease, diabetes and arthritis (Scott et al., 2011). Thus although negative health outcomes are most strongly tied to a PTSD reaction to a traumatic event, there is evidence of health decline with exposure to trauma regardless of associated psychopathology (Spitzer et al., 2009).

The positive relationship between trauma exposure and physical disease can be considered in light of this study's higher reported rate of trauma (97%) than past studies of female veteran (e.g. 83% ; Escalona, et al., 2004). This elevated trauma rate may be related to inclusion of a broad array of types of traumas. For instance in the current study traumatic stressors included those that may not meet the criteria of PTSD in the DSM-IV

but have been found to be related to functional decline, such as the act of clearing homes or buildings (Hoge et al., 2004), in which soldiers search buildings for enemy combatants and are at increased risk of being attacked or ambushed. In addition, participants were given the designation of having a history of trauma exposure regardless of whether or not they reported the DSM-IV PTSD A2 distress criteria as there is evidence of trauma morbidity independent of this criteria (Anders et al., 2011). Results of the current study support the relationship of this broader definition of trauma to pathology in the form of greater physical disease and reduced functioning.

Physiological and cognitive sequelae of trauma may be key factors in understanding the relationship between trauma exposure and health difficulties in the absence of comorbid psychopathology. First, a meta-analysis of trauma, PTSD and cognitive functioning studies (Brewin, Kleiner, Vasterling & Field, 2007) found that trauma exposure was associated with neurocognitive deficits in participants who did and did not have a PTSD reaction to the trauma. As hypothesized by D'Andrea, Sharma, Zelechoski & Spinazzola (2011), trauma – induced cognitive difficulties may result in distress in reacting to normative daily life stressors, leading to elevated physiological stress reactivity and thus a susceptibility to physical illness. Similarly, dysregulated physiological responses to stress have been noted in trauma survivors without psychiatric diagnoses, including cortisol suppression (de Kloet et al., 2007), and such dysregulation is associated with physical morbidity.

The previously proposed mechanisms are avenues by which trauma may adversely impact health. However as this study was cross-sectional in nature, it is unclear whether increased trauma led to impaired health or whether compromised health predisposed the participants to trauma exposure. There is evidence that biological markers of physical disease are related to compromised cognitive function (Sparkman et al., 2006), which may result in increased vulnerability to experiencing a traumatic event. For example, among veterans, lower cognitive ability at military enlistment was reported

to predict future alcohol abuse (Gale et al., 2008) and in turn among women greater alcohol use has been found to predict risk for rape (Messman-Moore, Coates, Gaffey & Johnson, 2008). It is thus possible that compromised cognitive function may result in engaging in behavioral risk factors for future trauma. This pathway is unlikely in the relationship between childhood trauma and current physical health, but is a possibility with relatively recently experienced traumas. These mechanisms were not examined in the current study.

Depression - Disease Associations

In all models, depression had the strongest relationship to physical disease of any predictor. This finding is in agreement with the well-characterized literature documenting a strong association between depression and illness, including IMIDs. For instance, depression is three times more common in rheumatoid arthritis patients than in the general population (Dickens, McGowan, Clark-Carter & Creed, 2002) and has been reported to predict physical health decline more strongly than other comorbid conditions (Moussavi et al., 2007).

Multiple pathways may explain the relationship between depression and both the disease prevalence and functional decline components of the physical disease outcome variable in the current study. The cross-sectional nature of this study does not allow determination of causation, thus reciprocal relationships between these constructs will be considered. First, it is possible that in this study elevated depression conferred risk for both disease occurrence and worse physical functioning. In support of this hypothesis, baseline depression has been found to predict incidence of inflammatory bowel disease controlling for disease at study initiation (Leue et al., 2005). In addition depression was found to contribute to functional decline in patients with inflammatory-related diseases such as hypertension and asthma (Kessler, Ormel, Demler & Stang, 2003). Moreover in women there appear to be genetic contributions to the chronic effects of depression on disease (Kendler, Gardner, Fiske & Gatz, 2009).

In contrast, there is evidence that disease severity is a risk factor for depression. For example, in rheumatoid arthritis patients, functional disability, disease activity and duration are all predictors of elevated depression (Covic, Tyson, Spencer & Howe, 2006). Research also suggests that depression and disease are related through a shared etiology of inflammatory dysregulation. The elevated peripheral inflammation common to IMIDs has been found in depression as well (Blume, Douglas & Evans, 2011; Miller, 2009 for a review), although the exact role of inflammation in depression is still under evaluation (Raison & Miller, 2011). Thus the current study adds to the substantial literature of an association between elevated depression and disease risk in newly returning female veterans and future research could examine the directionality of this relationship in this population.

Post Traumatic Stress Symptom – Disease Associations

There was partial support for the hypothesis that elevated post traumatic stress symptoms would be related to negative health outcomes. Bivariate correlations indicated that all three PTSD subscales were positively related to both IMID incidence and functional decline, with relationships strongest for functional decline. This is consistent with report from Pacella et al. (2012) that PTSD and posttraumatic stress symptoms were more strongly related to health symptoms than health diagnoses.

Results were mixed for the relationship between posttraumatic stress symptoms and physical disease when examined through SEM. Among women who reported a history of trauma, greater posttraumatic stress symptom report was found to be significantly related to worse physical disease, but only in a reduced model which excluded depression. When depression was included in the model, posttraumatic stress symptoms were unrelated to disease, both when posttraumatic stress symptoms were modeled as a latent variable encompassing all subscales and when PTSD subscales were examined individually (reexperiencing, avoidance and arousal). Moreover, in a reduced model depression was found to mediate the relationship between posttraumatic stress

symptoms and physical disease. In all models, greater depression was related to worse physical disease.

The significant relationship between posttraumatic stress symptoms and physical disease in both bivariate correlations and the reduced structural equation model adds to the well-developed literature documenting compromised health in those with elevated posttraumatic stress symptoms and PTSD, including recently returned OIF and OEF veterans (Andersen, Wade, Possemato & Ouimete, 2010; Nazarian, Kimerling & Frayne, 2012). Moreover the posttraumatic stress symptom-health relationship has been reported as being stronger in female veterans than female civilians (Pacella et al., 2012).

The lack of relationship between posttraumatic stress symptoms and physical disease when variance due to depression is modeled, and thus controlled, in the current study is in contrast to a subset of previous research in veterans. Frayne et al. (2004) found increased physical diagnoses and worse physical functioning in female veterans with PTSD regardless of whether or not they reported comorbid depression. Similarly, in recently returned veterans, PTSD was positively related to primary-care provider disease diagnoses (Andersen et al., 2010) and physical disease burden (Possemato, Wade, Andersen & Oimette, 2010) after controlling for depression.

In contrast, this study is consistent with past reports that depression is a strong predictor of disease in veterans with a history of trauma. For instance, combat veteran males with PTSD were three times more likely to have metabolic syndrome when comorbid depression was present (Jakovljevic et al., 2008). PTSD-depression comorbidity has been associated with reduced functioning above PTSD alone, including in war veterans (Ginzburg, Ein-Dor & Solomon, 2010). Moreover among veterans a diagnosis of depression, but not PTSD, was associated with increased mortality after controlling for demographic factors and medical comorbidity (Kindler et al., 2007). Hence although there are numerous studies documenting a strong relationship between posttraumatic stress symptoms and health compromise after controlling for the variance

due to depression, there is empirical support for depression or PTSD-depression comorbidity having a stronger relationship to physical disease than PTSD or posttraumatic stress symptoms alone.

The impact of depression on the relationship between PTSD and physical disease is important to consider given high rates of PTSD-depression comorbidity (Keane & Kaloupek, 1997; Kessler et al., 2005). The etiology of this comorbidity was explored in a longitudinal study of the sequential relationship between PTSD and depression in war veterans (Ginzburg et al., 2010). A prolonged posttraumatic stress response was found to precede and possibly influence development of comorbid depression. In turn, negative affective states of depression and anxiety confer disease risk through both biological and behavioral pathways (Cohen, Janicki-Deverts & Miller, 2007). Results of the current study suggest that physical disease may be more strongly related to the occurrence of depression following protracted stress than to the post traumatic stress itself.

Negative affectivity may be a key factor in understanding why posttraumatic stress symptoms were unrelated to physical health in the presence of depression. A two-factor structure of internalizing disorders has been reported, consisting of fear and distress (Kendler, Prescott, Myers & Neale, 2003; Watson, 2005). In these models, the distress disorders include depression, dysthymia, PTSD, and generalized anxiety disorder, and the common distress has been described as negative affect. Thus there is emerging evidence of a trans-diagnostic negative affect factor in both PTSD and depression (Post, Zoellner, Youngstrom & Feeny, 2011; Simms et al., 2002). Negative affect, in turn, has been reported to be a strong predictor of both medical conditions and symptoms (Vassend & Skrondal, 1999). As previously discussed, SEM models allow for exploration of multiple construct relationships in one analysis, thus examining relationships while accounting for multiple other sources of variability. It is possible that in the full model the effect of negative affect on physical disease was represented by the relationship of depression with disease and thus statistically removed from the

posttraumatic stress symptom - physical disease relationship. In this scenario the posttraumatic stress symptom – physical disease relationship would have been largely due to either negative affectivity or another construct overlapping with depression.

Physiological disease indicators and health behaviors may represent mechanisms by which depression or negative affect may mediate the relationship between PTSD and physical disease. First, depression may mediate the association between trauma and physiological markers of disease. Among survivors of Hurricane Katrina, heart rate variability to trauma reminders was more strongly related to depression than PTSD (Tucker, Pfefferbaum, Jeon-Slaughter, Khan, & Garton, 2012). The authors describe the contribution of heart rate variability to cardiac disease. Data from the current study indicate that both trauma and depression were related to greater physical disease, including cardiac disease. Thus it is possible that among the participants of the present study, depression influenced physiological disease risk factors. In addition, depression may mediate the trauma – disease relationship by influencing health behaviors. In the recent Heart and Soul study, PTSD was related to greater smoking and medication non-adherence in cardiovascular disease patients. However the PTSD – health behavior relationship was fully explained by adjustment for comorbid depression (Zen, Whooley, Zhao & Cohen, 2012). The results of these studies as well as the current investigation suggest that depression plays an equal or larger role than PTSD in maintaining the effects of traumatic stress on the body through mechanisms such as dysregulated physiological disease markers and poor health behaviors and thus conferring risk for disease. These mechanisms were not examined in the current study. In addition, it is also possible that PTSD mediates the relationship between depression and physical disease in this sample of female veterans; however this relationship was not explored in the current study. Since this mediation relationship was not explored, the relative contributions of PTSD and depression to physical disease remain uncertain.

Finally, it is possible that the relationship between PTSD and physical disease is confounded with physical injury sustained at the time of a traumatic event, as combat injury is predictive of both PTSD and depression (Grieger et al., 2006). However previous research also suggests a robust relationship between PTSD and physical health problems in veterans after adjustment for traumatic stressor-related physical harm risk factors including extent of physical injury (Hoge, Terhakopian, Castro, Messer & Engel, 2007) and chemical exposure (Jakupcak, Luterek, Hunt, Conybeare & McFall, 2008). Thus although the current study did not examine the contribution of injury to the PTSD-disease relationship, there is previous support for the contribution of both PTSD and depression to physical disease regardless of the presence of traumatic stressor-related physical injury.

Maladaptive Repetitive Thought – Disease Associations

Contrary to hypotheses, the posttraumatic stress symptom-MRT interaction was unrelated to physical disease in all models. In addition, MRT as a stand-alone variable was unrelated to physical disease in a parsed model that did not include depression. When depression was included in the model, reduced MRT was associated with *greater* physical disease. Moreover this negative relationship between MRT and physical disease was significant, albeit small, when controlling for additional covariates of childhood trauma and health behaviors. Thus results of this study did not support the perseverative cognition hypothesis that increased MRT is related to compromised health outcomes (Brosschot et al., 2006).

The lack of relationship between the PTSD and MRT interaction term and physical disease was contrary to expectations. Previous research has suggested that the relationship between MRT and physical disease may be exacerbated by trauma-related distress. For instance, MRT has been reported as more frequent in depressed patients with PTSD than depressed patients without PTSD or a trauma history (Birrer & Michael, 2011), suggesting that either trauma or a PTSD reaction to the trauma was more strongly

related to MRT than depression. Moreover the interactive effects of anxiety and MRT were found to predict difficulty in disengaging attention to threat in an experimental paradigm (Verkuil, Brosschot, Putman & Thayer, 2009). Continued engagement with threat stimuli could maintain physiological distress that is related to disease, suggesting that a posttraumatic stress symptom – MRT interaction should be related to greater disease. Statistical difficulties with interaction terms represent an explanation for the lack of relationship between the posttraumatic stress symptom - MRT interaction and physical disease. The product variable used to model the interaction effect will always be less reliable than the original variables, and thus have reduced power of detecting interaction effects (Dimitruk, Schermelleh-Engel, Kelava & Moosbrugger, 2007). As such, it is possible that the reciprocal relationship between posttraumatic stress symptoms and MRT does exist in this population but that the way it was operationalized in the current study was underpowered to detect this effect.

When the stand-alone MRT variable was modeled without depression, MRT was unrelated to physical disease. This is in contrast with previous work which has reported that MRT, including brooding rumination, is associated with poor health outcomes (Fortune et al., 2003; Holman et al., 2008; Siegle et al., 2004). Moreover in the present study, MRT *was* related to both increased disease incidence and decreased physical functioning when examined through bivariate correlations which did not control for depression, childhood trauma or health behaviors. It is possible that MRT as measured in this sample was not as salient a predictor of physical disease than other constructs in the model such as childhood trauma or health behaviors. In contrast, MRT as measured by several repetitive thought questionnaires has been found to adversely impact immune response and this relationship was not mediated by depression (Segerstrom, Schipper & Greenberg, 2008). It is thus possible that MRT is in fact related to physical disease independent of depression but was inadequately measured in this study to detect such a relationship.

In analyses that included both MRT and depression, elevations in MRT were related to better health. This finding is initially counterintuitive. However there are several potential reasons for the negative relationship between MRT and physical disease when statistically controlling for depression. First, similar to the PTSD-health relationship above, the inclusion of a depression factor in the model may have statistically removed negative affect from MRT. While the exact nature of a MRT variable parsed for negative affect is unclear, consideration of the function and valence of repetitive thought may provide some clarity. As was described previously, the valence and function more than total amount of repetitive thought has been described as influential to both mental and physical health (Kashdan, Young & McKnight, 2012; Segerstrom et al., 2010). MRT is generally beneficial when the valence is positive and/or the function is error correction or goal attainment. It is possible that MRT with negative affect controlled in this model reverts to conceptually resemble a beneficial form of rumination such as the Reflection subscale of the Ruminative Response Scale, a theory which was endorsed by the scale author, Dr. Nolen-Hoeksema (personal communication, 8/15/2012).

One mechanism by which adaptive repetitive thought could influence physical disease is through regulation of negative affect. In a prospective study, Kashdan et al. (2012) found that adaptive repetitive thought was concurrently related to greater negative affect but prospectively predicted less negative affect. Conversely, negative affect was not related to future repetitive thought (Kashdan et al. 2012). Similarly, Watkins (2004) found greater emotional recovery from an upsetting event among individuals randomized to an adaptive, experiential repetitive thought condition versus those in a maladaptive conceptual-evaluative condition. If adaptive repetitive thought serves to reduce future negative affect, it may also reduce the long-term physiological wear and tear of negative affect and be protective against physical disease. In support of this hypothesis, previous work has suggested a protective effect of adaptive repetitive thought on physiological disease correlates. Segerstrom et al. (2008) found that while MRT was associated with

poorer antibody response to a vaccine, adaptive repetitive thought was related to a better antibody response. Hence it is possible that in this study repetitive thought with depression controlled mitigated the effect of stress, leading to reduced physical disease. As the current study variables were measured at one time-point, the effect of repetitive thought on future depression and health could not be measured.

The cross-sectional nature of this study means that the relationship between repetitive thought and physical health are correlational and directionality of causation is unclear. As a result, the effects of physical disease on repetitive thought need to be considered. A second hypothesesis for the negative relationship between repetitive thought and physical disease is the effect of disease on psychological functioning. As discussed previously, poor somatic health can result in negative psychological outcomes. Segerstrom, Roach, Evans, Schipper and Darville (2010) hypothesize that increased distress may result in elevations in both MRT about the negative mood and adaptive repetitive thought such as emotional processing as a tool to reduce the distress. However this hypothesis cannot be examined in the current study since the model with depression as a mediator of the relationship between repetitive thought and physical disease exhibited poor model fit.

Health Behavior – Disease Associations

In the current study, health behaviors were proposed to mediate the relationship between the PTSD x rumination interaction and physical disease. As the interaction was unrelated to disease, this hypothesis was not examined. However structural equation models did explore the individual relationship of each health behavior (sleep, alcohol use and smoking) with physical disease. Analysis covariates included posttraumatic stress symptoms, MRT, childhood trauma and, in all but one model, depression. In structural equation models sleep was negatively related to physical disease as predicted, but only in a reduced model which excluded depression. In all other models sleep was unrelated to physical disease. Moreover depression was found to fully mediate the relationship

between sleep and physical disease. Alcohol use was consistently related to physical disease, but in the opposite direction than predicted; lower levels of alcohol use were related to greater disease. Also contrary to hypotheses, smoking was unrelated to physical disease in all models. These unexpected findings may be due to the moderate average levels of all three health behaviors reported in this study, with modest deviations from those means (as shown in Table A4). It is possible that participants were underreporting poor health behaviors and that sleep, smoking and alcohol use are in fact independently related to worse physical health in this population.

Since the negative health outcomes associated with disturbed sleep are well characterized (Taylor, Lichstein & Durrence, 2003), it was unexpected to only find this relationship in a model which excluded depression. In previous research, self-reported sleep has been independently associated with inflammatory disease risk above the effects of depression in women (Ayas et al., 2003) and in fact has been reported as a mediator in the relationship between depression and disease (Gangwisch et al., 2010). In contrast, model analyses from the current study suggest that in female veterans, depression may mediate the relationship between sleep and physical disease. This finding is partially supported by recent data examining the relationship between sleep, depression and pain in rheumatoid arthritis patients (Irwin et al., 2012). Similar to the current study, in the arthritis patients sleep loss was related to increased depression. However the authors also report that sleep disturbance predicted worse disease-related functioning in the form of pain and that the sleep-pain relationship was not mediated by depression. In contrast, among female veterans in the current study data suggest that the relationship between sleep and physical disease was fully mediated by depression. The measurement of sleep may be a key factor in understanding the lack of independent association between sleep and physical disease. While sleep was defined in the current study by a single item assessing the average number of hours per day, Irwin et al. evaluated severity of sleep disturbance through the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk,

Berman & Kupfer, 1989) and studies which operationalized sleep as persistent sleep problems (lasting over one year) were also likely to predict disease (Nicholson, Fuhrer & Marmot, 2005). It is possible that sleep problems evaluated in such formats would be associated with disease in the current participants. Another possible explanation is the overlapping influence of depression and sleep on the inflammatory pathways believed to play a role in IMID onset (Irwin, Olmstead, Ganz & Haque, 2012; Joynt, Whellan & O'Connor, 2003). It is possible that in this study depression represented these physiological processes more strongly than sleep.

In contrast to the effects of sleep with physical disease, alcohol use was consistently related to physical disease in the current study. However contrary to hypotheses alcohol was negatively related to physical disease, and the relationship was roughly linear. Recently substance use disorders, including alcohol use, have been found to be associated with increased odds for medical diagnoses in newly returning OIF / OEF women, although PTSD was found to be more strongly related to medical diagnoses than substance use disorders (Nazarian et al., 2012). The moderate use of alcohol reported by the current sample (1.5 drinks per day) may help explain the direction of this relationship. There is evidence that low to moderate alcohol consumption is related to lower levels of inflammation markers in arthritis patients (Roseman, Truedsson & Kapetanovic, 2012). It is thus possible that moderate alcohol use in these female veterans was protective of IMIDs and physical functioning through regulation of the physiological markers associated with IMIDs.

The hypothesis that smoking would be related to poor health outcomes was not supported. Specifically, smoking was unrelated to physical disease in all models. This is contrary to a significant literature which has found smoking to predict disease, including IMID incidence, and associated physiological dysregulation. For instance, smoking has been associated with both an increased risk of rheumatoid arthritis (Klareskog et al., 2006) and the increased inflammatory response associated with arthritis (Roseman et al.,

2012). However the above studies did not account for the possible variance due to depression. Zen (2012) found that the relationship between PTSD and cigarette smoking was largely accounted for by adjustment for depression. Thus it is possible that in the current study cigarette smoking is not independently associated with physical disease above the effects of depression. However another possibility is that this study was underpowered to detect the relationship between smoking and physical disease, as cigarette use was unexpectedly minimal in this sample. In addition, operationalization of smoking as current packs per day may have influenced the relationship with disease. Zen et al. (2012) measured tobacco use as mean pack years of smoking, thus it is possible that this construct would be more strongly related to disease outcomes measured in that format. It is also possible that cigarette use was underreported in the current study, making results more difficult to interpret.

Taken together, the results from the primary and secondary analyses suggest that in newly returning female veterans with a history of trauma exposure, physical disease is associated with greater depression, childhood trauma but lower levels of repetitive thought and alcohol use, after accounting for covariates. Unexpectedly, smoking, sleep and the interaction between post traumatic stress symptom and MRT interaction were generally unrelated to physical disease in this sample. The relationship between greater levels of both depression and childhood trauma with health compromise is well characterized in the literature. The lack of an association between the interaction of posttraumatic stress symptoms and MRT and physical disease may be due to reduced statistical power inherent to interaction terms. An absence of relationship between posttraumatic stress symptoms and physical disease appears to be explained by adjustment for depression. The unanticipated finding that physical disease is related to *less* MRT may be a result of MRT parsed for negative affect coming to conceptually resemble *adaptive* repetitive thought. An adaptive form of repetitive thought may have been protective of disease processes, as has been found by previous studies. Conversely,

those with greater physical disease may be more likely to use adaptive repetitive thought to cope with disease-related stressors. Thus although support was not found for the Perseverative Cognition Hypothesis, the results of this study have relevance to relationships between women's emotional and physical health, and for female veterans in particular.

Implications for Clinical Practice

Female veterans represent a historically high 20% of new military recruits (Yano et al., 2010) and over 44% of OEF / OIF female veterans have enrolled for VA health care (Hayes & Krauthamer, 2009). Many female VA patients have compromised functioning, are intensive users of VA services and have a high rate of retention within the VA system (Friedman et al., 2011). Moreover, reduced quality of interventions for female versus male veterans has been noted (Yano, 2010). Accordingly, investigators working with female veterans have noted the need for research which examines relationships between mental and physical health conditions to inform sound clinical practice (Yano et al., 2011).

This study addresses these goals by describing behavioral and psychological factors which are associated with physical disease in female veterans. Specifically, depression and repetitive thought were found to be related to disease, and both are modifiable through psychosocial intervention. Results of this study reinforce that these constructs may be important to address in psychosocial interventions with women who have either experienced trauma, are coping with a long-term disease or both. This is important as trauma-related psychopathology is high in primary-care settings but medical providers often feel they do not have the resources to address the disorder (Gill & Szanton, 2011). Moreover female veterans are less likely than male veterans to be screened for depression, especially in primary care settings (Yano et al., 2011). The relationship between depression and physical disease in this study supports the urgency to both screen and provide intervention for women with elevated depressive symptoms.

In a review of the consequences of repetitive thought, Watkins (2008) notes that while the harmful consequences of maladaptive repetitive thought are well-documented, there is a relative paucity of research documenting the effects of adaptive repetitive thought. He noted that benefits of adaptive repetitive thought in extant studies include cognitive processing of trauma-related distress, improvements in depressive symptoms, and adoption of health-promoting behaviors. In addition adaptive repetitive thought has been associated with improved regulation of physiological disease markers (Segerstrom et al., 2008). However little has been published on the relationship of adaptive repetitive thought with established disease and physical functioning outcomes. Moreover, researchers have described the specific need for interventions tailored to trauma survivors with associated physical comorbidities (Seng, 2011). This study expands the current literature by suggesting that since greater physical disease is associated with less adaptive repetitive thought and greater depression, there may be clinical utility in implementing interventions which address these factors.

Adaptive repetitive thought has been characterized as active reflection on corrections that can be made to past mistakes rather than focusing on the implications of failure, as well as non-judgmentally and fully experiencing the distress associated with such upsetting events (Kashdan et al., 2012). A number of existing interventions facilitate adoption of these qualities. For example, some aspects of adaptive repetitive thought have been reported to be similar to the psychological state of mindfulness, which can be defined as focusing one's attention on the present moment in a nonjudgmental/accepting way (Kabat-Zinn, 1994). Evans and Segerstrom (2011) found that adaptive repetitive thought in the form of positively-valenced repetitive thought was significantly associated with mindfulness qualities of describing, being non-judgmental and non-reactive and acting with awareness. Mindfulness-based interventions have been shown to improve regulation of immune response (Davidson et al., 2003), reduce psychopathology and improve well-being (see Baer, 2003 for a review). Moreover

mindful attention has been associated with resilience in trauma survivors (Bernstein, Tanay & Vujanovic, 2011).

A number of mindfulness-based interventions have been developed with empirically demonstrated benefits in patients with chronic medical and / or psychosocial problems, including Mindfulness-Based Stress Reduction (Kabat-Zinn, 1990), Mindfulness-Based Cognitive Therapy (Segal, Williams, & Teasdale, 2002), Acceptance and Commitment Therapy (Hayes, Strosahl, & Wilson, 1999) and Dialectical Behavior Therapy (Linehan, 1993). Some of mindfulness-based interventions also address the problem-solving aspect of adaptive repetitive thought which encompasses reflection on mistake correction. For instance, Acceptance and Commitment Therapy emphasizes values clarification and increasing value-guided behavior, skills which enhance one's ability to correct problematic behavioral patterns. Thus psychosocial treatments which facilitate increases in adaptive repetitive thought, such as mindfulness interventions, may provide psychological and possibly physiological benefit to patients with trauma-related psychopathology and medical disease comorbidity.

Limitations

The results of the current study must be interpreted in light of certain limitations. The sample for the current study was largely Caucasian. Although the sample is representative of the geographic area from which it was drawn, it is not representative of the diversity of the larger nation, limiting generalizability of study findings. Since significant differences were found for ethnic groups on the outcome variable of IMID diagnosis, it would be informative to examine the relationship between ethnicity and disease outcomes in a more representative sample. For example, participants reporting an ethnicity of Native American reported more IMID diagnoses than those reporting ethnicities of Asian, Black, Caucasian, Multi-race or Other, a finding that is similar to previous reports of inflammatory disease incidence in those reporting a Native American heritage (Del Puente et al., 1989). As Native American participants were

underrepresented in this study (.3% of the sample) it would be helpful to see whether this effect remains in a more diverse sample. Moreover the limited representation of ethnic groups other than Caucasian precluded subgroup analyses in the current study.

The study design represents another limitation. All measures were collected at one time-point and were self-report in nature. The cross-sectional study design precludes understanding of the direction of relationship among study variables. As all relationships are correlational in nature, causation cannot be determined and the study should be considered exploratory in nature.

The measure of health by self-report rather than independent verification by a physician or medical record represents another considerable limitation. Self-reported health may bias results as it has been suggested to be more strongly related to negative affectivity than objective disease (Watson & Pennbaker, 1989), However, recent research has suggested that while distress does contribute to self-reported health, objective health is significantly related to self-reported health after controlling for negative affect (Vassend & Skrondal, 1999). In addition, self-rated health is a salient predictor of health service utilization (Bosworth, Butterfield, Stechuchak & Bastian, 2000), suggesting that although flawed, it still has clinical utility.

One hypothesis of the current study was that trauma, and related distress, would contribute to the number of IMIDs and associated physical function decline. Thus ideally IMID onset and related physical function decline would be included only if initiated post-trauma. However, as a measure of premorbid health was not available in the present study, physical disease and physical functioning prior to the trauma experience was not available and could not be controlled. Inclusion of a childhood trauma variable did account for very early trauma exposure, but a more nuanced measure of pre-trauma health would be useful in future studies.

Relatedly, the assessment of trauma history represents another limitation of this study. In the current study, the wording of questions assessing trauma history precluded

definitive categorization of early versus late traumas. Since disease occurrence and related functional decline may increase with a greater amount of time since trauma occurrence, future research should explicitly assess the number of years since the participant's first traumatic experience.

MRT in this study was operationalized by a relatively brief 5-item measure representing just one form of repetitive thought, brooding rumination. In the current study, an association between MRT and physical disease was not found when depression was not included in the model. While other studies have found maladaptive rumination to be related to both disease incidence and physiological disease markers, in those studies rumination was measured with multiple scales (Siegle, Moore & Thase, 2004; Zoccola, Dickerson & Zaldivar, 2008). Thus in the current study additional measures of repetitive thought may have allowed detection of a relationship between MRT and physical disease. In fact, researchers have emphasized the importance of using a number of measures to represent the multiple dimensions of repetitive thought (Segerstrom et al., 2003). In addition, since adaptive rumination measures were not available in the present study, comparisons could not be made among the differential relationships of maladaptive and adaptive repetitive thought to physical disease.

The operationalization of health behaviors (sleep, alcohol use and smoking) with a single item each represents another limitation of the current study. Sleep was defined in the current study as the average number of hours of sleep per day, and in structural equation models this item was found to be unrelated to physical disease when depression was included as a covariate. It is possible that alternate measurements of sleep would have been more likely to predict disease, such as persistent sleep problems or the use of validated measures of sleep quality. Greater alcohol use as measured by drinks per day was found to be related to less disease in the current sample, contrary to predictions. A more precise definition of alcohol use, such as grams of alcohol per week (Roseman, Truedsson, Kapetanovic, 2012), or measurement of alcohol use disorder rather than

alcohol use (Nazarian et al., 2012) may have allowed detection of a relationship between elevated alcohol use and greater physical disease in the current population of female veterans. In addition, in this study smoking was unrelated to physical disease in all models. While smoking was measured as current packs per day in this study, a smoking-disease relationship may have emerged with alternate forms of operationalization, such as mean pack years of smoking (Zen et al., 2012).

Similarly, the operationalization of physical disease incidence as the number of IMIDs diagnosed represents another limitation of the current study. Disease incidence has been defined in this way in past research in veterans and found to be significantly related to posttraumatic stress symptoms (Boscarino, 2004). However it is unclear whether incremental increases in diseases diagnosed, such as from 2 to 3 diseases, truly represent greater underlying physical pathology. The current interpretation of IMID incidence is meant to give a broad overview of the relationship between physical disease and both psychological and behavioral risk factors to illustrate the need for additional investigations of these concepts. Future research could utilize alternate definitions of disease incidence, such as biological measures of immune dysregulation.

The current study explored the relations between posttraumatic stress symptoms, MRT, depression, childhood trauma and health behaviors with physical disease. However, although the study models evidenced good fit, there are many untested models which would include additional salient predictors of physical disease. Additional theoretical models should be explored so that competing explanations of psychosocial predictors of disease can be tested.

Future Directions

A number of future directions are suggested by the current study. Further studies should attempt to replicate the current findings in a more diverse sample of participants to determine how well the model presented here generalizes to other individuals, measures and designs. For instance, substance use in the current sample was relatively moderate

and may not represent substance use in other samples of trauma-exposed individuals. It is also possible that substance use was underreported in this study. Thus it may be useful for future research to examine the relationship between repetitive thought, posttraumatic stress symptoms and depression in participants with a history of trauma and reporting greater substance use. In addition, as there were a limited number of inflammatory-related diseases included in this study, it may be useful to examine these relationships with inclusion of a greater array of inflammatory disorders accompanied by physician verification of the medical condition or biological measures of physiological dysregulation.

Inclusion of additional measures of repetitive thought to represent more nuanced dimensions of this construct would clarify the relationship between repetitive thought and physical disease. For example repetitive thought constructs which have been explored by other researchers include emotional processing, intrusions associated with trauma, worry, rumination and reflection (Segerstrom et al., 2003 for examples of measures). There are examples of relatively new measures which have been designed to specifically address both maladaptive and adaptive forms of repetitive thought. For example, the Event Related Rumination Inventory (Cann, 2011) was designed to assess both trauma-related intrusive thoughts and deliberate problem-solving focused thought.

Longitudinal studies would allow sorting of true risk-factors from co-occurring phenomena. For example, although it makes sense that adaptive repetitive thought could be protective of physical disease, it is also likely that physical disease could result in a reduced capacity to engage in repetitive thought. It is also possible that a third variable, such as dysregulated immune markers, underlie both phenomena. Moreover this study unexpectedly found that PTSD was not related to physical disease when depression was included as a covariate. It may be useful to examine the contribution of PTSD to health when premorbid depression is controlled. Cross-lagged studies can explore temporal influences on these constructs.

The current study examined repetitive thought in female veterans. Military training and combat-related service involve increased vigilance and attentiveness which can be adaptive to task achievement. Such vigilance may be related to especially adaptive forms of repetitive thought. Future research could examine the relationship of military-related attentional focus and repetitive thought, including whether vigilance training is related to changes in repetitive thought form, function or frequency. For example, the focus of attention between military attentiveness and the repetitive thought construct examined in this study is likely to differ, with military-related attentiveness focused on activity outside the self versus the self-focus of repetitive thought. On the other hand, it is possible that military vigilance training promotes an active, solution-seeking thought pattern that promotes adaptive over maladaptive self-focused repetitive thought patterns. These relationships could be clarified in future studies. In addition, future work could examine the prevalence of different forms of repetitive thought in military populations and whether the rates of repetitive thought differ between military and civilian populations.

Empirical investigation of relationships between repetitive thought and aspects of physical health and functioning may be useful. For instance, repetitive thought type could be manipulated, using a paradigm similar to Watkins (2004) in which participants write about a failure experience, either evaluating the failure ("Why did you feel this way?"; maladaptive repetitive thought) or directly experiencing the failure ("How did you feel moment-by-moment?"; adaptive repetitive thought). Groups could be compared on dimensions of physical functioning, such as pain perception, self-rated health, or an objective measure of physical function such as a stress test.

Past research has found childhood trauma to be associated with chronic disease after controlling for effects from associated psychopathology. The current study extends the research by suggesting that the relationship of childhood adversity and disease may also be independent of behavioral patterns, here cigarette and alcohol use and repetitive

thought style. Research is needed to elucidate additional pathways by which early life experiences may affect chronic disease status and physical functioning.

Finally, this study did not examine the possible contribution of physical injury sustained during a traumatic stressor to the relationship between PTSD, depression and physical disease. Inclusion of severity of physical problems would assist in clarifying the relationship between traumatic stress and health.

In conclusion, the results of this study of female veterans are consistent with the hypothesis that physical disorders and related functional decline are greater in trauma-exposed individuals and that depression, childhood trauma and repetitive thought have independent associations with physical disease. Although the cross-sectional nature of these data precludes strong causal inference, the results are consistent with current theories of a protective effect of adaptive repetitive thought on physical disease and functioning. Results of this study suggest that it may be useful to examine the effects of interventions which increase adaptive repetitive thought on both disease occurrence and physical functioning. It also indicates a need for future studies to investigate the prospective role of trauma-related distress and repetitive thought in predicting a range of chronic physical conditions, while taking into account the long time frame for the expression of associations between these risk factors and later disease and functioning outcomes.

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APPENDIX A: TABLES

Table A1. Constructs and Measures for Current Investigation.

Variables	Measure	Subscale(s)
Predictor Variables		
Posttraumatic Stress Symptoms	PCL	Intrusions, Avoidance and Arousal
MRT	RRS	Brooding Rumination
Depression	PHQ-9	
Childhood Trauma	CTQ	
Health Behaviors	MCSQ	Smoking, Alcohol Use and Sleep
Outcome Variables		
IMID	MCSQ	
Physical Functioning	SF-12	PCS

Table A2: Demographic Characteristics of the Study Sample (N=661)

Variable	M (SD)
Age	37.9 (10.4)
Annual household income	$79,540.13 ($58,031.77)

Variable	%
Education	
Less than high school	.2
High school graduate	28.6
Some college or technical training	16.7
Associates degree, nursing or college graduate	39.5
Post-graduate degree	14.6
Employment	
Work full-time	65.1
Work part-time	14.4
Currently looking for work	6.9
Retired from civilian employment	1.1
Unable to work due to physical health difficulty	2.0
Unable to work due to emotional health difficulty	.8
Unable to work for another reason	4.5
Relationship Status	
Single, never married	27.1
Married, living with a spouse	49.6
Married but separated	1.7
Married but geographically separated	3.6
Living with a partner	1.4
Divorced	18.0
Widowed	1.4
Ethnicity	
American Indian	0.3
Asian	1.5
African American or Black	15.9
Native Hawaiian or Pacific Islander	0.5
Caucasian	79.5
More than One Race	0.8
Other	1.5
Deployment Category	
Never deployed	21.2
Deployed elsewhere (never to Iraq or Afghanistan)	26.0
Deployed to Iraq or Afghanistan once	40.9
Deployed to Iraq or Afghanistan more than once	12.0

Table A2 - Continued

Variable	%
Trauma Experiences Reported	
Serious accident, fire or explosion	41.5
Natural disaster	43.3
Non-sexual assault	18.8
Attempted sexual assault	29.1
Forced sex	26.1
Imprisonment	2.3
Life-threatening illness	9.6
Witnessed someone being seriously injured	40.9
Witnessed someone being killed	16.2
Seen a dead body or human remains	72.1
Sudden death of a close friend or relative	78.1
Care for wounded soldiers	38.6
Sight, sound or smell of someone dying	59.3
Receiving incoming artillery, rocket or mortar fire	48.6
Engaged in direct combat, discharged your weapon	5.9
Responsible for the death of an enemy combatant	1.8
Ill or injured civilians you were unable to help	22.6
Been wounded or injured	9.0
Cleared or searched homes or buildings	7.7
Had an IED or booby trap explode near you	13.9
Felt you were in great danger of being killed	33.6
Interacted with enemy POW soldiers	14.7
Been responsible for body searches	14.8
Left by members of your unit during a mission	2.0
Observed children being run over by vehicles	2.7
Other traumatic events in military or civilian life	15.9

Table A3: Clinical Characteristics of the Study Sample (N=643)

Variable	%
Inflammatory-Related Disease	
Fibromyalgia	2.0
Rheumatoid arthritis	2.7
Lupus	0.0
Crohn's disease	0.2
Ulcerative colitis	0.0
Chronic fatigue syndrome	0.5
Cardiovascular disease	14.4
Distress	
PTSD	14.8
Depression	16.7

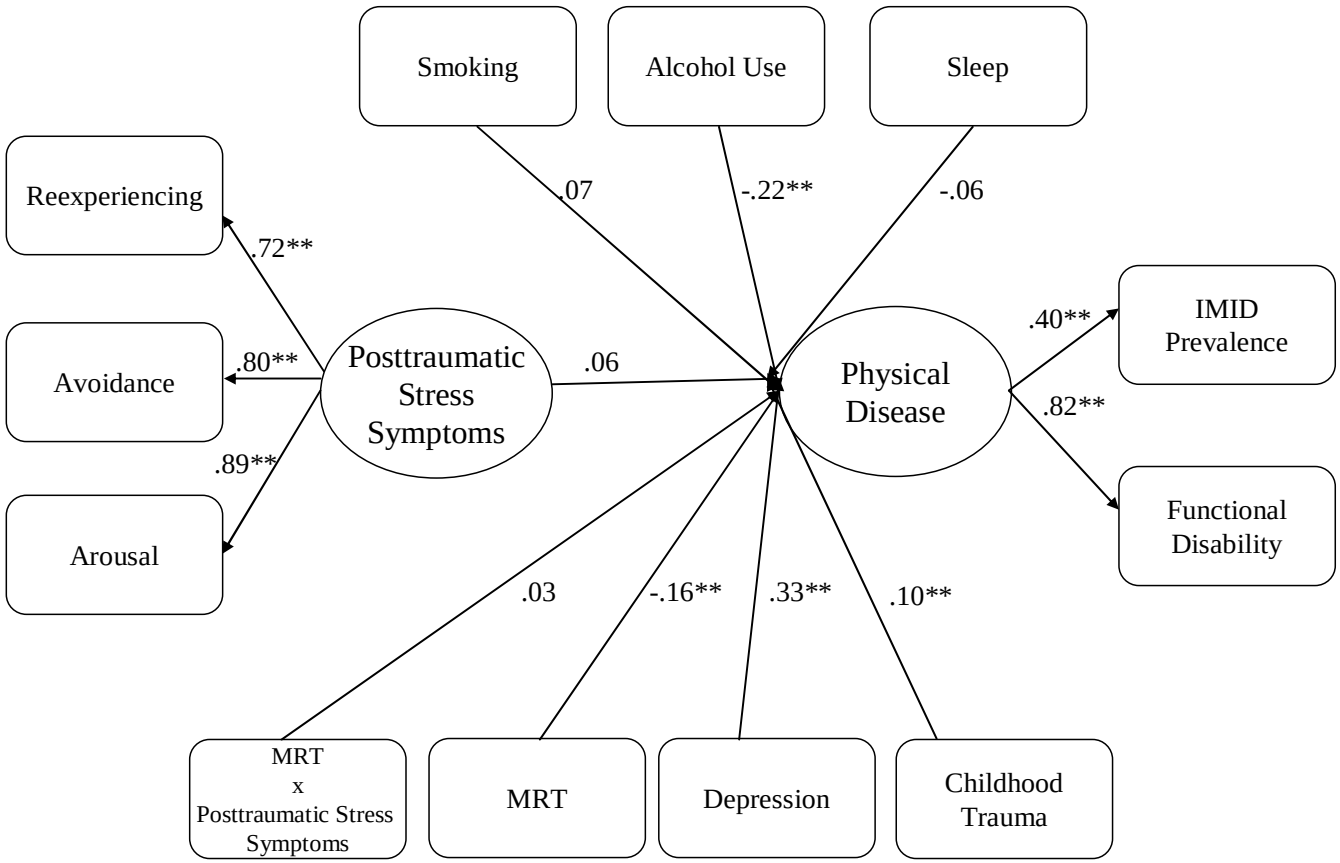
Table A4: Means, Standard Deviation and Zero-order Correlations among Study Constructs.

Construct	Mean	S.D.	1	2	3	4	5	6	7	8	9	10	11
1. IMID Total	.20	.50	**x**										
2. Physical Functioning[1]	50.03	9.18	-.26**	**.82**									
3. Reexperiencing	7.27	3.44	.11**	-.27**	**.88**								
4. Avoidance	10.17	5.05	.15**	-.30**	.76**	**.88**							
5. Arousal	8.31	4.47	.12**	.29**	.66**	.75**	**.87**						
6. MRT	8.72	2.85	.10**	-.11**	.36**	.39**	.41**	**.81**					
7. Depression	11.81	4.80	.18**	-.45**	.53**	.66**	.69**	.46**	**.88**				
8. Childhood Trauma	10.08	4.08	.18**	-.17**	.17**	.20**	.14**	.20**	.21**	**.80**			
9. Smoking	.28	.70	-.01	-.08*	.09**	.10*	.08**	.01	.07	-.02	**x**		
10. Alcohol Use	1.53	1.55	-.01	.15**	.04	.09*	.09**	.11**	.04	-.00	.21**	**x**	
11. Sleep	6.72	1.45	-.13**	.19**	-.19**	-.22**	-.24**	-.17**	-.32**	-.12**	-.02	.06	**x**

Note. *N*= 643. Coefficients alpha are on the diagonal in boldface; "x" indicates that measure is a single item thus alpha cannot be computed. * Correlation is significant at p <. 05; ** Correlation is significant at p < .01. [1]Indicates scale is reverse-keyed when included in model analyses.

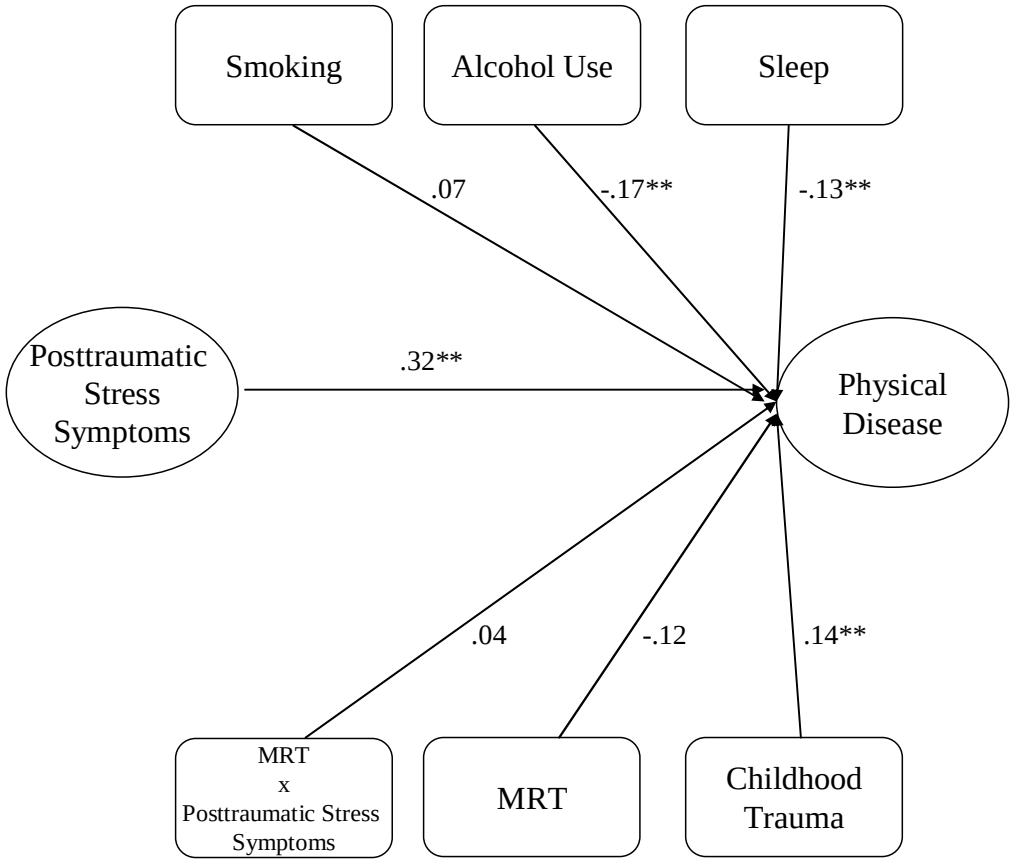
APPENDIX B: FIGURES

Figure B1: Measurement and Structural Model for Relations Between Posttraumatic Stress Symptoms, Maldadaptive Repetitive Thought, Depression, Childhood Trauma, Health Behaviors and Physical Disease.



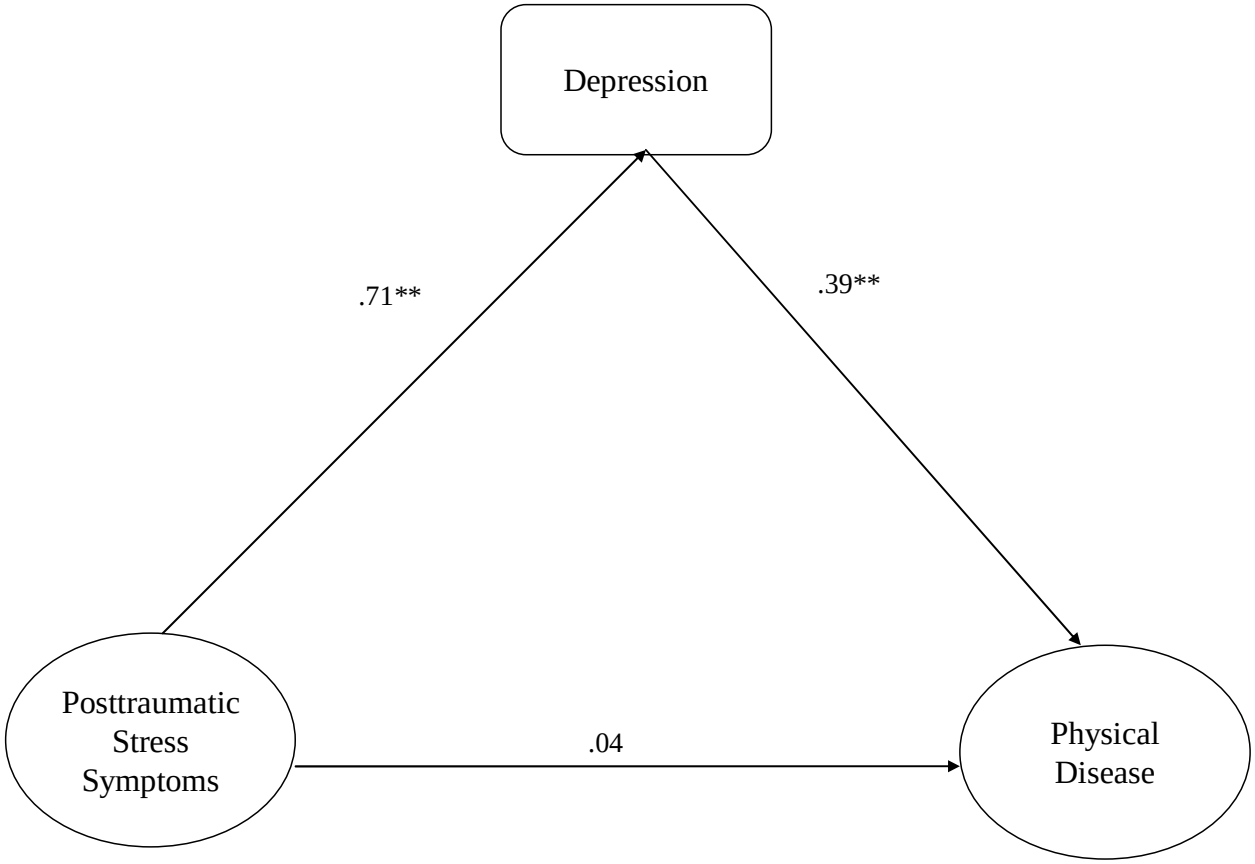
Note. $^{**}p < .01$. Standardized path coefficients are shown.

Figure B2. Structural Model for Relations Between Posttraumatic Stress Symptoms, Maladaptive Repetitive Thought, Childhood Trauma, Health Behaviors and Physical Disease.



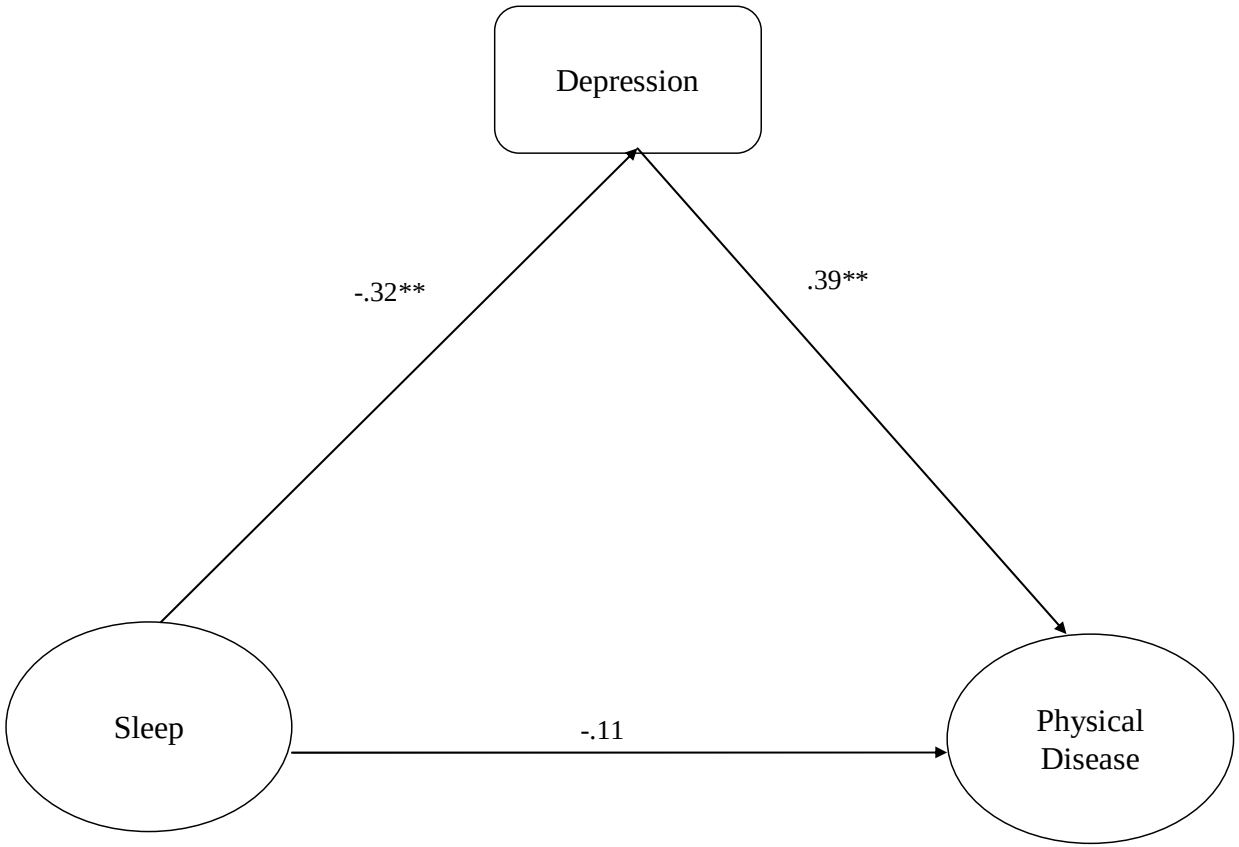
Note. ***p* < .01. Standardized path coefficients are shown.

Figure B3. Structural Mediation Model with Posttraumatic Stress Symptoms as the Predictor, Depression as Mediator and Physical Disease as Outcome Variable.



Note. $^{**}p < .01$. Standardized path coefficients are shown.

Figure B4. Structural Mediation Model with Sleep as the Predictor, Depression as Mediator. and Physical Disease as Outcome Variable.



Note. ***p* < .01. Standardized path coefficients are shown.

APPENDIX C: MEASURES

Ruminative Responses Scale (RRS): Brooding Rumination Subscale

Now I am going to read you some statements about things people sometimes say and do when they are feeling distressed. Please tell me what you generally do, not what you think you should do.

1	2	3	4
Never	Sometimes	Often	Always

1. Think “What am I doing to deserve this?”
2. Think “Why do I always react this way?”
3. Think about a recent situation, wishing it had gone better.
4. Think “Why do I have problems other people don’t have?”
5. Think “Why can’t I handle things better?”

PTSD Checklist (PCL)

Now I am going to read a list of problems that people sometimes have after experiencing a traumatic event. I'd like for you to rate each problem with respect to your experience of (traumatic experience). I will ask you to tell me which best describes how often that problem has bothered you in the past last month.

1	2	3	4	5
Not at all	A little bit	Moderately	Quite a bit	Extremely

(In the last month…)

1. How often have you had repeated, disturbing memories, thoughts or images of a stressful experience from the past?

2. How often have you had repeated, disturbing dreams of a stressful experience from the past?

3. How often have you suddenly acted or felt as if a stressful experience were happening again (as if you were reliving it)?

4. How often have you felt very upset when something reminded you of a stressful experience from the past?

5. How often have you had physical reactions (e.g., heart pounding, trouble breathing, or sweating) when something reminded you of a stressful experience from the past?

6. How often have you avoided thinking about or talking about a stressful experience from the past or avoided having feelings related to it?

7. How often have you avoided activities or situations because they remind you of a stressful experience from the past?

8. How often have you had trouble remembering important parts of a stressful experience from the past?

9. How often did you experience loss of interest in things that you used to enjoy?

10. How often have you felt distant or cut off from other people?

11. How often have you felt emotionally numb or unable to have loving feelings for those close to you?

12. How often have you felt as if your future will somehow be cut short?

13. How often have you had trouble falling or staying asleep?

14. How often have you felt irritable or had angry outbursts?

15. How often have you had difficulty concentrating?

16. How often have you experienced being "super alert" or watchful on guard?

17. How often have you felt jumpy or easily startled?

Traumatic Experiences

The following questions are about experiences you may have had over the course of your life, not just during military service.

How often have you experienced any of the following?

1	2	3	4
Never	Once	A few times	Many times

1. (How often have you experienced) a serious accident, fire, or explosion: for example, an industrial, farm, car, or boating accident?

2. (How often have you experienced) a natural disaster: for example, a tornado, hurricane, flood, or major earthquake?

3. (How often have you experienced) non-sexual assault: for example, being mugged, physically attacked, shot, stabbed or held at gunpoint?

4. (How often have you experienced) imprisonment (for example, being held hostage) ?

5. (How often have you experienced) a life-threatening illness?

6. (How often have you) witnessed someone being seriously injured?

7. (How often have you) witnessed someone being killed?

8. (How often have you) seen a dead body or human remains?

9. (How often have you) experienced the sudden death of a close friend or relative? READ RESPONSES AS NEEDED

10. (How often have you) cared for wounded soldiers?

11. (How often have you) been exposed to the sight, sound or smell of someone dying?

The following questions are about experiences you may have had while deployed to Iraq or Afghanistan. Since 2001, how many times have you experienced the following during deployment?

12. Receiving incoming artillery, rocket or mortar fire?

13. (Since 2001, how many times have you …) engaged in direct combat where you discharged your weapon?

14. (Since 2001, how many times have you…) been responsible for the death of an enemy combatant?

15. (Since 2001, how many times have you …) seen a dead body or human remains?

16. (Since 2001, how many times have you …) seen ill or injured civilians you were unable to help?

17. (Since 2001, how many times have you…) been wounded or injured?

18. (Since 2001, how many times have you…) cleared or searched homes or buildings?

19. (Since 2001, how many times have you…) had an improvised explosive device (IED) or booby trap explode near you?

20. (Since 2001, how many times have you …) felt that you were in great danger of being killed?

21. (Since 2001, how many times have you…) Interacted with enemy soldiers who were taken as prisoners of war?

22. (Since 2001, how many times have you…) been responsible for body searches checking for hidden weapons or explosives?

23. (Since 2001, how many times have you …) been left by members of your unit during a mission?

24. (Since 2001, how many times have you …) observed children being run over by vehicles?

25. During your lifetime, has anyone, male or female, using force or threat of harm, ever attempted to sexually assault you? By attempted sexual assault, I mean that an attempt was made but penetration did not occur.
1. yes 2. no

26. During your lifetime, has a man or boy, using force or threat of harm, ever made you have sex by putting his penis in your vagina; or has a male or female put their tongue, fingers or objects in your vagina or anus?
1. yes 2. no

27. Have you experienced any other traumatic event in military or civilian life, that we have not asked about?
1.yes 2. no

Millenium Cohort Study
(Selected health behavior and disease items)

1. What is your **current** marital status? Choose the single best answer.
    a. Single, never married
    b. Now married
    c. Separated
    d. Divorced
    e. Widowed

2. What is the highest level of education that you have completed?
    a. Less than high school completion / diploma
    b. High school degree / GED/ or equivalent
    c. Some college, no degree
    d. Associate's degree
    e. Bachelor's degree
    f. Master's, doctorate, or professional degree

3. Over the past month, how many hours of sleep did you get in an average 24-hour period?
    a. _____ hours per day

4. In a typical week, now many drinks did you have? _____

5. When smoking, how many packs per day did you or do you smoke?
    a. Less than half a pack a day
    b. Half to 1 pack per day
    c. 1 to 2 packs per day
    d. More than 2 packs per day

In the last 3 years, has your doctor or other health professional told you that you have any of the following?

1. Hypertension (high blood pressure)
2. Coronary heart disease
3. Had a heart attack
4. Angina (chest pain)
5. Any other heart condition
6. Fibromyalgia
7. Rheumatoid arthritis
8. Lupus
9. Crohn's disease
10. Ulcerative colitis
11. Chronic fatigue syndrome

Medical Outcomes Study Short Form-12 (SF-12)

These next questions are about your health now and your current daily activities.

1. In general would you say that your health is:

   READ RESPONSES
   1. Excellent
   2. Very good
   3. Good-fair
   4. Poor

Now I am going to read a list of activities that you might do during a typical day.

2. First I want to ask you about moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf.
   Does your health now:

   READ RESPONSES
   1. limit you a lot
   2. (limit you)a little
   3. not (limit you) at all

3. When climbing several flights of stairs, does your health now:

   READ RESPONSES AS NECESSARY
   1. limit you a lot
   2. (limit you) a little
   3. not (limit you) at all

4. During the past four weeks, have you accomplished less than you would like as a result of your physical health?

   1. Yes 2. No

5. (During the past four weeks,) were you limited in the kind of work or other regular daily activities you do as a result of your physical health?

   1. Yes 2. No

6. (During the past four weeks,) have you accomplished less than you would like as a result of any emotional problems, such as feeling depressed or anxious?

   1. Yes 2. No

7. (During the past four weeks,) did you not do work or other regular daily activities as carefully as usual as a result of any emotional problems, such as feeling depressed or anxious?

   1. Yes 2. No

8. (During the past four weeks,) how much did pain interfere with your normal work, including both work outside the home and housework? Has it interfered:

   READ RESPONSES
   1. not at all
   2. slightly
   3. moderately
   4. quite a bit
   5. extremely

9. (During the past four weeks,) how much of the time has your physical health or emotional problems interfered with your social activities like visiting with friends or relatives. Has it interfered:

   READ RESPONSES
   1. all of the time
   2. most of the time
   3. some of the time
   4. a little of the time
   5. none of the time

10. (During the past four weeks,) How much of the time have you felt calm and peaceful?

    READ WHEN NECESSARY
    1. All of the time
    2. Most of the time
    3. A good bit of the time
    4. Some of the time
    5. A little of the time
    6. None of the time

11. (During the past four weeks,) How much of the time did you have a lot of energy?

    READ WHEN NECESSARY
    1. All of the time
    2. Most of the time
    3. A good bit of the time
    4. Some of the time
    5. A little of the time
    6. None of the time

12. (During the past four weeks,) How much of the time have you felt downhearted and blue?

    READ WHEN NECESSARY
    1. All of the time
    2. Most of the time
    3. A good bit of the time
    4. Some of the time
    5. A little of the time
    6. None of the time

Childhood Trauma Questionnaire

Now I am going to read you some statements about experiences that children may have when they are growing up. Please tell me how accurately they describe your childhood experiences.

1	2	3	4	5
Never true	Rarely true	Sometimes true	Often true	Very often true

1. When I was growing up, I felt like there was someone in my family who wanted me to be a success.

2. (When I was growing up), my family was a source of strength and support.

3. (When I was growing up), people in my family hit me so hard that it left me with bruises or marks.

4. (When I was growing up), someone tried to make me watch sexual things.

5. (When I was growing up), I lived in a group or foster home.

6. (When I was growing up), I knew that there was someone to take care of me and protect me.

7. (When I was growing up), I felt like there was someone who believed I had what it takes to succeed in a job or career.

Patient Health Questionnaire-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?

1	2	3	4
Not at all	Several days	More than half the days	Nearly everyday

1. Little interest or pleasure in doing things.
2. Feeling down, depressed, or hopeless
3. Trouble falling or staying asleep, or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down
7. Trouble concentrating on things, such as reading the newspaper or watching television
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual