

CHAPTER e48

Neuropsychiatric Illnesses in War Veterans

Charles W. Hoge

Neuropsychiatric sequelae are common in combat veterans. Advances in personal protective body armor, armored vehicles, battlefield resuscitation, and the speed of evacuation to tertiary care have considerably improved the survivability of battlefield injuries, resulting in a greater awareness of the “silent wounds” associated with service in a combat zone. Although psychiatric and neurologic problems have been well documented in veterans of prior wars, the conflicts in Iraq and Afghanistan have been unique in terms of the level of commitment by the U.S. Department of Defense (DoD) and Department of Veterans Affairs (VA), Veterans Health Administration (VHA) to support research as the wars have unfolded, and to utilize that knowledge to guide population-level screening, evaluation, and treatment initiatives.

These conflicts, like previous ones, have produced hundreds of thousands of combat veterans, many of whom have received or will need care in government and civilian medical facilities. Studies have shown that service in the Iraq and Afghanistan theaters is associated with significantly elevated rates of mental disorders. Two conditions in particular have been labeled the signature injuries related to these wars: posttraumatic stress disorder (PTSD) and mild traumatic brain injury (mTBI)—also known as concussion. Although particular emphasis will be given in this chapter to PTSD and concussion/mTBI, it is important to understand that service in all wars is associated with a number of health concerns that coexist and overlap, and a multidisciplinary patient-centered approach to care is necessary.

EPIDEMIOLOGY OF WAR-RELATED PSYCHOLOGICAL AND NEUROLOGIC CONDITIONS

Service members from the current decade of war have faced multiple deployments to two very different high-intensity combat theaters, and the cumulative strain has negatively impacted marriages, parenting, educational goals, and civilian occupations. The stresses of service in these conflicts have led to a significant increase in the rate of suicide in personnel from the two branches of service involved in the greatest level of ground combat (army, marines).

Service in a war-zone can involve extreme physical stress in austere environments, prolonged sleep deprivation, physical injury, exposure to highly life-threatening events and hazards such as explosive devices, sniper fire, ambushes, indirect fire from rockets and mortars, and chemical pollutants. Certain events such as loss of a close friend in combat, leave indelible scars. All of these experiences have additive effects on health, likely mediated through physiologic mechanisms involving dysregulation of neuroendocrine and autonomic nervous system (ANS) functions.

Veterans of virtually all wars have reported elevated rates of generalized and multisystem physical, cognitive, and psychological health concerns that often become the focus of treatment months or years after returning home. These multisystem health concerns include sleep disturbance, memory and concentration problems, headaches, musculoskeletal pain, gastrointestinal

symptoms (including gastroesophageal reflux), residual effects of war-time injuries, fatigue, anger, hyperarousal symptoms, high blood pressure, rapid heart rate (sometimes associated with panic symptoms), sexual problems, and symptoms associated with PTSD and depression. In order to provide optimal care to veterans with these symptoms, it is important to understand how the symptoms interrelate, and to consider the possibility that there may be underlying combat-related physiologic effects.

POSTWAR SYMPTOMS

The overlapping and multisystem health symptoms reported by warriors from every generation have been given different labels, and have led to debates among medical professionals as to whether these are mediated primarily by physical or psychological causes. For example, World War I produced extensive debate about whether “shell shock,” diagnosed in more than 80,000 British soldiers, was neurologic (“commotional” from the brain being shaken in the skull by concussive blasts) or psychological (“emotional” or “neurasthenia”) in origin. World War II veterans were said to suffer from “battle fatigue,” Korean war veterans developed “combat stress reactions,” and Vietnam veterans developed the “post-Vietnam syndrome.” The role of environmental exposure (e.g., agent orange) and psychological causes (alcohol addiction, drug addiction, and PTSD) continue to be debated.

Gulf War I led to extensive debates as to whether Gulf War syndrome, also known as multisystem illness, was best explained by environmental exposures (e.g., oil fires, depleted uranium, nerve gas, multiple vaccinations) or the psychological stress of deployment to a war zone where there was anticipation of high casualty rates from chemical and biologic weapons and stressful training exercises involving the use of impermeable full-body protective uniforms (made from rubber, vinyl, charcoal impregnated polyurethane, and other materials) in desert conditions under extreme temperatures. Although no clinical syndrome was ever definitively confirmed among the nearly 1 million service members who deployed in 1990–1991, studies consistently found that military personnel who served in the Gulf experienced elevations in generalized symptoms across all health domains (e.g. physical, cognitive, neurologic, psychological) compared with service members who deployed elsewhere or did not deploy. In addition, there is good evidence that deployment to the Persian Gulf region during this period was associated with subsequent development of PTSD; other psychiatric disorders including generalized anxiety disorder, depression, and substance abuse, particularly alcohol abuse (Chap. 392); functional gastrointestinal symptoms such as irritable bowel syndrome (Chap. 296); and chronic fatigue syndrome (Chap. 389).

The conflicts in Iraq and Afghanistan have led to similar debates as to whether postwar symptoms such as headaches, irritability, sleep disturbance, dizziness, and concentration problems are best attributed to concussion/mTBI or to PTSD. Several studies have shown that either PTSD or depression explains the majority of the postdeployment “postconcussive” symptoms attributed to concussion/mTBI, a finding not well received by some experts in traumatic brain injury (TBI) but consistent with civilian studies on risk factors for developing persistent symptoms after concussion. As in past wars, it has taken years to understand how PTSD and concussion/mTBI interrelate with other deployment-related health concerns, and the implications for designing effective evaluation and treatment strategies.

Veterans understandably may become angry at the suggestion that their postwar health concerns are stress-related or psychological, and thus it is necessary for primary care professionals to be sensitive to this concern.

■ PTSD

PTSD is the most common mental disorder documented following war-zone service. Studies from the conflicts in Iraq and Afghanistan have found PTSD prevalence rates of 2–6% before deployment (comparable to civilian general population samples) and rates of 6–20% postdeployment, depending primarily on the level of combat frequency and intensity. Many other veterans experience subclinical PTSD symptoms after war-zone service, sometimes termed post-traumatic stress (PTS) or combat stress. These subclinical symptoms can contribute to distress and affect health, even if overall functioning is not as impaired as in the full disorder.

PTSD is defined by the American Psychiatric Association as persistent (>1 month) symptoms occurring after a life-threatening traumatic event in which there was an immediate response of fear, helplessness, or horror. The symptoms must be associated with significant distress or impairment in social or occupational functioning. Symptoms are grouped into three categories: (1) re-experiencing symptoms in which the person has nightmares, flashbacks, or intrusive thoughts and memories connected with the traumatic event; (2) hyperarousal symptoms in which the person is physiologically revved up, hyperalert, startles easily, and experiences sleep disturbance, anger, and/or concentration problems; and (3) avoidance symptoms where the person loses interest in things that previously brought enjoyment, and avoids places, situations, or other stimuli that serve as reminders of the traumatic event (for example a crowded mall that triggers heightened alertness to threat). Additional symptoms, currently categorized with the avoidance cluster, but which will likely become a fourth category in future definitions of PTSD, include emotional numbing, feeling distant or cutoff from others, and a foreshortened sense of future (**Chap. 391**). While PTSD is a clinical symptom-based case definition, it is best to think of PTSD not as an emotional or psychological/psychiatric condition, but rather as a physiologic-based response to life-threatening trauma that is associated with physical, cognitive, emotional, and psychological symptoms.

PTSD has strong biologic correlates, based in fear-conditioning responses to threat and responses to extreme stress involving neuroendocrine dysregulation and ANS reactivity. Numerous studies have shown that PTSD is highly correlated with generalized physical and cognitive symptoms—including hypertension, chronic pain, and cardiovascular disease—as well as cell-mediated immune dysfunction and shortened life expectancy. PTSD is frequently comorbid with other mental disorders such as major depressive disorder, generalized anxiety, substance use disorders (SUDs), as well as risky behaviors (e.g., aggression, accidents); it has been estimated that up to 80% of patients with PTSD exhibit one or more comorbid conditions. Misuse of alcohol or substances is most prevalent, often reflecting self-medication. PTSD is also associated with tolerance and withdrawal symptoms related to prescription pain and sleep medications; as well as nicotine dependence (**Chap. 395**).

Clinicians should understand the limitations of the definition of PTSD when applied to responses to trauma occurring in the occupational context of military service (similar to police, firefighters, and other first responders). Service members are trained to respond to traumatic events, and relatively rarely report fear, helplessness, or horror, which are characteristic responses of civilian victims of trauma. In addition, the reactions that are labeled as symptoms of PTSD are based on the adaptive survival responses of warriors in a combat environment. For example, physiologic hyperarousal, use of anger, and being able to shut down other emotions are very useful skills in combat, and can be present prior to traumatic events when there is tough realistic training. These responses only become symptoms when they impair functioning after warriors return home.

■ CONCUSSION/MTBI

TBI (**Chap. 378**) gained increased recognition during the conflicts in Iraq and Afghanistan because of the widespread exposure of troops to improvised explosive devices. Contributing to heightened concern were high prevalence estimates of deployment-related TBI that did not distinguish concussion/mTBI from moderate or severe TBI; data from animal models of blast suggesting that explosions may cause a different kind of concussion associated with inflammatory changes; and speculation that repetitive blast exposure may lead to future dementia, based on case series of professional athletes (e.g., boxers, football players) exposed to highly repetitive injuries linked to chronic traumatic encephalopathy (previously termed *dementia pugilistica*). Many veterans of Iraq and Afghanistan reported experiencing multiple concussions during deployments, and many also reported ignoring concussions and not seeking treatment at the time of injury.

TBI includes closed and penetrating head injuries; closed head injuries are categorized as mild (mTBI or concussion), moderate, or severe based on the duration of loss of consciousness, duration of post-traumatic amnesia, and the Glasgow coma score (GCS) (**Table 378-2**). Several studies have estimated that 10–20% of all military personnel deployed to Iraq or Afghanistan sustained one or more concussion/mTBI events during deployment, most commonly from exposure to blasts.

Although there is a neurophysiologic continuum of injury, there are stark clinical and epidemiologic distinctions between concussion/mTBI and moderate or severe TBI (**Table e48-1**). Concussion/mTBI is defined as a blow or jolt to the head that results in brief loss of consciousness (LOC) for <30 minutes (most commonly only a few seconds to minutes), posttraumatic amnesia (PTA) of <24 hours (most commonly <1 hour), or transient alteration in consciousness (AOC) without loss of consciousness. The majority of concussions in Iraq or Afghanistan have involved AOC without LOC or PTA (which soldiers may refer to as getting their “bell rung”). GCSs are usually normal (15 out of 15). Concussion is treated with rest to allow the brain time to heal, and almost never results in air-evacuation from the battlefield unless there are other injuries.

In contrast, moderate, severe, or penetrating TBI, which account for <1% of all battlefield head injuries in Iraq and Afghanistan, are characterized by LOC \geq 30 minutes (up to permanent coma), PTA \geq 24 hours (also may be permanent), and GCSs as low as 3 (the minimum value). These virtually always result in air-evacuation from the battlefield and can result in severe long-term neurologic impairment and requirement for rehabilitative care.

Symptoms following concussion/mTBI can include headache; fatigue; concentration, memory, or attention problems; sleep disturbance; irritability; balance difficulties; and tinnitus, among other symptoms. Recovery is usually rapid, with symptoms usually resolving in a few hours to days, but in a small percentage of patients' symptoms may persist for a longer period or become chronic (referred to as persistent “postconcussive symptoms” or “PCS”).

Establishing a clear causal connection between a deployment concussion injury and persistent PCS months or years after return from deployment is difficult and often confounded by other post-war conditions that cause similar symptoms, including injuries not involving the head, other medical disorders, sleep disorders, PTSD, depression, substance use disorders, chronic pain, and the general physiologic effects of wartime service. Contributing to the difficulty in establishing causation is the fact that the concussion/mTBI case definition refers only to the acute injury event and lacks symptoms, time-course or impairment; case definitions for persistent postconcussion syndrome are not well validated. Several studies found that PTSD was a much stronger predictor of postdeployment PCS after

TABLE e48-1 Comparison Between Concussion/mTBI and Moderate/Severe TBI

	Mild TBI (concussion)	Mod/Severe TBI
Clinical case definition		
Loss of consciousness	<30 min (usually few seconds to minutes)	≥30 min to indefinite
Altered consciousness	<24 h (usually <30 min)	≥24 h to indefinite
Posttraumatic amnesia	<24 h (usually <30 min)	≥24 h to indefinite
Glasgow Coma Score	13–15 (usually 15)	As low as 3
Focal neurologic signs	None or transient	Frequently present
Traditional neuroimaging (CT/MRI)	Usually negative	Diagnostic
Clinical usefulness of neurocognitive testing after acute injury period	Usually inconclusive	Essential and valuable
Neuronal cell damage	Metabolic/ionic processes associated with axonal swelling, which can lead to disconnection	Direct injury effects plus metabolic/ionic effects
Sequelae, natural history, and recovery	Full recovery expected in majority of individuals; No consensus on natural history; the percent who develop persistent symptoms is debated	Based directly on injury characteristics; may be severely disabling
Predictors of persistent postconcussive symptoms or disability	Intensely debated Risk factors found to be most predictive include psychiatric conditions (e.g., depression, PTSD) and negative expectations	Not debated, predictors are directly related to injury severity and clinical progress with rehabilitation treatment

combat deployment than concussions/mTBIs, and one study even found that objective neuropsychological impairment after deployment was entirely explained by PTSD. These data do not minimize the importance of concussion/mTBI, but highlight the complex interrelationships of war-related health problems.

Studies of veterans who sustained concussions in Iraq or Afghanistan have suggested that blast mechanisms produce similar clinical outcomes as nonblast mechanisms, in contrast to expectations based on animal models. An explosion can produce serious injury from rapid atmospheric pressure changes (primary blast wave mechanism), as well as from flying debris (secondary blast mechanism) or by being thrown into a hard object (tertiary blast mechanism). Secondary and tertiary mechanisms are similar to other mechanical mechanisms of concussions sustained during accidents. The possibility of a unique head injury from the primary blast wave in otherwise uninjured soldiers appears to be low, but cannot be discounted.

Multisystem health problems that lack clear case definitions do not lend themselves well to uniform public health strategies such as screening. Nevertheless, mass population screening for concussion/mTBI was mandated for all U.S. service members returning from Iraq or Afghanistan and all veterans presenting for care at VA health care facilities. These screening processes, which attempt to apply the acute concussion case definition (lacking symptoms, time-course, or impairment) months or years after injury, led to sharp criticism that they were encouraging clinicians to misattribute common postwar symptoms to concussion/mTBI.

Management is largely symptom-focused, and ideally carried out within primary-care based structures of care. Optimal care avoids unnecessary specialty referrals, use of nonevidence-based interventions, or poor communication that results in negative expectations. Concussion research has shown that negative expectations are one of the most important risk factors for persistent symptoms.

While many questions remain regarding the long-term health effects of concussions (particularly multiple concussions) sustained during deployment, these are important battlefield injuries that

require careful attention. However, they need to be addressed within the context of all other war-related health concerns.

STIGMA AND BARRIERS TO CARE

Adding to the complexity of treating veterans is stigma and other barriers to care. Despite extensive education efforts among military leaders and service members, perceptions of stigma have shown little change over the many years of war; warriors are concerned that they will be perceived as weak by peers or leaders if they seek care. Studies showed that less than one-half of service members with serious mental health problems receive needed care. Many factors contribute to this, including the pervasive nature of stigma in society in general (particularly among men), the critical importance of group cohesiveness of military teams, the nature of avoidance symptoms in PTSD, and sometimes skepticism that mental health professionals will be able to help.

APPROACH TO THE PATIENT

Evaluation of Veterans with Neuropsychiatric Health Concerns

Evaluation should begin with a careful occupational history as part of the routine medical evaluation; this includes the number of years served, military occupation, deployment locations and dates, illnesses or injuries resulting from service, and significant combat traumatic experiences that may be continuing to affect the individual (Table e48-2). The clinician should evaluate the degree to which the patient's current difficulties reflect the normal course of readjusting after the intense occupational experience of combat. It is helpful to reinforce the many strengths associated with being a professional in the military: courage, honor, service to country, resiliency in combat, leadership, ability to work as cohesive workgroup with peers, and demonstrated skills in handling extreme stress.

One of the challenges with current medical practice is that there may be multiple providers with different clinical perspectives. Care should be coordinated through the primary care clinician, with the

TABLE e48-2 Specific Considerations in the Medical Evaluation of Veterans

Occupational context of health concerns	Deployment locations and dates, combat experiences or other deployment stressors, frequent moves, separations from family, impact of deployment on civilian occupation (for reservists)
Medical problems during deployment	History of deployment-related injuries (including concussions), environmental exposures, sleep pattern during deployment, use of caffeine/energy drinks, use of other substances
Current medical history	Current symptoms, level of chronic pain, sleep problems, evidence of persistent physiologic hyperarousal (hypertension, tachycardia, panic symptoms, concentration/memory problems, irritability/anger, sleep disturbance), chronic use of caffeine or energy drinks, chronic use of nonsteroidal anti-inflammatory medications, chronic use of narcotic pain medications, chronic use of nonbenzodiazepine sedative-hypnotic medications, chronic use of benzodiazepines for sleep or anxiety.
Mental health assessment	Screen for PTSD, major depressive disorder. Ask about suicidal or homicidal ideation, intent, or plans, as well as access to firearms
Alcohol/substance use	Screen for alcohol and substance use disorders, quantity and frequency of use and evidence of tolerance. Inquire about “self-medication” (e.g., use of alcohol for sleep, “calm down,” or “forget” war-zone experiences)
Functional impairment	Impact of current symptoms on social and occupational functioning. High-risk behaviors (e.g., drinking and driving, reckless driving, aggression)
Social support, impact of military service on marriage and family	Level of social support. Readjustment stress on spouse, children, or other family members.

assistance of a care manager if needed. It is particularly important to continually evaluate all medications prescribed by other practitioners and assess for possible long-term side effects, dependency, or drug-drug interactions. Particular attention should be given to the level of chronic pain and sleep disturbance, self-medication with alcohol or substances, chronic use of nonsteroidal anti-inflammatory agents (which can contribute to rebound headaches or pain), chronic use of sedative-hypnotic agents, chronic use of narcotic pain medications, and the impact of war-related health concerns on social and occupational functioning.

Screening for PTSD, depression, and alcohol misuse should be performed routinely in all combat veterans. Three screening tools, which are in the public domain, have been validated for use in primary care, and have been used frequently in veterans: the four-question Primary Care PTSD Screen (PC-PTSD), the two-question Patient Health Questionnaire (PHQ-2), and the three-question Alcohol Use Disorders Identification Test-Consumption module (AUDIT-C) (Table e48-3).

Since the clinical definition of an acute concussion/mTBI does not include symptoms, time-course, or impairment, there is currently no clinically validated screening process for use months or years after injury. However, it is important to gather information about all injuries sustained during deployment, including any that resulted in loss or alteration of consciousness or loss of memory around the time of the event. If concussion injuries have occurred, the clinician should assess the number of such injuries, the duration of time unconscious, and injury mechanisms. This should be followed by an assessment of any postconcussive symptoms immediately following the injury event (e.g., headaches, dizziness, tinnitus, nausea, irritability, insomnia, and concentration or memory problems), and the severity and duration of such symptoms.

TREATMENT**Neuropsychiatric Illnesses in War Veterans**

Given the interrelationship of postwar health concerns, care needs to be carefully coordinated. Specific techniques that have

been found to be helpful include scheduling regular primary care visits instead of as needed visits, establishing care management, utilizing good risk-communication principles, establishing a consultative step care approach that draws on the expertise of specialists in a collaborative manner (instead of immediately referring the patient to a specialist and relying on the specialist to provide care), and having behavioral health support directly within primary care clinics (both for referrals and to provide education and support to primary care professionals prescribing treatment for depression or PTSD).

It is important not to implicitly or explicitly convey the message that physical or cognitive symptoms are psychological or due to stress. Even if depression or anxiety plays a large role in the etiology of physical health symptoms, the treatment approach should be designed within a patient-centered primary care structure, and referrals managed from within this framework. For example, it might help to explain that the primary goal of referral to a mental health professional is to improve sleep and reduce physiologic hyperarousal, which in turn will help with treatment of war-related chronic headaches, concentration problems, or chronic fatigue. If however, the primary care professional conveys the message that the cause of headaches or concentration problems is anxiety or depression, and this conflicts with the patient’s own viewpoint, then this could damage therapeutic rapport and in turn exacerbate the symptoms.

Specific questions related to military service (Table e48-2) combined with screening for depression, PTSD, and alcohol use disorders (Table e48-3) should be a routine part of care for all veterans. A positive screen for depression or PTSD should prompt follow-up questions related to these disorders [or use of a longer screening tool such as the (PHQ-9) or National Center for PTSD Checklist], as well as risk assessment for suicide or homicide. It is important to assess the impact of depression or PTSD symptoms on occupational functioning and interpersonal relationships.

A positive screen for alcohol misuse should prompt a brief motivational intervention that includes bringing attention to the elevated level of drinking, informing the veteran about the effects of alcohol on health, recommending limiting use or abstaining, exploring and setting goals related to drinking behavior, and follow-up and referral to specialty care if needed. This type of

TABLE e48-3 Primary Care Mental Health Screening Tools

PC-PTSD Screen		
1. Have you ever had any experience that was so frightening, horrible, or upsetting that, in the past month, you:		
Have had nightmares about it or thought about it when you did not want to?	Yes	No
Tried hard not to think about it or went out of your way to avoid situations that remind you of it?	Yes	No
Were constantly on guard, watchful, or easily startled?	Yes	No
Felt numb or detached from others, activities, or your surroundings?	Yes	No

Note: Two or more “yes” responses (three or more a more specific cutoff) is considered a positive screen.

Source: A Prins et al: The Primary Care PTSD Screen (PC-PTSD): Development and operating characteristics. *Prim Care Psychiatr* 9:9, 2004.

PHQ-2 Depression Screen

2. Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all (0)	Few or several days (1)	More than half the days (2)	Nearly every day (3)
Little interest or pleasure in doing things.	0	1	2	3
Feeling down, depressed, or hopeless.	0	1	2	3

Note: If either (or both) questions are marked 2 or 3 (“more than half the days or higher), this is considered a positive screen for depression.

Source: K Kroenke et al: The Patient Health Questionnaire-2: Validity of a two-item depression screener. *Med Care* 41:1284, 2003.

AUDIT-C Alcohol Screen

3a. How often do you have a drink containing alcohol?

Never (0) Monthly or less (1) Two or four times a month (2) Two to three times per week (3) Four or more times a week (4)

3b. How many drinks containing alcohol do you have on a typical day when you are drinking?

1 or 2 (0) 3 or 4 (1) 5 or 6 (2) 7 or 9 (3) 10 or more (4)

3c. How often do you have six or more drinks on one occasion?

Never (0) Less than Monthly (1) Monthly (2) Two to three times per week (3) Four or more times a week (4)

Note: A positive AUDIT-C screen is defined as a total score for men ≥ 4 ; for women ≥ 3 . A report of drinking 6 or more drinks on one occasion should prompt an in-depth assessment of drinking.

Source: K Bush et al: The AUDIT Alcohol Consumption Questions (AUDIT-C): An effective brief screening test for problem drinking. *Arch Intern Med* 158:1789, 1998.

brief primary care intervention has been found to be effective, and should be incorporated into routine practice. One way to facilitate dialogue about this topic with veterans is to point out how hyperarousal associated with combat service can lead to increased craving for alcohol as the body searches for ways to modulate this. Veterans may consciously or unconsciously drink more to help with sleep, reduce arousal, or avoid thinking about events that happened “downrange.” A key educational strategy is to help the veteran to learn that drinking to get to sleep actually damages sleep architecture and makes sleep worse [e.g., reduces rapid eye movement (REM) sleep initially followed by rebound REM activity and early morning wakening].

SPECIFIC TREATMENT STRATEGIES FOR PTSD AND COMORBID DEPRESSION

PTSD and depression are highly comorbid in combat veterans and the evidence-based treatments are similar, involving either antidepressant medications, cognitive behavioral therapy (CBT), or both. Psychoeducation that assists veterans to understand that their symptoms of PTSD have a basis in adaptive survival mechanisms and skills they exhibited in combat can facilitate therapeutic rapport. Remaining hyper-vigilant to threat, being able to shut down emotions, being able to function on less sleep, and using anger to help focus and control fear are all adaptive beneficial survival skills in a

combat environment. Therefore, PTSD for warriors is both a medical disorder and a set of reactions that have their roots in the physiologic adaptation and skills they successfully applied in combat.

It is important to know that combat is not the only important trauma in a war-zone environment. Rape, assault, and accidents also occur. Rape or assault by a fellow service member, which affects a greater number of women veterans, can be particularly devastating because it destroys the vital feeling of safety that individuals derive from their own unit peers in a war environment.

The treatments for PTSD considered by most consensus guideline committees to have an A level of evidence include CBTs and medications, specifically selective serotonin reuptake inhibitors (SSRIs) (of which paroxetine and sertraline received FDA approval for PTSD). Although lacking a specific FDA indication, there is increasing evidence that serotonin norepinephrine reuptake inhibitors (SNRIs) (e.g., venlafaxine and duloxetine) and mirtazapine are also effective. (See Table 391-3 for recommended dosages.)

CBT interventions include narrative therapy (often called “imaginal exposure”), in vivo exposure focused on retraining the body not to react to stimuli related to traumatic reminders (e.g., a crowded mall), and techniques to modulate physiologic

hyperarousal (e.g., diaphragmatic breathing, progressive muscle relaxation). A number of complementary alternative medicine approaches including acupuncture, mindfulness meditation, yoga, and massage are also being tested in PTSD. Although not evidence-based treatments per se, if they facilitate a relaxation response and alleviation of hyperarousal symptoms, they can be considered useful adjunctive modalities.

There have been no head-to-head comparisons of medication compared with psychotherapy for treatment of PTSD. It is reasonable for primary care clinicians to consider initiating treatment for mild to moderate PTSD symptoms with an SSRI, and refer patients to a mental health professional if there are more severe symptoms, significant comorbidity, safety concerns, or limited response to initial treatment. All PTSD treatments are associated with a sizable proportion of individuals who fail to respond adequately, and it is often necessary to add modalities or switch treatment. SNRIs may be useful alternatives to SSRIs if there has been nonresponse, side effects, or if there is comorbid pain (duloxetine, in particular, has indications for pain). Both SSRIs and SNRIs can increase anxiety initially; patients should be warned about this possibility and treatment should be initiated with the lowest recommended dose (or even one-half of the lowest dose for a few days) and gradually increased thereafter. Mirtazapine use can cause drowsiness and weight gain. Antidepressants also are likely to be useful in comorbid depression, which is common in veterans with PTSD. All antidepressants have potential drug-drug interactions that must be considered.

Many other medications have been used in PTSD, including tricyclic antidepressants, benzodiazepines, atypical antipsychotics, and anticonvulsants. In general, these should be prescribed in conjunction with psychiatric consultation, because of their greater side effects and risks. Benzodiazepines, in particular, should be avoided in combat veterans. Studies have shown that they do not reduce core PTSD symptoms, are likely to exacerbate substance use disorders that are common in veterans with PTSD, and may produce significant rebound anxiety. Veterans with PTSD often report symptomatic relief upon initiation of a benzodiazepine, but this is generally short lived and associated with a high risk of tolerance and dependence that can worsen recovery. Atypical antipsychotics, which have gained widespread popularity as adjunctive treatment for depression, anxiety, or sleep problems, have significant long-term side effects, including metabolic effects (e.g., glucose dysregulation), weight gain, and cardiovascular risks.

Sleep disturbance should be addressed initially with sleep hygiene education, followed by consideration of an antihistamine, trazodone, or non-benzodiazepine sedative-hypnotic such as zolpidem, eszopiclone, or zaleplon. However, the non-benzodiazepine sedative-hypnotics should be used with caution in veterans as they can lead to tolerance and rebound sleep problems similar to those seen with benzodiazepine use.

TREATMENT STRATEGIES FOR CONCUSSION/MTBI AND POST-DEPLOYMENT POSTCONCUSSIVE SYMPTOMS

Concussion/mTBI is best treated at the time of injury with education and rest to allow time for the brain to heal and protect against a second impact syndrome (a rare but life-threatening event involving brain swelling that can occur when a second concussion occurs before the brain has adequately healed from an initial event). Randomized trials have shown that education regarding concussion that informs the patient of what to expect and promotes the expectation of recovery is the most effective treatment in preventing persistent symptoms.

Once service members return from deployment and seek care for postwar health problems, treatment is largely symptom focused, following the principles of patient-centered and collaborative care models. Cognitive rehabilitation, which is very useful in moderate and severe TBI to improve memory, attention, and concentration, has generally not been shown to be effective for mTBI in randomized clinical studies, though consensus groups have supported its use.

General recommendations for the clinical management of persistent, chronic postconcussive symptoms include treating physical and cognitive health problems based on symptom presentation, coexisting health problems, and individual preferences; and addressing coexisting depression, PTSD, substance use disorders, or other factors that may be contributing to symptom persistence. Headache is the most common symptom associated with concussion/mTBI, and the evaluation and treatment of headache parallels those for other causes of headache (Chap. 14). Stimulant medications for alleviating neurocognitive effects attributed to concussion/mTBI are not recommended. Clinicians should be aware of the potential for cognitive or sedative side effects of certain medications that may be prescribed for depression, anxiety, sleep, or chronic pain.

Treatment of neuropsychiatric problems must be coordinated with care for other war-related health concerns, with the goal of treatment to reduce the severity of symptoms, improve social and occupational functioning, and prevent long-term disability. Understanding the occupational context of war-related health concerns is important in communicating with veterans and developing a comprehensive treatment strategy.

DISCLOSURE

This material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense.

FURTHER READINGS

AIARZAGUENA JM et al: A randomized controlled trial of a psychosocial and communication intervention carried out by GPs for patients with medically unexplained symptoms. *Psychol Med* 37:283, 2007

BELINGER HG et al: Cognitive sequelae of blast-related versus other mechanisms of brain trauma. *J Int Neuropsychol Soc* 15:1, 2009

DEKOSKY ST et al: Traumatic brain injury—football, warfare, and long-term effects. *N Engl J Med* 363:1293, 2010

DEPARTMENT OF DEFENSE: Department of Defense Task Force for the Prevention of Suicide in Members of the Armed Forces. The challenge and the promise: Strengthening the force, preventing suicides, and saving lives. 2010. Available at <http://www.health.mil/dhb/downloads/Suicide%20Prevention%20Task%20Force%20final%20report%208-23-10.pdf>

DEPARTMENT OF VETERANS AFFAIRS, DEPARTMENT OF DEFENSE: Evidence-based clinical practice guideline: Management of concussion/mild traumatic brain injury (mTBI), version 1.0, April 2009. Available at http://www.healthquality.va.gov/mtbi/concussion_mtbi_full_1_0.pdf

—: Clinical practice guideline for management of substance use disorders, version 2.0, August 2009. Available at http://www.healthquality.va.gov/HEALTHQUALITY/sud/sud_full_601f.pdf

—: Clinical practice working group. Management of post-traumatic stress. Washington, DC, Department of Veterans Affairs, Department of Defense, 2010 publication 10O-CPG/

- FTSD-04. 2004. Available at http://www.healthquality.va.gov/Post_Traumatic_Stress_Disorder_PTSD.asp
- ENGEL CC et al: Managing future Gulf War syndromes: International lessons and new models of care. *Philos Trans R Soc Lond B Biol Sci* 361(1468):707, 2006
- ESCOBAR JI et al: Effectiveness of a time-limited cognitive behavioral therapy type intervention among primary care patients with medically unexplained symptoms. *Ann Fam Med* 5:328, 2007
- FOA EB et al (eds): *Effective Treatments for PTSD: Practice Guidelines from the International Society for Traumatic Stress Studies*, 2d ed. New York, Guilford Press, 2009
- HOGUE CW: *Once a Warrior—Always a Warrior: Navigating the Transition from Combat to Home, Including Combat Stress, PTSD, and mTBI*. Guilford, CT, Globe Pequot Press, 2010
- et al: Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med* 351:13, 2004
- et al: Association of posttraumatic stress disorder with somatic symptoms, health care visits, and absenteeism among Iraq War veterans. *Am J Psychiatry* 164:150, 2007
- et al: Mild traumatic brain injury in U.S. soldiers returning from Iraq. *N Engl J Med* 358:453, 2008
- et al. Care of veterans with mild traumatic brain injury: Flawed perspectives. *N Engl J Med* 360:1588, 2009
- HOWE LL: Giving context to post-deployment post-concussive-like symptoms: Blast-related potential mild traumatic brain injury and comorbidities. *Clin Neuropsychol* 23:1315, 2009
- INSTITUTE OF MEDICINE: *Committee on Gulf War and Health. Health Effects of Serving in the Gulf War, Update 2009*. Washington DC, National Academies Press, 2010
- MARX BP et al: Association of time since deployment, combat intensity, and posttraumatic stress symptoms with neuropsychological outcomes following Iraq war deployment. *Arch Gen Psychiatry* 66:996, 2009
- PIETRZAK RH et al: Posttraumatic stress disorder mediates the relationship between mild traumatic brain injury and health and psychosocial functioning in veterans of Operations Enduring Freedom and Iraqi Freedom. *J Nerv Ment Dis* 197:748, 2009
- SCHNEIDERMAN AI et al: Understanding the sequelae of injury mechanisms and mild traumatic brain injury incurred during the conflicts in Iraq and Afghanistan: Persistent postconcussive symptoms and posttraumatic stress disorder. *Am J Epidemiol* 167:1446, 2008
- SMITH RC et al: Primary care clinicians treat patients with medically unexplained symptoms: A randomized controlled trial. *J Gen Intern Med* 21:671, 2006
- THOMAS JL et al: Prevalence of mental health problems and functional impairment among active component and national guard soldiers 3 and 12 months following combat in Iraq. *Arch Gen Psychiatry* 67:614, 2010
- VAN DER FELTZ-CORNELIS CM et al: Randomized controlled trial of a collaborative care model with psychiatric consultation for persistent medically unexplained symptoms in general practice. *Psychother Psychosom* 75:282, 2006
- WILK JE et al: Mild traumatic brain injury (concussion) during combat: Lack of association of blast mechanism with persistent post-concussive symptoms. *J Head Trauma Rehabil* 25:9, 2010