MEDICAL ACUPUNCTURE
Volume 23, Number 4, 2011

DOI: 10.1089/acu.2011.0840

Acupuncture for the Trauma Spectrum Response: Scientific Foundations, Challenges to Implementation

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ABSTRACT

The long wars in Iraq and Afghanistan have produced extensive and often repeated trauma to United States service members and their families. These injuries occur to the mind, the brain, the body and the soul. The current approach to management of these injuries follows the standard medical model that attempts to isolate the pathophysiological locations and processes affected by the injury and provide specialized care for that part of the person—psychological treatment for mind injuries, neurological treatment for brain injuries, and surgical and rehabilitation approaches for body injuries. This model is overwhelmingly dominated by the use of drugs for symptom management. Yet, research has shown that, no matter where an injury is located, its impact and the healing responses to it cut across these boundaries resulting in a common symptomatic and functional spectrum. The authors of this article have called this the war-related trauma spectrum response (wrTSR) and propose a better approach to this spectrum, which is to induce whole-person healing responses not specialized to addressing the injury cause or location. Acupuncture appears to be such an approach. This article reviews the conceptual and scientific foundations of wrTSR, makes the case for managing it in a holistic manner, and reviews the evidence for using acupuncture as a treatment across the trauma response spectrum. This article then discusses the challenges to implementing of acupuncture in the military and veterans' systems and proposes direct comparative effectiveness, health services, and program evaluation approaches to providing the evidence needed to broaden acupuncture's use.

Key Words: Acupuncture, Military, Pain, Trauma Spectrum Response, TBI, PTSD, Depression, Anxiety, Moral Injury, Integrative Medicine

INTRODUCTION

The current wars in Iraq (Operation Iraqi Freedom, OIF) and Afghanistan (Operation Enduring Freedom, OEF) are returning thousands of warfighters with psychological mind injuries, such as post-traumatic stress disorder (PTSD), and physical mind–body injuries such as traumatic brain injury (TBI), many with long-term symptomatic and functional consequences.[1,2] The multicomponent and overlapping nature of injuries in returning warfighters are appropriately considered as war-related, trauma spectrum responses (wrTSR) and may be of a different character and require a different approach than the civilian trauma stress response (TSR). Trauma to the head and neck occurs in 15%–20% of all battle injuries, and mild TBI (mTBI) may afflict up to 28% of all deployed warfighters.[3,4]

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**The opinions and assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the United States Air Force Medical Corps, the Air Force at large, or the Department of Defense. The author indicates that he does not have any conflicts of interest.*

More than 46% of blast patients and 55% of amputees at Walter Reed Army Medical Center (WRAMC) have sustained comorbid brain injuries. Nearly 20% of soldiers returning from the wars in Iraq and Afghanistan suffer from diagnosable post-traumatic stress disorder (PTSD),[5,6] and nearly 40% report stress-related symptoms and dysfunctions that significantly prevent reintegration into a full, productive life. As stated by Potash, the wounded veteran presents the health care system with ''new challenges'' not the least of which is the ''growing number of patients with co-morbid chronic pain…brain trauma and…attendant cognitive issues.''[7]

Triggered by combined mind–brain/body injuries (MBIs), the various manifestations of wrTSR share many common pathophysiological and recovery mechanisms. Evidence supports the potential for the development, expression and durability of certain types of pain and psychopathologies in which genotypic factors could be either latent or code for phenotypes (e.g., of ion channels, neurotransmitters, receptors and synaptic elements) that are differentially expressed from factors from the internal and external environments. In such genotypically predisposed individuals, environmental and/or psychosocial insult can induce a core constellation of common symptoms that includes: (1) psychological and emotional distress (e.g., depression, anxiety, or anger); (2) cognitive impairment; (3) chronic and, often refractory, pain of organic and psychosomatic origins; (4) drug/opioid desensitization (with abuse potential); and (5) somatic (sleep, appetite, sexual, and energy) dysfunction.

Best estimates suggest that multiple comorbidities after exposure to trauma may be present in a substantial percent of wounded military personnel. Villano et al.,[8] and Shipherd and coworkers[9] have shown that psychiatric conditions, such as depression and anxiety, appear to be responsible for the co-occurrence of a syndrome of chronic pain and heightened stress-reactivity, including frank presentation of PTSD, in between 24% and 66% of combat-wounded veterans of OIF/OEF. The impairment of cognitive abilities in patients with chronic pain and PTSD, and the reported incidence and prevalence of chronic pain, PTSD, other neuropsychiatric conditions, and cognitive deficits in wounded OIF/OEF troops has also been described by Beck and colleagues.[10,11] These results are strengthened by the report that more than 60% of these soldiers have been diagnosed with some form of brain-injury condition or apparent constellation of cognitive, emotional, and behavioral features resulting from neural insult.[9] When induced by exposure to deployment and battle, we refer to this constellation of trauma-related manifestations as wrTSRs (Fig. 1).

The current authors hypothesize that the effects of mind–brain injury are approached better by assessing the full spectrum of trauma-related morbidities—rather than dividing them into subcomponents—and then treating the whole person with an approach that enhances the patient's inherent

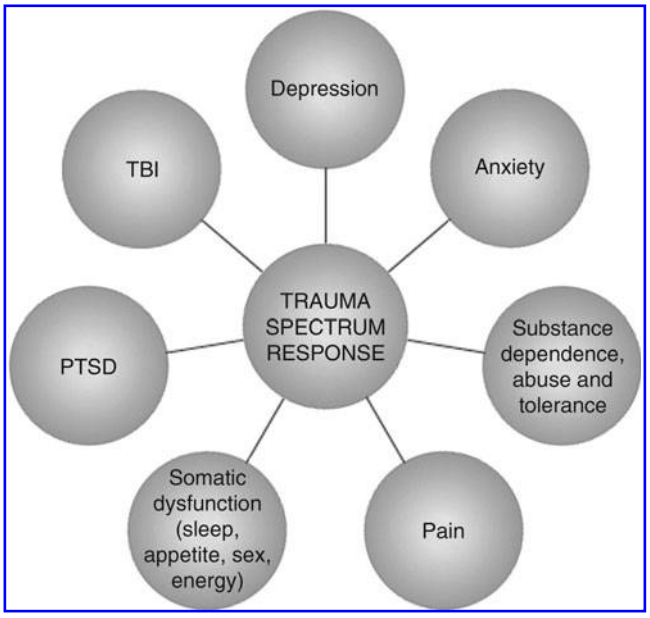

FIG. 1. Trauma spectrum response components. TBI, traumatic brain injury, PTSD, post-traumatic stress disorder.

healing mechanisms and capacities.[12] The current authors hypothesize that this can be done with a standardized acupuncture method. Using this approach, the authors will test the efficacy of acupuncture on Health Related Quality of Life (HRQoL) and wrTSR comorbidities in service members with TBI and PTSD drawn from several Department of Defense (DoD) and Veterans Affairs (VA) sites across the country.

PTSD AND wrTSR

PTSD as a Component of wrTSR

PTSD (from psychological or mind injuries) is a widely recognized consequence of combat trauma and frequently accompanies wrTBI and bodily injury. The PTSD prevalence rate in OIF/OEF active duty, deployed service members is estimated to be between 15.6% and 17.1%.[13] A more-recent study by the RAND Corporation put this rate at nearly 20%.[6,14]Likewise, the National Vietnam Veterans Readjustment Study (NVVRS[15]) found that more than 15% of male Vietnam theater veterans (VTVs) met criteria for current PTSD, and 30% met diagnostic criteria for lifetime PTSD, while 9% of female VTVs met current PTSD criteria and 27% met lifetime criteria for PTSD related to Vietnam combat trauma. High rates of PTSD and depression (ranging from 9% to 31%, depending on the level of functional impairment reported) are accompanied in nearly half the cases by alcohol abuse or aggressive behavior comorbidity.[14] According to the official report of the Joint Mental Health Advisory Team 7 (J-MHAT 7),

2010 prevalence rates of acute stress, depression and anxiety among deployed OIF/OEF service members are 17.4%, 7.9%, and 8.8%, respectively.[16]

PTSD (especially combat-related PTSD) commonly co-occurs with other psychiatric disorders. In fact, the majority of individuals with PTSD meet criteria for at least one other psychiatric disorder and many for three or more[17,18] including: depression,[19,20] suicide,[21–23] substance abuse disorders,[15,24] anxiety disorders,[18] and chronic pain.[25–28] Comorbid diagnoses are particularly common among people suffering from combat-related PTSD with many in more than 50%.[29,30] Any additional disorders in the presence of PTSD complicates the treatment process and weakens the prognosis for recovery.[17,31,32]

Injury and Trauma to the Soul

In combat, perpetrating, failing to prevent, or witnessing acts that transgress deeply held values can shatter an individual's beliefs about the purpose and meaning of life, challenge belief in God, induce moral conflict, and even precipitate an existential crisis.[34] In December 2009, Veteran's Administration mental health professionals described a new concept of the consequences of spiritual and psychological trauma: ''moral injury,'' defined as ''perpetrating, failing to prevent, or bearing witness to acts that transgress deeply held moral beliefs and expectations.''[35] Clinicians have observed that moral injury is a significant contributor to clinical depression, addiction, violent behavior, and suicide, and that the current wars create conditions that increase the exposure to moral injury.[36] Signs and symptoms of moral injury include misconduct, violence, other disciplinary problems, social alienation, alienation from self, loss of faith, and loss of meaning.[37]

Prevalence rates for moral injury are not yet available, because it is a relatively new construct, and a well-validated metric is lacking. (A 14-item Moral Injury Scale [MI Scale] has been developed as part of the Marine Resiliency Study [MRS][38] but this scale has not yet been validated in the military.) However, surrogate statistics can be used to estimate the magnitude of the problem. The 2010 MHAT-VII survey found that $< 15\%$ of soldiers report high or very high individual morale, and 13% report suicidal ideation. Suicide rates among active duty military and veterans are currently alarmingly high and rising.[39] Suicide rates have doubled among Marines in the last 3 years, and these rates remain more than double the national average among Army personnel.

PTSD and Substance Abuse

Substance-use disorders (including alcohol and drug abuse, and dependence) represent another class of disorders commonly co-occurring with PTSD. In two community studies of Vietnam veterans with PTSD, 22%[33] and 39%[24] also had current alcohol abuse or dependence. One hypothesis for this phenomenon is that people with PTSD use alcohol and drugs as a means of self-medicating to relieve their debilitating symptoms.[18] This hypothesis is supported by the finding that a diagnosis of PTSD increases a person's risk of developing an alcohol and drug use disorder. However, research has also demonstrated that people with PTSD (particularly males) are more likely than others with a similar background to have an alcohol use disorder that preceded PTSD.[40,41]

Whatever the cause of comorbidity between PTSD and alcohol/drug use disorders, it is clear that excessive use can worsen the symptoms related to PTSD, including sleep disturbance, difficulty in concentrating, emotional numbing, social isolation, anger and irritability, depression, and hypervigilance. Alcohol can also reduce a person's ability to cope with traumatic memories and stress. A number of factors complicate the treatment of comorbid PTSD and alcohol-use disorder. While, to a patient, alcohol use may appear to help symptoms of PTSD by decreasing the severity and number of nightmares, alcohol may also exacerbate the cycle of avoidance that occurs in PTSD.[42] Furthermore, people with comorbid PTSD and alcohol abuse/dependence are at increased risk for premature termination of therapy, and take a longer time to remit from an episode of chronic PTSD.[31,32]

PTSD and Pain

A number of studies have been conducted to assess the co-occurrence of PTSD and chronic pain symptoms. Benedikt and Kolb reported that 10% of 225 patients referred to a VA pain clinic met criteria for PTSD.[25] Muse reported that 9.5% of a sample of patients attending a multidisciplinary chronic pain center met criteria for ''posttraumatic pain syndrome.''[43] Patients referred for assessments of chronic pain resulting from a traumatic event have an even higher prevalence of PTSD. In a study conducted to determine the extent to which work-related injuries were associated with PTSD, assessments of 139 injured workers with chronic pain referred to a rehabilitation program indicated that 34.7% reported symptoms consistent with PTSD.[44] Rates of PTSD in patients for which pain is secondary to a motor vehicle accident range from 30% to 50%.[45–47] Geisser et al. examined self-reports of pain, affective distress, and disability in pain patients with and without PTSD symptoms.[48] The results of this study indicated that patients with accident-related pain and high PTSD symptoms reported higher levels of pain and affective distress, compared to patients with accident-related pain who did not have PTSD.

Studies examining the prevalence of chronic pain in patients with a primary diagnosis of PTSD have reported even higher rates of other comorbid conditions. McFarlane et al. reported that pain was the most common physical complaint (45% back pain and 34% headaches) in a sample of PTSD patients reporting physical symptoms.[26] Beckham et al.

performed a study to investigate chronic pain patterns in Vietnam veterans with PTSD[27] and found that 80% reported the presence of a chronic pain condition. In addition, increased levels of PTSD involving reexperiencing of symptoms were associated with increased pain levels and pain-related disability. White and Faustman reported that 60% of 543 veterans treated for PTSD had an identified medical problem and that 1 in 4 had signs some type of musculoskeletal or pain problem.[28]

The co-occurrence of pain and PTSD may have implications for both conditions. Patients with chronic pain related to trauma and PTSD experience more intense pain and affective distress,[48,49] higher levels of life interference,[50] and greater disability than pain patients without trauma or PTSD.[51] Chibnal and Duckro found that patients with PTSD and traumatic headache pain had higher levels of depression and suppressed anger than non-PTSD traumatic headache pain patients.[46] In addition, patients with post-traumatic headache reported more frequent pain and had a poorer prognosis than did nontraumatic headache patients.[52] Thus, the presence of both PTSD and chronic pain may increase the symptom severity of either condition. In the proposed study, acupuncture treatment in combat-injured soldiers is intended to improve recovery from both conditions and interrupt the trajectory of chronic PTSD and pain symptoms.

Traumatic Brain Injury and wrTSR

TBI is a major cause of death and disability in young people, involving more than 5 million Americans and an annual cost of nearly $50 billion.[53–55] More than 7000 noncombat patients are admitted to VA and military hospitals for TBI annually, with an additional 1700 resulting from problems related to the recent wars in Iraq and Afghanistan.[3,4] Approximately 28% of service members (SMs) with battle injuries requiring evacuation to WRAMC have had TBI.[4] Trauma to the head and neck occurs in 15%–20% of all SMs with battle injuries and mild TBI (mTBI) may afflict up to 28% of all deployed warfighters.[3,4] More than 46% of blast patients and 55% of amputees at WRAMC have sustained comorbid brain injuries.[56,57]

Symptoms and dysfunction, from mild-to-moderate TBI cross the spectrum of dimensions in wrTSR and may include physical symptoms (headache, dizziness, balance, visual

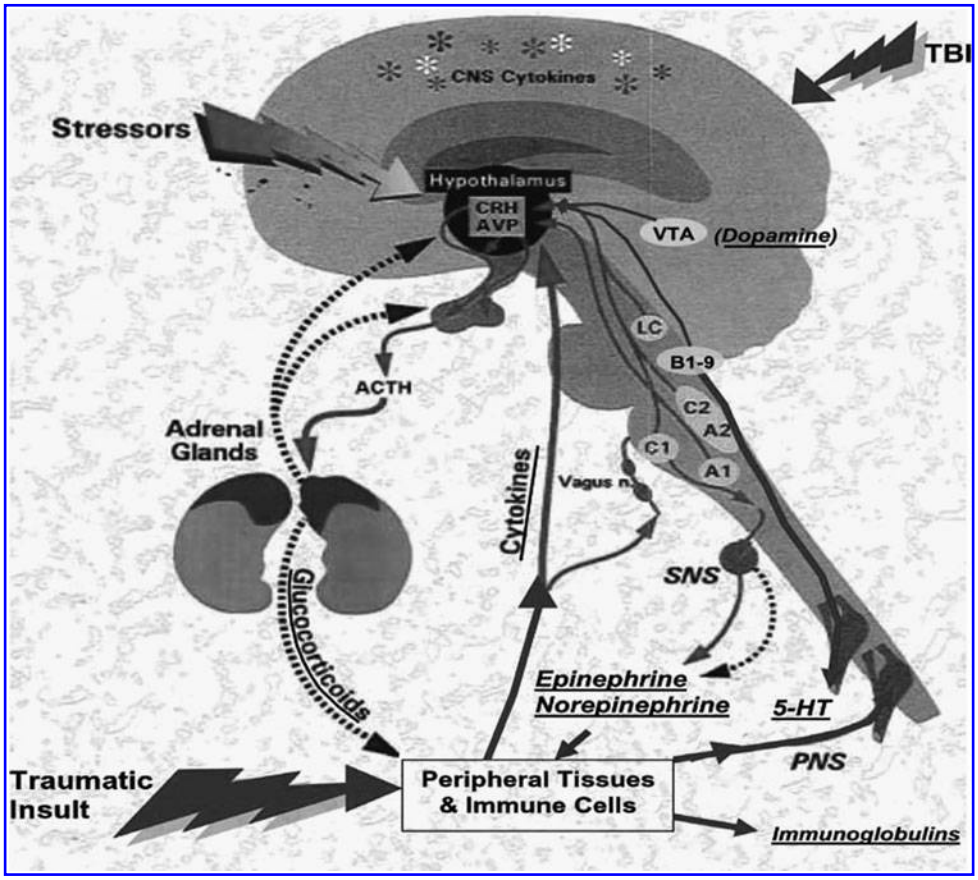

FIG. 2. The hypothalamic–pituitary–adrenal (HPA) axis. Dotted lines represent negative regulatory pathways, solid lines represent positive regulatory pathways. Reprinted with permission from *Annual Review of Immunology*, Volume 20, 2002 by Annual Reviews (www.annualreviews.org). TBI, traumatic brain injury; CRH, corticotrophin releasing hormone; AVN, arginine vasopressin; ACTH, adrenocorticotrophin hormone; SNS, sympathetic nervous system; PNS, parasympathetic nervous system.

changes, and pain), cognitive dysfunction (memory, attention, and concentration difficulties), and psychological or behavioral problems (depression, anxiety, anger, mood swings, social and family dysfunctions).[58] Patients admitted to the hospital for other injuries may have sustained previously unrecognized brain injuries or suffer from psychological and stress traumas. The mechanisms and manifestations of TBI from combat blast injuries may have different and more complex characteristics than civilian blunt head injuries.

Wounded military personnel also have unique demographic factors that cause trauma-related physical and psychological injuries to manifest in a particular way. First, this patient population may be comprised of young(er) individuals with characteristically multiple, compound traumas that involve substantial alterations in physical and mental status, and which require acute, subacute, and long-term therapeutic support in both curative and palliative domains.[59] Second, the personal protective equipment that is currently used by the military has undergone significant improvement over its iterations in previous wars. But while such gear has proven to reduce combat-related mortality, the enhanced survival afforded by Kevlar head and torso equipment has led to an increased morbidity of IED-induced injuries, including blast-generated appendicular fractures, projectile wounds, traumatic amputation(s), and compression wounds as well as concussive (and cerebral contusive) insults.[4]

Finally, such external-blast TBI (ebTBI) is more often accompanied by skull fractures, seizures, and limb amputations. (For a summary, please see Warden and French 2005 and Warden 2006.[3,4]) Rates of post-concussive symptoms (PCS) may occur at increased frequency than found in civilian populations.[4] MTBIs sustained in battle may be difficult to distinguish from, and are often accompanied by, PTSD. Thus, both MTBI and PTSD often manifest with similar sets of symptoms and dysfunctions.[60]

Converging Mechanisms of wrTSR

As illustrated in Figure 2, there are interactive peripheral and central mechanisms that affect the progression of the constellation of features representative of wrTSR. Both physical insult to peripheral tissues and the concomitant stress that such an injury evokes induce this cascade of events to produce early and late effects across the trauma spectrum. These interacting mechanisms produce high levels of inflammatory mediators, including the cytokines (most notably interleukins [IL]–1 and −6), tumor necrosis factor–alpha (TNF-α), neurotropic factors and the tachykinins (including substance P).[61] These ''bottom-up'' mediators can affect the central nervous system (CNS), both by engagement of the peripheral nervous system and by accessing the CNS via altering the vascular integrity and permeability of the brain, to evoke neuroinflammatory changes within the brain parenchyma. The cytokines and tachykinins affect glial metabolism and disrupt glial–neuronal calcium regulation, leading to increased neural uptake and endocellular release of calcium.

Acting as an intracellular messenger, calcium produces ''downstream'' effects to induce early and late-stage transcriptional factors and promotes translation of ion channel, synaptic, enzymatic, and receptor proteins that can lead to disrupted neural function in several brain areas (for a summary see Carofoli and Klee, 1999).[62] This aberrant neural and glial activity is manifested in alteration of both neurochemistry (of neurotransmitter and metabolic systems; for example, epinephrine, norepinephrine, serotonin [5-hydroxytryptamine; 5-HT], and dopamine, as well as other peptidergic and amino-acid transmitters) and of more global network properties to produce ''top-down'' brain–mind effects that induce pathological change(s) in mentation, cognition, and psychological states (see Fig. 2). Thus, while initial effects may be transitory, more durable sequelae are evidenced in those systems with the highest ''vulnerability,'' namely, those neural networks and systems that have sustained direct neurological damage and those with genetic-phenotypic predispositions. These factors are strong predictors of the development of chronic pain, pain syndromes, and psychopathology following trauma.[63]

Some of these effects are overt and acute, while others are more subtle and delayed, reflecting the slower changes that occur as a central consequence of inflammatory processes, with resultant alterations in neural and glial function, and disruption and/or remodeling of neurological networks. The lack of explicit, first-order signs and symptoms may result in a return to combatant status, or, if other wounds are sufficiently grave, triage to a secondary- or tertiary-care facility. Often, it is in these settings—or in the home—that the signs and symptoms reflective of progression along the pain and neuropsychopathologic spectrum of wrTSR (i.e., co-occurrence of depression and anxiety—including PTSD—disorders) are more saliently expressed and and in evidence. This is not incidental; rather, it may at least partially be the result of the psychophysiological effects of increased allostatic loads incurred by social, familial, occupational, and/or economic stressors.[64] The reciprocity and cyclicity of these events are such that:

1. Large-scale peripheral injury augments the inflammatory effects within the CNS.
2. Geno- and phenotypic factors are induced/provoked that are ultimately expressed as pain and psychopathology.
3. These pathologies become chronic, with possible functional and structural remodeling of CNS micronetworks
4. These networks mediate dysfunctional responses and reactions to environmental factors.
5. This adaptational dissonance enhances stress loads.
6. The condition(s) may worsen as discordant interactions between the underlying neural state and environmental factors become increasingly synergistic (Fig. 2).[12,65]

While symptomatic assessment is important, if not essential, to diagnose syndrome expression accurately within this spectrum disorder, and, ultimately, to determine the best type(s) of care, it is equally important to attempt to identify peripheral and central biological markers (e.g., IL 1 and 6, immunoglobulin G, cortisol) and endproduct metabolites of adrenergic (i.e., 3-methoxy, 4-hydroxy phenylglycol [MHPG]), dopaminergic (i.e., homovanillic acid [HVA, dihydroxyphenylacetic acid [DOPAC]), and serotonergic (i.e., 5-hydroxyindole acetic acid [5-HIAA]) neurotransmission (see below, also Fig. 2) that reflect particular syndromes or subsyndromes of the TSR continuum, and physiologic effects of both pathological variables and those of various treatments.

This pathological progression advances many patients to treatment failure, symptomatic worsening, chronic illness, psychosocial stress, and family and life disruption. As described below, there is good evidence to believe some integrative medicine approaches, especially acupuncture, can disrupt this pathological progression and offer an opportunity to reverse this cycle and lead to enhanced recovery, quality of life and function.

PTSD, wrTSR, RESEARCH, AND THE HEALTH CARE SYSTEM

Failure to Address the Full wrTSR and the Overuse and Underuse Burdens on Health Care

The expression of wrTSR complex often manifests following treatment of the acute neuropsychological symptoms caused by in-theater trauma, with signs and symptoms reflective of progression along this neuropsychopathological spectrum in these wounded military personnel.[61] This pathological progression may be the result of psychophysiological effects of increased allostatic loads incurred by social, familial, occupational, and/or economic stressors, and it advances many patients down the slippery slope of treatment failure, symptomatic worsening, psychosocial stress, and life disruption.[62]

These patients are classified into categories based on mind, brain, or bodily damage and sent to specialty clinics (psychiatry, neurology, rehabilitation medicine, etc.) that address selected components of the wrTSR (psychological, neurological, or physical). Often, these SMs simply do not show up for care (avoiding treatment altogether for symptoms that carry a social stigma) or show up repeatedly at a later time in primary care clinics with a variety of somatic complaints involving dysfunctions in sleep, appetite, energy, and/or sexual activity. The former results in underdiagnosis and treatment, and the latter increases the burden on primary care resulting from chronic, unremitting illness. The latter may arise from so-called ''subthreshold'' PTSD or ''mild-to-moderate'' TBI, which often goes undiagnosed or is treated ineffectively.[63] These patients present weeks to months after trauma exposure with symptoms and dysfunctions that chronically burden the DoD or VA health care delivery systems.[7,63] Clearly, the zero-sum nature of this situation is opprobrious to the sound practice of medicine—both technically and ethically—and calls for a more innovative and comprehensive approach to addressing the full consequences of mind–brain/body injuries (MBI).

The Need to Focus Research on the Whole Person wrTSR Response

Clearly, these epidemiological and mechanistic data indicate a large and growing clinical problem (with recent estimates of this pattern of comorbidity within this population of wounded at as much as $n = 10{,}000$)[66] and suggest that these patterns of comorbidity may reflect underlying, common patho-etiologic variables and mechanisms; compel the need for additional research to define these variables and mechanisms more fully; and equally compel and sustain the need for ''the development of intervention based on a new integrated care model.''[9] In addition, the long-term impact of MBI goes far beyond individuals and affects their families and communities, which, too often, go unaddressed by the health care system.[67] Thus, from the perspectives of the person, family, and community, there is good reason to consider the full wrTSR (rather than individual components) and to investigate integrative, multidimensional (mind, body, symptom, function) approaches to classification and treatment.

Because of this complex nature of the trauma response, the current standards of care for wrTSR are probably not maximally effective, nor do they address fully the biopsychosocial aspects and spectrum effects of wrTSR. Thus, there is a need for additional research to define and understand TSR more completely so as to develop interventions based upon both neuroscientific information and new integrated care models. Such care should address the whole-person experience of wrTSR and seek to facilitate prevention, cure, and healing as an integrated paradigm that includes contextual understanding of patient-specific variables, uses innovative therapeutic approaches based on rigorous methods of empirical evaluation, and narrows the gap between research and clinical practice.[8] Complementary and integrative approaches, and acupuncture in particular, may be able to address many of these challenges to wrTSR treatment.

Complementary and Integrative Practices

Complementary and integrative medicine (CIM) refers to a family of holistic practices used in conjunction with conventional medicine to enhance health, stimulate recovery, and reduce side-effects. CIM therapies are being increasingly utilized within comprehensive care models[68] and may provide major contributions to patient recovery. Local

surveys in military treatment facilities have shown that more than 70% of DoD beneficiaries may use CIM at certain sites.[69] A large survey conducted by the Samueli Institute (Alexandria, VA) in conjunction with the DoD Health Behaviors Survey showed that more than 45% of active duty military members have used CIM and more than two thirds used dietary and nutritional supplements in a 12-month period. Surveys, such as the Klemm Analysis Group[70] and Healthcare Analysis and Information Group[71] reports, showed extensive use of CIM practices by Veterans Health Administration (VHA) health care practitioners.[62] The wide acceptance of CIM for addressing various health issues suggests that, were a CIM approach to prove effective for treating PTSD, many people who have mixed feelings about psychiatric treatment might use CIM.[73] Current research is shifting its primary focus from managing and mitigation of PTSD to one that also promotes post-traumatic adaptation, development, and resurgence. Ai and Park[74] describe three interrelated trends in mental health research that are based on a broader view of (1) the positive psychology movement, (2) the recognition of the role of spirituality and religion in health and well-being, and (3) stress-related growth.[74] Similarly, research on the use of optimal healing environments for the treatment (and possible prevention) of the negative effects of PTSD is emerging.[75]

For the treatment of wrTSR, CIM approaches fall into two basic categories:

1. Actions people do for themselves that enhance self-care and self-treatment skills, such as mind–body practices[76] (imagery, relaxation response,[77] mindfulness training,[78] and yoga[79]), self-care skills (community self-care practices, diet, and exercise training), device-assisted biofeedback (heart-rate monitoring, breathing, and virtual reality), and diet and supplements for enhancing cognitive/physical fitness and psychological resilience
2. Nondrug and nonpsychiatric approaches used by CIM professionals to complement conventional treatments and facilitate healing, such as acupuncture,[80,81] Reiki, osteopathic manipulation,[82] chiropractic, and integrative medicine team approaches.

RESEARCH ON ACUPUNCTURE FOR PTSD AND wTSR

Preliminary Data for the Effectiveness of Acupuncture for HRQoL and wrTSR Comorbidities

Arguably, the most promising CIM intervention for TSR is acupuncture. Originating in China, acupuncture has been used as a medical treatment modality for more than 2500 years, but only relatively recently has it received attention in the United States. It is based on a concept of health and disease that is very different from conventional Western scientific thinking. Acupuncture theory holds that energy, called Qi, travels along pathways (meridians) within the body. Disease states result from disruption or blockage of proper Qi flow. To influence this energy flow, thin metal acupuncture needles are inserted at specific points along the meridians. The stimulation of those points may also be accomplished by other techniques, such as electrical stimulation, laser, moxibustion, and pressure.[83,84]

Acupuncture is used to treat many conditions. Even as far back as 1998, it was estimated that more than 1 million people in the United States collectively received 10 million acupuncture treatments.[85] Treated disorders included acute and chronic pain of various etiologies, nausea, stress and anxiety states, depression, substance abuse, allergic rhinitis, asthma, gastrointestinal disorders, infectious disease, and brain injury from stroke.[84] Overall studies show that acupuncture helps reduce stress, anxiety, and pain, and is effective for treating depression and insomnia, which are all symptoms with diagnostic groups that are part of the complex of the trauma spectrum.[86–91] The relevant studies are summarized next.

Controlled Clinical Studies of Acupuncture

There is evidence, demonstrated via controlled clinical trials, that acupuncture can be effective for treating many of the specific comorbidities that comprise wrTSR in TBI and PTSD. Recent randomized, controlled, blinded studies support the efficacy of acupuncture for treating pain associated with fibromyalgia, knee arthroscopy, and labor.[92–94] These findings are consistent with many prior investigations showing the amelioration of pain caused by diverse conditions in both humans and animals.[95] Strong evidence also exists for treating postoperative nausea and vomiting with acupuncture, resulting in minimal side-effects.[96] Several clinical trials have demonstrated acupuncture's effectiveness for ameliorating stress and anxiety and for facilitating a mentally relaxed state.[97–106] Studies in healthy volunteers have demonstrated reduction in stress scores and levels of subjective stress achieved by acupuncture,[107,108] while another study showed an increase in vagal tone, with suppression of sympathetic tone in healthy volunteers, suggesting a direct effect on CNS control.[109] Acupressure has reduced anxiety and stress as well as perceived pain of treatment in emergency patients being transported to the hospital via ambulance.[101] Electrical stimulation of acupuncture points has been shown to increase ''mental relaxation'' in patients with chronic physical disorders,[110] and, in another controlled study of acupuncture, muscle sympathetic nerve activity was reduced in heart failure patients undergoing mental stress testing.[111]

Furthermore, acupuncture is effective for addressing other symptoms that comprise wrTSR, including insomnia[112–115] and somatic and postoperative pain.[95,116–121]

While research results for the effectiveness of acupuncture for treating drug addiction is mixed, there are national standards for using ear acupuncture in drug addiction, with reported effectiveness, and several states mandate a trial of acupuncture for treating drug addition.[122] Several studies in patients with stroke have found that acupuncture can enhance cognitive and physical functioning in patients with brain damage above and beyond conventional rehabilitation approaches.[123] In a study by Hollifield (the acupuncture trainer and consultant on this project) and colleagues, acupuncture was as effective as cognitive behavioral therapy and markedly more effective than a wait-list control for alleviating symptoms of PTSD in veterans.[124] In addition, large randomized controlled trials of acupuncture for treating various chronic pain conditions have shown acupuncture to be more effective than guideline-based standard therapy.[125,126] Finally, numerous case reports, case series, and observational studies have reported benefits in patients after surgery and head trauma.[126–131]

Acupuncture studies frequently use the Short Form (SF)–36/SF-12 for measurement of HRQoL, which will be the primary outcome measure for this study. Across heterogeneous populations, acupuncture consistently improves SF-36 scores by 5–7 points,[132–135] a change that is considered to be clinically significant.

Acupuncture Research in the Military

Several studies overseen by the primary author of this article have been done on acupuncture use in the military for the comorbidities of trauma response. These include studies on acute pain,[73] chronic and refractory pain,[127] and PTSD.[128] The authors are currently testing a simplified field deployable acupuncture technique to be used for headache called Battlefield Acupuncture (BFA), also known as Auricular Stimulation Procedure (ASP), previously tested for pain.[81] This simple Five Point ear acupuncture technique reduced pain by 23% over controls.[81] The authors of the current article have recently completed two studies at WRAMC using acupuncture. One in the Deployment Health Clinical Center found that acupuncture over 12 weeks was acceptable and effective as an adjunct in OIF/OEF patients being treated for PTSD.† A second study done in the rehabilitation clinic examined the effect of scalp acupuncture for treating phantom-limb pain in amputees from the war.‡ In a pilot study, Niemtzow et al.[130] and Gambel et al.¶ found acupuncture effective for addressing this otherwise refractory pain condition. A follow-up study is being planned that will parallel and coordinate data collection with this proposed study. The current authors have also conducted a Rapid Evidence Assessment of the Literature (REAL©; which is also reported in this special issue by York et al., pages 229–236). The REAL was conducted to survey the literature on acupuncture research conducted in the military population and to evaluate the quality of the research available—there is a paucity of published reports in this area and further research is necessary, as acupuncture is becoming more readily chosen for military populations in the field for treating various conditions.

Translation of effective therapies is of prime importance for the military. The current authors are currently evaluating the feasibility of training Air Force physicians in the BFA technique for possible widespread use as a pain treatment modality in military primary care. The current study will use an approach recently shown by Hollifield et al. to be effective for trauma spectrum comorbidities in veterans with PTSD. Hollifield et al. used a semi-standardized acupuncture technique that was carefully developed from Traditional Chinese Medicine and matched to trauma response syndromes. In a randomized controlled trial, this approach was found to be easily teachable, as effective as cognitive behavioral therapy, and markedly more effective than a wait-list control for alleviating symptoms of PTSD in veterans.[124] Hollifield also found that this approach was effective for addressing other trauma comorbidities, including pain, insomnia and quality of life.§

Common, Interacting Mechanisms of Acupuncture in wrTSR Conditions

Acupuncture may have such ubiquitous effects because it appears to simultaneously influence several common, interacting mechanisms involved in trauma response and recovery. Acupuncture is known to have effects on the autonomic nervous system and the prefrontal cortex—systems that are involved in the pathophysiology of the emotional, pain, and cognitive dysfunctions of TSR.[136–138] It has been established that acupuncture stimulates the release of endogenous opioids and that analgesic effects are blocked in a dose–response manner by naloxone, an opioid antagonist.[95] Cho et al. have demonstrated specifically that the cingulate gyrus and the thalamic areas, activated in the presence of applied pain stimulation, show brain activity that correlates with decreased pain sensation in human subjects.[139] There is evidence that electroacupuncture may affect the pressor response, resulting in decreased oxygen demand in the presence of myocardial ischemia[140] and cardiovascular reactivity and hypertension.[141] Thus, acupuncture appears to cause a broad matrix of CNS responses involving the amygdala, hippocampus, hypothalamus,

†Cooper J, Walter J, Ader D, Niemtzow RC. Outcomes and Cost Assessment of Acupuncture in the Treatment (OCAT) of Pain Patients at Malcolm Grow. Unpublished.

‡Engel C, Benedek D, Armstrong D, Osuch E, et al. Acupuncture for the Treatment of Trauma Survivors. Unpublished.

¶Gambel J, Niemtzow RC, Burns SM, Penhollow T, et al. Acupuncture for Post Amputation Limb Pain. Unpublished.

§Jonas WB and Hollifield M. Personal communication about acupuncture techniques effective for trauma. Washington, DC, 2008.

cerebellum, basal ganglia, anterior cingulate, insula, and other limbic structures, as evidenced by functional magnetic resonance imaging, positron emission tomography, and electroencephalographic studies.[136] Responses by the CNS may be dependent on the type and frequency of acupuncture treatment.[136,142,143] In this proposed study, the authors will use an acupuncture approach previously developed and found to be effective for addressing TSR.[124]

Specific and Nonspecific Effects of Acupuncture

The many potential mechanisms for the efficacy of acupuncture on the trauma recovery spectrum has both pros and cons for testing its efficacy. The apparent ''multimechanism'' whole-person's response acupuncture seems to provide a compelling rationale for testing acupuncture effects on quality of life and function in two heterogenious populations—the authors expect both to improve significantly. The down side for collecting evidence about acupuncture efficacy is that it becomes difficult to select an appropriate control procedure without knowing its precise mechanism. Three competing mechanisms exist: (1) the traditional Chinese theory of ''point specificity''; (2) the more Western explanations related to facia and the induction of facia/neural/inflammatory ''matrix'' responses; and (3) the ''therapeutic meaning and expectancy'' theory of acupuncture as a placebo. While all three of these potential mechanisms cannot be disentangled in a single clinical trial, the acupuncture control methods will be specifically selected to control for all three mechanisms simultaneously in the following manner.

Clinical trials testing the therapeutic claims of acupuncture have focused on the efficacy of needling at specific sites on the body surface (acupuncture points), using selected needling techniques. The choices of acupuncture points and needling techniques are guided by traditional and modern theories and diagnostic procedures. However, insertion of needles into the body can also induce a range of physiological effects that are not dependent on the location of stimulation and are thus considered nonspecific.[144,145] Among these nonspecific effects likely to be associated with the microtrauma of acupuncture are stimulation of cutaneous microcirculation,[146,147] heterosegmental analgesic mechanisms (i.e., diffuse noxious inhibitory control),[148,149] and aspects of the relaxation response.[150,151] Even ''needle grasp''—a biomechanical phenomenon traditionally associated with acupuncture, needle insertion, and manipulation—has been shown to occur to a marked, albeit lesser, extent at control points relative to acupuncture points.[152] The realization that acupuncture treatment elicits nonspecific and specific effects has led to adoption of the term ''sham acupuncture'' for control needling procedures in randomized controlled trials (RCTs) of acupuncture, because the term ''placebo'' is generally applied to control procedures that are believed to be inert.

Nonspecific effects of needling may well have contributed to the outcomes of recent large-scale German trials of acupuncture (involving several hundred to several thousand patients per trial) in which sham acupuncture, delivered as superficial needling at non-acupuncture points with no needle manipulation, was found to be as effective as true acupuncture for treating low-back pain[132,153] and migraine.[135,154] Invasive sham acupuncture cannot be discarded as a control procedure in acupuncture trials, however, in part because another of the German trials, one on osteoarthritis of the knee,[133] found acupuncture to be statistically superior to the same type of ''minimal acupuncture'' provided in the low-back pain and migraine trials cited above.

The likelihood that invasive needling at non-acupuncture points induces some level of nonspecific healing has led to the development of an alternative type of sham acupuncture involving noninvasive needling.[155,156] This procedure utilizes needles with blunted tips, designed such that contact with the skin leads to retraction into the shaft instead of penetration of the skin. Despite nonpenetration, the sham needle is held ''upright'' because it perforates the tape used to hold a small O-ring in place that surrounds the needle placement site[155] or the sham needle perforates a small square of Styrofoam that is attached at the site of ''needling.''[156] In either procedure, the patient sees the needle shorten and believes that true acupuncture has occurred—an expectation that has been confirmed by questionnaires. A review of the literature over the period since these nonpenetrating sham needles were introduced in 1999 reveals 19 RCTs that utilized a sham needling telescoping device, of which 8 trials were positive, 9 negative, and 2 mixed with regard to their authors' stated primary outcomes. The summative situation with respect to trial results is similarly inconclusive in acupuncture trials that used invasive needling as a sham control procedure.[157]

At this stage in the development of acupuncture research methodology, it seems clear that an appropriate sham procedure cannot be designed or agreed upon until a clearer understanding emerges regarding the mechanism by which the acupuncture needle elicits its response.[158] Given the present dilemma, the current authors have chosen to utilize a noninvasive needling procedure for a sham control in the present 3-arm trial of acupuncture for HRQoL in TBI and PTSD. This procedure will be designed to control for the ''meaning responses'' (placebo)[159] associated with the delivery of acupuncture and, when compared to true acupuncture, will allow an assessment of the treatment benefit that results from acupuncture needling-related responses.

CONCLUSIONS

There is a need for new approaches for treatment of trauma that induce a whole-person healing response. The current medical approaches that divide an individual into

subspecialties increase the precision of diagnosis and treatment but create complicated management approaches, which are, in some cases, counterproductive. Healing approaches such as acupuncture provide an alternative model to the current biomedical model and provide an opportunity for widespread healing with fewer medications and subspecialty oversight, and are nonstigmatizing.

However, the costs of differing strategies for delivery of acupuncture may vary substantially. Little research has evaluated the cost effectiveness of acupuncture treatment or determined which strategies are optimal for adoption. A recent panel conducted by the RAND–Samueli Program on Integrative Medicine Policy focused on economic analysis issues in CIM, which will help inform the DoD about the best approaches for evaluating these differing strategies. The report and toolkit from that panel should be out before the end of 2011. Given the growing interest in acupuncture and integrative approaches for treating wrTSR, such as that incorporated to the recent DoD Pain Task Force Report, and given the increased suffering likely to emerge as warriors return from the battlefield with the coming drawdown, it would behoove the military and the VA to substantially accelerate the development and evaluation of programs delivering acupuncture. SMs and families who are suffering the consequences of these long wars deserve nothing less than the optimal healing environments we can provide.

ACKNOWLEDGMENTS

The authors would like to thank Cindy Crawford, BA, and Jarrad Davis, BA, for assistance in preparation of the manuscript and Jim Giordano, PhD, for contributions to the concept of wrTSR. This study article was partially funded by a grant from the Department of Defense Telemedicine and Advanced Technology Research Center.

DISCLOSURE STATEMENT

The authors have neither conflicts of interest nor financial disclosures to report.

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