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TRADITION SHAPES THE FUTURE

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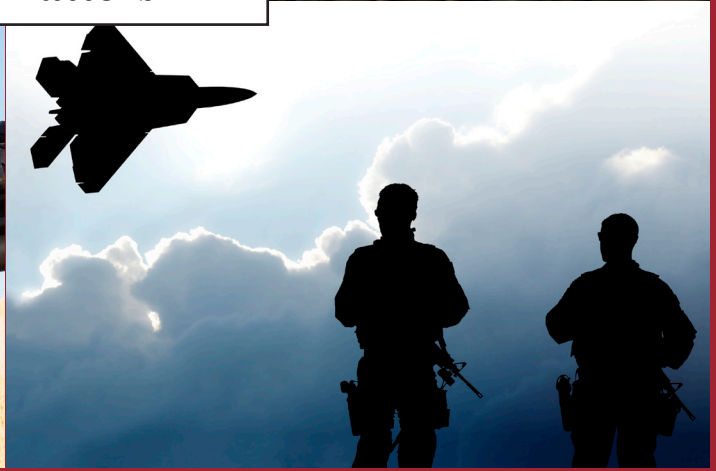
Special July 4th Issue on Military Matters



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Disclaimer: Dr. Berkowitz was not involved in the editorial decision to publish the articles he co-authored, which was left up to the editorial committee of the journal.

Correction: In the article "Manipulative Methods of Dr. Still" by Jamie Archer, DO (UK), from the December issue of *The AAO Journal*, the quote from Dr. Edwards in the fifth paragraph of page 20 was misattributed to Dr. Still. On page 23, the following sentence was omitted in reference to Figures 4 and 5: According to the dictionary the very word "swinging" refers to an oscillating, rotary or repetitive movement. Finally, "Figure 8: Hip Treatment" should have been labeled "Figure 9: Hip treatment." *The AAO Journal* apologizes for these errors.

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The mission of the American Academy of Osteopathy is to teach, advocate and research the science, art and philosophy of osteopathic medicine, emphasizing the integration of osteopathic principles, practices and manipulative treatment in patient care.

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View From the Pyramids

A resource journal on traumatic brain injury and post-traumatic stress disorder in veterans

Murray R. Berkowitz, DO, MA, MS, MPH

As part of the 2011 White House Joining Forces Initiative aimed at taking action to better serve America's military families, the American Association of Colleges of Osteopathic Medicine (AACOM) looked at the manner in which the curricula taught at the nation's osteopathic medical colleges provide instruction in military-related medical issues. An analysis of the complete curricula taught at these schools was performed. When the AACOM effort was first announced in December 2011, this Editor sought to provide a special, themed issue of the *AAO Journal* that would emphasize the problems of traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) in our veterans to coincide with the January 11 public announcement of the Joining Forces Initiative. For a number of reasons, this could not be accomplished in the very short time that was available. Our colleagues at the American College of Osteopathic Family Physicians (ACOFP), however, were able to publish a special, themed issue of the *Osteopathic Family Physician* in March 2012. My congratulations to Jay Shubrook, DO, Editor, and Meredith Norris, DO, Associate Editor.

This month's special, themed issue is the first for the American Academy of Osteopathy and its *Journal*. Specific content includes, but is not limited to, post-traumatic stress disorder (PTSD), traumatic brain injury (TBI), depression and psychosocial issues related to military culture and families. It was envisioned that this issue may serve as a resource for physicians, especially non-veteran civilian physicians, who must be aware of how veterans can slip through the cracks of the Veterans Affairs system and have issues tied to their military service.

Our Guest Editor, Dr. William Bograkos, received his Disaster and Chemical, Biological, Radiologic, Nuclear and Explosive (CBRNE) training during his 28 years of military service. He is a retired Colonel in the U.S. Army Medical Corps, and has served both the Army and the U.S. Air Force as a military Flight Surgeon and Family Practice and Emergency Medicine Physician. Dr. Bograkos served with a Special Operations Weapons of Mass Destruction Detachment prior to, and during, the millennium. He served in the Balkans as a Division Surgeon and NATO Multi-National Peacekeeper from September 2001 to April 2002. Dr. Bograkos chaired the U.S. Special Operations Command's Curriculum Examination Board for the Advanced Tactical Practitioner (SOF EMT-P) from 2004 to 2006. He served the Pentagon's Civil Military Emergency Preparedness office as a Bioterrorism/Medical Consultant for the Black Sea Initiative, and briefed at the First Interpol Global Conference on Preventing Bioterrorism in Lyon, France, in 2005.

Of the contributing authors, several are veterans. Andrew Lovy, DO, FACN, DMOR, was the second DO to be commissioned into the U.S. Army Medical Corps. Dr. Lovy served in Vietnam with the 506th Infantry Regiment as part of the famed 101st Airborne Division ("Screaming Eagles"). During World War II, the 506th jumped into France in the opening hours of D-Day, and fought their way out of Bastogne during the Battle of the Bulge. Dr. Lovy took part in the 1968 Tet Offensive. For those not familiar with the DMOR (Distinguished Member of the Regiment) designation, it is a special award conferred by the Department of the Army and sanctioned by the unit. Since the inception of the 506th, approximately 40,000 troops have been in the unit, and 112 have been so awarded. Until this year, Dr. Lovy was the only physician so awarded, and of the four medics who have since received the award, three served with him in Vietnam. This award is special because it is given by one's peers to acknowledge service of the highest magnitude.

Murray R. Berkowitz, DO MA, MS, MPH, served on active military duty as a Medical Corps Officer in the United States Army. Before attending medical school, Dr. Berkowitz served in numerous assignments in the U.S. Army and U.S .Air Force (USAF). He ultimately received a Direct Commission in the U.S. Army as an Armor/Cavalry Officer and served assignments as an Officer Candidate

School (OCS) Instructor/Tactical Officer, Transportation Officer, Chemical Officer and Infantry Company Commander with the Army, the Reserve, and the National Guard. He transferred to the USAF in January 1981. His Air Force assignments included service with the Strategic Air Command, Military Airlift Command, Defense Communications Agency, USAF Headquarters (Pentagon) and the Office of the Secretary of Defense (OSD). He served for more than seven years in the space program, including assignments as Staff Development Engineering Manager for the space shuttle, Space Launch and Control Division; Directorate of Space Systems and Command, Control, Communications; Deputy Chief of Staff/Research in the Department of Development and Acquisition at the USAF Headquarters; Airborne Space Command, Control, Communications Flight Test Engineering Manager at the OSD; with attachment to the 89th Military Airlift Wing (Special Air Missions/Presidential Support) at Andrews AFB in Maryland; and as the Special Assistant for Space and Command, Control, Communications to the Chief Scientist of the Air Force. During the first Gulf War, Dr. Berkowitz served as a Special Assistant to the Director of Plans; Directorate of Plans; and following cessation of hostilities, Chief of Research Services for the Secretary's Gulf War Study. Dr. Berkowitz is a disabled veteran, medically separated from the military due to service-related disabilities. A former "Line of the Air Force" Lieutenant Colonel, he was a military aviator and parachutist, and also holds the Master Space Badge and the Office of the Secretary of Defense Identification Badge. He has received 26 military awards and decorations.

Natalie A. Nevins, DO, MSHPE, is a former Major in the United States Air Force Medical Corps. Dr. Nevins was assigned to the 61st Medical Squadron at Los Angeles Air Force Base as a Family Practice Physician, where she held positions as Chief of Medical Field Response; Clinical Director for Laboratory Services; Chairman of the Infection Control Department; and Director of Radiology Services. She lectures for the California Preparedness and Education Network on issues related to Disaster Preparedness, Bioterrorism, Chemical and Radiological Warfare and Emerging Infectious Diseases.

Finally, I would like to gratefully acknowledge the many editing and other contributions of Ms. Tessa Boeing. Without her continuing efforts, this special issue of the *Journal* would have been delayed.

Osteopathic Considerations in Systemic Dysfunction: Common Clinical Problems

July 20-22, 2012, at New York College of Osteopathic Medicine (NYCOM)

Course Description

This course presents a practical, hands-on osteopathic manipulative treatment (OMT) approach to everyday patient systemic complaints—ranging from sinusitis to pneumonia, gastritis to irritable bowel syndrome and headache to angina. The program centers on designing rational osteopathic care that integrates the five osteopathic care models and can be delivered in a clinically-effective, time-efficient manner.

It will teach clinicians to seek regional and segmental diagnostic somatic clues to enhance and speed differential diagnosis. Participants will learn to integrate Chapman's reflexes, collateral abdominal ganglia, and segmental diagnosis of the entire spine and sacroiliac joint. In treatment, the course will center on skills used to enhance homeostasis. Participants will master skills including sphenopalatine ganglia technique; collateral ganglia inhibition; spleen pump; myofascial spray and stretch; ischial rectal fossa technique; mesenteric lifts; rib raising; lymph pumps; liver pump; diaphragm redoming; and direct and indirect OMT techniques to remove somatic dysfunction in the cranial, cervical, thoracic, costal, lumbar and sacral regions.

While a number of techniques will be taught, emphasis will be placed on developing skills and strategies to speed diagnosis and recovery. Residents, residency trainers and directors of medical education will be accorded special tips for maximizing integration of these skills and strategies into their specific programs.

Faculty

Hugh Ettlinger, DO, FAAO, is a 1987 graduate of NYCOM, where he serves as an Associate Professor of Osteopathic Manipulative Medicine (OMM) and director of the NYCOM/St. Barnabas NMM/OMT Residency Program.

Michael Kuchera, DO, FAAO, is a 1980 graduate of Kirksville College of Osteopathic Medicine. He currently directs the OMM Research and Human Performance and Biomechanics Laboratory at Philadelphia College of Osteopathic Medicine. He is also clinical director of the Center for Chronic Disorders of Aging and secretary-general of the International Federation of Manual/Musculoskeletal Medicine.

CME

20 hours of Category 1-A AOA CME credit is anticipated.

Course Location

NYCOM at New York Institute of Technology
Northern Boulevard
Old Westbury, NY 11568
(516) 686-3747

Course Times

Friday and Saturday: 8:00 am - 5:00 pm (lunch provided)
Sunday: 8:00 am - 12:00 pm (lunch on your own)

Travel Arrangements

Call Tina Callahan of Globally Yours Travel at (800) 274-5975.

American Academy of Osteopathy Registration Form

Osteopathic Considerations in Systemic Dysfunction...
July 20-22, 2012 at NYCOM

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AAO Calendar of Events 2012-2013

Mark your calendar for these upcoming Academy meetings and educational courses.

July 17	AAO Board of Trustees Meeting—AOA Headquarters, Chicago, IL
July 17-19	AOA Board of Trustees Meeting—The Farimont Hotel, Chicago, IL
July 20-22	AOA House of Delegates Meeting—The Farimont Hotel, Chicago, IL
July 20-22	*Osteopathic Considerations in Systemic Dysfunction: Common Clinical Problems* Hugh Ettlinger, DO, FAAO; Michael Kuchera, DO, FAAO—NYCOM, Old Westbury, NY
August 10-11	Education Committee Meeting—University Place Conference Center & Hotel, Indianapolis, IN
August 10-11	SAAO Council Meeting—University Place Conference Center & Hotel, Indianapolis, IN
August 16	Membership Committee Teleconference, 8:30 pm EST
September 7-8	*Ultrasound Guided Injections*—Millicent K. Channell, DO; Sajid Surve, DO UMDNJSOM, Stratford, NJ
October 6	*Fine-Tuning Your HVLA* (Pre-AOA Convention) John G. Hohner, DO, FAAO—San Diego, CA
October 7	AAO Board of Trustees Meeting—San Diego, CA
October 8-10	AAO Program at the AOA Convention: *Osteopathic Considerations for Head and Neck Disorders* Millicent K. Channell, DO, Program Chair—San Diego, CA
October 25-27	*Prolotherapy Weekend*—Mark S. Cantieri, DO, FAAO; George J. Pasquarello, DO, FAAO UNECOM, Biddeford, ME
November 9	AOBNMM Meeting—Wyndham Hotel West, Indianapolis, IN
November 10	AOBNMM Oral & Practical Exams—Wyndham Hotel West, Indianapolis, IN
November 11	AOBNMM Written Exam—Wyndham Hotel West, Indianapolis, IN
Nov. 30-Dec. 2	*Oscillatory & Energetically Integrated Osteopathic Medicine in a Contemporary Setting* Zachary J. Comeaux, DO, FAAO—NSUCOM, Fort Lauderdale, FL
Jan. 18-20, 2013	*Osteopathic Approach to Clinically Relevant Myofascial Trigger Points* Michael Kuchera, DO, FAAO—AZCOM, Glendale, AZ
Feb. 1-2, 2013	Education Committee Meeting—Indianapolis, IN
Mar. 17-19, 2013	Peripheral Nerve course (Pre-Convocation)—Kenneth J. Lossing, DO—Rosen Shingle Creek Resort, Orlando, FL
Mar. 18-19, 2013	Pediatric ENT course (Pre-Convocation)—Program Chair TBD—Rosen Shingle Creek Resort, Orlando, FL
Mar. 18-19, 2013	*Osteopathic Considerations in Systemic Dysfunction of the Geriatric Patient* (Pre-Convocation) Drs. Kuchera and Ettlinger—Rosen Shingle Creek Resort, Orlando, FL
Mar. 20, 2013	*Cellular Biology and the Cellular Matrix* (Pre-Convocation)–Frank H. Willard, PhD Rosen Shingle Creek Resort, Orlando, FL
Mar. 20-24, 2013	AAO Convocation—*Mechanotransduction and the Interstitium: The World In Between* Gregg C. Lund, DO—Rosen Shingle Creek Resort, Orlando, FL

"The difference a DO makes" in welcoming home our troops

William Bograkas, DO, MA, FACOEP, COL, MC, FS USA (retired)

The human spirit has not changed since Sun Tzu addressed moral influence with the five fundamentals in *The Art of War*[1] and Homer wrote of Odysseus's journey to and from Troy in *The Illiad*[2] and *The Odyssey*.[3] What has changed, however, is technology and the art of medicine. After World War II, our troops returned home by ship. They returned home from Vietnam by plane. During the long "War on Terror," our casualties have been treated and stabilized through the modular Emergency Medical Services (EMS) system of Joint Medical Force 2010.

Through excellence in military EMS, survivors, not victims, have received care and returned stateside within 72 to 96 hours. Today, a surge of military patients require the unity of efforts between the Department of Defense, the Department of Veterans Affairs and our civilian medical communities. We shall be judged by the homecomings of those we deploy.

Our own Civil War influenced the teaching and practice of Major Andrew Taylor Still. Let us not forget his teachings when we welcome our Veterans home. The laying of hands on these patients will restore tissue perfusion and relieve tissue congestion (tissue memory). We all need to feel the safety of home.

We all need to remember "an Osteopath asks no favor of drugs"[4] and be respectful of opiates. Fifty percent of patients with post-traumatic stress disorder (PTSD) self medicate—a great challenge in soldiers' homecomings. Our teachers have taught us the importance of treating both body and mind. Let us do no harm as we receive our returning Veterans.

As we treat and unwind the soma, memories release. Trauma to the autonomic nervous system (ANS) is seen in all disasters, not just man-made (war) disasters. Major depression, anxiety disorders, PTSD and substance abuse are all reported in the disaster psychiatry literature. As osteopathic physicians, we can make a difference through the restoration of the ANS, and through our support of those in recovery.

I hope the reader will find these journal readings of value. I am confident that our profession will continue to welcome our troops home and practice "the difference a DO makes."

Recommended reading for those who care for veterans can be found at: www.ncptsd.va.gov, www.DCoE.health.mil and www.biausa.org.

References

1. Sun T. *The Art of War*. Griffith SB, trans. Oxford: Oxford University Press;1963.
2. Homer. *The Iliad*. Lattimore R, trans. Chicago: University of Chicago Press; 1951.
3. Homer. *The Odyssey.* Butcher SH and Lang A, trans. New York: P.F. Collier & Son, 1909–14.
4. Truhlar RE*, ed. Doctor A. T. Still in the Living: His Concepts and Principles of Health and Disease.* Cleveland, OH: privately published; 1950.

Ultrasound-Guided Injections

September 7-8, 2012, at UMDNJSOM in Stratford, NJ

Course Description

This course is designed for physicians who are novices at sonographic guidance for injections. Under the direction of physiatrist Sajid Surve, DO, course participants will be introduced to the basic principles of ultrasound, learn proper injection techniques with ultrasound guidance and learn proper billing and coding for this procedure. Cadavers will be available for practice, and table trainers will facilitate a low faculty-to-participant ratio. The course will focus on the injection of the major joints: glenohumeral, sacroiliac, hip, and knee.

Course Objectives

Upon completion of this course, participants will be able to:

- Apply the basic principles of musculoskeletal ultrasound
- Comfortably navigate the necessary equipment required for sonographic guidance of injections
- Utilize proper injection techniques under sonographic guidance for the glenohumeral, sacroiliac, hip and knee joints.
- Bill, code and document correctly for ultrasound-guided injections
- Avoid common pitfalls associated with the above procedures

CME

16 hours of AOA Category 1-A credit is anticipated

Course Directors

Millicent K. Channell, DO, FAAO, is a 2001 graduate of the Philadelphia College of Osteopathic Medicine. After completing her Family Medicine residency and Neuromusculoskeletal Medicine/Osteopathic Manipulative Medicine (NMM/OMM) residency, she joined the faculty of UMDNJSOM in the departments of OMM and Family Medicine. She has made numerous scholarly contributions to osteopathic medicine, most notably as co-author of the book *The 5-Minute Osteopathic Manipulative Medicine Consult.*

Sajid A. Surve, DO, is a 2005 graduate of the UMDNJSOM. After completing a traditional rotating internship at Delaware County Memorial Hospital in Drexel Hill, PA, he became an inaugural resident, and the first Chief Resident, of the Physical Medicine and Rehabilitation residency at Long Beach Medical Center in Long Beach, NY. He joined the faculty of UMDNJSOM in 2009, and completed an NMM/OMM residency in 2010.

Course Location

UMDNJSOM

One Medical Center Drive
Stratford, NJ 08084

Course Times

Friday and Saturday: **8:00 am - 5:30 pm** (lunch provided)

Travel Arrangements

Call Tina Callahan of Globally Yours Travel at (800) 274-5975.

Registration Form

Ultrasound-Guided Injections
September 7-9, 2012

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Understanding blast-induced traumatic brain injury (bTBI) through mechanisms and patterns of injury

Patrick M. Malie, MS, OMS III; Marc Quentin Sonnier, Jr., MS; Murray R. Berkowitz, DO, MA, MS, MPH

Abstract

Objective of review: To provide clinicians and researchers with a comprehensive, evidence-based overview of blast-induced traumatic brain injury (bTBI) and the implications for a multi-disciplinary approach to treating military personnel. Understanding the effects of that injury on the human brain is difficult due to the complexity of explosive forces. This review introduces new tools and innovations being applied within the context of bTBI research. Understanding blast injury—a common occurrence in military combat— by evaluating benchmarks for concussive or mild traumatic brain injury (mTBI) with computational tools, neuroimaging, epidemiology and neurophysiology in a multi-disciplinary approach to treatment, will help delineate subsequent effects that may complicate recovery and produce the majority of manifestations associated with this type of injury.

Recent findings: Body and vehicular armor reduces combatants' risk of higher severity blast exposure, which tends to increase the rate of bTBI incidence. An increase of mTBI literature has been found in a diverse range of science and medical journals from the fields of immunology, epidemiology, neuroscience and psychiatry, to computer science and blast forensics. This has improved understanding of what differentiates bTBI, post-concussive syndrome and post-traumatic stress disorder (PTSD) with the goal of improving diagnosis.

Conclusions: In the current state of the U.S. medical crisis, cost-effective solutions are needed to manage the new condition of chronic bTBI in our veterans. Understanding neurodegeneration with biomarkers, axonal damage, personality aberrations and inflammatory responses aimed at building treatment protocols improves both patient outcomes and scientific research progress. Through a multidisciplinary approach to understanding the mechanisms and patterns of injury of blast-induced traumatic brain injury, research scientists and physicians hope to achieve optimal patient outcomes.

Introduction

As many as 320,000 American military combat veterans who have served in the current wars in Iraq and Afghanistan are estimated to have sustained a traumatic brain injury (TBI) as of January 2008.[1] TBI has been described as the "signature injury" of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).[2-5] The growing number of conflicts in recent years has led to an unprecedented increase in the use of weaponry resulting in blast-induced TBI (bTBI). Such weaponry includes improvised explosive devices (IEDs), rocket-propelled grenades (RPG-7 to RPG-29), thermobaric "enhanced-blast explosives," and explosive-formed projectiles.[6] The negative effects of these devices are felt not only by military personnel, but also civilians. In 2007, roughly 14,000 terrorist attacks occurred worldwide, resulting in more than 44,000 injuries and 22,000 deaths, a 20 to 30 percent increase from 2006.[7] Moreover, as a result of modern warfare, it is estimated that 10 civilians are killed for every one combatant casualty.[8] The study and management of blast-related injuries is not a recent phenomena, despite its increased prevalence in recent times. The first known documented study of blast-related head trauma occurred more than 90 years ago.[9]

During World War I, British Army physicians Drs. Gordon Holmes and Fred Mott studied soldiers subjected to blasts who developed neuropsychiatric symptoms.[10] Holmes and Mott had trouble differentiating between emotional trauma and physical brain injury.[9,11] Such difficulties persisted into World War II—some physicians believed there was no brain injury, while others noted electroencephalography changes similar to those previously seen in closed head injuries.[12] Although it was evident that secondary and tertiary blast injuries could result in brain damage, it remained unresolved whether primary blast injuries could directly damage the brain.

TBI Overview

TBI is defined as damage to the brain from an external mechanical force, including impact, acceleration or deceleration, penetration by a projectile and blast waves.[13-14] It is an acquired form of brain injury. TBI is a complex injury with a broad spectrum of disabilities and symptoms that can be classified as mild, moderate or severe, depending on the extent of the damage inflicted on the brain.[15] Brain injury is also known as intracranial injury

or head injury, although the latter does not necessarily connote neurological defects. TBIs are divided into two subcategories: (1) primary injury and (2) secondary injury. Primary injuries occur at the moment of trauma, while secondary injuries occur after the trauma, and may persist for an extended period.[16]

Primary injuries can manifest as focal injuries, such as skull fractures, intracranial hematomas, contusions, lacerations, and penetrating wounds, or they can be diffuse, as in diffuse axonal injury.[15] Secondary injury is promoted through biochemical cascades and further cellular damage from the effects of the primary injury, and can take hours to days to present following the initial injury.[17] Almost half of all TBI patients deteriorate after the initial injury, and many succumb days to weeks later.[18]

Secondary and tertiary bTBIs involving cerebral contusion, direct parenchymal damage and intracranial hemorrhage comprise most central nervous system (CNS) injuries; however, primary blast forces are suggested to cause brain injury as well.[21-22] Primary blast injuries to the brain and spinal cord have been noted to include concussion and barotrauma (physical damage produced from pressure differences), with the latter resulting from acute air embolism.[21] Air embolisms, or gas embolisms, can occur whenever a blood vessel is open and a pressure gradient exists, favoring the entry of air. Cernak, et al.,[22] demonstrated that exposure to blast overpressure induces ultrastructural and biochemical impairments in the brain hippocampus, with the associated development of cognitive deficits, including long-term memory and spatial navigation. Moreover, with the increased use of body armor in the military, injuries that were once considered to result from secondary and tertiary blast effects, such as unconsciousness and coup/contrecoup injuries, are now increasingly being attributed to primary blast effects.[21]

bTBI vs. Civilian TBI

bTBI injuries present unique and new challenges among the medical community; however, it remains an incurable condition. An important challenge is the difficulty in differentiating biological from psychological symptoms. According to Masel, et al., TBI is a chronic disease process with long-lasting effects on the CNS.[23-25] Military mobilizations from 2001 to 2011 yielded many surviving battle casualties as well-armored soldiers engaged aggressors who retaliated with novel weaponry, such as the IED. This provides research opportunities to study the long-term effects in greater detail due to the increased survivability of battle injury. Although there is no cure for battle TBI, medical professionals are encouraged to evaluate and treat bTBI with some of the latest research findings.[26-32]

Prior to 1990, there were insufficient clear-cut bTBI medical findings, largely due to only a rudimentary understanding of its symptoms-based classification. Physical examinations of this illness typically yielded problems of similar magnitude, which consequently became grouped under a single, disparate pathophysiological process, and left physicians with an imprecise method classification.[33] Since 2001, with the injurious effects of IEDs adding to the concerns of military medical clinicians, Vanderploeg raised attention to the serious risk of undiagnosed concussion or mTBI due to the fact that treatment for obvious injuries are of higher priority in most cases. Newly submitted research findings within the last several months are beginning to address this classification deficit and provide guidance and much-needed solutions for this swiftly growing cohort of mTBI military personnel.

Previously lacking significantly large bTBI cohorts, there is an inadequate understanding of the wide variety and mass of injuries sustained by U.S. military forces and subsequently presenting in today's civilian medical practice upon their return. (There were FBI reports of 15,700 bombings with 3,176 injuries and 355 deaths between 1990 and 1995).[34] Computational data models provide one of the latest tools for medical professionals and researchers to look deeper into the effects of explosive blasts, so that more promising medical solutions may be explored. Comparative studies between mTBI-injured soldiers of the Vietnam-era and the Iraq and Afghanistan combat theaters had to control for the psychiatric conditions of soldiers in the latter group that predated the existence of this current injury classification.[35,36]

The civilian definition of mTBI is a cerebral concussive force produced by the acceleration or deceleration forces acting on the brain to produce a period of confusion and/or amnesia followed by a complex of the following symptoms: physical (headache, fatigue, sleep disturbances, dizziness, sensory changes and various pains and discomforts); cognitive (attention and concentration difficulties, diminished ability to process, learn and retain new information and solve complex problems); and behavioral-affective (irritability, diminished frustration tolerance, social isolation, interpersonal difficulties, diminished confidence and self-esteem, fatigue, an increased need for sleep and depression).[37] Civilian TBI is usually the result of mechanical forces during collisions or sudden mechanical forces.[38] As a result of dynamic loading, which is comprised of impulsive loading and impact loading, angular loads deliver the insult to brain tissue. As a result of this rotational injury, higher rates, rather than longer durations, tend to do more damage. Focal injury tends to occur with the more direct impact loading in the absence of widespread injury.

Unfortunately, military-associated blast TBI is much more complex. Diffuse axonal injury occurs as a result of rotational acceleration accompanying indirect loading. Of these rotational injuries, we are most susceptible to sheer strain. This is due to the large cross-sectional area of the CNS providing many mediatory paths for contradicting force vectors and causing both acceleration and deceleration forces. Animal models associate rotational acceleration with concussion and linear acceleration with contusions and subdural hematomas without loss of consciousness. As the lowest of TBI severity, mild bTBI has a reported prevalence of 80 percent spanning three decades of civilian traumatic brain injury.[33,39-41]

It is evident that many of the features observed in animal models mimicking focal and diffuse TBIs are also seen in bTBI.[42] According to Cernak and Noble-Haeusslein,[42] common features include vasospasm and barrier disruption, electroencephalogram (EEG) abnormalities, oxidative stress, elevated ICP, metabolic disturbances and energy failure. Although some reports propose varying temporal and spatial profiles, as well as a different frequency of pathological changes in bTBI versus non-explosive TBI, other studies suggest a lack of strong evidence that blast is categorically different than other mechanisms of TBI.[43-45] For instance, Ling, et al.,[44] propose that the occurrence of vasospasm, which is often the cause of delayed neurological deterioration, appears to be more typical following bTBI than other types of TBI, such as penetrating TBI (pTBI) and closed head TBI (cTBI). As a result, military neurosurgeons have had to perform decompressive craniectomies more often than is typical for pTBI or cTBI. Moreover, there was an increased incidence of PTSD symptoms reported among bTBI participants in a study designed to compare patterns of performance on neuropsychological measures.[45] However, with respect to cognitive sequelae, it was argued that there is no strong evidence that blast is categorically different than other mechanisms of TBI.[45]

Despite the aforementioned cases noting differing features between bTBI and TBI from other mechanisms, it is still a challenge to confirm or refute a unique signature clinical description for bTBI. Epidemiologic data alone is not sufficient in differentiating the less-studied blast injury features from the more well-known components of pTBI and cTBI.[44] Further complicating the issue is that individuals who experience bTBI are also likely to experience other severe injuries, including hemorrhagic shock and limb amputation.[42] Addressing other such injuries can mask features attributable to bTBI.

Predicting Arousal Defects as a Long-Term Consequence of Blast-Induced mTBI

mTBI diagnosis is difficult due to its heavy reliance on patient recall of the history of the trauma. In the best-case scenario, eyewitness accounts can substitute for the memory of the injured. As a diagnostic component of mTBI, loss of consciousness (LOC) is a result of functional degradation of both cerebral hemispheres of the reticular activating system (RAS). Blyth proposes that mTBI-associated alteration of consciousness is caused by injury to consciousness as a state-dependent structure that includes the RAS. This structure is excited by input from surrounding sensory tracts, and transmits this excitation to the cortex to induce generalized cortical and behavioral arousal. Within the brainstem reticular formation, it extends from the top of the spinal column to the rostral midbrain with extensions into the thalamus and hypothalamus.[33,46]

Significant Forces of Blast Effects

Blast-induced TBI acts through multiple simultaneous events occurring in succession, and as a result, can be categorized according to three distinct actions of injury.[47] Blast waves traverse the explosives' surrounding environment with an initial high-pressure shock wave leading to over-pressurization. An explosion creates ballistic projectiles within a viscous medium, giving rise to blast-pressure waves. These projectiles, such as blast debris, lose energy as they propagate toward the greater forces generating the pressure waves. The magnitude of these waves is the sum of interfering wave points created as it propagates, signature waves from conserved areas of spatial expansion with a consequentially causal collapse, and reflected waves from stiffer boundaries. This property of energy dissipation is the inherit magnitude of explosive blast waves.[48]

The over-pressurization mentioned earlier is followed by a subsequent blast wind that causally follows the subsequent negative pressure created by the shock wave similar to an elastic-like pressure recoil. The ultimate vector of this reverse wind is directed toward the explosive source, leading to rapid under-pressurization.[49] The negative transient pressures associated with reverse wind can create cavitation bubbles that are toxic to neurons. *In vitro* studies of mild TBI discovered induced circuit crosstalk as a consequence of single, mild blast exposures. Multiple blasts increase neuronal tissue susceptibility to damage associated with excitotoxic insult. The action of primary blast injury relates to the wave action that the blast produces through the mediums it traverses. Tympanic membrane rupture is generally considered a reliable patient presentation for primary blast exposure, but interestingly,

less than two percent of cases in the Madrid, Spain, train station explosion experienced pulmonary injury lacking this indicator.

Factors that complicate blast outcomes include explosive type, peak over-pressure and its duration, impulse as complex wave forms, location of the explosion and its relative proximity, environmental hazards, body orientation to the blast and barriers. All these factors impact, as well as facilitate, bodily insult due to blast exposure. Secondary acts by blast waves propulsion on fragmented objects that become projectiles. This bTBI is more associated with penetrating injury where, in the case of neurotrauma, the integrity of the skull becomes compromised by the blast's projectiles. These projectiles create superficial pathology that is more apparent than the latter. Mild blast seldom causes injury of higher blast severity, but multiple exposures, like those seen in many military personnel overseas, creates acceleration/pressure forces that result in neuron associated soma swelling, nuclear prominence and sometimes neuronal death.[50] *In vitro* studies focusing on the effects of direct laceration by cell scratching produced findings that proposed the effects of micro-laceration induced a greater amount of neuronal cellular death than compared to glial cells.

Tertiary is relevant to the surroundings in which the blast's action mediates a collision. Likely damage can be expected between the hemispheres separating the cerebrum from the cerebellum due to sheer strains. Cytoskeletal alterations, organelle disruption and derangement have occurred in studies by Chen[51] when tertiary effects were quantified *in vitro* as an affect of mechanical deformation and quaternary involved burns to surface tissues proximal to those in contact with air, such as the respiratory tracts and skin. These are commonly seen with explosive weapons capable of radiation delivery over large areas. Injury findings of this type of blast would likely demonstrate the neuronal damage similarly seen with heavy cellular phone use.[42,51-58]

Computational Modeling of Blast Injury

Chen describes researchers contrasting the virtual representation of geometric deformations of blast waves to that of experimentally similar effects of induced blast trauma as an injury predictor.[51] With the aid of embedded monitoring systems consisting of cost-effective, helmet-based nanosensors capable of relaying digitalized force injury characteristics to a field hospital, medical teams are able to explore new possibilities of guided, long-term treatment into structurally precise areas of perceived damage.[59] Some are concerned that helmets, especially with the added weight of electronic sensors, may contribute to increased cerebral damage. But recent computational, three-dimensional analysis discredited this hypothesis with findings that are suggestive of danger only when forces are so high that the damage would be similarly destructive either with or without protective headgear. The combined advantage of both recorded collateral damage characteristics as input for computational cell-deformation and cell-stretching modeling allows for estimates of boundary zones between damaged and undamaged areas in the brain. These data would be used to provide additional information to the more obvious clinical findings. The precision of finite element models representing blast dynamics upon brain tissue will inevitably increase with more research to meet the level of confidence needed to be useful for diagnosticians to develop a structured approach to differential diagnosis for blast-related mTBI.[51,52,54,60-64]

Experimental Study of Blast Effects

The more commonly studied methods for investigating blast effects are either by open-air blast, which is often done on large specimens, or closed-pressure systems well suited to investigate blast wave kinetics with smaller specimens in a more controlled fashion. Open-air blast studies, while lacking the scalar precision and objectivity of closed-air studies, presents the more realistic, multi-dimensional variability of forces experienced by U.S. military forces. One such study has attempted to combine the more precise, closed-air blast tube investigation with the varied, multi-mode shock of open blast studies in a cost-effective and highly subjective TBI screening experiment as an alternative to the expensive Helium-based experiment. The hypothesis is that multi-mode shock draws correlate the severity of brain insult with a pressure-time signature of varied blast signatures in an attempt to associate a higher relevance to the variety and occasionally overlapping nature of injuries experienced by deployed combat troops.

Using several characteristically different gas types in the experiment, expensive helium used to improve the velocity performance of closed shock tube research was replaced with relatively inexpensive oxyhydrogen. It also reduces conditional ischemia as an inherent property of the closed experiment's atmospherically isolated environment. This pressure-time signature compensates for the traditional lower resolution peak pressure as a measure of the many different components of blast effects. The six parameters studied were shock wave velocity, positive phase magnitude, positive phase duration, positive phase impulse, negative phase magnitude, and the impulse difference between reflected and free-field pressures. This allows the degrees of damage to be predicted as potential contributions of individual blast components. Greater cerebral vascular damage was seen using compressed air

rather than oxyhydrogen of similar peak pressure. This suggests that this method may be a more realistic and cost-effective approach to blast study.[65,66]

Long-Term Effects Associated with Blast mTBI

Long-term effects of mTBI on the CNS are elusive because conflicting findings in scientific and medical literature are unclear regarding mechanisms relative to the nervous system. The combination of IEDs, along with dramatically improved soldier survivability since the infancy of defining PTSD at the end of the Vietnam War era, has bolstered a significant interest in blast-induced neural injury. Although animal studies have indeed proven that, of the many varied mechanisms of injury, blast overpressure waves seem to cause the diffuse axonal-type of neuropathological injury.[67] TBI injury findings of these mechanisms illustrate primary blast wave as a unique mechanism and injury variable.[49]

Blast-induced mild traumatic brain injury (bmTBI), whether occurring in a combat theater or berthing areas, is typically associated with instant, combustion-induced cephalic blunt trauma, resulting in temporary debilitation of neurological functionality.[23]

Helmet Protection from Blast mTBI

There has been much debate to whether helmet protection adds to or lessens bTBI. Service members wearing helmets were more likely to withstand both lower TBI severity and Injury Severity Scores when compared to those who weren't, even though the helmet participated in blast mechanisms. Less than 40 percent of IED attacks were accounted for by helmetless TBI as compared to the larger 82 percent of operatives wearing helmets. This small percentage of victims unprotected from IED blast was likely attributable to a combination of convoy-required helmet use established by military protocol, and the increased vulnerability that predisposes mobilized ground vehicles to this type of attack. Consequently, higher TBI severity associated with projectile-type weapons, including their associated injury specifics, was significantly higher when helmet protection wasn't available. This is likely the result of ambush or unexpected attacks on military servicemen in berthing areas where it is more difficult for militant extremists to exercise timely IED staging, thus warranting the use of focused weaponry. Unfortunately, these servicemen are most vulnerable because of laxed precaution in these areas, leading to helmet disrobe and subsequent maximum morbidity. Therefore, these results, along with current findings, seem fairly agreed that helmets do reduce TBI severity. But new helmet designs are needed for improved facial protection to optimize TBI reduction during explosive exposure.[62,68]

Conclusions

Symptoms are not only dependent on the type and severity of TBI, but also by the particular region of the brain that is affected.[15] Mild TBI may result in loss of consciousness, while other symptoms include nausea, vomiting, headache, dizziness, difficulty balancing, lack of motor coordination, blurred vision, lightheadedness, fatigue or lethargy, tinnitus and changes in sleep patterns.[13,19] Emotional and cognitive symptoms associated with mild TBI include behavioral or mood changes, confusion, as well as impairment of concentration, attention, and thinking.[15] An individual with moderate or severe TBI may present the same symptoms associated with mild TBI, as well as persistent headache, vomiting and nausea, agitation, restlessness, confusion, loss of coordination, slurred speech, dysarthria, aphasia, weakness or numbness of limbs, convulsions and dilation of one or both pupils.[13,15,19] Long-term symptoms of moderate or severe TBI include cognitive changes, such as issues with attention sustainment, processing speed and executive function, as well as changes in typical social behavior and judgement.[20]

Cerebral concussive syndromes are common among those subjected to explosions, with cognitive deficits and substantial memory dysfunction typically resulting.[69] These results indicate that bTBIs are capable of causing cognitive deficits, particularly problems with memory.

Hoge, et al.,[70] found mild TBI occurring among soldiers deployed in Iraq was strongly correlated with PTSD and other physical health issues months after returning home. Furthermore, it was suggested that both PTSD and depression were critical mediators of the relationship between mild TBI and physical health problems.[70-74] Significant correlation was found between tympanic perforation and unconsciousness in blast-injury victims, suggesting a relationship between concussive brain injury and tympanic perforation.[5] It has also been noted that both tympanic perforation and primary blast injury were scarce in service members subjected to explosions in the recent US-Iraq conflict.[69,75] This may suggest that tympanic perforation may correlate with concussive brain injury, but not with other primary blast-induced injuries. Further studies need to be conducted to provide insight into the relationship between tympanic perforation and concussive brain injury.

Currently, many features of bTBI remain unknown. The relatively recent increase in the occurrence of bTBI has warranted a research push to allow for a better characterization of the injury. In so doing, the clinical personnel will be better able to provide proper assessment and treatment techniques. Furthermore, family members and friends of bTBI victims will be better prepared for coping with effects that may last a lifetime.

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Address correspondence to:
Patrick M. Malie, MS, OMS III; Marc Quentin Sonnier, Jr., MS; Murray R. Berkowitz, DO, MA, MS, MPH
Department of Osteopathic Manipulative Medicine
Philadelphia College of Osteopathic Medicine—Georgia Campus
625 Old Peachtree Road NW
Suwanee, Georgia 30024
murraybe@pcom.edu

Clinical management and multipotential treatment strategies for blast-induced traumatic brain injury (bTBI)

Patrick M. Malie, MS, OMS III; Murray R. Berkowitz, DO, MA, MS, MPH

Abstract

Objective of review: To gain an understanding of current clinical management, treatment strategies and sequelae of blast-induced traumatic brain injury (bTBI). Due to the nature of bTBI, the focus is placed on military populations.

Recent findings: With the increased use of body armor in the military, injuries that were once considered to result from secondary and tertiary blast effects are increasingly being attributed to primary blast effects. The occurrence of vasospasm and post-traumatic stress disorder (PTSD) symptoms appear to be more frequent in bTBI than with other mechanisms of brain injury. Diketopiperazine therapy and hyperbaric oxygen therapy are multipotential treatment designs for bTBI.

Conclusions: Due to the increased occurrence of bTBI as a result of modern warfare, a collaborative effort is required by all medical personnel involved in the clinical management, assessment and treatment processes in order to increase the probability of favorable outcomes.

Introduction and TBI Overview

It is estimated that by January 2008, as many as 320,000 American armed forces serving in the current Iraq and Afghanistan wars experienced a traumatic brain injury (TBI).[1] The growing number of conflicts in recent years has led to an unprecedented increase in the use of weaponry resulting in blast-induced TBI (bTBI), so much so that TBI has been designated as the "signature injury" of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).[2-5]

TBI is defined as damage to the brain from an external mechanical force, including impact, acceleration or deceleration, penetration by a projectile and blast waves.[6,7] TBI is a complex injury with a broad spectrum of disabilities and symptoms that can be classified as mild, moderate or severe, depending on the extent of the damage inflicted on the brain.[8] Brain injury is also known as intracranial injury or head injury, although the latter does not necessarily connote neurological defects. TBI is divided into two subcategories: (1) primary injury occurring at the moment of trauma and (2) secondary injury occurring after the trauma per se, which may persist for an extended period.[9] Secondary injury is promoted through biochemical cascades and further cellular damage from the effects of the primary injury, and can take hours to days to present following the initial injury.[10] Almost half of all TBI patients deteriorate after the initial injury, and many succumb days to weeks later.[11]

Symptoms are not only dependent on the type and severity of TBI, but also by the particular region of the brain affected.[8] Mild TBI may result in loss of consciousness, while other symptoms include nausea, vomiting, headache, dizziness, difficulty balancing, lack of motor coordination, blurred vision, lightheadedness, fatigue or lethargy, tinnitus and changes in sleep patterns.[6,12] Emotional and cognitive symptoms associated with mild TBI include behavioral or mood changes, confusion, as well as impairment of concentration, attention and thinking.[8] An individual with moderate or severe TBI may present the same symptoms associated with mild TBI, as well as persistent headache, nausea and vomiting, agitation, restlessness, confusion, loss of coordination, slurred speech, dysarthria, aphasia, weakness or numbness of limbs, convulsions and dilation of one or both pupils.[6,8,12] Long-term symptoms of moderate or severe TBI include cognitive changes, such as issues with attention sustainment, processing speed and executive function, as well as changes in typical social behavior and judgement.[13] Cerebral concussive syndromes are common among those subjected to explosions, with cognitive deficits and substantial memory dysfunction typically resulting.[14] These results indicate that bTBIs are capable of causing cognitive deficits, particularly problems with memory.

According to Hoge, et al.,[15] mild TBI occurring among soldiers deployed in Iraq was strongly correlated with PTSD and other physical health issues months after returning home. Recent studies have suggested that tympanic perforation, or rupture of the eardrum, may foreshadow concussive brain injury, but not necessarily for other primary blast-induced injuries.[5,14,16]

It is evident that many of the features observed in animal models mimicking focal and diffuse TBIs are also seen in bTBI.[17] According to Cernak and Noble-Haeusslein,[17] common features include vasospasm and barrier disruption, electroencephalogram (EEG)

abnormalities, oxidative stress, elevated intracranial pressure (ICP), metabolic disturbances and energy failure. Though some reports propose varying temporal and spatial profiles, as well as a different frequency of pathological changes in bTBI versus non-explosive TBI, other studies suggest a lack of strong evidence that blast is categorically different than other mechanisms of TBI.[18-20] For instance, Ling ,et al.[19] proposes that the occurrence of vasospasm, which is often the cause of delayed neurological deterioration, appears to be more typical following bTBI than other types of TBI, such as penetrating TBI (pTBI) and closed head TBI (cTBI). As a result, military neurosurgeons have had to perform decompressive craniectomies more often than is typical for pTBI or cTBI.

Clinical Management

Clinical care for bTBI begins on the battlefield and is carried out in accordance with the ‘‘Guidelines for Field Management of Combat-Related Head Trauma.”[19] A primary objective of the guidelines is to serve as a resourceful tool for all the individuals involved in the management process, including the physician, commanding officer, logistician and combat medic.[21] They provide evidence-based support for military medical personnel in the assessment, treatment and transport of TBI combat casualties. One of the assessment techniques included in the guidelines involves the combatant’s Glasgow Coma Scale (GCS) score.

A more detailed clinical assessment should be made upon arrival at a combat support hospital, beginning with an immediate CT to identify lesions such as skull fractures, intracranial hemorrhage and cerebral edema.[22] Critical issues to attend to include maintaining proper oxygen levels, controlling ICP and ensuring proper cerebral perfusion pressure.[21] A frequent observation among clinicians is the presence of both hyperemia and severe edema in the acute period, which tends to occur more readily when a traumatic subarachnoid hemorrhage is observed.[19] A delayed increase in ICP has been observed in some individuals occurring two to three weeks after severe bTBI, although it may be attributable to other complications such as vasospasm.[18] In the first study to analyze the effects of blast injury on cerebral vasculature, Armonda, et al.[18] found that clinical outcomes in bTBI victims with traumatic vasospasm were worse when compared to those who presented without it. Because investigations into the effects of blast injury on cerebral vasculature have only recently begun, further studies will need to be conducted to determine if a significant relationship exists between the two.

General management of increased ICP includes controlling the airway, elevating the patient’s head to 30 degrees and administering Mannitol (0.5 to 1 g/kg over 10 min).[23] Mannitol (Osmitrol) is a weak renal vasodilator that is used as an osmotic diuretic. Hypertonic saline solutions are an option that has shown efficacy in patients suffering from an increase in ICP.[19] In particular, intravenous injection of 23 percent NaCl can be used to alleviate acute elevations of ICP, followed by repeated infusions of two percent and three percent NaCl to stabilize ICP.[23] A critical aspect of hypertonic saline therapy is that serum osmolality can be increased without compromising intravascular volume, as many victims of severe blast injury present with hemorrhagic shock.[22] Unfortunately, many patients suffering from intracranial hypertension do not respond upon implementation of the aforementioned strategies, and further intervention is required.

Decompressive craniectomy is one such intervention that played a critical role in alleviating adverse effects of severe brain swelling following bTBI in OIF.[24] In a decompressive craniectomy, part of the skull is removed to permit space for the swelling brain to expand. Aside from easing the effects of increased ICP, it also improves brain oxygenation, cerebral blood flow and increases compliance.[25] Some studies have suggested improved outcomes after decompressive craniectomy following bTBI.[24,26] For instance, Aarabi, et al.,[24] indicated an association between improved functional outcome and decompressive craniectomy in patients with unmanageable ICP and/or brain herniation. More than 61 percent of patients in an observational study with increased ICP demonstrated favorable outcomes (defined as good recovery or moderate disability), following decompressive craniectomy.[26] Moreover, decompressive craniectomy resulted in more favorable outcomes in patients with higher GCS scores.[22] Current randomized trials in Australia and the United Kingdom could provide further insight into decompressive craniectomy’s role in improving outcome after severe head injury.[27,28]

Positron emission tomography (PET) is an effective and resourceful technique for quantifying ischemic burden after TBI.[29] TBI studies implementing PET have shown that early reductions in cerebral perfusion can result in cerebral ischemia, which is correlated with adverse outcomes.[29,30] PET has demonstrated that in TBI, the threshold of cerebral blood flow (CBF) below which irreversible tissue damage occurs varies from the classical CBF threshold for stroke.[30]

Treatment

Stoica, et al.,[31] discussed a multipotential treatment design that has shown effectiveness for TBI and spinal cord injury. The approach was based on thyrotropin-releasing hormone (TRH)—a tripeptide hormone that is metabolized to a cyclic dipeptide (CHP). CHP can be

classified as a diketopiperazine—a class of cyclic, organic secondary metabolites with a wide variety of biological functions.[32] Similar to other diketopiperazines, CHP is able maintain substantial physiological function.[32] Of all the diketopiperazines structurally similar to CHP that were developed by Faden, et al.,[33] 1-ARA-35b (35b) has been evaluated both *in vitro* and *in vivo* experiments, and showed neuroprotection in both necrotic and apoptotic cell death models.[31,34] When introduced intravenously, 35b lowered lesion volume by almost 70 percent and improved both cognitive and motor skills in mice after either fluid percussion-induced (FPI) TBI or controlled cortical impact (CCI).[31] 35b is presently being investigated for human clinical trials in head injury.

Another multipotential treatment strategy that may be beneficial in treating bTBI is hyperbaric oxygen therapy (HBOT). HBOT utilizes oxygen at pressures greater than atmospheric pressure in an enclosed chamber to treat certain disease processes, such as anemia, carbon monoxide poisoning and air embolism.[35] The physiologic effects of HBOT are dependent on the underlying pathology of the disease. For instance, HBOT has been shown to cause proliferation in both normal and diabetic human fibroblasts *in vitro*.[36] Furthermore, HBOT has demonstrated the ability to lower apoptosis and improve mitochondrial recovery in hypoxic neurons.[37] It is suggested that the enhancement in mitochondrial function facilitates cognitive recovery and lowers hippocampal neuron loss after TBI.[37]

In a case report conducted by Wright, et al.,[38] two U.S. servicemen who had suffered mild TBI from a roadside IED showed improvements in Automated Neuropsychological Assessment Metrics (ANAM) testing following HBOT. ANAM is a library of more than thirty electronic-based test modules designed for a broad range of clinical and research applications across all service branches within the Department of Defense.[39] Specifically, ANAM4™ serves as a neurocognitive assessment tool that has been customized in the aforementioned case report to be sensitive to cognitive changes that typically coincide with mild TBI.[39] Following seven months of persistent mild TBI symptoms, the injured servicemen drastically improved within ten days of HBOT. In particular, their headaches and sleep disturbances decreased, while their irritability, cognitive and memory defects improved more slowly.[38] Due to the reliability of the ANAM testing, and that HBOT was the only treatment received by the servicemen, the efficacy of HBOT in bTBI is noted.

bTBI-related sequelae

The sequelae of bTBI are diverse and can persist for a patient's lifetime. Due to the scarcity of literature on the subject, as well as an overlap of symptoms associated with certain manifestations, understanding post-TBI disorders has proved troublesome for clinicians.[40] The chronic sequelae of TBI can be grouped into different categories based on the various neuropsychiatric symptoms associated with each grouping. Specifically, they can be discussed as cognitive impairments, neurobehavioral disorders, somatosensory dysfunctions and somatic symptoms.[13] Other post-injury manifestations that do not delineate into separate entities include post-concussion syndrome (PCS) and substance dependence.[41]

Any impairment of a sensory organ system can be considered a somatosensory dysfunction. Auditory disruption has become the most prevalent individual, service-connected disability, with compensation totaling more than one billion dollars per year.[42] In particular, peripheral hearing loss, tinnitus, central auditory processing deficits and vestibular impairment (leading to dizziness) can occur in bTBI.[42] Visual impairments, such as anomalies of light sensitivity, accommodation and vergence (convergence or divergence) may also be present.[43] Although disruption of olfactory and taste senses has not been thoroughly investigated in bTBI, alterations in sense of smell may alter social interactions, immune functions and emotions.[44]

Chronic pain is a common complication of TBI, both in civilian and military populations. Nonetheless, somatic symptoms (i.e., chronic pain syndromes such as headache) represent an underdiagnosed result of TBI.[13] It is suggested that PTSD might arbitrate some TBI-induced somatic symptoms; however, brain injury seems to associate independently with chronic pain.[15] According to Nampiaparampil,[45] chronic pain syndromes are independent of neurobehavioral disorders, and are typical among individuals with relatively minor brain injuries. Although it is thought that chronic pain is more likely to occur in patients with mild TBI, more studies will need to be conducted to establish a significant correlation between the two.[45]

Although cognitive dysfunctions are commonly reported following bTBI, their precise prevalence is poorly understood, partly because of the difficulties associated with the classification of such conditions.[46] Cognitive dysfunctions can include impairments in attention, memory, language and communication, executive function and visuospatial cognition.[13] Problems with memory are among the most common dysfunctions following bTBI, and can be acute or chronic. Attention deficits are also common following bTBI and are observed throughout all TBI severities.[47] In particular, it is suggested that a pathophysiological association between TBI and attention deficit hyperactivity disorder (ADHD) may

exist.[47] Impairment of executive function, which can be characterized as an integration of specific cognitive functions that allow an individual to perform daily tasks, has been associated with poor social integration post-injury.[48] Injury to the temporal and parietal lobes is associated with apraxia and agnosia; however, the prevalence and incidence of both conditions in mild or moderate TBI is unknown.[13] Finally, there are an array of communication deficits associated with TBI, with the precise location and severity of TBI determining the particular type and degree of language dysfunction.[49]

As with cognitive dysfunctions, evidence of specific associations between TBI and neurobehavioral disorders is scarce. The neurobehavioral sequelae of bTBI include depression (mood down), mania (mood up), PTSD and other anxiety disorders, psychosis and other psychotic disorders, and libido.[46] The incidence of TBI-induced depression ranges from about 15 percent to 30 percent while the prevalence ranges from about 19 percent to 61 percent[41,50] The broad ranges are due in part to the overlap of depression symptoms with post-concussive type symptoms, including fatigue, sleep disruptions, and concentration impairments.[13] The incidence of TBI-induced mania is nine percent, while the prevalence ranges from about one percent to 22 percent[51] While the majority of manic cases develop after one year following TBI, some studies report a delay of four to five years after TBI.[52,53] A strong relationship exists between OIF/OEF veterans and PTSD. In particular, about 11 percent of returning veterans screen positive for PTSD, while about 62 percent of those with mild TBI screen positive.[54] The incidence of post-TBI psychosis is about 20 percent, while the prevalence has not been determined.[55] Because the average onset of psychosis occurs twelve years after TBI and manifests in many variations, diagnosing psychosis has proved troublesome.[41] Finally, although sexual dysfunction is common after TBI, data relating sexual health and veterans with bTBI is scarce.[56] Nonetheless, typical issues include impulsiveness and a decrease in both libido and sexual frequency.[56]

The criteria for PCS are intricate in that both somatic and cognitive impairments are included and its pathophysiological nature is contentious.[57] According to the International Classification of Diseases-10 (ICD-10), three or more symptoms from a total of eight must be present to classify as PCS.[41] The symptoms include headache, dizziness, fatigue, irritability, insomnia, concentration impairment, memory impairment, and intolerance of stress, emotion or alcohol.[41] It is suggested that the term "PCS" may be deceptive in that it could falsely imply that the condition is solely the result of an observable brain injury.[57] Supportive of that argument are the high rates of PCS found in individuals without brain injury.[58] Acute pain seemed to arbitrate acute outcome in mild TBI, while symptoms were more evident in patients with mild TBI comorbid with PTSD than those without comorbid PTSD.[59] Thus, even though bTBI may play a part in causing PCS, the relationship between PCS and other causative factors devalues its role as a marker for TBI severity and outcome.

Conclusions

As a result of the nature of modern warfare, bTBI has become an increasingly occurring injury with devastating effects, both acute and chronic. Since many of the acute effects may not be observable by the naked eye, bTBI can be referred to as "the invisible wound of war." Because several of the chronic effects can persist for a patient's lifetime, the costs associated with bTBI can be deemed incalculable. Thus, not only is a patient forever affected, but so are the friends and family members of the injured individual. Clinical management and treatment of patients with bTBI require a multidisciplinary team approach. Primary care, neurology, physical medicine and rehabilitation, and neuromusculoskeletal medicine physician specialists must team up with physical and occupational therapists and nurses to provide the breadth and depth of care necessary to manage patients with the complex of symptoms inherent in those afflicted with bTBI.

The present review highlights the need for an investigative surge so that bTBI can be better characterized. Studies encompassing both pharmacologic and non-pharmacologic multipotential treatment strategies, such as HBOT, demonstrate the potential of combination therapies for bTBI. Since there are currently no clinically proven biomarkers for brain injury, further research should be conducted on ways to improve and expedite the detection of bTBI. Furthermore, a collaborative effort is needed by all medical personnel involved in the clinical management process to become more aware of the tendencies and patterns of bTBI. Finally, mandatory education programs should be incorporated into the training regimens of military personnel stressing the importance of brain injury recognition and communication so fewer brain injuries will go unnoticed and misdiagnosed.

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Address correspondence to:
Patrick M. Malie, MS, OMS III;
Murray R. Berkowitz, DO, MA, MS, MPH
Department of Osteopathic Manipulative Medicine
Philadelphia College of Osteopathic Medicine—Georgia Campus
625 Old Peachtree Road NW
Suwanee, Georgia 30024
murraybe@pcom.edu

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2. To diagnose somatic dysfunction in junctional areas.
3. To formulate the manipulative prescription for each area.
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Program Director

John G. Hohner, DO, FAAO, is a 1987 graduate of Midwestern University Chicago College of Osteopathic Medicine (CCOM). He is certified by the American Osteopathic Board of Special Proficiency in Osteopathic Manipulative Medicine and the American Osteopathic Board of Family Physicians, and is in private practice in Oak Forest, IL. He is a professor of Osteopathic Manipulative Medicine (OMM) and Family Practice at CCOM, where he is also Division Director for the OMM's Department's MS-I curriculum. He currently serves on the AAO Board of Trustees, and is the former chair of the Education Committee.

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Blast-induced mild traumatic brain injury as etiology of post-traumatic stress disorder in military veterans

Marc Quentin Sonnier, Jr., MS; Murray R. Berkowitz, DO, MA, MS, MPH

Abstract

Objective of Review: To provide clinicians and researchers with a comprehensive, evidence-based overview of mild traumatic brain injury (mTBI) and the implications for a multi-disciplinary approach to the treatment of military personnel. Blast injuries occur in a variety of ways, but grasping a comprehensive understanding of their effects on the human brain is difficult due to the chaotic nature of explosive forces. Less obvious are the effects of mTBI. Confusion over adequate testing methods to examine these effects continues to occur. Advanced methods within this field of research are just beginning to reveal a new understanding of the debilitating effects of blast-related mTBI. These new discoveries are producing a significant understanding of the causes of reduction in both life quality and life expectancy. Along with this come new insights into treating mTBI.

Recent Findings: Body and vehicular armor reduces military combatants' risk of higher severity blast exposure, which tends to increase the rate of mTBI incidence. This, along with a proliferation of sabotage explosive attacks, has resulted in an awareness of injury patterns seen in a large proportion of U.S. military ground combat units exposed to mTBI. An unraveling of the overlap of mTBI with post-traumatic stress disorder (PTSD) and post concussive syndrome (PCS) has progressed, as well as neurophysiological associations with excite-toxic damage occurring with further blast exposure. This has improved our understanding of what separates biological manifestations, such as mTBI, PTSD and PCS, from other indicators that might complicate the differential diagnosis.

Conclusions: In the current state of the U.S. medical crisis, it is imperative that cost-effective solutions are created to manage the new chronic disease of mTBI in our demobilized military forces. Understanding neurodegeneration indicated with biomarkers, axonal damage, personality aberrations and inflammatory responses aimed at building treatment regimes have improved both patient outcomes and the progression scientific research. Through patterns of injury characteristics and standardizing baselines of physical and psychological fitness risk, patient assessments and follow-ups will help to establish relative foundations from which mTBI disease manifestation can be measured on an individual level. A multidisciplinary approach by physicians and research scientists is necessary to achieve optimal patient outcomes.

Psychological manifestations and co-morbidity related to blast mTBI

Patterns of mTBI should be distinguished from blast trauma to build a greater understanding of their psychological effects. The incidence of hospitalization associated with non-blast mTBI in adults encompasses 300/100,000 per year. With transient symptoms typically transpiring within a time frame of days to weeks, this trauma can be easily overlooked. Evidence of developing a psychiatric disorder was 2.8 times greater for mTBI patients.[1] Studies performed in Level I trauma centers reveal the influence mTBI has on the risk of manifesting psychiatric illness. Comparing mTBI to the lack thereof, injured patients had a greater likelihood of developing PTSD, panic disorder, agoraphobia and social phobia at 12 months in a study outlined by Bryant.[2] More than a third of mTBI patients had a coexisting diagnosis of PTSD in a Veterans Affairs study for screening accuracy. Inconsistent mTBI screening systems between civilian and military healthcare are believed to be a major confounder to PTSD research related to TBI.[3,4] Damage associated with the frontal brain compromises emotional control, which is believed to mediate the stress of traumatic injury. But evidence that disproves the linkage between mTBI and greater post-injury functional impairment make it difficult to predict subsequent health problems in afflicted military personnel following control of both PTSD and depressive effects. It is noteworthy that psychological disorders among military personnel could be sustained, if not increased, during combat theaters.[5-8]

Health problems occurring with mTBI and associated with PTSD begin to appear three to four months after soldiers return home.[9] The term post-traumatic stress disorder (PTSD) refers to the development of a set of specifics symptoms following exposure to a psychologically distressing event that is outside the range of usual human experience.[10] These symptoms share a stronger association than any other pair of injuries in recent military theaters.[11] But Meares has shown that

mTBI diagnosis wasn't a reliable predictor of acute PCS, whereas pain was associated with the two.[12] Evidence among non-blast studies suggest traumatic events at the onset of mTBI play a protective role against causal memory retention for PTSD.[10,13] This contradicts PTSD as a more probable sequela of mTBI (compared to more severe trauma) because of its likelihood to occur in less severe brain injury.[14] This may in part be due to the lower incidence of memory defect hindering the experiential recall of traumatic events. The co-morbidity of dually diagnosed PTSD and mTBI may make it difficult to reduce the differential diagnosis because of the association with traumatic memory retention or loss in both.[10,15] Some of the persistent symptoms are of a somatic, cognitive and psychological nature.[16] While PCS shares many overlapping symptoms with mTBI, patients may present less than the full spectrum of symptoms. Because civilian PTSD carries a clinician's warning not to diagnose mTBI or PCS, military doctors are confronted with the complications of warfare trauma within the context of patient assessment.[3,17-20]

Associated symptoms

Symptoms of military personnel exposed to blast mTBI when other bodily injuries were present did not differ. The Department of Veteran Affairs demonstrated contrasting patterns of injury between blast and non-blast polytrauma. Excluding brain injury from similar cases of polytrauma didn't improve negative neurological problems. High rates of neurobehavioral symptoms from polytrauma are similar to those leading to PCS. The significance of predicting and treating PCS continues to increase in the fragile healthcare crisis in the U.S.[14,21-23] The mTBI group had more reported injuries overall. They also had higher reporting of PTSD with increasing injury severity. Overexposure to combat-related stressors acted to compound psychological dissolution and fatigue, which ultimately lead to chronically high states of alertness and thus predisposing blast victims to experience more symptoms.[24]

Soldiers' environments and internal states throughout combat operations worked to exacerbate these effects (in particular, the response to environmental stressors and the reciprocal reaction to their environment due to internal stressors) through deviations in normal functional response and regression (consequences of poor interdependence between cognition and response). Poor outcomes, as a result of additive chronic symptoms, were best protected against when emotional disorders were taken into account during clinical investigation, the functional outcomes of which were mediated by PTSD as it relates to symptoms of mTBI.[11,25] PTSD findings and depression can make recovery from such injuries exceedingly difficult. Evidence has suggested that a large portion of mTBI damage inducing PTSD causes neural network disruption. Damage to the amygdale, contained in the pre-frontal cortex, could perpetuate anxieties through emotionally charged trauma associated with an injury event. Almost half of the service members with burn injuries were exposed to mTBI and 32 percent had PTSD.[21]

Retrospective reviews of Operation Iraqi Freedom (OIF) clinical cases involving mTBI have shown certain blast dynamics that are often apparent upon examination for specific injury patterns. In one of the largest sample sizes of Iraq combat operatives to date, 95 percent of participants were injured by blast mechanics and 90 percent sustained mTBI. The demographics revealed that injuries were 89.3 percent likely to involve mTBI when case findings were stratified against TBI severity. This is significantly greater than moderate and severe TBI, with 4.3 percent and 6.4 percent, respectively. Head injuries sustained without skull fracture were 99.6 percent likely to have mTBI symptom presentations.

Injuries from improvised explosive device (IED) explosions dominated all TBI instances. Afflictions from the detonation of these ordinances showed up in a large percentage of mTBI clinical cases. In recent years, military activity has delivered a payload of mild brain trauma in significantly greater numbers than any previous engagements because of the stockpiles of these ordinances. Without guidance equipment or tactical platforms to launch from, these otherwise useless "dumb bombs" of old warfare fill the effectiveness gap between the heavily armored modernized forces and resourceful militant guerilla fighters who are less likely to directly engage the enemy with traditional gunfire. This leads to a greater contrast between that of mild and the historically more frequent TBI of greater severity associated with gunshot wounds.

Other bodily injuries that predominate higher severity TBI are sub-clavicular and sub-cervical. In particular, simulation injuries to upper and lower extremities were not heavily present in mTBI, except when the spine or back was involved. Blast mechanisms appeared in a greater percentage of these type of injuries, which raises the possibility that the effective blast radius associated with mTBI may exert a greater force of injury than initially thought. Macgregor, Dougherty and Galarneau theorize that if the spine is involved in some cumulative force that serves to magnify the injurious effects on the CNS (including the brain and spinal cord), the blast wave spread over a larger, cross-sectional area may mediate an increase in the qualitative effects that blast vectors force on the nervous system. But these observations are purely speculative.[26]

Demographic findings of blast mTBI

mTBI in recent, war-related demographics has been taken ever more seriously because of the high risk for physical and mental degradation due to the corrosive effect imposed on biological processes associated with exposure to extreme stress. When a blast creates sensory impairments, repercussions might worsen depending on how much of a sense remains or what can be restored from its baseline. Multiple sensory losses can have drastic implications to quality of life and create increased risks for depression. Dual sensory disabled patients struggled to recover functional independence and required more assistance that dampened motor-function conditioning. This was made worse by the dizzying sequela following a blast's effect on vestibular balance. Soldiers serving in Afghanistan and Iraq frequently complain of vestibular symptoms that are not typical of blunt head trauma and significantly worsen if the gap between time of injury and presentation of symptoms increases.[21] The civilian clinical screening and treatment guidelines for mTBI lack sufficient specificity for environmental effects of combat, and make the discernment of the overlapping alteration of mental status with dissociative symptoms of acute stress disorder, post-concussive symptoms and PTSD that much more difficult.

In an effort to assess the prevalence and significance of combatants' self-reported history of mTBI three to four months after an incident, epidemiologic data was used to advance the prevention and treatment strategies of health professionals. Due to the effects of combat-related TBI, the debilitation that persistent post-concussive symptoms leave behind might pose a serious threat to the livelihood of many recent veterans for years to come. These long term effects concern mTBI, which is characterized by brief loss of consciousness or altered mental status as a result of deployment-related head injuries, particularly those resulting from proximity to blast explosions. From a population of 2,525 soldiers with injury, 124 (4.9 percent) reported loss of consciousness and 260 (10.3 percent) reported altered mental status without loss of consciousness. The significance of injury reports, including those related to mTBI, lies in the likelihood that the incident coincided with high intensity combat, a blast mechanism of injury, more than one exposure to an explosion and hospitalization during deployment. While PTSD was strongly associated with mTBI, in cases with loss of consciousness, 43.9 percent met criteria for the diagnosis of PTSD; logistical regression demonstrated that this was significant only when associated with combat intensity.[11,21]

Neurophysiology and anxiety-related sequelae

PTSD and its association with anxiogenic effects on the amygdala have been established as the fundamental mechanisms underpinning the conditioned fear reactions plaguing many mTBI-exposed veterans. Mild blast TBI has been the suspected culprit for the large majority of cases of prefrontal cortex blast shearing, which exerts forces that cause the frontal region to collide against the skull. But just as it is possible for mTBI to impair one's capacity to regulate the exaggerated fear response, recent findings suggest that the amygdala possesses a built-in anxiety reversal circuit.

The prevalence of anxiety is approximately 28 percent for lifetime disorders and, within the scope of this paper, there exists equal implications for understanding what neuronal circuitry plays a role in neurological and psychological dysfunctions associated with mTBI. Exploring the underpinnings of anxiety with cellular precision, the amygdala micro-circuitry was optogenetically dissected using viruses that induced the synthesis of photo-responsive proteins similar to those expressed within retinal cells. This allows individual cells to be stimulated by selectively induced depolarization using light. The majority glutamatergic basolateral amygdala and the centrolateral nuclei of the amygdala together compose a neural substrate for real-time bidirectional modulation of unconditioned anxiogenic activity.[27]

Mild TBI, upon initial examination, is differentiated into complicated and uncomplicated types based on structural injury that is visualized on imaging and/or acute neurological signs.[28] Complicated mTBI better parallels the symptom pathology of moderate TBI in severity. This is likely to include Alzheimer's disease because TBI is its best known environmentally related exposure. In a retrospective cohort study of World War II veterans with documented closed head injury, Blyth is clear to point out an increased risk of Alzheimer's type dementia when compared to non head-injured controls (hazard ratio 2.00, 95 percent CL 1.03-3.90).[29]

Vasterling explored the effects of deployment on neuropsychological health. Some important differences are now being noted between severe and penetrating CNS trauma and increasing emphasis on battle-related mTBI. Behavioral discharges among military personnel following mTBI increased 1.8 fold, and when confounded with alcohol or drugs, ultimately increased 2.6 fold. Hypovolemic shock from hemorrhage is the most detrimental to cerebral blood flow, making the brain highly susceptible to post-traumatic hypoxemia, the long-term effects of which need further investigation.[21,30]

Blast mTBI has the potential to cause neuronal damage that subjects otherwise long, healthy lives to multiple brain-related disturbances. When characterized as a chronic, mild discomfort, neglected treatment can often promote irrational mood swings that can disturb social structures and seclude patients from healthy neurobehavioral habits. Because pharmacological and psychiatric therapies for mTBI remain largely unknown, it is critical to isolate adverse effects from the baseline before further therapies are pursued. The neuropsychological effects of blast mTBI present challenges that warrant an interdisciplinary approach at both the microscopic neuronal level, as well as the macroscopic neuroanatomical and neurophysiological levels.

Much of the newly relevant medical and scientific literature commonly expresses a need for further investigation into these stratified layers of depth. This is necessitated by the difficulty of blast trauma differential diagnosis. Animal research with primary blast waves adversely affected the white matter of the brain and consequently affected areas by neuronal death-induced astrocyte proliferation. The hippocampus, at a cellular level, had abnormal myelin with cytoplasmic vacuoles. Although the likelihood of these effects being seen in blast mTBI cases is small, it has occurred.[31] This may involve altered neurobehavioral patterns with implications of hippocampal defects associated with memory and special awareness.[32-35]

Reporting errors involving blast mTBI can manifest anomalies, such as false symptoms, remediation and recovery, when environmental variables of post-deployment aren't taken into consideration.[31] When examined for the neurophysiological outcomes of deployment, a prospective cohort-controlled study of OIF revealed an associated risk of increased compromise in learning and memory with alterations in response times. The study was based on differences recorded among two separate deployments, each with subdivisions of deployed and non-deployed personnel, and measured the outcomes for each. The first deployment group had a sample size of 600 personnel drawn from a unit of 1,368 personnel and a sample of 300 non-deployed personnel. There was a 94 percent compliance rate in the deployed volunteer group and a 75 percent compliance rate in the non-deployed volunteer group. Comparisons between the two found that the second deployment group performed significantly poorly in visual reproductions of immediate recall ($P < .001$).[30] Primary outcomes as a function of deployment revealed significant losses with greater distress when tested for Profile of Mood States confusion and tension ($P < .001$). The Neurobehavioral Evaluation System (third edition) revealed significantly less proficiency toward omission errors ($P < .001$), and the Wechsler Memory Scale (third edition) similarly revealed proficiency compromise ($P = .003$) in verbally paired associated learning trials.

Although visual-spatial impairments were significantly less proficient when it came to percent retention of visual reproduction in the Wechsler Memory Scale ($P < .001$), there was a significant increase in simple reaction time throughout proficiency in the Automated Neuropsychological Assessment Metric test ($P = .003$). This improvement is suggested to be a conditioned survival response advantageous in reacting swiftly toward an aggressor. This is likely attributed to an autonomic associated neuroendocrine effect of the hypothalamic-pituitary-adrenal axis in response to life-threatening stimuli within combat settings. While initial benefits pertain to deployed infantrymen, this may yield a false sense of security likened to that of a Western quick draw. In these operations, a soldiers' safety heavily relies on their wits and tact to counter the cunning tactics aimed at outsmarting a modern military.

Once more, these findings point out negative outcomes that cannot be attributed to pre-existing neuropsychological outcomes that are ruled out from baseline measurements. Significantly poor effects on sustained attention, learning and memory have little if any likelihood of inaccuracy due to variability between subjects because of relatively short, intermittent deployment times and score compensation for worsening PTSD and/or depression symptoms. Neurobehavioral outcomes demonstrated skewed associations with emotional symptoms that were found to be independent from emotional responses to deployment-related neuropsychological alterations. These may, in fact, be due to varying degrees of coping mechanisms developed to diminish the emotional burden of warfare. Even without evidence to associate mTBI as a mechanism of injury, the findings clarify that war deployment has shown negative health outcomes that compromise neuropsychological functions.[30]

Compromised brain stress systems have been hypothesized to promote a compulsory dependence on reward-seeking behavior. This behavior can lead to a vicious cycle with a perceived resolution of anxiolytic effects. The paradox has to do with the way this stress-related behavior depresses the gamma-aminobutyric acid (GABA) activity associated with stress relief. Corticotrophin-releasing factor (CRF) localized in components of the amygdala, whereby it, along with norepinephrine binding to the $\alpha 1$ receptors, participates in allostatically related addictive tendencies. Within the

context of the emotional state, CRF engages hypothalamic and midbrain systems that reciprocate norepinephrine-induced release of more CRF from the amygdala.

Alcohol-augmented GABA release in the central nucleus of the amygdala can be linked to CRF depreciation, as its effects also depreciate the ability to motivationally overcome drug/alcohol-seeking behavior. Similarly, anxiolytic drugs used to treat PTSD might sabotage an mTBI-exposed patient's successful treatment neurophysiological alterations due to the fact that it depresses GABA transmission in the brain. The resultant modifications in regions downstream to the amygdala might compromise the healthy, synergistic rationale of emotionally driven behavioral response.[36,37]

The amygdala comprises a role in the CNS that is as emotionally prevalent as it is complex. The amygdala neurocircuits contain associated GABA pathways that perform mixed inhibitory and stimulatory roles that are important to the mechanics of anxiety disorders like PTSD. Neurocircuits comprised of basolateral amygdala, centrolateral and centromedial nuclei within the nuclei are considered causally anxiogenic. As basolateral pyramidal neurons have mixed roles, centrolateral nuclei inhibit centromedial nuclei output associated with stimulatory effects toward autonomic and behavioral responses associated with fear and anxiety by feed-forward inhibition. The centromedial, containing the majority of GABA neurons, is the primary output region of the amygdale, and is therefore associated with fear- and anxiety-related projections within the brain. But stimulation to the amygdaloid basolateral terminals in the central nucleus of the amygdala reflected a measured reduction in anxiety. These circuits, therefore, illustrate a bidirectional equilibrium effect between the anxiogenically associated, centrolaterally induced diminishment of inhibition to the centromedial output and the anxiolytically associated, basolateral amygdaloid terminals within the central nucleus of the amygdala. For mTBI patients with compromised memory, learning and emotional compromise associated with blast sequel, these illuminate strong implications of brain arousal/stress systems affecting the amygdala. As components relating to mood and general well being, induced negative emotional states are the driving force of the substance dependencies of war veterans that magnify the damages of conflict. Interestingly, Trudeau mentions that persons with attention-deficit/hyperactivity disorder (ADHD) are more prone to mTBI.[38]

Some of the psychological outcomes following mTBI are of great preventative importance in targeting secondary and tertiary disabling sequelae. The prevalence of psychiatric illness following mTBI within the first year was 34 percent. For those who did not succumb within this time frame, the adjusted relative risk of psychiatric illness post-mTBI following an additional six months was 2.8, with a 95 percent confidence interval and P value less than .001. With prior psychiatric illness post-mTBI, the adjusted relative risk was 1.6, with a 95 percent confidence interval and P value of .005. Within the age range of 15 to 44 years, greater TBI effects were often seen in mTBI cases without prior psychiatric illness. For those adjusted for exposure, mTBI disorders were not significant until following the second year. When the incidence of the exposed was expressed as a proportion of the unexposed, substance abuse became significant in groups without prior psychiatric illness and individual significance continued for 30 months. This may illustrate a risk of prior conditioning of substance mediation of emotional stress propitiated by the emotional cost of war-related trauma.

Nearly all substance abusers with TBI had mTBI. Substances being used to minimize prior, sub-level psychiatric illness may explain this finding. A relatively longer subsequence of relative psychiatric illness risk was nominally statistically significant for mTBI. This prolonged pattern of elevated risk exhibited by pre-nonpsychiatric mTBI eventually surpassed that of TBI of higher severity, suggesting mTBI may contribute to a significantly large proportion of the population whose persistent symptoms continue to perplex healthcare professionals. Etiologically related, post-TBI psychiatric symptoms with neurophysiological effects may have been a contributing factor in subjects with prior pre-psychiatric mTBI.[1,39]

PCS presents injurious outcomes in addition to mTBI, and represents more than 500,000 new cases after mTBI annually. The disabling nature of this disease marks causes great concern considering today's economic fragility.[1] Blast mTBI treatment planning and management could be more effectively planned if an identifying rule outlined patients for high or low risk of PCS. One study examined how effective testing for PCS in non-blast mTBI comparatively, using both logistical regression (LR) and recursive partitioning (RP), might help shed light on this risk determinant. LR helped determine relative risk and RP used an intuitive tree design more easily understood by clinicians. The combination of LR and RP found notably high, similarly low and distinctly divergent high-risk PCS patients following mTBI injury, reducing the difficult-to-classify middle zone. Males with mTBI were less prone to succumb to PCS symptoms over time than women with mTBI.[40]

Neuroimaging may eventually prove the existence of a cerebellar cognitive affective syndrome where cerebellar and subcortical brain structures exhibit relative

hypometabolism and neuroanatomy of cortico-cerebellar-cortical circuits. As these afferent cortical projections converge in the pons and pass through the cerebellar peduncles to the cerebellar hemispheres and vermis, leading to efferent convergence in the deep cerebellar nuclei, they traverse the peduncles returning to the thalamus where they associate with motor cortices. Functional imaging analysis of mTBI veterans demonstrated further posterior cerebellar cortex lesion impairments to executive, visual-spatial and linguistic impairments, along with vermal lesion impairments of affective dysregualtion. Animal tests explain the vulnerability cerebellar Purkinje neurons have toward mechanical trauma.

These chronic, post-concussive symptoms between OIF and Operation Enduring Freedom (OEF) may therefore be due to repetitive, blast-related acute mTBI damage to the infratentorial and medial temporal brain regions.[41-43] Neuroimaging was also used to study major depression's effects on veterans from the two recent combat theaters to analyze what other effects mTBI may have on neuroanatomically related damage. Major depressive disorder, when compared to its absence, demonstrated significantly greater activity within the bilateral amygdala during fear processing. Since there were not any relatively noticeable behavioral changes, either group's brain activity was unlikely to be driven by behavioral differences.

Whole-brain analysis revealed significantly greater activation in the cerebellum, thalamus and middle temporal gyrus, with only a lowered level of cortical activity. Diffusion tensor imaging showed significantly lower fractional anisotropy by a count of white-matter associated tracts. These included the corona radiata, corpus callosum and superior longitudinal fasciculus. The superior longitudinal fasciculus connects the dorsolateral prefrontal cortex with a wide distribution of nodes in the parietal, occipital and temporal lobes. This comprised heteromodal neural network is of paramount importance to core processing executive to attention, memory, language and emotional processing with modulation. This lowered level of fractional anisotropy was significantly related in the left superior longitudinal fasciculus, as was demonstrated in post-mTBI major depressive disorder. These hypothesized microstructural changes caused by the mechanistic forces of concussive, blast-induced trauma dampen normal, healthy emotional processing and regulation, leading to risky cognitive states for major depressive disorder.[44-46]

The major depressive disorder group also exhibited a significantly negative correlation of fractional anisotropy in the left superior longitudinal fasciculus and the Beck Depression Inventory-II,[44,45] which tests depression severity based on psychodynamic prospective instead of thoughts. As a salience detector, the amygdala orchestrates the same somato-motor, visceral and cognitive responses utilized by rigorous, repetitive conditioning used in military basic training self-defensive exercises. This neurostructure, as its role in threat response implicates, is deeply rooted and has been shown to preferentially participate in negative emotional states. Neuroanatomical structures additionally involved with emotional processing of stimuli, such as the cerebellum and middle frontal gyrus, also exhibited a heightened fear response. This was shown to be associated with major depressive disorder and hyperactivity of emotional processing circuitry and hypoactivity in structures of emotional regulation. The hyperactivity was caused by blast-induced disruptions of white matter tracts, but whether or not these changes were structural or functional remains to be discovered. Major depressive disorder due to mTBI, as it relates to microstructural and functional changes, is hypothesized to be the emotionally and cognitively responsive driving force that comprises a major depressive disorder symptom complex.[41,47]

Blast mTBI symptoms as they related to the adverse effects on normal homeostasis

Pain following mTBI can be associated with lesional damage at any point along the ascending pathways. This referred or central pain can be attributed to trauma delivered at the first synapse in the dorsal horn of the spinal cord or trigeminal nuclei, thalamic pathways, subcortical white fibers and cerebral cortex. The ventroposterior thalamus, and to be more specific, damage to the ventroposterior thalamic nucleus causes central pain if lesions occur. Interestingly, the reticular thalamic nucleus as a GABA projection plays an inhibitory role in pain perception, and a lesion in this area will lead to hypersensitivity to pain. If patients suffering from mTBI-related central pain are not treated in a fashion that's conducive to a healthy lifestyle, this may causally contribute to worsening neuropsychological outcomes. Chronically administered pain medication will lead to increased dosages, which have a high risk of addiction and may create or worsen a patient's substance abuse. These risks present patients returning from deployment with significant concern over their general stress and discomfort levels. The attributed euphoric effects may temporarily resolve these stressors psychologically, and establish a functional dependency to cope with civilian life in a post-recession economy.[48]

Chronic pain, like that of post-mTBI headaches, is often associated with troubled sleep. This, along with sleep cycle disruption due to nightmares, can desynchronize hormones and lead to excessive daytime drowsiness. Consequentially, more time is needed to

reach a sleeping state due to over-resting throughout daytime hours. This desynchronization may largely be attributed to the impaired attention and reduced learning and memory capacity of OIF/OEF veterans. Many studies demonstrate that these cognitive processes suffer because the consolidation and intergradation they require are part of sleep-dependent processes.[49,50] With a prevalence of 30 percent to 70 percent, post-TBI sleep disturbance is an important differential diagnosis sequela for the purpose of normalization of blast victims. This is especially true for mTBI-associated sleep disturbances, which are significantly more frequent than those of any greater severity.

Insomnia is also a common occurrence with TBI injury.[51] A survey of 452 TBI patients found that up to half met the criteria for insomnia and more than half went untreated. Not only was there a greater incidence of sleep dysfunction, there were also reportings of higher frequencies of sleep disturbance. These circadian aberrations all surmount to more somnolence arousal events during sleep and longer sleep-onset latency. Strangely, these dysfunctions and their related symptoms are more prevalent in mTBI. In an overall sleep study of 175mTBI patients there was a two- to three-fold increase in sleep disturbance from a time frame of 11 days to 6 weeks following injury. This coincides with the physiological outcome of animal exposure to mTBI and a post-day seven normalization of increased of heart rate, followed by a day 14 return to increased heart rate. Therefore, these, along with discharge complaints of greater neurobehavioral impairments that impair occupational outcomes, aggravate mTBI-associated risk factors that include higher levels of fatigue, depression and pain.

Some studies suggest that mTBI, to a greater degree than any other severity of TBI, contributes to daytime sleepiness scores in excess of 10 on the Epworth Sleepiness Scale. When driving, a score greater than nine can be life threatening. Sleepiness becomes a disease when it places individuals at higher risks of adverse consequences.[52] Some might argue that sleep deprivation may contribute to a protective mechanism through resultant insomnia-related memory loss. As memory consolidation and encoding are heavily sleep-dependent, sleep deprivation may extinguish implicit fear recognition and physiological response to fear lingering from a spontaneously forgotten traumatic event memory.[53] If this is the case for civilians, then mTBI exposed deployed and veteran military service members could be less likely to experience PTSD symptoms. mTBI's increased prevalence with insomnia over other blast TBI severities could better explain the controversy over whether or not it shares any causality with PTSD. A civilian study of mTBI found it was associated with lower sleep efficiency, more nocturnal wake time and more awakenings lasting longer than three minutes. These same patients presented altered sleep architecture with significantly higher proportions of Stage 2 sleep over Rapid Eye Movement slumber. This can lead to deficits in the healthy replenishment of neurotransmitters and subsequently poor neurophysiological outcomes.

Electroencephalogram analysis in an awakened state revealed significantly greater delta activity and less alpha activity—a pattern indicative of sleep deprivation and/or a sleep disorder. Low hypocretin-1 levels within cerebral spinal fluid, an indicator of hypothalamic damage, have also been observed six months after TBI. In excess, low levels of hypocretin-1 are associated with post-traumatic excessive daytime sleepiness, and are therefore a potential biomarker for service members ailing from sleep-related symptoms post-mTBI.[54] If the evidence of endocrine damage substantiates civilian sleep disturbance, a greater risk ism, in fact, likely to affect military blast victims due to blast's effects on the brain's inflammatory responses on neurophysiology. Other animal studies have found that direct brain injury produces diffuse degeneration of white matter or diffuse axonal injury. These injuries, produced by angular accelerations, inflict blunt trauma onto areas closely associated with sleep-wake mechanisms in the septum pellucidum, corpus callosum, deep gray matter and dorso-lateral pons and midbrain. Subsequent biochemical processes associated with mTBI injury and response, including excitotoxicity, inflammation, free radicals, hyperglycolysis, hyperglycemia and apolipoprotein E e4 synthesis, likely increase the severity of sleep dysfunction.

For post-rest period somnolence in particular, sleepwalking can be associated with damage to the peri-locus coeruleus area. This type of sleep disturbance can be triggered by excitatory impulses, which are typically suppressed during Rapid Eye Movement sleep, and reach the nucleus reticularis magnocellularis within the medulla. This can lead to the unintended activation of motor pathways as the spinal motorneurons of the ventrolateral reticularspinal tract have become hyperpolarized.[49,55-60]

Predicting the psychological and physical outcomes of blast mTBI

For military injury related to blast exposure, stress is rarely excluded from TBI, PTSD or PCS symptoms. To what degree does stress add to mTBI injury insult? In a newly published study by Kwon, mice exposed to stress, with and without mild blast exposure, were studied to examine what complications stress-induced anxiety has on blast exposure. An open field test used to measure

anxiety found significantly higher levels in stressed blast rats. This normalized after one to two months. In contrast, anxiety levels measured by the count of rat entrance onto an exposed, elevated ledge that projected from an enclosure were significantly greater for stressed non-blast rats in the first 48 hours.

These results draw on differences between the two methods, and therefore imply that fear perception may be a factor. Three to eight days post-blast, spatial learning and memory testing found that stressed non-blast rats needed significantly more time to locate the escape box entrance. Similar effects for the stressed blast rats were not seen until 33 to 36 days after. The stressed blast rats also performed very poorly in Barnes maze, a less stressful alternative to water a maze, after day 64. Histological tissue from the prefrontal cortex and hippocampus were examined two months post-injury as a proteomics and immunohistochemical analysis of mental defects.

Tissue samples showed elevated levels of S100β, VEGF, GFAP, Tau-protein and IFNγ in both the neural structures of stressed blast rats, with IL-6 only having a significantly higher level in the hippocampus of stressed non-blast rats. Stress alone had no effect on IFNγ levels in the hippocampus. Cellular examinations to subjugate these observations found that stressed blast rats experienced an increase in glial fibrillary acidic protein (GFAP) immunoreactivity of the prefrontal cortex and ventral hippocampus. Such findings were significant for long-term memory impairments associated with conditions similar to those our military forces confront. Unlike that related blast exposure, stress alone was found to cause a transient increase in anxiety, but no lasting memory impairments.

A recent surge in astrocyte research involving neurodegenerative disease has proliferated TBI findings, which is not to be excluded from this study. Increased stellar morphology characteristic of reactive astrocytes was in the previously mentioned structures of stressed blast rats. TUNEL-measured neuronal apoptotic activity in the ventral and dorsal hippocampus was significantly increased in stressed blast rats. Overall, stress alone contributed no major cellularly or molecularly induced defects, unlike stress combined with blast. Neuroinflammatory, vascular, neuronal and glial causally destructive outcomes are believed to contribute primarily to increased anxiety and chronic memory faults. The tress aspect of war-related blast exposure might selectively impair regeneration of inflammatory damage as chronic levels of anxiety significantly reduce somal volume of astroglia of the hippocampus.[62]

The long-term effects of mTBI aren't limited to cognitive deficits. mTBI can also have longstanding consequences related to increased mortality. Compared to greater severity trauma, veteran mTBI is marginally greater in the significance of premature death. All injury prevention accounted for on the battlefield only delays fatality to a later time if long-term medical care isn't properly maintained. Given that today's military combatants are frequently exposed to mTBI, prototypical medical discharge should always follow a plan for scheduled checkups throughout the lifespan of these patients. TBI is a chronic disease, which could lead to untimely death if its progression goes unchecked.[63,64]

Conclusions

Blast mTBI has been, and continues to be, a major hurdle in the recovery of many military personnel and veterans faced with debilitating occurrences, including significant changes made on both the patients' lives and those with whom they share them. Injuries related to blast mTBI are more prevalent, and even more so for multiple insults. This review covered a broad spectrum of findings and correlations about mTBI. In this review, it also becomes apparent that research tools, combined with a diversity of novel investigatory approaches, may lead to what wasn't available to veterans of Vietnam and Desert Storm– a new chance at living better lives.

This review describes the complexity of findings in which clinical methods may be more fruitful when overlapping with cutting-edge research tools. Unlike lethal diseases such a cancer, mTBI clinical trials are more concerned with more quality of life than certain mortality, which argues the necessity of risky endeavors, such as those taken in chemotherapy treatments. The exception for mTBI is that the quality of life lost is progressive and unpredictable in nature. This provocation is not to make a difficult situation more hopeless—in fact, quite the contrary. mTBI patients stand at the forefront of where new medicine can make great strides to develop innovative practices among a community of interconnected physicians and researchers in this digital age.

New branches in astrocyte research are opening doors for a new understanding of human neurophysiology in the hope that brain-injured veterans can aid in the study of other related neurological diseases. Research scientists and physicians are working to turn state-of-the-art medical research into state-of-the-practice medical care. Moreover, there was an increased incidence of PTSD symptoms among blast TBI participants in a study designed to compare patterns of performance on neuropsychological measures.[65] However, with respect to cognitive sequelae, it was argued that there is no strong evidence that blast is categorically different than other mechanisms of TBI.[65]

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Address correspondence to:
Marc Quentin Sonnier, Jr., MS;
Murray R. Berkowitz, DO, MA, MS, MPH
Department of Osteopathic Manipulative Medicine
Philadelphia College of Osteopathic Medicine—Georgia Campus
625 Old Peachtree Road NW
Suwanee, Georgia 30024
murraybe@pcom.edu

Prolotherapy Weekend

October 25-27, 2012, at UNECOM in Biddeford, ME

Course Outline

Thursday, October 25, 5:00 pm - 10:00 pm: Physicians who have not taken a prior course in prolotherapy are required to attend this session. It will include an introduction to prolotherapy, wound healing, degenerative postural cascade, coding and billing.

Friday and Saturday, October 26-27, 8:00 am - 5:30 pm: Participants will be divided into two groups—beginners and advanced. These two groups will alternate between lectures in anatomy and injection technique, and time in the anatomy lab performing injections under supervision and reviewing prosections.

Principles of Prolotherapy by Cantieri MS, Pasquarello GJ and Ravin TH, will serve as the course syllabus. Please see http://principlesofprolotherapy.com/index.html for details.

Prerequisites

Functional anatomy: (1) Level I course or equivalent.

Participants must indicate upon registration whether they are a beginner or advanced prolotherapy student. If you are unsure, please contact Lisa Susemichel at the AAO.

CME

20 hours of AOA Category 1-A credit is anticipated

Travel Arrangements

Call Tina Callahan of Globally Yours Travel at (800) 274-5975.

A rental car is recommended since the campus is located about 15-20 minutes from most hotels and restaurants.

Course Directors

Mark S. Cantieri, DO, FAAO, is a 1981 graduate of Des Moines University College of Osteopathic Medicine, and is board certified in NMM/OMM. He has served on various hospital staffs as a consultant in OMM—treating newborns, post-operative patients and patients in intensive care units. He currently operates a private practice, Corrective Care, PC, in Mishawaka, IN, which specializes in the treatment of chronic musculoskeletal pain. Dr. Cantieri is a Past President and Secretary-Tresurer of the AAO.

George J. Pasquarello, DO, FAAO, graduated from UNECOM in 1993. Board-certified in NMM/OMM, he has served as a Residency Program Director and Associate Professor of OMM at UNECOM. He has also worked as a clinical specialist at Maine Spine & Rehabilitation and University Healthcare. He is currently in private practice at East Greenwich Spine & Sport in East Greenwich, RI. Dr. Pasquarello is a Past President of the AAO.

Course Location

University of New England College of Osteopathic Medicine
11 Hills Beach Road
Biddeford, ME 04005
(207) 283-0171

Registration Form

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October 25-27, 2012

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Sociodemographic analysis of psychiatric emergency services in a state with greater than average veteran density

Livia Cara, MS; Murray R. Berkowitz, DO, MA, MS, MPH

Abstract

Objective: The purpose of this study is to examine the socio-demographic and clinical characteristics of psychiatric patients who utilize the emergency department (ED) of a hospital in the Northeast part of the state of Alabama as a resource for treatment. The results of this study have the potential to help healthcare providers in early detection and intervention strategies. One objective of this research is to expose the prevalence of mental health emergencies and the importance of management of psychiatric crises in the state of Alabama and the nation at large.

Methods: This study analyzed regression model data collected from an emergency department in the Northeast region of Alabama from May 2010 to July 2010 of all patients presenting with mental health-related issues. Statistical Package for the Social Sciences (SPSS) software was used to analyze descriptive statistics.

Results: During this three-month period, 502 psychiatric patients were seen in the emergency department. A random sample of 218 patients was used for statistical analysis. The average age was 36.7 years, and 54.6 percent of the patients were female. Mood disorders were the most frequent diagnosis with 41.3 percent, followed by anxiety disorders with 37.6 percent, suicidal ideation in 10.2 percent and psychosis in 10.2 percent. Suicidal ideation was present in 49.1 percent of patients, and more were discharged from the hospital than were admitted (47.2 percent).

Conclusions: This research demonstrates the importance of understanding the population served, as well as the characteristics of the care delivered to psychiatric patients seeking emergency services. This research also revealed the need for further attention to developing strategies that could provide greater support to the ever-increasing demand for mental healthcare.

Introduction

The use of emergency departments as a source for treatment for psychiatric and social problems has increased dramatically in the last decade.[1] Overcrowding in emergency departments has led to a state of crisis all over the nation, with an even greater concern in the state of Alabama, where local laws and a decreased number of psychiatrists and psychiatric inpatient beds have contributed to this chaotic situation.[2,3]

The National Institute of Mental Health estimated that 26.2 percent of Americans ages 18 and older (about one in four adults) suffer from a diagnosable mental disorder in a given year.[4] In the 2004 census, this figure translated to 57.7 million people. The Centers for Disease Control and Prevention's (CDC) National Vital Statistics System reported that suicide was the fourth-leading cause of death in the U.S. for adult ages 18 to 64 years.[5]

The lack of available and appropriate psychiatric services, especially for short-term care and stabilization, has turned emergency departments into holding areas for patients in crisis.[6] This consumes limited emergency department resources (e.g., staff, beds and ancillary personnel), thus prolonging the amount of time that all patients spend waiting for services.[7]

One objective of this research is to expose the prevalence and characteristics of mental health emergencies, and examine whether there is a need to improve the management of psychiatric services in the state of Alabama and the nation at large to prevent exacerbation of an already existing crisis.

Psychiatric Services in Alabama

Statistics provided by the Substance Abuse and Mental Health Services Administration (SAMHSA) and other federal agencies reveal that Alabama has 7.1 practicing psychiatrists per 100,000 persons, compared with the entire Southeast region of the U.S. having a ratio of 8.2 per 100,000, and with the New England region having a ratio of 26.9 per 100,000.[8,9] An important factor that needs to be taken into consideration in the state of Alabama is its number of veterans. Alabama's civilian population consists of 12.8 percent veterans. Male veterans in the general U.S. population are twice as likely as their civilian peers to die by suicide. Compared with civilian men who died by suicide, veterans were 58 percent more likely to use a firearm to end their lives.[10] By taking this important concept into consideration, more appropriate psychiatric emergency services can be made available in a given location.

Northeast Alabama Regional Medical Center

Northeast Alabama Regional Medical Center (RMC) is located in the city of Anniston. RMC is a 330-bed hospital. The emergency department (ED) is a Level II Trauma Center with 35 beds, and sees approximately 55,000 patients annually. The hospital has an inpatient adult psychiatric program and a geriatric inpatient psychiatric program, as well as outpatient and partial-day treatment programs. RMC does not treat adolescent psychiatric patients, who must be transferred to another facility.

Methods and Materials

This study analyzed regression-model data collected from an emergency department in the Northeast region of Alabama from May 1, 2010, to July 31, 2010, of all patients presenting with mental health-related issues. A random sample of 218 was drawn from the population of 502 psychiatric emergency patients seen during this three-month period.

Statistical Package for the Social Sciences (SPSS) software was used to perform the analyses. All the analyses were descriptive statistics. The mean and standard deviation was calculated on the continuous variables and frequencies, and percentages were calculated for the categorical/ordinal data. Logistic-regression analysis was performed.

Results and Discussion

Analysis of the socio-demographic characteristics of the patients in this study revealed that 54.6 percent were female. Their ethnicity was overwhelmingly Caucasian (78.6 percent). The majority of the patients seen were either unemployed (49.9 percent) or disabled (22.9 percent) (Table 1). Mental health-related visits to the emergency department between sexes were consistent with national reports, showing a prevalence of females over males.[11] Ethnicity was not consistent with national trends, however, which showed a prevalence of African Americans over Caucasians.[12] The national prevalence of any disability among those with a mental disorder is 69.8 percent.[13] People with mental disorders were twice as likely to be unemployed than those with no disorder (49.6 percent compared with 24.5 percent). Our research results were remarkably similar to the national results.[14]

Among this research of mental health-related visits, the most common diagnoses were acute depression (22.9 percent), followed by anxiety (12.8 percent) and suicidal ideation (10.1 percent) (Table 2). The overall consolidated diagnosis data (Table 3) shows the most common diagnosis was that of a mood disorder (41.3 percent), followed by that of an anxiety disorder (37.6 percent); the results were

Variable	n	%
Gender		
Female	119	54.6
Male	99	45.4
Race		
American Indian	1	0.5
Asian	1	0.5
Black	42	19.5
Caucasian	169	78.6
Hispanic	2	0.9

Table 1. Descriptive statistics for patient demographics

Variable	n	%
Affective psychosis	3	1.4
Anxiety-depression	16	7.3
Anxiety-generalized	12	5.5
Anxiety-in transient adjustment	4	1.8
Anxiety-panic attack	17	7.8
Anxiety	28	12.8
Anxiety disorder	5	2.3
Bipolar-depression	1	0.5
Bipolar affective disorder	8	3.7
Bipolar depression	8	3.7
Bipolar effective disorder	1	0.5
Bipolar manic	6	2.8
Depression-acute	50	22.9
Depression-prolonged	16	7.3
Neurosis-anxiety	1	0.5
Neurosis-anxiety, panic type	1	0.5
Psychosis	19	8.7
Suicidal ideation	22	10.1

Table 2. Descriptive statistics for patient diagnosis

the same for suicidal ideation (10.2 percent) and psychosis (10.2 percent).

Comprehensive research done by Larkin and Associates using data from the National Hospital Ambulatory Medical Care Survey (NHAMCS) was used for comparison. The NHAMCS surveys emergency healthcare services nationwide annually. Larkin and his colleagues reported that the most prevalent national mental health-related diagnoses were substance-related disorders (30 percent), mood disorders (23 percent) and anxiety disorders (21 percent).[12] Our research revealed that 66.1 percent of the patients had positive results in a drug or alcohol screening (Table 3). Table 3 also shows that suicidal ideation was reported in 49.1 percent of the patients, and a well thought-out plan for suicide was present in 40.4 percent. Plans ascertained for furtherance and lethality varied, with the most common being self-mutilation with 35 percent, closely followed by overdose with 31.6 percent and shooting oneself with 12.7 percent. Forty-two percent of all the patients reported being suicidal in the past, 17.9 percent reported suffering from domestic violence, and a positive family history of psychiatric illness was seen in 26.5 percent.

More than 300,000 people attempt suicide each year in the United States.[15] This research, as well as other reports, reveal that suicidal behavior is a frequent problem in psychiatric ED patients. In two similar studies, suicidal ideation was present in 38 percent[16] and 39 percent[17] of the patients. It is our interpretation that a ten percent increase in the suicide rate in the state of Alabama may be due to the lack of involuntary commitment laws, which make the patient more comfortable to state suicidal ideation without being forced to be hospitalized for a 72-hour period for mental evaluation.

It is possible that our study may have been subjected to under-reporting of suicidal behavior.[18] Suicidal ideation data was also obtained from the patients' family members, emergency medical personnel and police reports, but if the patient denied being suicidal while answering the face-to-face suicide risk assessment tool, he/she was not considered to be at risk for suicide. Past studies have concluded that face-to-face assessments of suicidal behavior reveal lower rates of suicide risk when compared with anonymous surveys.[19, 20]

Psychiatric treatment was received by 46.8 percent of the patients in the ED. This percentage is lower compared with the percentage obtained from NHAMCS in a nine-year research study, which showed that 61 percent of patients receive psychiatric medication while in the ED.[12] Among suicidal patients, 40.4 percent reported having a well-thought out plan for suicide.

Variable	n	%
Consolidated Diagnosis		
Anxiety	82	37.6
Bipolar Disorder	23	10.6
Depression	67	30.7
Neurosis	2	0.9
Psychosis	22	10.2
Suicidal Ideation	22	10.2
Suicidal		
No	111	50.9
Yes	107	49.1
Plan		
No	130	59.6
Yes	88	40.4
Type of Plan		
Cutting	28	35.4
Hang Self	5	6.3
Hitting Self	3	3.8
MVC	6	7.6
Overdose	25	31.6
Poison Self	1	1.3
Set Self on Fire	1	1.3
Shoot Self	10	12.7

Table 3. Descriptive statistics for patient information

The incidence and pattern of drug abuse is reported in Table 4. Fifty-five percent of the patients tested positive for drug use. Marijuana (THC) was the most common drug used by the patients that were seen in the emergency room for mental health evaluation. THC was followed by benzoates and cocaine as the drugs of choice for these patients. For the patients who tested positive for two or more drugs, the combination varied, but the most common combinations were amphetamines and THC, benzoates and ecstasy, and benzoates and THC (Table 4). In agreement with the SAMHSA (Substance Abuse and Mental Health

Service Administration), THC is the most common substance abused by psychiatric patients, followed by cocaine and opiates.[2]

Surprisingly, only 11.1 percent of the patients had positive alcohol screenings, and their mean blood-alcohol level was found to be 150.77 milligrams per deciliter (mg/dL). The SAMHSA reported alcohol abuse in 35.7 percent of the patients—a far higher percentage than the 11 percent reported by our patients.[22] Blood-alcohol level is reported in milligrams per deciliter. At present, 32 states have laws making it illegal to drive with a blood-alcohol level of 80 mg/dL or above.[23]

Conclusion

In summary, 502 psychiatric patients were seen in the ED during the specified three-month period. A random sample of 218 patients was used for statistical analysis. The average age was 36.7 years, and 54.6 percent of the patients were female. Mood disorders were the most frequent diagnosis with 41.3 percent, followed by anxiety disorders with 37.6 percent, suicidal ideation with 10.2 percent and psychosis in 10.2 percent. Suicidal ideation was present in 49.1 percent of cases, and more patients were discharged from the hospital than were admitted (47.2 percent).

Drug	n	%
One Drug		
Amphetamines	1	1.20
Barbiturates	2	2.41
Benzoates	13	15.66
Cardiac	10	12.05
Cocaine	6	7.23
Ecstasy	4	4.82
Opiates	2	2.41
THC	18	21.69
Two Drugs		
Amphetamines/THC	4	4.82
Barbiturates/Benzoates	1	1.20
Benzoates/Cocaine	1	1.20
Benzoates/Dilatin	1	1.20
Benzoates/Ecstasy	3	3.61
Benzoates/Methadone	1	1.20
Benzoates/Opiates	2	2.41
Benzoates/THC	3	3.61
Cocaine/Opiates	1	1.20
Cocaine/THC	2	2.41
Three or More Drugs		
Amphetamine/Benzoates/Ecstasy	1	1.20
Amphetamines/Benzoates/Cocaine/Opiates	1	1.20
Amphetamines/Ecstasy/Opiates	1	1.20
Amphetamines/Opiates/THC	1	1.20
Barbiturates/Benzoates/THC	1	1.20
Benzoates/Cocaine/Acet	1	1.20
Benzoates/Opiates/THC	2	2.41

Table 4. Descriptive statistics for postive drug screenings

The socio-demographic analysis was very similar to that of other studies, with the exception that patients' ethnicity was overwhelmingly more Caucasian in our research compared with African American in the national data. The most common diagnoses in other studies were substance-related disorders, whereas, in our study, mood disorders were more predominate. Furthermore, alcohol abuse had very low incidence in our research with only 11 percent compared to nation results of 32.4 percent.[21]

Suicidal ideation was 10 percent higher in our research compared to the national data. Our patients were more likely not to receive treatment while in the ED when compared with patients seen in other EDs across the nation. Admission rates for all patients were also higher in our research.

According to the SAMHSA, in 2002, out of the $1.6 trillion of all healthcare expenditures, $100 billion was spent on mental healthcare.[24] Mental healthcare represented around six percent of all medical expenditures in the United States. Mental healthcare expenditures are tied with cancer as the nation's third costliest medical conditions.[25]

These statistics show the need for mental health services to continually be researched and evaluated in order to improve the gaps that exist in the healthcare system related to psychiatric services and costs. Significant changes in treatment methods and service delivery have occurred during the past 50 years, with deinstitutionalization being the most striking transition.[3,26] These changes mandate that psychiatric emergency services be available to provide psychiatric patients with crisis evaluation, management and treatment outside of inpatient settings. However, due to political and economic forces, mental healthcare services have declined.[27,28] A lack of resources and community support, underpaid providers and a decline in psychiatric inpatient beds all increase the chances of relapse in patients with mental illnesses. With nowhere appropriate to go, these patients have been seeking care in emergency departments.[29,30]

Analysis of the characteristics of psychiatric patients is important because it has the potential to reveal diversity in the clinical decisions made by different providers in the emergency department. Since general physicians and practitioners are the ones making the decision between hospitalizing a patient and referring him/her to an outpatient mental health service, it is of great importance that an analysis of these characteristics is done.[31] Inaccurate recognition of symptoms has been associated with the overuse of expensive services such as hospitalization.[32]

Pain, cognitive disorders, post-traumatic stress disorder[33] and depression[34.35] are often found among veterans, especially those of the recent conflicts in Iraq and Afghanistan. Many of these veterans have been found to self-medicate with various drugs or alcohol. The sociodemographics of this study is consistent with past results.[33-35] This research demonstrates the importance of understanding the population served, as well as the characteristics of the care delivered to psychiatric patients seeking emergency services. This research also reveals the need for further attention to developing strategies that could provide greater support for the ever-increasing demand for mental healthcare.

Lastly, this data provides insight on the different type of issues psychiatric emergency systems face in the state of Alabama. It allows public officials to recognize gaps and consider the implantation of more hospital beds for psychiatric patients and the improvement of resources available for outpatient treatment, using other states and national data as models for a more plausible mental healthcare system. This analysis is limited with respect to its generalizability beyond the local rural area of this single state. Questions comparing veteran vs. non-veteran sociodemographics could not be analyzed due to the lack of patient data regarding veteran status in this civilian medical center. Questions regarding whether the sample is representative of both the general U.S. population and the veteran population remain. More research is warranted.

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Address correspondence to:
Livia Cara, MS; Murray R. Berkowitz, DO, MA, MS, MPH
Department of Osteopathic Manipulative Medicine
Philadelphia College of Osteopathic Medicine—Georgia Campus
625 Old Peachtree Road NW
Suwanee, Georgia 30024
murraybe@pcom.edu

Oscillatory and Energetically Integrated Osteopathic Medicine in a Contemporary Setting

November 30-December 2, 2012, at NSUCOM in Fort Lauderdale, FL

Course Description

The course will give practitioners an introduction to, or an organized context in which to use, rhythmic force in the application of osteopathic manipulation—either to complement their current methods or as a new alternative strategy. Three major trains of thought emerge, namely the use of the mechanical percussion vibrator updated from Dr. Fulford's introductory view; a purely manual application (Facilitated Oscillatory Release); and a phenomenological approach to mindfulness in manipulation. Contemporary neuroscience and cognitive science pertinent to these skills will be reviewed. Each of the three areas will be dealt with conceptually, but also with practical exercises intended to integrate them rapidly into practice.

Dr. Comeaux's attitude toward each is that vibratory methods should be most appropriately viewed not as separate models, but as part of an eclectic, integrated approach to the intended end, facilitating normal function. This includes engagement on multiple levels of dynamic physiology. Integration relies on having strategies and skills, but also a perceptive, mindful approach. The use of oscillation and managed perception, furthermore, develop insight into the common features of many approaches to subtle Osteopathy and advanced practice.

CME

20 hours of AOA Category 1-A credit is anticipated

Course Directors

Zachary J. Comeaux, DO, FAAO, a student/protegé of Robert C. Fulford, DO, has researched neuroscience/cognitive science relevant to Dr. Fulford's "energetic" patient/practitioner interraction. The result is an integrative synthesis taught to avid osteopathic communities overseas for years. As president of the World Osteopathic Health Organization and active in the Osteopathic International Alliance, he has a broad view of osteopathic history, concept and practice. A 1988 graduate of OUCOM, he is certified in FM and NMM, and carries this integrative perspective into workshops.

Prerequisites

Level I course and basic understanding of functional anatomy.

Course Times

Friday and Saturday: **8:00 am - 5:30 pm** (lunch provided)
Sunday: **8:00 am - 12:30 pm** (lunch on your own)

Course Location

NSUCOM
3301 College Ave.
Fort Lauderdale, FL 33314
(800) 541-6682

Travel Arrangements

Call Tina Callahan of Globally Yours Travel at (800) 274-5975.

Registration Form

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November 30-December 2, 2012

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Holistic osteopathic approach to the care of veterans with post-traumatic stress disorder: Case report

Andrew Lovy, DO, FACN, DMOR; Murray R. Berkowitz, DO, MA, MS, MPH

Abstract

Post-traumatic stress disorder (PTSD) is an anxiety disorder, the differential diagnosis of which includes generalized anxiety, somatoform disorder, major depression with or without psychosis, secondary chemical dependency and schizophreniform disorder. The epidemiology and etiology of PTSD are briefly discussed. Pharmacotherapy is presented. The purpose of this paper is to alert physicians of what to look for, since the clues are sometimes in the musculoskeletal system, but do not respond to Osteopathic Manipulative Medicine (OMM) treatment until the origin of the trauma is also discovered.

Introduction

PTSD is a valid diagnosis, with many different valid treatment options that work for some. There is an overabundance of contradictory medical literature. In general, we are doing a poor job with the diagnosis, treatment, and even validation of, PTSD. The purpose of this paper is to alert physicians of what to look for, since the clues are sometimes in the musculoskeletal system, but do not respond to OMM treatment until the origin of the trauma is also discovered. Since September 11, 2001, even World War II veterans have been having symptoms they cannot explain until they receive therapy and PTSD is uncovered. We now have many Iraq and Afghanistan veterans facing the terrors of their tour(s).

Post-traumatic stress disorder (PTSD) is an anxiety disorder, the differential diagnosis of which includes generalized anxiety, somatoform disorder, major depression with or without psychosis, secondary chemical dependency, and even schizophreniform disorder when in the middle of an "attack."[1]

- Approximately 20 percent of women and eight percent of men who have been exposed to significant traumatic events will eventually develop symptoms of PTSD. The lifetime prevalence of this disorder is approximately 10 to 14 percent for women and five to six percent for men.[2]
- PTSD is a debilitating anxiety disorder seen in 25 to 30 percent of individuals who experience a traumatic event.[2]
- PTSD has been described throughout American military history, originating in veterans of the American Civil War. Then called "Da Costa syndrome" or "soldier's heart," it was characterized by cardiac symptoms associated with irritability and increased arousal. During World War I, "shell shock" was thought to result from brain trauma caused by exploding shells.
- In World War II, the terms "combat neurosis" and "operational fatigue" were used to describe combat-related symptoms. The Vietnam War significantly influenced the current concept of PTSD, with the lifetime prevalence of the disorder in these veterans estimated to be approximately 30 percent.[2]

Etiology of PTSD

Although the etiology of PTSD is unknown, patients with a personal or family history of major depression or anxiety disorder may be at risk for symptom development.[2-4]

- Overall, there is "an increased likelihood of suffering from physical health conditions with increased exposure to traumatic events, in a linear pattern."[2]

- Some people are more likely to develop PTSD after a traumatic event. Risk factors include severe or prolonged trauma, trauma/abuse during childhood, pre-existing history of psychiatric illness, comorbid substance abuse,[5] poor social support and female gender.
- Common forms of trauma that cause PTSD include involvement in military conflict (particularly combat or medical roles), violent crime, rape and other sexual assault, torture, natural disasters and severe injury or medical illness.[2]
- Current evidence suggests that the underlying physiology of PTSD probably involves dysregulation of multiple neurochemical systems, including those regulated by noradrenalin, the hypothalamic-pituitary-adrenocortical (HPA) axis, the thyroid and endogenous opioid systems.
- Major medical illnesses are common among people with severe PTSD.
- In a large cohort of Vietnam veterans examined approximately 20 years after their combat experiences, there was a higher lifetime prevalence of circulatory, digestive, musculoskeletal, endocrine, nervous system, respiratory and non-sexually-transmitted infectious diseases among veterans with PTSD.[2]

- There is considerable evidence to suggest that noradrenergic mechanisms play a fundamental role in the underlying neurophysiology of PTSD, in particular with respect to disturbances of arousal response and memory function.

Troops serving in Iraq and Afghanistan may be more vulnerable to mental disorders for several reasons:

- Due to the lack of a formal battlefront, soldiers deal with constant threat and combat uncertainty.
- Many of the troops are from National Guard units. These soldiers frequently receive much less training than active-duty units.
- Tours of duty are long and frequently include direct-combat exposure.
- Many military service members face re-deployment.

According to the DSM-IV, for a diagnosis of PTSD, a person has to have been exposed to a traumatic event in which both of the following were present:[1]

- The person experienced, witnessed, or was confronted with, an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of oneself or others.
- The person's response involved intense fear, helplessness or horror. Note: In children, it may be expressed instead by disorganized or agitated behavior.

True trauma, in the clinical sense, refers to situations in which one is rendered powerless and great danger is involved. The fundamental dynamic underlying PTSD is a cycle of re-experiencing the trauma, followed by attempts to bury the memories of the trauma and the feelings associated with it. This cycle of intrusive recall, followed by avoidance and numbing, has a strong biological component. The patient experiences persistent avoidance of stimuli associated with trauma and a numbing of general responsiveness. The patient experiences hyperarousal symptoms ("fight or flight" and "freeze" reactions). This results in impaired functioning. It is possible for individuals to develop PTSD without meeting this stressor criterion. There also appears to be a genetic predisposition to developing PTSD.[6]

PTSD is more likely to develop if one dissociates (defense mechanism); has the perception that they were responsible or acted inappropriately; perceives that they are alone or isolated; has post-trauma factors; the recovery environment is negative; there is emotional unavailability; the victim is disbelieved, stigmatized, shamed or shunned; the victim does not receive treatment; or the victim has ineffective coping skills. There are various triggers: sensory (visual–seeing blood, etc.–sound, smell, taste); physical/bodily; tactile; pain; significant dates or seasons of the year; stressful events/arousal; and strong emotions, thoughts, memories or behaviors. Symptoms may come "out of the blue" when the patient is tired, relaxing or his/her defenses are down. These symptoms may appear in various combinations.

Pharmacotherapy for PTSD

Pharmacotherapy should be directed at the core symptoms of PTSD and attempt to reduce the

frequency and intensity of symptoms and their disability. The primary target symptoms for pharmacotherapy include difficulties with sleep, hypervigilance, exaggerated startle response, irritability or outbursts of anger, and difficulty concentrating or completing tasks.

Antidepressants are currently the preferred medication for PTSD, with the most substantial evidence available to support the use of the selective serotonin reuptake inhibitors (SSRIs). The SSRIs should be regarded as the first-line pharmacotherapy for PTSD. Antipsychotic medications may be helpful, particularly in cases where there are severe hyperarousal symptoms or psychotic phenomena; these include Olanzapine, Quetiapine and Aripiprazole. Adrenergic modulators appear to be effective in treating symptoms of PTSD. There is considerable evidence to suggest that noradrenergic mechanisms play a fundamental role in the underlying neurophysiology of PTSD, in particular with respect to disturbances of arousal response and memory function.

An estimated 70 to 87 percent of patients suffering from PTSD experience sleep disruption. Prazosin, a highly lipophilic α_1-adrenergic receptor blocker that is traditionally used to treat hypertension and benign prostatic hyperplasia, has been shown to decrease the occurrence of trauma nightmares in both combat veterans and patients with non-combat-related PTSD. Drawbacks to the medication include the side effects of weight gain, Diabetes Mellitus and Tardive Dyskinesia.

For years, the treatment for the depression component of those with PTSD was Buproprion (Wellbutrin). This is a very good dopaminergic medication and an especially good one for depression. However, the depression of PTSD is predominantly serotonergic. It is the decrease in serotonin, possibly due to the shock of the incident or incidents, that depletes the serotonin, and it is that replacement that is crucial during the effective treatment of PTSD. Patients who were switched to Zoloft (sertraline), or any other SSRI, did better. Now we understand that the replacement of serotonin is not the single answer; it is part of the chemicals the brain needs in order to then process the therapy. So, as is frequently the case, no single therapeutic modality addresses the issue. The medication makes the brain more amenable to therapy; the therapy cannot proceed as well without the medication; the groups; the returning in the mind, if not actually physically, to the original site of the trauma—all are part of the situation. For many, it is a lifelong struggle, since the damage to the brain is irreversible, but can be attenuated. For others, once the therapy proceeds and is successful, the symptoms relent, possibly forever.

Cases

At a medical conference, one doctor (a psychiatrist) came up to me and told me that he had never been in combat or ever assigned to a combat unit; his job was to counsel newly returning veterans from combat zones and help them re-adjust and get their new assignments. The horrors they talked about to him, over and over again, caused him to develop a full-blown case of PTSD, meeting all the criteria. This emphasizes the criterion of being personally involved in the horrors—hearing about it enough times, and personalizing it, can lead to developing PTSD.

Another case, one that is still in my active files, is that of an airborne paratrooper suffering from PTSD. He was on patrol, had a Vietcong person in his sights, and shot first, killing the person. When they went to the site, they found that the person was a woman, and brought him back her bloodied bra. He sees this in his dreams continually, has nightmares about it and cannot get it out of his mind, even when he is not thinking about it. When we chatted years ago, I mentioned that, at the time, this was not a woman, but a dedicated enemy and, had he not fired, she surely would have killed him. He looked at me and said that most of his life, he wished she would have, so he would not have to go through this for the rest of his life.

Another case is that of a 60-year-old veteran who has had PTSD symptoms since a few years after he left the military. One of his symptoms was that he could not stand changing the diaper of his children, or even being in the same room as his grandchildren when their diapers were being changed. We worked on this for six months. I did relaxation therapy and OMM to his very tight muscles

when he described his symptoms and discomfort (he babysat his grandchildren frequently). Then, one day while working with him in therapy and doing myofascial release, he had a flashback in my presence. He was in the South Pacific and watching a Canberra (twin-engine British aircraft) that was landing, when an engine broke loose and went ahead of the plane. It then turned around and went through the cabin, burning and dismembering the occupants. One of his tasks was cleanup—picking up burnt body parts and bagging them. It finally hit him that the smell of burning flesh and diesel fuel smelled (to him) very much like a soiled baby's diaper! Once that was revealed, he went through a catharsis, and in a few months, his symptoms completely disappeared and he could change diapers. For some reason, locked in the way the brain works, once the original issue is discovered and worked through, and the emotional and physical are recombined in the present, the symptoms either disappear or are sufficiently attenuated to no longer be so pervasive as to prevent function.

PTSD is not limited to military situations, but a common result of any type of trauma, such as rape, murder, sudden death, etc. I work with two nurse practitioners, and it surprises me just how many ladies in this rural area meet the criteria for PTSD, having been in terrible relationships, beaten, accosted, etc.

It has been reported that children in California, thousands of miles away from ground zero on September 11, 2001, have the same incidence of PTSD as those at Ground Zero, so distance is not a factor.

Women face the same situations and dangers as their male counterparts, plus the additional trauma inherent in being women. Accurate data was presented to me by a female Colonel in the Army, who had statistics that, in addition to dealing with combat-related issues, almost 75 percent of women in the military, sometime during her career, will be sexually harassed, raped or accosted by their male counterparts. If the theories are correct regarding origins and etiological mechanisms, any severe trauma can lead to repressed or unrepressed memories resulting in PTSD.

I have seen many cases over the years of patients who have had muscle aches and pains, and musculoskeletal or somatic issues, where the origin is not in the tissues themselves, but in the tissues reacting to the emotional component. Unless physicians are sensitive to this possibility, they can fail to identify the root cause(s) and miss coming to the correct, overarching diagnosis.

Conclusion

The parameters for making a diagnosis of PTSD are constantly changing. We still have many more questions than definitive answers. Much has been made of genetic vulnerability that is valid. Current state-of-the-practice places more emphasis on early diagnosis, and even more on effective ways to attenuate it when there is suspicion of it occurring now or in the future. Treatments can be very effective, perhaps in spite of the theories rather than because of them.

Physicians need to recognize that the brain can compartmentalize and move psychic trauma to unconscious levels so the individual can function. They must also understand that if anything pushed into the unconscious or subconscious is not resolved, it may make a full-blown return under certain circumstances. There are somatic functional complaints that do not resolve with appropriate and effective somatic therapy until and unless the original insult to the body and/or brain is also exposed, understood and worked through.

There are five fundamental "victim" questions:

- What happened?
- Why did it happen?
- Why did I act as I did then?
- Why do I act as I have since then?
- How will I act if it happens again?

Patients with PTSD often experience guilt over acts they performed or observed—"survivor guilt," gaps in awareness, depersonalization and de-realization. In addition to the management of core PTSD symptoms, it is also

necessary for clinicians to address important associated comorbidities, most notably, substance-use disorders and mood disturbances.

It is a myth that PTSD will go away and be forgotten if you do not talk about it. Treatment can be very helpful, and is recommended if the patient's symptoms are causing considerable suffering; the symptoms are interfering with his/her capacity to work, enjoy life and connect to others; his/her symptoms are causing physical illness;[7] symptoms do not lessen within one to three months; the patient experiences suicidal thoughts; or if the patient is taking any medications for his/her symptoms.[5]

Physicians, especially non-veteran civilian physicians, need to be aware of how veterans can slip through the cracks of the military and VA systems, and have issues tied to their military service. Somatic dysfunctions may not only reflect viscerosomatic reflexes, but may also announce that the patient is suffering from psychic trauma. This psychic trauma may be the reflection of wartime experiences presenting as PTSD.

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Address correspondence to:
Andrew Lovy, DO, FACN, DMOR;
Murray R. Berkowitz, DO, MA, MS, MPH
Department of Osteopathic Manipulative Medicine
Philadelphia College of Osteopathic Medicine—Georgia Campus
625 Old Peachtree Road NW
Suwanee, Georgia 30024
murraybe@pcom.edu

CME QUIZ

The purpose of the quiz found on page 48 is to provide a convenient means of self-assessment for your reading of the scientific content in "Holistic osteopathic approach to the care of veterans with post-traumatic stress disorder: Case report" by Andrew Lovy, DO, FACN, DOMR and Murray R. Berkowitz, DO, MA, MS, MPH.

Please answer each question listed. The correct answers will be published in the September 2012 issue of the *The AAO Journal*.

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Author(s): Andrew Lovy, DO, FACN, DMOR; Murray R. Berkowitz, DO, MA, MS, MPH

Publication: *The AAO Journal*, Volume 22, No. 2, Summer 2012, pp. 43-47.

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1. **D**
2. **B**
3. D
4. A

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1.Which of the following mechanisms are believed to play a fundamental role in the neurophysiology of PTSD, in particular with respect to disturbances of arousal response and memory function?
A) Adrenergic
B) Exogenous opioid systems
C) Noradrenergic
D) Serotonergic

2.Which of the following should be regarded as first-line pharmacotherapy for PTSD?
A) Antipsychotics
B) MAOIs
C) SNRIs
D) SSRIs
E) TCAs

3.Musculoskeletal somatic dysfunctions due to the depression of PTSD may not be resolved with OMT until the emotional component is successfully addressed.
A) True
B) False

4.Which of the following is NOT one of the DSM-IV criteria for PTSD?
A) Avoidance
B) Exposure
C) Hypoarousal
D) Impaired functioning
E) Re-experiencing the trauma

Biomarkers and neuroimaging techniques to detect blast-induced traumatic brain injury (bTBI)

Patrick M. Malie, MS, OMS III; Murray R. Berkowitz, DO, MA, MS, MPH

Abstract

Detection of blast-induced traumatic brain injury (bTBI) is discussed by looking at potential biomarkers of injury and current neuroimaging techniques. Due to the nature of bTBI, the focus is placed on military populations. Biomarkers of injury that have demonstrated pre-clinical potential include glial fibrillary acid protein (GFAP), myelin basic protein (MBP), S-100β and neuron specific enolase (NSE). The application of neuroimaging techniques to the evaluation and management of patients who have suffered bTBI is presented. Additional translational research is needed to study the effectiveness and efficiency of using biomarkers of injury and neuroimaging techniques in the evaluation and management of patients with suspected exposure to bTBI.

Introduction

It is estimated that, by January 2008, as many as 320,000 American armed forces serving in the current Iraq and Afghanistan wars have experienced a traumatic brain injury (TBI).[1] TBI has been designated as the "signature injury" of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).[2-5] The nature and effects of blast-induced traumatic brain injury (bTBI) are more fully reviewed and described elsewhere.[6]

Biomarkers for bTBI

A thorough understanding of the biomarkers of bTBI is yet to be achieved. One reason is because the symptoms of bTBI often do not manifest until sometime after the injury has occurred.[7] Another is that brain injuries, mild and moderate in particular, often go undiagnosed and untreated since medical attention is issued toward more visible injuries.[8] Although there are currently no biomarkers with proven clinical utility for bTBI, or any mechanism of brain injury for that matter, there are several proteins that have demonstrated pre-clinical potential.[9] The candidates include glial fibrillary acid protein (GFAP), myelin basic protein (MBP), S-100β and neuron specific enolase (NSE).

GFAP is a filamentous protein found in the astroglial cytoskeleton, and is not located outside the central nervous system (CNS).[10] In a study conducted by Nylen, et al.,[11] on severe TBI patients, those with unfavorable outcomes had significantly higher maximal serum GFAP (s-GFAP) levels in the acute phase than patients with favorable outcomes. Another study indicated that GFAP had the capability to distinguish injury severity based on the Marshall scale classification of computed tomography (CT) scans.[12] The Marshall scale is a classification scale of intracranial pathology as observed by CT, and has been shown to be predictive of clinical outcome.[13] Although GFAP has not been studied in mild or moderate brain injury, it demonstrates potential as a diagnostic tool in predicting outcome after severe TBI. Furthermore, it shows potential in discriminating brain injury magnitude, and may prove to be a better diagnostic tool than S-100β, since it is specific for brain tissue and not affected by hemorrhagic shock or extracranial trauma.[9]

MBP, an abundant protein in white matter, is thought to be important in the myelination of nerves in the CNS.[14] It has been examined as a biomarker of axonal damage in many insults relevant to neurointensive care.[9] In TBI, serum and cerebrospinal fluid (CSF) levels of MBP have shown excellent specificity, but limited sensitivity.[15] More recently, it was shown that MBP serum levels, as well as NSE and S-100β serum levels, may function in predicting outcomes after pediatric TBI.[16] Specifically, Berger, et al.[16] demonstrated that initial MBP and NSE serum concentrations were more strongly correlated with outcomes in children younger than or equal to four years of age, as compared to children older than four. Because MBP is yet to be studied in bTBI, further research is needed to verify its utility as a biomarker of brain injury.

Among the most well researched biomarkers for TBI is S-100β, a small dimeric calcium binding protein most abundant in glial cells of the CNS (astrocytes) and PNS (Schwann cells).[9] A downside to S-100β as a biomarker for brain injury is that it is not exclusively located in the brain, as it has been found to be expressed in melanocytes, adipocytes and chondrocytes.[17] Many studies have shown an association between S-100β and injury outcome and magnitude in TBI.[15,16,18] In a study using patients with severe TBI, Korfias, et al.,[18] concluded that S-100β serum levels reflected TBI severity, improved prediction of outcomes, and may also have a role in assessing the

efficacy of treatment after severe TBI. Conversely, other studies have suggested that S-100β is a poor predictor of outcomes following brain injury, particularly mild and pediatric TBI.[19,20] Specifically, while attempting to determine the relationship between S-100β serum levels and long-term outcomes after mild TBI, Bazarian, et al.,[19] found no statistically significant correlation between marker levels and PCS three months after injury. Despite the contradictions, S-100β has potential as a biomarker for brain injury, and should be further studied in bTBI.

NSE is a protein located in the neuronal cytoplasm and is involved in regulating intracellular chloride levels.[21] Although NSE was originally believed to be exclusively neuronal, it was later located in both erythrocytes and platelets, decreasing its value as a biomarker for brain injury.[22] Elevated NSE levels have been observed after multiple trauma, however, systemic levels have increased by similar amounts with and without TBI, limiting its capability of distinguishing brain injury magnitude.[23] In addition, NSE has a half-life of more than twenty hours in serum, which may further limit its use as a biomarker for TBI.[22] Although associations of NSE serum levels with brain injury magnitude and outcomes are controversial, NSE measured in conjunction with S-100β has demonstrated utility in predicting TBI outcomes.[9,16] Further research will need to verify whether NSE concentrations alone are valuable in predicting and distinguishing bTBI outcome and severity, respectively.

Neuroimaging techniques

Ideally, a detailed clinical assessment should be made upon arrival at a combat support hospital, beginning with immediate CT to identify lesions such as skull fractures, intracranial hemorrhage and cerebral edema.[24] Although computed tomography (CT) and standard magnetic resonance imaging (MRI) structural images are efficient in demonstrating bleeds and large focal contusions (i.e., TBIs characterized by bruises in specific locations), they are less effective in detecting diffuse axonal injury.[25] Diffuse axonal injury is one of the more common and destructive types of TBI, and is characterized by extensive lesions in the white matter. Diffuse axonal injury can be detected by diffusion tensor imaging (DTI), or indirectly by volumetric analysis (brain volume loss).[25]

DTI is an MRI technique that enables the measurement of the restricted diffusion of water in certain tissues in order to produce neural tract images.[26] Data is used to produce images rather than for the purpose of assigning contrast or colors to pixels in a cross-sectional image.[27] DTI is resourceful when a tissue, such as the neural axons of white matter in the brain, has an internal fibrous structure that is similar to the anisotropy of some crystals.[28] The value that describes the degree of anisotropy of a diffusion process is known as the fractional anisotropy (FA), and when applied to diffusion imaging, it provides a measure of fiber density, axonal diameter and myelination in white matter.[29] Some DTI studies have shown reductions in FA at sites of traumatic axonal shearing injury, corresponding to a loss of microstructural fiber integrity.[29,30] An increasing number of DTI studies in TBI have been emerging recently, a couple of which indicate correlations between DTI findings and neurocognition.[31,32] For instance, Salmond, et al.,[31] demonstrated a significant correlation between learning and memory indices and diffusivity in areas known to subserve the cognitive functions. Moreover, DTI was found to be sensitive to white matter injury three months after the occurrence of a moderate or severe TBI.[32]

Positron emission tomography (PET) is an effective and resourceful technique for quantifying ischemic burden after TBI.[33] TBI studies implementing PET have shown that early reductions in cerebral perfusion can result in cerebral ischemia, which is correlated with adverse outcome.[33,34] In addition, PET has been employed to demonstrate that, in TBI, the threshold of cerebral blood flow (CBF) below which irreversible tissue damage occurs varies from the classical CBF threshold for stroke.[34] Aside from PET, many studies have confirmed the potential of single-voxel proton MR spectroscopy (^{1}H-MRS or MRS) for the detection of neuronal injury following TBI.[35-40] MRS is a metabolic screening technique that has been shown to be more sensitive than PET in depicting metabolic abnormalities of the temporal lobe in individuals with epilepsy.[41]

MRS is resourceful in that it allows for the acquisition of biochemical (metabolic) information from tissues in a non-invasive manner. While MRI can determine the location of a particular injury, MRS has the capacity, in theory, to determine the severity of the injury.[41] A common finding among the MRS studies is the presence of altered metabolite concentrations that appear normal on structural MR images, suggesting diffuse neuronal tissue damage. Specifically, a significant correlation has been found between N-acetylaspartate (NAA), a biomarker of neuronal integrity, and adverse clinical outcome in studies using single-voxel methods.[42,43]

A method similar to MRS, known as proton MR spectroscopic imaging (MRSI), collects spectroscopic information from multiple voxels during the same imaging acquisition.[25] Thus, MRSI differs from MRS in that the data acquired is not restricted to a single region or voxel. However, both have been found resourceful in finding

metabolic abnormalities that present as markers for long-term sequelae, which includes neuronal loss and glial proliferation.[36] Moreover, some studies have implemented MRS and MRSI in the effort of finding a correlation between metabolic abnormalities and neurocognitive effects.[44,45] In short, Friedman, et al.,[45] found that the association between neurometabolic levels and behavioral function supports the hypothesis that diffuse axonal injury is an important contributor to brain dysfunction after TBI. Furthermore, it was determined that acute MR spectroscopy of the pediatric brain injury patient improves prognostic ability and may provide valuable information for early treatment and intervention planning.[44]

Studies using functional MRI (fMRI) in individuals with TBI demonstrate unusual patterns of brain activation when compared with healthy control subjects.[46-48] Functional MRI is a type of specialized MRI scan that measures the hemodynamic response, or change in blood flow, related to neural activity in the brain or spinal cord of humans and other animals.[49] It uses blood-oxygen-level dependent (BOLD) contrast that enables detection of changes in the concentration of oxygenated hemoglobin, which becomes altered by the hemodynamic response.[49] Prigatano et al.[46] demonstrated that the different patterns of brain activation in individuals with TBI compared to healthy controls can be observed even when the level of behavioral performance between groups is generally within normal parameters.

Furthermore, it was concluded that the impairment of working memory in TBI seems to be correlated with alterations in functional cerebral activity.[48] Another variation of MRI, known as dynamic contrast-enhanced perfusion-weighted MRI (PW-MRI), is a method that can provide information about the functional status of cerebral tissue with a high spatial resolution of morphology.[50] Although PW-MRI has demonstrated that regions of both normal-appearing and contused brain can have an unusual regional cerebral blood volume (rCBV), and that changes in rCBV can play a role in determining the clinical results of patients, there have not been any publications using PW-MRI in TBI patients.[51]

Conclusions

Since many of the effects of bTBI may not be observable by the naked eye, bTBI has been referred to as "the invisible wound of war." Since there are no clinically proven biomarkers for brain injury to date, further research should be conducted on the potential candidates to improve and expedite the detection process. Furthermore, the application of neuroimaging techniques to the evaluation and management of patients who have suffered bTBI was briefly presented. Additional translational research is needed to study the effectiveness and efficiency of using biomarkers of injury and neuroimaging techniques in the evaluation and management of patients with suspected exposure to bTBI so that fewer brain injuries will go unnoticed or misdiagnosed.

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Address correspondence to:
Patrick M. Malie, MS, OMS III;
Murray R. Berkowitz, DO, MA, MS, MPH
Department of Osteopathic Manipulative Medicine
Philadelphia College of Osteopathic Medicine—Georgia Campus
625 Old Peachtree Road NW
Suwanee, Georgia 30024
murraybe@pcom.edu

The safety and efficacy of osteopathic manipulation in the treatment of mTBI (mild traumatic brain injury) in U.S. service members as validated by SPECT scan: A report of planned research

Natalie A. Nevins, DO, MSHPE; Marcel Fraix, DO, FAAPMR

Introduction

Traumatic brain injury (TBI) is one of the signature wounds of the Global War on Terrorism (GWOT). TBI is a common injury in Unites States service men and women who have served in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF). The Armed Forces Health Surveillance Center (AFHSC) report to the Department of Defense (DoD) from February 2012 states that there have been 233,425 TBIs, including all levels of severity in all branches of the Armed Forces from 2000-2011. Additionally, of these, 178,961 were classified as mild in nature.[1]

The Centers for Disease Control (CDC) approximates that 1.7 million individuals sustain a TBI in the United States each year.[2] In 2007, The Report to the Surgeon General from the Traumatic Brain Injury Task Force commented that, if mild TBI (mTBI) is also accounted for, then at least 5.3 million Americans currently have long-term or life-long disabilities resulting from TBI. [3] TBI is clearly a factor affecting the overall function and productivity of both U.S. military personnel and those in the general population.

The leading causes for non-military TBI include falls, motor vehicle accidents and assault involving head trauma. According to the Defense Manpower Data Center, explosive devices, including Improvised Explosive Devices (IED), are responsible for two-thirds of the wounded-in-action casualties from the conflicts in Iraq and Afghanistan.[4] IEDs are the leading cause of blast-induced mTBI. The financial burden of direct medical costs and indirect costs (i.e., loss of productivity) resulting from TBI totaled an estimated $60 billion to $76.5 billion in the U.S. in 2000.[5,6,7] Additionally, the one-year costs for military service members with TBI accessing the health care system in 2007 ranged from $27,259 to $32,759 for mild cases, and $268,902 to $408,519 in moderate to severe cases.[8]

TBI is often referred to as one of the invisible wounds of warfare. Our service men and women are returning with mental health and cognitive dysfunctions, many of which are directly related to TBI. Research related to the long-term treatment of TBI is lacking and underfunded. At the Concussion Restoration Care Center at Camp Leatherneck in Helmand province, Afghanistan, patients with a history of acute concussion and possible mTBI receive a neurological evaluation, balance assessment and evaluation via Automated Neuropsychological Assessment Metric (ANAM), which is an advanced neurocognitive test. Current test results from ANAM are compared with a baseline study that was established back in the States prior to deployment. Additionally, the patient may receive a CT or MRI scan.[9] Treatments are designed to be comprehensive and may include acupuncture, osteopathic manipulative therapy, occupational or physical therapy, counseling and chaplain visits. Rest, both physical and mental, is emphasized for all patients. This treatment protocol has 98 percent of Marines treated at the center returning to their units in theater. Before it opened in August 2010, the Marine Expeditionary Force in Regional Command-Southwest was losing about 20 Marines a month to concussions.[10]

Definition of TBI

The definition of TBI has been continually evolving over the last 10 years, with no consensus definition agreed upon by those treating these patients. The Defense and Veterans Brain Injury Center defines TBI simply as a blow or jolt to the head that disrupts the normal function of the brain. The severity of the TBI is determined at the time of the injury, and may be classified as mild, moderate or severe.[11] The DoD definition is far more explanatory—a traumatically induced structural injury and/or physiological disruption of brain function as a result of external force that is indicated by new onset or worsening of at least one of the following clinical signs, immediately following the event:

- Any period of loss of or a decreased level of consciousness;

- Any loss of memory for events immediately before or after the injury;
- Any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.);
- Neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient;
- Intracranial lesion.

External forces may include any of the following events: the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, a foreign body penetrating the brain, forces generated from events, such as blast or explosion, or other force yet to be defined.[12]

The severity of TBI is based on the status of the patient at the time of injury, based on observable signs. Severity of injury does not predict the functional or rehabilitative outcome of the patient.[13] (Table 1).

Signs and Symptoms of TBI

Common signs and symptoms are generally broken down into physical, emotional and cognitive changes. The National Academy of Sciences published an executive summary, which provides a general description of the symptoms of TBI.[14] It states that the majority of people who sustain a TBI are mobile and able to care for themselves, but physical health problems are common. Such problems include balance and motor coordination, fatigue, headache, sleep disturbance, seizures, sensory impairments, slurred speech, spasticity and tremors, problems with urinary control, dizziness and vestibular dysfunction, and weakness. Psychiatric sequelae can also occur after TBI, with major depressive disorder being the most common in civilian and military populations. Other psychiatric diagnoses associated with TBI include generalized anxiety disorder, PTSD, bipolar disorder and personality changes.[15, 16,17] Other symptoms can include memory impairment and disordered thinking. [18] (Table 2).

Mild	Moderate	Severe
Normal structural imaging	Normal or abnormal structural imaging	Normal or abnormal structural imaging
LOC = 0-30 min	LOC >30 min and < 24 hours	LOC > 24 hrs
AOC = a moment up to 24 hrs	AOC >24 hours. Severity based on other criteria	AOC >24 hours. Severity based on other criteria
PTA = 0-1 day	PTA >1 and <7 days	PTA > 7 days

AOC – Alteration of consciousness/mental state

LOC – Loss of consciousness

PTA – Post-traumatic amnesia

Table 1. Severity of TBI

Physical	Headache, sleep disturbances, dizziness, balance problems, nausea/vomiting, fatigue, visual disturbances, light sensitivity, ringing in ears
Cognitive	Slowed thinking, poor concentration, memory problems, difficulty finding words
Emotional	Anxiety, depression, irritability, mood swings
Co-occurring disorders	PTSD

Table 2. Common signs and symptoms of mTBI

Purpose of Study

The purpose of our study is to measure neurobehavioral and brain changes following the application of osteopathic manipulation in the treatment of chronic mTBI. Current standards of evaluation in mTBI will be recorded before and after treatment to validate outcomes. Single-photon emission computer tomography (SPECT) imaging will be used to evaluate the brain before and after treatment.

The objectives of this study are:

- To assess the safety of osteopathic manipulative treatment (OMT) in participants experiencing chronic mTBI;
- To measure the response to OMT by using SPECT imaging and neurobehavioral testing in participants experiencing chronic mTBI.

Methods

Design: Prospective randomized controlled cohort comparative effectiveness study

1. Evaluation

a. Outcome Measures

i. Neuropsychological Testing

ANAM testing is conducted prior to deployment, and can be used to identify and monitor changes in function before and after an injury. ANAM is a proven, computer-based cognitive assessment tool used by the U.S. military designed to detect the speed and accuracy of attention, memory and thinking ability. It records every service member's performance through responses provided on a computer.[19] Additionally, we will use the Neurobehavioral Symptom Inventory (NSI) and the Amen Brain System and Symptom Checklist.

ii. SPECT Imaging

"SPECT is a functional imaging technique used to determine blood flow in the brain based on the distribution of radioactive pharmaceuticals in the brain. The radiopharmaceuticals are injected into the bloodstream of patients and, as the radioisotope decays, the photons emitted are detected and recorded by gamma cameras. This produces tomographic images of the activity of the radiopharmaceutical in the brain. These images can then be reconstructed in three dimensions."[20]

The most common radiopharmaceutical used for SPECT imaging in the brain is technetium-99 m-hexamethylpropyleneamine oxime (99mTc-HMPAO). Technetium-99 m is a metastable radionuclide that releases the photons detected by the SPECT scan.[21] "99mTcHMPAO is injected, and accumulates in areas of blood flow with detectable concentrations for up to 24 hours, and is therefore utilized as a resting state functional neuroimaging technique, similar to functional magnetic resonance imaging methods."[22] "Given the long half-life of the SPECT radionuclide, subjects can be injected and time can be taken to establish a calm and quiet environment to eliminate background brain activity."[23]

Given the disturbances to metabolism that are expected to occur after brain injury, it is expected that blood flow would be altered in mTBI. SPECT is an ideal tool for making blood flow assessments after mTBI due to its availability, and non-invasive nature. As a result, there is a rich body of medical and scientific literature surrounding the use of SPECT in brain injury.[24]

It is agreed that imaging studies are not necessary for all mTBI patients. The absence of pathologic signs on computed tomography (CT) does not rule out the presence of mTBI. Structural magnetic resonance imaging (MRI) has a low incidence of positive findings in mTBI.[25] It is contraindicated in patients with shrapnel and is of limited use with acute mTBI. SPECT and functional MRI (fMRI) may be more useful for patients who manifest symptoms of cognitive dysfunction after the acute phase of TBI has passed.[26]

b. Intervention

OMT will be used as an intervention in this study. Patients will receive OMT with the objective of treating diagnosed somatic dysfunction, which will entail the use of specific indirect and direct techniques. These can include soft tissue, inhibitory, myofascial release, Osteopathy in the Cranial Field, articulatory and high-velocity/low-amplitude (HVLA) techniques, but not muscle energy techniques, which are active, and passive motion maneuvers that could confound the data. Direct-action OMT procedures, including HVLA, involve the application of a force in the

Technique	Description
Counterstrain	Somatic dysfunction is considered to be due to continuing inappropriate strain reflex, which is inhibited by applying a position of mild strain in the direction exactly opposite to that of the reflex; this is accomplished by specific directed positioning about the point of tenderness to achieve the desired therapeutic response.
Myofascial Release	With continual palpatory feedback, the myofascial tissues are engaged by guiding them in the direction of least resistance until tissue release occurs and increased movement is achieved.
Balanced Ligamentous Tension	The ligaments and joints are placed in a position that facilitates release of tension and increased motion.
Soft Tissue	A technique that usually involves lateral stretching, deep pressure, traction and/or separation of muscle origin and insertion while monitoring tissue response and motion changes by palpation.
HVLA	An osteopathic technique employing a rapid, therapeutic force of brief duration that travels a short distance within the anatomic range of motion of a joint, and that engages the restrictive barrier in one or more planes of motion to elicit release of restriction.
Articulatory	A low velocity/moderate to high amplitude technique where a joint is carried through its full range of motion with the therapeutic goal of increased range of motion. The activating force is either a repetitive springing motion or repetitive concentric movement of the joint through the restrictive barrier.
Osteopathy in the Cranial Field (OCF)	A system of diagnosis and treatment by an osteopathic practitioner using the primary respiratory mechanism and balanced membranous tension. Refers to the system of diagnosis and treatment first described by William G. Sutherland, DO. *primary respiratory mechanism*: 1. A conceptual model that describes a process involving five interactive, involuntary functions: (1). The inherent motility of the brain and spinal cord. (2). Fluctuation of the cerebrospinal fluid. (3). Mobility of the intracranial and intraspinal membranes. (4). Articular mobility of the cranial bones. (5). Mobility of the sacrum between the ilia (pelvic bones) that is interdependent with the motion at the sphenobasilar synchondrosis.

Table 3. OMT techniques

direction of restricted joint motion in order to resolve somatic dysfunction. Indirect techniques, including counterstrain, balanced ligamentous tension and myofascial release, entail applying a force away from the restrictive barrier of a joint or soft-tissue structure. A descripton of these techniques is listed in Table 3. Each participant in the intervention groups using OMT will receive a total of three treatments spaced approximately one week apart. The same physician will perform all the OMT to ensure it is applied as consistently as possible. Additionally, OMT will not be restricted to a specific region of the body, since there is not evidence that demonstrates that somatic dysfunction of a specific region causes, or is correlated with, mTBI. This is also in keeping with the theory of Osteopathy, which attempts to resolve structural imbalances and improve the overall function of the body.

The schedule for each group regarding evaluation and treatment is illustrated in Table 4.

Participants

Subjects: Men and women who have served in the U.S. armed forces above the age of 18. Participants will not be excluded based on their race, color, national origin, religion, disability, gender or sexual orientation.

Inclusion criteria:

- Diagnosis of mTBI during deployment;
- Baseline ANAM testing done before deployment.

Exclusion criteria:

- Pre-existing psychiatric disorder;
- Refusal to participate in the study.

Timeline: We will recruit participants and randomly assign them to the varying treatment arms of the study. The treatment phase of the study will last one month. Data will be collected pre-treatment and immediately post-treatment.

Data Analysis: After the treatment phase of the study is completed and data from SPECT and the neurobehavioral testing is collected, descriptive statistics will be used to characterize the study population at baseline and at the conclusion of treatment. Frequencies and percentages will be computed for categorical variables; means, standard deviations, medians and ranges will be computed for continuous variables. Pre- to post-treatment change scores will be computed and reported in terms of both absolute and percentage changes. Ninety-five percent confidence intervals for the differences between pre-treatment and post-treatment measures will be computed, and general linear modeling will be used to estimate and test the effects of treatment on SPECT and neurobehavioral testing changes. Data management and statistical analyses will be conducted with Microsoft Excel and SAS (version 9.1, Cary, NC).

	Control Group	**OMT Group**
Visit One Week One	Initial testing: SPECT & Neurobehavioral testing	Initial testing: SPECT & Neurobehavioral testing
Visit Two Week Two	*Evaluation:* Somatic Dysfunction	*Evaluation:* Somatic Dysfunction *Treatment:* OMT
Visit Three Week Three	None	*Treatment:* OMT
Visit Four Week Four	None	*Treatment:* OMT
Visit Five Week Five	SPECT & Neurobehavioral testing	SPECT & Neurobehavioral testing

Table 4. Group schedule for evaluation and treatment

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Address correspondence to:
Natalie A. Nevins, DO, MSHPE
Downey Regional Medical Center
Director/Medical Education/DRMC
11500 Brookshire Ave. - PO Box 7010
Downey, CA 90241
docnnevins@aol.com

From the Archives

Edited by Raymond J. Hruby, DO, MS, FAAO; From: Still AT. *The Autobiography of A.T. Still*. Kirksville, MO: Published by the author; 1908: 71-81.

In September 1861, at Fort Leavenworth, I enlisted in the Ninth Kansas Cavalry, in Company F, T. J. Mewhinne, captain. The regiment was composed mainly of Kansas men who had been christened in the baptism of fire during the pro-slavery contest. Soon after enlisting, we drew our clothing and equipment. We were men who meant business and had started out to do some very severe and successful fighting. From Leavenworth, we were ordered to Kansas City to complete our outfit, and were placed in the brigade of James H. Lane, then commissioned to organize the Western army. In a short time, we received marching orders to report at Springfield, MO.

We left Kansas City on the day that Mulligan surrendered to General Price at Lexington. Price, from some cause, chose to march his army south by way of Springfield. Each night we camped on the ground, which Price had camped on the night previous, until Springfield was reached. During this march, the rebel army seemed aware of the fact that pursuers were in their rear. Though we did not come in sight of the Confederates during the march, we took down many flags that Price had flung to the breeze. At Pleasant Hill, Greenfield and other points, the stars and bars were lowered to give place to the stars and stripes. Many loyal hearts that had sought concealment during Price's march came forth from the woods and bushes to fall in with us and swell our numbers, so by the time we reached Springfield, our brigade was considerably larger than when we left Kansas City. We arrived at Springfield just before General Fremont was removed from command of the Western Department.

The whole army assembled at Springfield was then given in round numbers at 120,000 men. The east and west sides of a forty-acre field were protected by lines of artillery a quarter-of-a-mile long. We remained at Springfield until about the first of November, and were then ordered back to Fort Scott, and then to different points along the Missouri border, until we finally reached Harrisonville, where we went into winter quarters. During the winter that followed, we were continually harassed by bushwhackers, who not only ambushed and shot our soldiers, but loyal citizens as well. This guerrilla warfare grew to be such an annoyance that a Colorado brigade under Colonel Ford, to whom we had reported, set out to take summary vengeance on the enemy. The Colorado troops were cavalry, and in squads of 20 to a company, scoured the country from Kansas City to the Osage River. It was reported that they killed 1,700 in that Territory in 11 days. I counted 62 fresh graves in one graveyard near Harrisonville. For some time after this, there was no trouble from guerrillas.

About the first of April 1862, the Third Battalion of the Ninth Kansas was disbanded, which let me out of the service. I went home and organized a company of Kansas militia, and about May 15, 1862, was commissioned Captain of Company D, 18th Kansas militia. I received orders to drill my men once a week, and patrol the road known as the Old Santa Fe Trail, running from Kansas City to Old Mexico. My beat extended east and west across Douglas County, KS. The drilling and training continued until an order was issued to organize the 18th Regiment of Kansas militia, of which I was chosen major.

A few months later, there came another order to consolidate with some other battalions, by which I was transferred and commissioned major of the 21st Kansas militia. I did service in this capacity in Kansas until the autumn of 1864, when on the 10th of October, General Curtis ordered us to the borderline between Missouri and Kansas to fight General Price, who was expected at Kansas City or Independence at an early day. Militia regiments from Kansas were hurried to the border until our numbers equaled 127,000. By the addition of General Totten, we numbered 35,000. We were stationed south of Westport, forming a line extending for ten miles. During Thursday and Friday of October 22 and 23 there was heavy fighting at Lexington and Independence. On the morning of 24th, General Price moved west, formed his men and opened the battle, from Westport running south to the Little Blue, a distance of six miles. He took the aggressive, and we met and fought his forces, who were under the command of Joe Shelby, Quantrell and numerous other Confederate commanders.

About four o'clock on Saturday the 24th, the battle raged all along the line, from Westport to the Little Blue, on which ground the 21st Kansas State Militia was stationed. Being east of the Kansas line, General Joe Shelby seemed to regard us as intruders, and expressed his conviction by showers of bullets. We considered this an uncivil way to

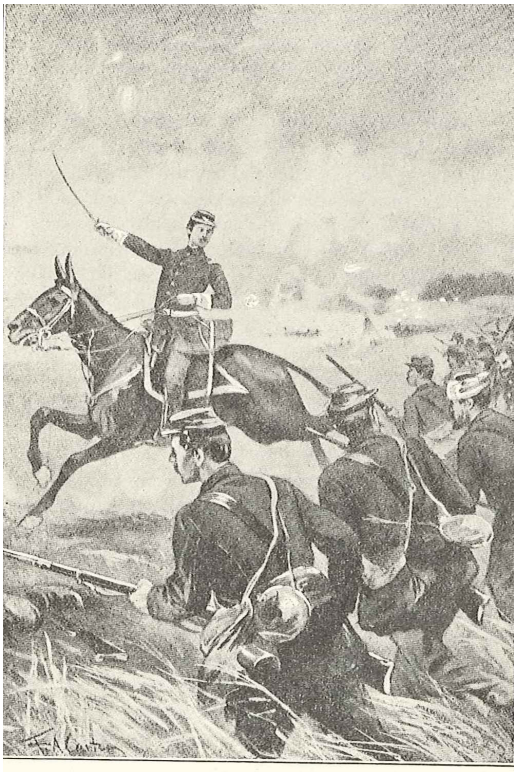
treat visiting neighbors, and resented by an equally hot fire. The 21st Kansas nobly held its ground while we were surrounded by fire, smoke and blood. I remembered the good old Scriptural admonition, that "it is more blessed to give than to receive," and told the boys to give them the best they had—and we gave them 42 rounds—not without a charge, but with a charge behind each one of them.

During the hottest period of the fight, a musketball passed through the lapels of my vest, carrying away a pair of gloves I had stuck in the bosom of it. Another minie ball passed through the back of my coat, just above the buttons, making an entry and exit about six inches apart. Had the rebels known how close they were to shooting Osteopathy, perhaps they would not have been quite so careless. During this engagement, I was mounted on the same mule, which had walked the log with me back in Kansas. The antics of this creature when the leaden balls came whizzing thickest about her were amusing. She seemed under the impression that they were nit flies, while I was thoroughly convinced they were bullets.

Many amusing incidents occurred during our conflict. Some of our boys fell to praying for the Lord to save them. Under the circumstances, I deemed it best to suspend devotional services and get into line to fight the rebels, who were spattering us with lead, so I leaped from my mule, and planting my foot close behind some of them, I broke the spell. They closed up the front and made good soldiers throughout the remainder of the fight. We held the field until Price's forces withdrew, leaving 52 dead on the ground and 127 horses, which fell into our hands.

Shortly after the departure of the enemy, night spread her friendly mantle over the scene, shutting out from our sight the horrors of war. Our regiment marched west two miles, then north six, east one, and went into camp near Shawneetown. About six o'clock the next morning, the artillery under General Totten opened fire east of Westport and south for six or eight miles—28 pieces joining in the chorus with a spattering of small arms, which made a sullen roar, rolling along the entire line. The fighting was severe until about eight o'clock, when General Price began his retreat south. We followed him, skirmishing all the way, until we had pursued him a distance of 90 miles, had captured 28 cannon and were only a mile or two east of Fort Scott.

At this point, we decided not to escort General Price any farther, but leave him to take care of himself. Finding the Confederate General Marmaduke in bad company, we invited him to go home with us; and as we were prepared to enforce the invitation, he consented with some reluctance, for the general had "a hankering after the stars and bars."



OSTEOPATHY IN DANGER

After Price's forces began their retreat, the firing ceased for a while, and they had gone fully 20 miles before it was again resumed. The privilege was given the enemy to bury their dead, and soon a company of 140 of our brave foes came to my headquarters under a flag of truce, which we always respected. I ordered the captain and his men to dismount and stack their arms, which they did. I then instructed the officer in command to form his men in line before me, and stationed a guard over their arms.

Addressing the Captain, I asked, "How are you off for grub?" "Almost out, major!" he answered. Then in a tone and manner as serious as I could assume, I said, "I want you to listen to what I have to say for about five minutes, and not move a muscle until I get through." Then I went on to picture the horrors of war and the extreme measures sometimes necessary. I wound up by saying the rebels had been in the habit of shooting many of our men, and notwithstanding they had come in under a flag of truce, I intended to shoot the captain and every man with him.

At this, every cheek blanched and their breath came quick. Some were about to interpose, when I broke in with, "I mean I will shoot you all in the mouth with food and coffee, as I want to convert all your sorrows into joy. Break ranks, go to the commissary and get enough to fill up." The captain and officers gave me a friendly grasp, and regretted that war made us (who should be by all laws of nature

friends) enemies, and hoped that the Angel of Peace might soon spread her white wings over our beloved land. Those rebels certainly enjoyed that meal, and it was no doubt the first good meal the poor fellows had had for many days.

After chasing Price for 90 miles, as stated, we went into Kansas at De Soto, and on Tuesday morning, October 27, 1864, I received orders to disband the 21st Regiment and go home. I kept the order to myself, determined to try the grit of the boys and have a little fun at their expense. Ordering the whole regiment to be drawn up in line, I made a speech in which I said we had a very long march before us and a desperate battle at the end of it. I stated that I did not wish anyone to undertake this arduous march, or to engage in the terrible conflict, who was not fully equal to the emergency. If any felt too sick, faint or weak to accompany us, or for any cause felt they could not endure the hardship and danger, they would not be forced to go. All who would volunteer to go with me through any trial or danger were requested to step six paces to the front.

About one-third of the command stepped out six paces and thus declared their willingness to follow anywhere. Then, in a tone loud enough to be heard by all, I read the order for the disbanding of the regiment, told those who did not feel well enough to accompany us to go to the hospital under the doctor's care, and to the others said, "Boys, we will go home!" Shouts and roars of laughter drowned any further utterance, and in ten minutes, we had not a sick man in the regiment. The regiment was disbanded, we all went home and that ended my experience as a soldier.

AAOJ Submission Checklist

For more information on the elements in this checklist, see "*AAOJ* Instructions for Contributors" at www.academyofosteopathy.org

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- ☐ Submission e-mailed to *AAOJ*'s Scientific Editor at editoraaoj@gmail.com or mailed on CD-ROM to the *AAOJ*'s Managing Editor, American Academy of Osteopathy, 3500 DePauw Boulevard, Suite 1080, Indianapolis, IN 46268
- ☐ Manuscript formatted in Microsoft Word for Windows (.doc), text document format (.txt) or rich text format (.rtf)

Manuscript Components

- ☐ Cover letter addressed to the *AAOJ*'s Scientific Editor, Murray R. Berkowitz , DO, MA, MS, MPH, with any special requests (e.g., rapid review) noted and justified
- ☐ Title page, including the authors' full names and financial or other affiliations, as well as disclosure of the financial support related to original research described in the manuscript
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- ☐ "Methods" section
  - the name of the public registry in which the trial is listed, if applicable
  - ethical standards, therapeutic agents or devices, and statistical methods defined
- ☐ Four multiple-choice questions for the continuing medical education quiz and brief discussions of the correct answers
- ☐ Editorial conventions adhered to
  - units of measure given with all laboratory values
  - on first mention, all abbreviations other than measurements placed in parentheses after the full names of the terms, as in "American Academy of Osteopathy (AAO)"
- ☐ Numbered references, tables and figures cited sequentially in the text
  - journal articles and other material cited in the "References" section follow the guidelines described in the most current edition of the *AMA Manual of Style: A Guide for Authors and Editors.*
  - references include direct, open-access URLs to posted, full-text versions of the documents
  - photocopies provided for referenced documents not accessible through URLs
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- ☐ For manuscripts based on survey data, a copy of the original validated survey and cover letter

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- ☐ For authors serving in the U.S. military, the armed forces' approval of the manuscript and institutional or military disclaimers submitted

Financial Disclosure and Conflict of Interest

Authors are required to disclose all financial and non-financial relationships related to the submission's subject matter. All disclosures should be included in the manuscript's title page. See the "Title page" section of "*AAOJ* Instructions to Contributors" for examples of relationships and affiliations that must be disclosed. Those authors who have no financial or other relationships to disclose must indicate that on the manuscript's title page (e.g., "Dr Jones has no conflict of interest or financial disclosure relevant to the topic of the submitted manuscript").

Component Societies and Affiliated Organizations Upcoming Calendar of Events

July 15-18
Alabama Osteopathic Medical Association
22nd Annual Emerald Coast Conference
Hilton Sandestin Beach, Destin, FL
CME: 25 Category 1-A AOA credits anticipated
Phone: (256) 447-9045 Fax: (256) 447-9040
E-mail: **alosteoma@aol.com** Web site: **http://aloma.org/**

July 19-22
Opthalmalogic Principles and their Relationship to Osteopathy in the Cranial Field
Course Director: Paul Dart, MD
Private office, Eugene, OR
CME: 26 Category 1-A AOA credits anticipated
Phone: (317) 581-0411 Fax: (317) 580-9299
E-mail: **info@cranial academy.org**
Web site: **http://www.cranialacademy.org**

July 20-22
Manual Medicine: An Osteopathic Approach Introduction to Osteopathic Medicine and Evaluation & Treatment: Lumbar Spine
UNECOM, Biddeford, ME
CME: 20 Category 1-A AOA credits anticipated
Phone: (207) 602-2589 E-mail: **cme@une.edu**
Web site: **www.une.edu/com/cme/manualmedicine.cfm**

August 9-12
Colorado Society of Osteopathic Medicine
2012 Annual Meeting and Summertime CME: Primary Care Medicine in the Rockies
Beaver Run Resort & Conference Center, Breckenridge, CO
CME: 25 Category 1-A AOA credits anticipated
Phone: (303) 322-1752 Fax: (303) 322-1956
E-mail: **rachel@coloradodo.org**
Web site: **http://www.coloradodo.org**

August 17-19
Indiana Academy of Osteopathy & Indiana Osteopathic Association: A Sutural Approach to Osteopathy in the Cranial Field
Holiday Inn Indianapolis North, Carmel, IN
Program Chair: Charles A. Beck, DO, FAAO
Faculty: Edward G. Stiles, DO, FAAO
CME: 20 Category 1-A AOA credits anticipated
Phone: (317) 926-3009 Fax: (317) 926-3984
E-mail: **info@inosteo.org**
Web site: **http://www.inosteo.org**

September 7-9
Integrated Neuromuscular and Myofascial Release
Course Chairperson: Lisa DeStefano, DO
MSUCOM, East Lansing, MI
CME: 19 Category 1-A AOA credits anticipated
Phone: (517) 353-9714 Fax: (517) 432-9873
E-mail: **cme@com.msu.edu**
Web site: **http://www.com.msu.edu/cme/courses.html**

September 14-16
Osteopathic Physicians & Surgeons of California
23rd Annual Fall Conference - CME by the Bay
Intercontinental Clement Monterey Hotel, Monterey, CA
CME: 22 Category 1-A AOA credits anticipated
Phone: (916) 822-5246 Fax: (916) 822-5247
E-mail: **opsc@opsc.org** Web site: **http://www.opsc.org/**

September 21-23
Orthopedics, Posture and the Primary Respiratory Mechanism
Course Director: Maurice Bensoussan, MD
Associate Course Director: R. Paul Lee, DO, FAAO
Hilton Hotel, Providence, RI
CME: 21.5 Category 1-A AOA credits anticipated
Phone: (317) 581-0411 Fax: (317) 580-9299
E-mail: **info@cranial academy.org**
Web site: **http://www.cranialacademy.org**

September 21-23
Manual Medicine: An Osteopathic Approach Introduction to Osteopathic Medicine and Evaluation & Treatment: Thorax & Rib Cage
UNECOM, Biddeford, ME
CME: 20 Category 1-A AOA credits anticipated
Phone: (207) 602-2589 E-mail: **cme@une.edu**
Web site: **www.une.edu/com/cme/manualmedicine.cfm**

September 21-23
ACOFP Intensive Update & Board Review in Osteopathic Family Medicine
Intercontinental Chicago O'Hare Hotel, Rosemont, IL
CME: 21 Category 1-A AOA credits anticipated
Phone: (800) 323-0794 Fax: (847) 228-9755
Web site: **http://www.acofp.org/CME_Center/Conventions/Workshops/**