22 May 2020

DEFENSE AND VETERANS BRAIN INJURY CENTER RESEARCH REVIEW ON MULTIPLE TRAUMATIC BRAIN INJURY/MULTIPLE CONCUSSION

PURPOSE

The purpose of this Research Review is to summarize available peer-reviewed scientific literature regarding the epidemiology, special populations, risk factors, chronic effects, and treatment considerations or recommendations regarding multiple traumatic brain injury (TBI).

BACKGROUND

The term "multiple TBI" is applicable to TBI of any severity sustained by an individual who has a prior history of TBI. The Department of Defense (DoD) defines TBI as "…a traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force…" (Department of Veterans Affairs, Department of Defense, & The Management of Concussion/mTBI Working Group, 2016). More specifically, mild TBI (mTBI) is defined as a loss of consciousness ≤ 30 minutes, altered mental state or consciousness ≤ 24 hours, posttraumatic amnesia ≤ 1 day, Glasgow Coma Scale 13-15, and normal structural imaging (conventional MRI or CT scan) (Department of Veterans Affairs et al., 2016). The vast majority of TBIs are mild (Centers for Disease Control and Prevention, 2015; Defense and Veterans Brain Injury Center, 2019c), and most instances of multiple TBI result from an mTBI sustained by an individual with a history of prior mTBI. Accordingly, multiple TBIs are most often considered in the context of populations with routine exposure to repetitive mTBI risk – notably, military service members (SMs) and athletes.

Since the beginning of post-9/11 combat operations in Afghanistan and Iraq, the number of TBIs sustained by members of the U.S. Armed Forces has significantly increased (Defense and Veterans Brain Injury Center, 2019a), with many SMs likely sustaining multiple diagnosed or undiagnosed mTBIs from combat and combat support activities, including exposure to explosive blasts (Cernak & Noble-Haeusslein, 2010; Vanderploeg et al., 2012). The reported total number of SMs diagnosed with at least one TBI from 2000 to 2019 Quarter 3 is 413,858. (Defense and Veterans Brain Injury Center, 2019c). However, this is an underestimation of total TBIs, as this number does not count multiple TBIs sustained by a single SM. More than a decade ago, the Armed Forces Health Surveillance Branch (the DoD agency responsible for collecting TBI data) deliberately chose to report only one TBI per patient to avoid overinflating the numbers by counting a single TBI multiple times due to ambiguity in the medical records. To more accurately characterize the total number of injuries, the Defense and Veterans Brain Injury Center (DVBIC) Surveillance team has worked to estimate the incidence of repeat TBIs among SMs. In a cohort of SMs who sustained their first active duty TBI from 1 October 2015 to 30 September 2017, the model-derived probability scores found that approximately 2.32% of SMs are likely to sustain a repeat TBI within 2 years of their first injury (Agimi, Earyes, Deressa, & Stout, 2019). Work is ongoing to continue to identify and characterize multiple TBIs within the Military Health System.

The body of accumulated research regarding TBIs in sport – at least 90% of which are mild (Selassie et al., 2013) and typically referred to as "concussion"— is much more extensive. Consequently, over the past few decades, previous misconceptions have given way to better appreciation of the potential deleterious or cumulative effects of multiple concussion in sport (McAllister & McCrea, 2017), resulting in more conservative injury management and more restrictive return-to-play guidelines (Putukian & Kutcher, 2014). A comparison between two major sport concussion studies, the NCAA Concussion Study (1999-2001) and the CARE Consortium (2014-2017), illustrated that current management guidelines result in a time to return to play that is about 10 days longer when compared to earlier practices. Additionally, same-season repeat concussions were 41% lower in the CARE Consortium study under current practices when compared to previous management techniques in the NCAA Concussion Study (M. McCrea et al., 2019). Furthermore, in the CARE Consortium there was only one case of repeat concussion that occurred within 10 days of the initial injury (3.7% of within-season repeat concussions), but 92% of repeat concussions in the NCAA Concussion Study occurred within the first 10 days post-injury (M. McCrea et al., 2019). Although some reports suggest that the incidence of pediatric and sport-related mTBI has increased over time (Macpherson, Fridman, Scolnik, Corallo, & Guttman, 2014; Wasserman, Kerr, Zuckerman, & Covassin, 2016), this trend most likely reflects improvements in case detection and healthcare utilization (Bompadre et al., 2014; Macpherson et al., 2014) along with increased overall participation in sports and physical recreational activities (Selassie et al., 2013).

Outside of SMs and athletes, certain demographic characteristics and medical conditions may increase the risk for multiple TBIs. Individuals who may be at particular risk of multiple TBIs include those with medical conditions such as seizure disorders (Saunders, Selassie, Hill, Horner, et al., 2009; Saunders, Selassie, Hill, Nicholas, et al., 2009), those exposed to violence or who undertake high-risk behaviors, and those who are susceptible to falls (e.g., elderly individuals) (K. M. Iverson, Dardis, & Pogoda, 2017; K. M. Iverson, Sayer, et al., 2017; Olson-Madden, Forster, Huggins, & Schneider, 2012; Taylor, Bell, Breiding, & Xu, 2017). Risk factors identified by Hayward et al. (2018) in a sample of 50,744 patients treated for neurotrauma admissions and incorporated in the Michigan State Inpatient Database from 2006 to 2014 included the following: male gender, African-American race, and comorbid diagnoses such as depression, psychosis, or neurological disorders. Interestingly, age at first admission and socioeconomic status were unrelated to repeated neurotrauma, and individuals with comorbid alcohol and drug use were actually less likely to be readmitted for repeat neurotrauma (Hayward, Fessler, Buck, & Fessler, 2018).

Ascertaining prior TBI is often a challenge for both patients and clinicians. An emergency room survey found that most individuals who described sustaining a concussion within the last 12 months did not recognize the event as a concussion until prompted by a healthcare provider (Delaney, Abuzeyad, Correa, & Foxford, 2005). Studies in sports have found that athletes may not recognize previous injuries as TBIs (McCrory et al., 2017) or may be reluctant to report injuries to medical personnel (Kroshus, Garnett, Hawrilenko, Baugh, & Calzo, 2015). One survey of medical students and residents found that they had incomplete knowledge about mTBI diagnosis and management practices (Boggild & Tator, 2012). Since treatment is often not sought for mTBI, medical documentation of a previous TBI may be unavailable or may present an incomplete picture of the TBI history. Self-report via structured interview has been suggested as the "gold standard" for ascertaining a TBI history, (Corrigan & Bogner, 2007) and numerous TBI history reporting instruments have been developed for use in sports settings, the military, and other specific populations to capture a more comprehensive and accurate TBI history (Corrigan & Bogner, 2007; Fortier et al., 2014; Walker et al., 2015).

NEUROPHYSIOLOGY OF MULTIPLE MTBI

The physical forces that cause mTBI initiate a process of neurometabolic changes that alter cerebral physiology and may result in axonal impairment and cell death (Giza & Hovda, 2014). According to a number of pre-clinical studies, specific cellular pathology associated with multiple mTBIs can include excitotoxicity with dysregulation of glutamate and calcium, oxidative stress, dysmyelination, cell death, cerebral blood flow-metabolism uncoupling, blood-brain barrier dysfunction, astrocyte reactivity, microglial activation, and diffuse axonal injury (Fehily & Fitzgerald, 2017). Multiple mTBIs may also inhibit the recovery of cerebral white matter, which could contribute to patterns of white matter changes that have been associated with the development of long-term cognitive deficits (Bazarian et al., 2014). Recent advances in neuroimaging now allow for the assessment of the microstructural pathology. Research using diffusion tensor imaging (DTI) demonstrates that TBI patients differ from neurologically healthy controls on several metrics relevant to axonal structural integrity (Hulkower, Poliak, Rosenbaum, Zimmerman, & Lipton, 2013). However, to date there is no DTI literature exclusively examining the effect of multiple TBIs.

The term “Second Impact Syndrome” has been coined to describe a rare but catastrophic phenomenon in which a second TBI is sustained prior to full symptomatic recovery from the initial TBI. The additional neurometabolic strain on an already stressed system initiates cerebral swelling and brain herniation that can potentially result in death within minutes or hours of the second impact (Durand & Adamson, 2004; McLendon, Kralik, Grayson, & Golomb, 2016; Mori, Katayama, & Kawamata, 2006; Stovitz et al., 2017). While this phenomenon has been reported, the term “Second Impact Syndrome” and the existence of a definitive syndrome are regarded as controversial by some due to the rarity of cases and the lack of etiological data and clinical details (H. J. McCrea, Perrine, Niogi, & Hartl, 2013; McCrory, Davis, & Makdissi, 2012).

MULTIPLE CONCUSSIONS IN SPORT

Recreational activities and competitive sports are a common cause of concussions in both military and civilian populations. Specific to multiple TBIs, most research to date has focused on sports, particularly those with prominent person-to-person contact contributing to high rates of TBI such as football, boxing, hockey, soccer, and rugby (Casson, Viano, Powell, & Pellman, 2011; Delaney, Al-Kashmiri, & Correa, 2014; Levy et al., 2012; Neselius et al., 2012; Partridge, 2014). Findings from the NCAA Injury Surveillance Program from 2009-2010 to 2013-2014 academic years indicate an average concussion recurrence rate across 17 sports of 13.9% and 10.3% for men’s and women’s sports, respectively (Zuckerman et al., 2015). Men’s ice hockey represented the highest rate of multiple TBIs at 20.1%, while men’s baseball had a recurrence rate of 0.0% (Zuckerman et al., 2015). Among women’s sports, soccer (12.5%) and volleyball (5.4%) had the highest and lowest rates of recurrent concussions, respectively (Zuckerman et al., 2015).

Younger individuals may be particularly susceptible to sport-related mTBI (Selassie et al., 2013) and associated sequelae (Giza et al., 2013; Sariaslan, Sharp, D'Onofrio, Larsson, &

Fazel, 2016). Acutely, injury symptoms include a range of cognitive, somatic/sensory, vestibular, and/or emotional post-injury complaints (Cicerone & Kalmar, 1995; Vanderploeg et al., 2015) which typically resolve within 7 to 10 days following mTBI (Field, Collins, Lovell, & Maroon, 2003; Makdissi, 2009; M. McCrea et al., 2003; Pellman, Lovell, Viano, Casson, & Tucker, 2004). However, a proportion of concussed athletes may continue to have postconcussion symptoms, defined as symptoms that persist beyond traditional recovery periods (Mihalik et al., 2005; Willer & Leddy, 2006). While risk factors such as age (Williams, Puetz, Giza, & Broglio, 2015) and gender (Covassin, Elbin, Kontos, & Larson, 2010; Covassin et al., 2006; Kostyun & Hafeez, 2015) have been associated with symptom recovery time and risk of subsequent concussion, research in both sport-related TBI and military-related TBI points to a history of previous mTBI as more important than demographic factors in influencing outcome (Collins et al., 2002; Covassin, Stearne, & Elbin, 2008; Gaetz, Goodman, & Weinberg, 2000; Guskiewicz et al., 2003; Stein et al., 2016). In pediatric patients without a history of concussion, a greater number of symptoms and longer time to recovery associated with the incident concussion increased the risk for a repeat concussion (Curry et al., 2019). Additionally, history of two or more concussions has been associated both with a greater number of symptoms, greater severity of symptoms, and/or slower recovery from symptoms (Chen, Oddson, & Gilbert, 2019; G. L. Iverson, Gaetz, Lovell, & Collins, 2004; Johnson et al., 2012; Register-Mihalik, Mihalik, & Guskiewicz, 2009; Schatz, Moser, Covassin, & Karpf, 2011; Vynorius, Paquin, & Seichepine, 2016; Wasserman et al., 2016), especially headache (Chen et al., 2019; Guskiewicz et al., 2003; Mihalik et al., 2005; Sallis & Jones, 2000) and fatigue (Covassin, Moran, & Wilhelm, 2013). Greater total sleep disturbances have been reported proportional to the number of concussions (Oyegbile, Dougherty, Tanveer, Zecavati, & Delasobera, 2019). In those with three or more concussions, worse sleep disturbance was associated with greater symptomology and showed stronger correlations to cognitive dysfunction (Oyegbile et al., 2019). In addition, mTBI may results in balance problems. A study by Dierijck et al. (2018) assessed postural stability among male, junior elite football, hockey, and rugby players using center-of-pressure displacement and velocity. Pre-season tests of those with a history of three or more concussions were compared to tests of those with no history of concussion and revealed no significant effect of concussion history on postural control (Dierijck, Wright, Smirl, Bryk, & van Donkelaar, 2018). However, evidence to date regarding vestibular changes associated with repeat TBI has been limited and inconsistent (Howell, Beasley, Vopat, & Meehan, 2017; Murray et al., 2017).

A number of investigations have reported acute neurocognitive deficits, including problems with memory, processing speed, and new learning, in athletes who sustained multiple TBIs (Collins et al., 1999; Covassin et al., 2010; Covassin et al., 2013; G. L. Iverson, Echemendia, Lamarre, Brooks, & Gaetz, 2012; G. L. Iverson et al., 2004; Pedersen, Ferraro, Himle, Schultz, & Poolman, 2014; Ravdin, Barr, Jordan, Lathan, & Relkin, 2003; Wall et al., 2006; Yumul & McKinlay, 2016). However, other studies have found no evidence of cognitive differences in athletes with a remote history of multiple mTBIs compared to those with no history of mTBI (Brooks et al., 2016; Guskiewicz, 2002; G. L. Iverson, Brooks, Lovell, & Collins, 2006; Porter, 2003; Terry et al., 2012). These apparent discrepancies may be reconciled in part by acknowledging the limitations of cognitive assessments regarding a) sensitivity to clinically meaningful cognitive deficits, b) the use of a baseline tests vs population norms for post-injury comparisons, and c) accounting for the time between injuries.

Concerns about athletes returning to play before resolution of acute TBI symptoms led to the passage of the The Lystedt Law in Washington State in 2009. Provisions of this law include removal from play at the time of the concussion, no same-day return to play, evaluation and clearance by a trained healthcare provider prior to return to play, and required education for coaches, parents, and athletes on concussion injuries and appropriate management (Albano, Senter, Adler, Herring, & Asif, 2016; Bompadre et al., 2014). Less than 5 years after the enactment of The Lystedt Law, all 50 states and the District of Columbia have passed similar youth sport concussion legislation (Concannon, 2016). To date, surveillance data shows that these laws may have reduced the incidence of repeat concussion among high school athletes (Yang, Comstock, Yi, Harvey, & Xun, 2017).

MULTIPLE TBI IN THE MILITARY

SMs injured during support of Operation Enduring Freedom/Operation Iraqi Freedom are more likely to have sustained multiple TBIs than those not injured in battle (Galarneau, Woodruff, Dye, Mohrle, & Wade, 2008), though TBIs sustained during deployment are often not reported or diagnosed until after the SM has returned from deployment (Regasa, Agimi, & Stout, 2019). One post-deployment study found that 17% of SMs reported an mTBI (blast and non-blast) during their previous deployment, with 59% of these individuals reporting more than one mTBI (Wilk, Herrell, Wynn, Riviere, & Hoge, 2012). Explosive blast – usually the result of an improvised explosive device – is of particular relevance to SMs and is a primary reason why TBI is a "signature injury" of the wars in Iraq and Afghanistan (DePalma & Hoffman, 2018; Elder & Cristian, 2009; Galarneau et al., 2008; Warden, 2006). Currently, it is unclear how primary blast wave mechanisms may differ from the acceleration-deceleration forces of sports injuries and the resulting functional and clinical impact of these potential mechanistic differences (Elder & Cristian, 2009; Levin & Robertson, 2013; Rosenfeld & Ford, 2010). Further research is needed to identify the pathophysiological mechanisms of blast injury and to determine the potential cumulative effects of repetitive blast-related TBI on post-injury sequelae and neuropathological changes.

Among deployed military personnel, multiple TBIs have been associated with increased postconcussion symptomatology (Bryan & Clemans, 2013; Reid et al., 2014; Vanderploeg et al., 2012), including sleep disturbance, (Bryan, 2013), headache (Wilk et al., 2012), depression and PTSD (Bryan & Clemans, 2013; Vanderploeg et al., 2012), and anxiety (Vanderploeg et al., 2012). A particularly troubling finding is the potential for increased suicide risk among SMs with multiple TBIs. A study of deployed soldiers found that after controlling for depression, PTSD, and TBI symptom severity, 21.7% of those with multiple TBIs reported lifetime suicidal thoughts or behaviors compared with 6.9% of soldiers with a single TBI and 0% of soldiers with no history of TBI (Bryan & Clemans, 2013).

Active duty and reserve SMs are at greater risk for a TBI than are their civilian counterparts (Defense and Veterans Brain Injury Center), and many military SMs have sustained mTBI prior to military service (Ivins et al., 2003). Therefore, multiple TBIs in the military must be considered outside of the deployment arena as well. A study of non-combat injured military personnel found that individuals who sustained a TBI and had a previous history of one or more additional TBIs reported significantly more symptoms during the first 3 months post-injury compared to individuals who had not previously sustained a TBI (Miller, Ivins, & Schwab, 2013). This is consistent with findings in the sports TBI literature that recovery from TBI may be complicated or delayed in individuals with a history of a prior TBI.

MULTIPLE TBI IN THE GENERAL POPULATION

The impact of multiple TBIs on health outcomes has not been extensively explored in the general population, outside of the context of sports and the military. The proportion of the U.S. population that has sustained more than one lifetime TBI is unknown; some evidence suggests the prevalence rate may be near 20-30%. A TBI Model Systems National Database study of individuals who received rehabilitation following moderate-to-severe TBI found that 20% of the cohort had sustained at least one prior TBI (Corrigan et al., 2013), and a TRACK-TBI study of patients with mTBI reported 30.5% had a prior TBI (Stein et al., 2019).

Those with multiple TBIs may be at risk for behavioral or psychiatric disorders. Corrigan et al. (2013) observed that pre- and post-index TBI behavioral outcomes, particularly substance abuse, were highly associated with prior TBIs. Anxiety and depression were also significantly associated with prior TBIs, and TBI before age 6 was associated with an increased likelihood of psychiatric hospitalization and substance abuse (Corrigan et al., 2013). In another population-based study, epilepsy/seizure disorders were associated with sustaining a subsequent TBI (Saunders, Selassie, Hill, Nicholas, et al., 2009), and prior TBI in patients with mTBI has been reported as a significant predictor of 6-month postconcussive symptom severity (Cnossen et al., 2017).

MULTIPLE TBI & CHRONIC TRAUMATIC ENCEPHALOPATHY

There is evidence that multiple TBIs may contribute to long-term neurological degeneration, contributing to cognitive, psychological, or motor dysfunction. In an investigation of 2,552 retired football players, individuals who reported three or more mTBIs (24% of former players) were five times more likely to have been diagnosed with mild cognitive impairment and three times more likely to report significant memory problems compared to their counterparts without a history of mTBI (Guskiewicz et al., 2005). Studies of athletes and SMs also find that multiple TBIs increase the risk of depression (Bryan & Clemans, 2013; Guskiewicz et al., 2007; Kerr, Thomas, Simon, McCrea, & Guskiewicz, 2018) and may result in movement disorders or motor neuron dysfunction (Ozolins, Aimers, Parrington, & Pearce, 2016). Chronic traumatic encephalopathy (CTE), described as a progressive neurodegenerative disorder associated with hyperphosphorylated tau protein deposition, has been attributed to repetitive head trauma but not specifically repetitive mTBI. Currently, the diagnostic pathology can only be observed at autopsy, and a definitive cause-effect relationship between the degree of CTE pathology and history of brain trauma has not been demonstrated (Harmon et al., 2019; McCrory et al., 2013). The association between CTE and brain trauma is based on the observation that the pathologic hallmark of CTE frequently occurred in deceased individuals with a history of head trauma, most of whom were contact-sport athletes (Baugh, Robbins, Stern, & McKee, 2014; Erlanger, Kutner, Barth, & Barnes, 1999). To be sure, there is controversy regarding this association because the largest clinical studies suggesting a cause and effect are severely limited by selection bias. There is still much to be understood regarding the cause, pathology, progression, symptomology, and risk factors for CTE. A more detailed discussion of current research surrounding CTE is presented in a separate research review (Defense And Veterans Brain Injury Center, 2019b).

TREATMENT/MANAGEMENT CONSIDERATIONS

A number of tools and guidelines have been developed to help standardize the initial evaluation and care of concussed individuals. Within these tools, special consideration for multiple TBI is often considered. For civilian athletes suspected of having a concussion, the Sport Concussion Assessment Tool – 5th Edition (SCAT5) is commonly used. The SCAT5 includes questions on the number of prior concussions, time since last concussion, and time to recovery of last concussion ("Sport concussion assessment tool - 5th edition," 2017). Following the diagnosis of a sport-related mTBI, a six-stage rehabilitation progression is recommended, starting at Stage 1 "symptom-limited activity" and ending with Stage 6 "return to sport" (Harmon et al., 2019; McCrory et al., 2017). The return-to-play progression does not start until the athlete is asymptomatic and has a normal clinical examination (Broglio et al., 2014; McCrory et al., 2017). When an athlete has sustained more than one mTBI, particularly within a short period of time such as a single season, more conservative management is recommended (Elbin et al., 2013). Other modifying factors that call for more conservative management include repeated mTBIs "occurring with progressively less impact" or requiring progressively longer recovery times (Broglio et al., 2014). Although it has been suggested that retirement be considered in cases where additional mTBIs are being sustained from new injuries involving less force (Elbin et al., 2013), retirement from sport is not discussed in those guidelines (Broglio et al., 2014; McCrory et al., 2017), except to state that there are no evidence-based guidelines for disqualification (Harmon et al., 2019).

For the Military, in 2014, the DoD adopted a Pathway of Care approach across the Services, tasking the DVBIC as the manager of that pathway, for identifying, evaluating, and treating TBI (Assistant Secretary of Defense for Health Affairs, 2014). More recently, DoD Instruction 6490.11, titled "DoD Policy Guidance for Management of Mild Traumatic Brain Injury/Concussion in the Deployed Setting", (November 26, 2019) (Under Secretary of Defense for Personnel and Readiness, 2019), was updated to provide medical guidance for concussion screening, initial evaluation, and recurrent events by leveraging clinical tools produced by the DVBIC. Initial screening for concussion is conducted using the Military Acute Concussion Evaluation 2 (MACE 2), a tool designed to screen the SM following potentially concussive events. The MACE 2 has a section on injury history to account for recurrent concussions within the last 12 months (Defense and Veterans Brain Injury Center, 2018a). The revised DVBIC Progressive Return to Activity Clinical Recommendation (PRA CR) titled "Progressive Return to Activity Following Acute Concussion/Mild Traumatic Brain Injury: Guidance for the Primary Care Manager in Deployed and Non-deployed Settings" is to be used after initial screening with the MACE2 to direct clinical management during the initial weeks post-injury and guide appropriate rehabilitation. Similar to sport guidance, the PRA CR defines the stages of the progressive return to activity process, from Stage 1 "Relative Rest" to Stage 6 "Return to Full Duty" and provides an algorithm and guidelines for appropriate progression through the stages based on symptomatology. Specific guidance is given for SMs who have sustained the second concussion within a 12-month time period and mandates a minimum of seven days in the protocol prior to return to full duty (Defense and Veterans Brain Injury Center, Under Review). The DVBIC's "Recurrent Concussion Evaluation Card" provides additional guidance for those with three or more documented concussions within a 12-month time frame and directs the individual to have a comprehensive evaluation by a neurologist, neuroimaging as necessary, neuropsychological testing, functional assessments, and ultimately clearance by a neurologist for return to full duty (Defense and Veterans Brain Injury Center, 2018b).

The recently updated DoD Instruction 6490.11 (November 26, 2019) mandates that all SMs diagnosed with an mTBI have, at a minimum, 24 hours recovery unless the results of subsequent clinical evaluation indicate a longer period is needed. Per this instruction,

> *If two diagnosed mTBI/concussions have occurred within the past 12 months, return to duty is delayed for an additional 7 days following symptom resolution… If three diagnosed mTBI/concussions have occurred within the past 12 months, return to duty is delayed until a recurrent concussion evaluation has been completed. The recovery period for SMs experiencing recurrent concussions depends on the number of incidents. Recovery care includes uninterrupted sleep and pain management. All sports and other activities with risk of concussion are prohibited until the SM is cleared by a licensed independent practitioner… Additionally, a recurrent concussion evaluation may be performed any time it is clinically indicated, i.e., if symptoms are persistent. The recurrent concussion evaluation can be obtained on the DVBIC website at https://dvbic.dcoe.mil/material/recurrent-concussionevaluation-card.*

CONCLUSIONS

Multiple mTBIs are especially concerning in contact sport athletes and military SMs. The physical forces of multiple TBIs may result in dysregulated cerebral physiology or cumulative white matter alterations with potential long-term functional implications. In athletes, greater symptomology and longer recovery time have been associated with multiple concussions, but the effects on neurocognitive function are unclear. Recent conflicts have increased the number and risk of multiple TBIs in SMs, with a unique risk stemming from blast injuries. Similar to contact sport athletes, greater symptomology has been reported with a history of multiple TBIs. Chronic traumatic encephalopathy and other neurodegenerative conditions are reported by some to be associated with repetitive head trauma, though to date a causal relationship has not been established. Individuals with previous TBIs should be monitored and managed conservatively so as to reduce the risk of subsequent TBIs and allow for a more rapid recovery from post-TBI symptoms. Sustaining a second mTBI before fully recovering from the first results in a more prolonged recovery, and puts the SM at greater risk for neurologic injury. Clinical guidance about return to play or to work/military service, which may expose the patient to subsequent TBIs, should be made with consideration for an individual patient's risk factors and TBI history with a focus on opportunities for prevention. Both sport and military guidelines recommend a similar six stage progressive return to activity model following a TBI, with additional rest and evaluation for individuals with a prior TBI within the same year.

Future research is needed to examine the effects of and, ultimately, to mitigate the risk for repeat concussion. This will require continued examination of the impact of current progressive return to activity guidelines and recurrent concussion evaluations on reducing risk of repeat concussion, as well as impacts on long-term symptomology. Ongoing improvements in evaluation, documentation, and reporting among civilian and military health systems will facilitate improved understanding of multiple concussion prevalence and recovery.

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