Long-Term Consequences of Head Injury and Occupational Impairments

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ABSTRACT

Despite concerns about dire long-term consequences of blast induced military MTBI there have been few well-conducted prospective studies. The available data shows that much like in the civilian setting, symptom resolution occurs within days to weeks in the majority of individuals. Persistent post-concussive symptoms are present beyond three months ion up to a third of individuals and are frequently co-morbid with mental health diagnoses, particularly pots traumatic stress disorder. Only one study specifically examined occupational outcomes following MTBI. This showed and absolute and relative risk of medical unfitness in those with a history of deployment related MTBI. However, in the majority of those cases, mental disorder diagnosis and musculoskeletal injuries were primarily associated with a determination of medical unfitness. This highlights the need for a comprehensive and multidisciplinary approach in the rehabilitation of individuals with persistent symptoms following deployment related MTBI.

1.0 ACUTE SEQUELAE

Acute sequelae associated with MTBI have been measured in numerous studies, documenting both self-reported symptoms and neuropsychological impairments following MTBI acutely after injury. In a critical review of symptom recovery and neuropsychological test performance in adults with MTBI, Carroll et al [1] found that subjects injured while participating in sports commonly experienced symptoms immediately after concussion. Symptoms included headache, blurred vision, dizziness, self-perceived memory problems and confusion. Other adults with non-sports related MTBI reported similar symptoms after injury, including headache, fatigue, forgetfulness and sleep difficulties. Though such symptoms are not specific to MTBI, studies have found "…they are more common within the first month after MTBI than after other injuries or in the general population." Their review of cognitive sequelae measured with neuropsychological assessments likewise found evidence for acute effects of MTBI. Studies accepted in their review found consistent evidence of "…cognitive deficits within the first few days after the injury, including problems of recall of material, speed of information processing and attention. Resolution of symptoms and return to normal levels of cognitive functioning generally occurred within 3 to 12 months after injury, with *cognitive deficits* associated with MTBI generally resolving within 3 months." The authors recommended that future investigations include control groups and additional variables to measure confounding factors such as pain, prior TBI, other injuries, post injury events, and distress, in order to provide improved evidence on these issues.

Studies of the acute consequences of MTBI conducted after the review by Carroll et al [1] have confirmed frequent symptom reporting and problems of cognitive performance in the days and weeks following MTBI. Several of these studies have included analyses of possible confounding variables, comparisons with injury control groups, or included neuroimaging in order to further evaluate the meaning of symptoms and their clinical implications.

Emergency department patients with MTBI (n=246) were found to have poorer cognitive scores on learning and memory, orientation, and speed of information processing tested within 24 hours of injury than patients with orthopaedic injuries (n=102) [2]. Ponsford et al. [3] found that subjects with MTBI treated in the Emergency Department (ED) (n=123) more often had post-concussive symptoms, and impaired cognitive functioning in the emergency department and at 1 week post-injury than did a matched control group treated for general trauma (n=100). Kashluba and colleagues [4] compared MTBI patients treated in 2 emergency departments with matched controls within 1 month of injury and then again at 3 months. They found that symptom complaints were common for the MTBI patients at 1 month, but that by 3 months their complaints had diminished. MTBI patients continued to endorse only 3 of the 43 symptoms by 3 months follow-up ("doing things slowly," "fatiguing quickly," and "poor balance") as measured with a Bonferroni corrected effect size. However, MTBI patients reported higher severity levels of symptoms than did the controls (on 10 of the 43 symptoms). In contrast, Meares et al. [5] found that post-concussion syndrome was not specific to MTBI compared to non-brain injured trauma among patients treated in a level 1 trauma hospital within 14 days of injury (n=90 patients with MTBI; 85 trauma controls). Ponsford et al [3] suggest that measures of symptomatology based upon ICD-10 criteria of post-concussive disorder such as Meares' study, include a more limited set of the symptoms that can be experienced by patients with MTBI than were included in their study, and that this difference may explain the difference between Meares' findings and other studies. Multiple MTBIs have been linked to greater symptomatology in retired football players [5], and in active duty service members [4]. Guskiewicz and colleagues used surveys of retired professional football players to determine the relationship of mild cognitive impairment and memory problems with multiple concussions [6]. They found that retired players with three or more concussions were associated with clinically diagnosed mild cognitive impairment and self-reported significant memory impairments compared to retired players without a history of concussion [7].

Studies have reported inconsistent evidence of associations between symptoms after MTBI and neuro-imaging. DeGuise and colleagues [8] compared MTBI patients with (n=45) and without findings (n=176) on cerebral imaging (using CT) at two weeks post injury. Those with imaging findings more often showed auditory and vestibular system dysfunction; surprisingly, uncomplicated MTBI patients (those without cerebral imaging findings) reported more severe post-concussive symptoms than patients with cerebral imaging findings. Lange et al [9] found that MTBI patients (n= 60) reported more post-concussive symptoms than trauma controls (n=34), but they did not find a relationship between Diffusion Tensor Imaging (DTI) and ICD-10 post-concussive disorder. Using DTI, Henry et al. [10] found white matter differences between concussed athletes (n=18) compared to non-concussed athletes (n=10). They did not find that the number of regions showing alterations was associated with the number of symptoms reported, but number of regions altered was associated significantly with the number of concussions reported (3 concussions versus 1 or 2). Gosselin et al. [11] reported that compared to controls, symptomatic MTBI patients had more findings on functional magnetic resonance imaging (fMRI) and Event Related Potentials (ERP) months after injury (5.7 plus/minus 2.9 months post injury). (n=14 mTBI patients; 23 controls).

As with civilian populations, military populations with MTBI have, on average, more symptom complaints, and poorer cognitive performance when studied in the acute period after MTBI (generally defined as within 3 months of injury). For instance, this result was observed by Bryan and Hernandez [12] in an in-theatre study (N=116), that compared patients with and without MTBI who were referred for a TBI evaluation a median of 2 days post injury. Patients with TBI demonstrated greater declines across all subtests (ANAM) on several throughput scores (Simple Reaction Time, Procedural Reaction Time, Code Substitution-Learning, and Spatial Memory scores) than non-TBI patients when post-injury scores were compared to pre-deployment ANAM scores. Patients did not differ on accuracy scores, Code-Substitution Delayed, or Mathematical processing scores. Coldren et al. [13] also conducted a comparison of ANAM scores for patients with MTBI compared to non-concussed military subjects. They obtained pre-deployment ANAM scores for a subset of participants, and repeated ANAM testing at 5 or more days after injury. As with the Bryan and Hernandez study, Coldren et al. found significant differences in cognitive scores between concussed and non-concussed subjects immediately after injury (within 72 hours). They did not find differences at five or more days follow-up, suggesting that ANAM scores return to within normal levels within 5 to 10 days in the combat setting. The recovery of cognitive function is consistent with the sports literature. Caution needs to be used when testing cognitive performance, since poor effort has been measured in some returning service members [9], [14], similarly caution that symptom validity needs to be part of the evaluation of symptoms after MTBI.

Three or more concussive symptoms, were recalled by soldiers to have occurred immediately post injury in a large cohort drawn from an Army unit that served in Iraq. Headache and dizziness were most frequently reported post injury. Soldiers injured without TBI reported fewer of these symptoms post injury (33% of soldiers with TBI reported 3 or more symptoms immediately post injury compared to 3% of injured soldiers without TBI) [15]. Headache in MTBI patients presenting to a combat support hospital in Iraq were found to be associated with insomnia, loss of consciousness, PTSD symptoms, and slowed reaction time [12].

2.0 LONG-TERM SEQUELA OF MILITARY MTBI FOLLOWING BLAST

If symptoms and problems following MTBI persist for months or years and are attributable to MTBI, it would imply different treatment and evaluation strategies than if these problems resolved within weeks or months, or are explained by other, independent events or patient characteristics. Long-term consequences of MTBI identified in prior studies may be explained, at least in part, by other, often unmeasured factors such as pain and associated injuries. The risks of long term sequelae after MTBI are thought to be greater with multiple MTBIs,

MTBIs received before recovery is complete, MTBIs with overlapping PTSD or anxiety, pain, incentives for exaggerated symptom reporting, depression, and MTBIs resulting from close exposure to blasts. Research is ongoing and more evidence is expected in the near future.

Early cross-sectional studies suggested that as many as 10-20% of individuals reporting previous MTBI continued to have "persistent physical, emotional, and cognitive symptoms" months or years after injury. But, a number of investigators have questioned the existence of persistent symptoms due to MTBI or thought that the estimated percentage was too high, and suggested that base rates of these symptoms in non-injured populations, other patient characteristics, or subsequent injuries might explain the findings. Factors other than the MTBI itself were found in studies reviewed by Carroll et al. [1] as explaining or partly explaining persistent symptoms, including female gender, other injuries, prior brain illness, prior head injuries, psychiatric problems, pain, older age, acute stress disorder, ongoing litigation, and PTSD. However, other than PTSD and ongoing litigation, there was not enough consistency in the predictors studied or findings to conclude which factors contributed to persistent symptoms.

Because of alternate explanations for persistent symptoms in MTBI populations, researchers have increasingly used prospective studies with longitudinal follow-up and/or included control groups to investigate the association of persistent symptoms and MTBIs. Prospective longitudinal follow-up studies permit a closer link between the injury event and outcomes than do cross-sectional studies. Carefully designed control groups permit the comparison of outcomes between injured and non-injured subjects who are presumed to be comparable on other characteristics (measured and unmeasured). For example, in the study summarized above, Ponsford et al. [3] followed subjects for 3 months post-injury. Though the MTBI patients reported more symptoms early on than did the trauma control group, by 3 months post-injury, both injury groups had improved and did not significantly differ on any symptoms. There were also no differences in median pain scores, and both groups had similarly high return to work rates by 3 months. However, the MTBI group had poorer mean scores on the General Health, Vitality, and Mental Health components of the SF-36 Health-related quality of life. Additionally, the MTBI group had more ongoing impairment at 3 months on one of the subtests of the ImPact cognitive test (the Visual Memory subtest, which the researchers rate as the subtest requiring the most mental effort), and more often reported problems with concentration and memory than did controls at 3 months. Their findings are similar to several other studies that found evidence of improvements in symptoms over time, but with persistent symptoms in MTBI patients continued relative to trauma controls at 3 months [16], at 6 months [17] and 3 and 12 months post-injury [18]. Compared to reports of headache in other populations, TBI patients undergoing rehabilitation in the Model Systems Study reported frequent headaches more often through the first year following injury [19]. Masson et al [20] included subjects with MTBI in their population study in Aquitaine, France, and found that mild TBI subjects did not differ from moderate or severe TBI subjects in their complaints of headache, memory problems, anxiety, or sleep disturbance. All TBI subjects were more likely to report those complaints than control subjects (i.e., subjects with lower-limb injury). Selassie and colleagues found that among patients hospitalized with TBI, long term disability determined at 12 month follow-up was associated with TBI severity, but was associated for patients with mild TBI (i.e., no LOC, no intracranial injury) [21].

2.1 Neuropsychological Testing

In general, neuropsychological evaluations find cognitive impairments in the acute period after MTBI, and these generally resolve within days to months of injury. A few studies have found some continued neuropsychological differences between MTBI patients and controls, but generally the differences are small and/or isolated to a few subtests. In contrast, a larger percentage of MTBI patients *self-report* problems with cognition. Studies have found that self-reported cognitive problems were not associated with neuropsychological test performance at

6 months post-injury for MTBI patients [22], [23]. Stulemeijer et al. identified poor effort as a contributing factor to poor scores on neuropsychological assessment at 6 months post injury in these subjects [24].

2.2 Studies on the Chronic Effects of MTBI in Military Populations

Veterans of combat in OIF/OEF who screened positive for TBI in a Veterans Affairs Medical Center were found to have higher rates of neurological deficits (most commonly impaired olfaction) and PTSD with the greater the number of MTBI exposures with LOC [25]. Service members compared on self-rated health pre- and post-deployment to Iraq (i.e., "Overall, how would you rate your health during the past month?") who had experienced blast-related injuries reported poorer health at 6 months post injury. Those with MTBI were 5 times more likely than service members with other mild injuries to report a major negative change in their health [26]. Canadian military personnel with probable MTBI were more likely to have poorer physical health than military personnel with negative MTBI screens [27]. Alcohol abuse was slightly higher in combat injured service members with MTBI than in service members with other injuries (6.1% vs 4.9%; total n=3,123). However, MTBI was not associated with alcohol abuse in a multivariate analysis [28]. Various co-occurring conditions, including combat stress [29] are associated with increased concussive symptoms reporting in service members with MTBI.

The overlap of MTBI and PTSD has been identified in military populations [30] but also occurs in some civilian injured populations. Determining whether chronic problems are due to physical or psychological injury is challenging with available diagnostic tools. Jones, Fear and Wessely [31] remind us that the issue of determining the cause of shell-shock in World War I and II has parallels with the current debate over the causes of chronic symptoms in today's returning service members. They conclude that "…a clear-cut distinction between physical and psychological injury is unlikely to be realized, not least because the two coexist."

Charles Hoge and colleagues [32] investigated the effects of MTBI, PTSD, and depression on persistent MTBI symptoms in a sample of National Guard troops who had returned from service in Iraq, 3-4 months before the survey. After controlling for PTSD and depression in multivariate statistical analysis, they found that symptoms typically attributed to MTBI were no longer significantly related to MTBI. Only headache remained significantly associated with MTBI, once PTSD and depression were controlled. Various pathophysiology links and endocrine factors\ may help to explain the vulnerability of some injured service members. Several reviews of the literature have examined the overlapping symptomatology, various interpretations for the findings, and implications for clinical care [33]-[35]. Lack of gold standard measures to validly identify un-witnessed and/or distant MTBI presents a methodological challenge to the differential diagnosis of the two conditions in service members returning from deployment. Much of the data gathered thus far on the effects of MTBI, other types of injuries and associated conditions such as anxiety and PTSD upon chronic outcomes have come from cross-sectional studies that are subject to alternative explanations. Carefully designed longitudinal studies with appropriate control groups that are currently in process will assist in sorting out the validity of various competing hypotheses. Various explanations have been proposed for chronic symptoms in a percentage of service members with MTBI, including PTSD [30], pain, grief [36] the presence of prior symptoms, and prior depression.

3.0 OCCUPATIONAL OUTCOMES

As mentioned previously, the acute symptoms of MTBI largely resolve spontaneously within days to weeks after the injury. However, in some individuals these same symptoms remain beyond 3 months and are referred to as persistent post-concussive symptoms (PCS).

Estimates of the prevalence of persistent PCS vary. Up to 33% of US military personnel have reported persistent PCS symptoms following deployment and approximately 25% of Canadian military personnel. These estimates exceed those reported in civilian accident victims and sports related concussions (15%).

Although PCS in military MTBI has been the focus of several papers [32], [37], [38], none of these studies have explicitly explored occupational outcomes in term of the impact of MTBI on military fitness.

Strikingly, the literature on the occupational impact of MTBI in the civilian setting is also limited. The Worker's Compensation Board of the Province of British Columbia in Canada published in 2003 which examined the existing literature on this issue at the time and reported an analysis conducted on their database that covered worker disability claims in the province over the period of 1987-2001. The literature review showed that on average MTBI patients require 3-4 weeks off work post-injury. Up to 97% of MTBI cases will return to work 6 months post injury. Subsequent analysis of BC claims data showed that half of the MTBI claims were on short term disability for ≤ 1 week, 12.8% for 2 weeks, 10.2% between 3-4 weeks, 12.8% between 5-10 weeks and 14.7% for > 10 weeks.

The International Collaboration on Mild Traumatic Brain Injury Prognosis recently published the results of a systematic review examining return to work after MTBI. This review covered the period from 2001-2012 [39]. After 77, 914 records were screened, only 101 had a low risk of bias and re deemed scientifically acceptable, of which only 4 had return to work or employment outcomes. These limited studies showed that most workers returned to work within 3 to 6 months after MTBI; MTBI was not a significant risk factor for long-term work disability; and predictors of delayed return to work include a lower level of education (<11y of formal education, nausea or vomiting on hospital admission, extracranial injuries, severe head/bodily pain after injury, and limited job independence and decision making latitude. The authors were careful to point out that the findings are preliminary at best and that more well-designed studies are required to understand return to work and sustained employment after MTBI in the longer term (≥ 2 years).

Military service is arduous and the fitness standards exceed that of many civilian employment requirements. Consequently, the civilian literature on the occupational impacts of MTBI cannot be readily generalized to military populations. Despite concerns over the dire consequences of MTBI on the rate of service related disability in the military, there are few published reports that have explicitly examined this important outcome.

Schoenfeld and colleagues reported the findings of a longitudinal study that sought to determine the impact of musculoskeletal injuries incurred on deployment on occupational fitness amongst an Army Brigade that deployed to Iraq from 2006 to 2007 [40]. They specifically examined the effect of the injury on soldier ability to remain in active service as determined by a Physical Evaluation Board. Within their study cohort, Traumatic Brain Injury was the third leading cause of medical unfitness, exceeded only by Post-traumatic Stress Disorder and low back pain in that order. Because traumatic brain injury was not the focus of this paper there is no detail provide as to the nature and severity of the brain injury. Consequently the impact of MTBI as opposed to moderate or severe TBI on occupational fitness cannot be determined by this paper nor can the relative risk of MTBI on medical unfitness be more accurately estimated.

However, a recent Canadian paper sheds further light. The study was a retrospective cohort design that examined the risk of medical unfitness in 16, 193 Canadian Armed Forces personnel who deployed in support of the mission in Afghanistan and completed post-deployment screening over a period from January 2009 to July 2012. Previous analyses of this same cohort showed that a history of MTBI during the deployment was reported in 5.2% and multiple PCS was present in 21% of those with less severe MTBI (dazed/confused only) and 27% with more severe MTBI (loss of consciousness or post-traumatic amnesia), 3-6 months after their return from deployment [41]. Subsequent survival analyses looking at occupational fitness showed that MTBI was independently associated with a risk of medical unfitness (aHR=1.65, 95% CI 1.35 to 2.03). However, mental disorders and musculoskeletal condition were the primary diagnoses associated with medical unfitness (identified as the primary diagnosis in 55.4% and 25.9, respectively), and a neurological condition was only documented in 5.8% of those with MTBI who were letter deemed to be permanently medically unfit [42].

The discrepancy in the prominence of TBI as a cause of medical unfitness in the US study reported by Schoenfeld et al and the Canadian study is not easily reconciled. Some have argued that philosophical differences in symptoms attribution may in part contribute to this (Bryant and Hoge's Editorial). Nevertheless, both studies highlight the importance of comorbid diagnoses such as mental disorders and musculoskeletal conditions as major contributors to military occupational unfitness in cases of MTBI. This reinforces the need for a multidisciplinary approach in rehabilitation for those who sustain MTBI in any effort to limit disability and occupational impairment.

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