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Review Article

Long-Term Health Consequences of a Single Traumatic Brain Injury

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ABSTRACT

Contrary to previous beliefs that long-term health consequences resulted only from moderate-to-severe Traumatic Brain Injuries (TBIs) or repeat mild TBIs (mTBIs), there is mounting evidence that a single TBI-regardless of severity-can have life-long health consequences. Here we discuss the details of those of the heightened risks faced by those who have suffered even a single head trauma and how risk varies according to several factors. Traumatic Brain Injury (TBI) dynamically impacts the brain and can therefore impart lifelong detriments to health and wellbeing. Of those who suffer TBI, 30% experience worsening symptoms over the following 5 years.

Keywords: Traumatic brain injury; mTBI; Dementia; Psudomeniscus; Polypathology

INTRODUCTION

Critically, while it was once believed that these long-term health deficits were largely limited to repetitive head trauma, it is becoming increasingly clear that isolated TBI incidents are also associated with long-term, often progressive, health consequences [1-3]. While the number of TBIs may affect the severity of illness, a recent meta-analysis has demonstrated that the overall risk of illness associated with a single is comparable to that associated with repeated head injuries [4].

LITERATURE REVIEW

Several factors contribute to the long-term outcomes associated with TBI

Post-mortem studies on the long-term neuropathology that follows TBI have led to the description of the persistent and evolving brain abnormalities as Polypathology [3]. Several biological mechanisms may occur that lead to deficits in those who have suffered TBI. These mechanisms include apoptosis, demyelination, excitotoxicity, inflammatory events, neurodegeneration, seizures, and white matter pathology [5]. Several factors influence this underlying physiology and help to determine the long-term outcomes following a TBI. For instance, the severity of the trauma, the location of the impact, whether the TBI was concussive or blast-induced, and both the amount and depth of brain penetration affect long-term health outcomes, as do immunological stressors, genetics, and age at the time of injury [6-9]. In addition, repetitive injury may compound some of these risks [10].

All TBIs increase the risk for certain symptoms and brain pathologies

Longitudinal data that tracks long-term outcomes following single incidents of TBI are beginning to elucidate brain abnormalities and associated symptomatology that occur in higher frequency in those who have endured even just one TBI. For example, more widespread neurofibrillary tangles and greater density of amyloid-β plaques are observed in those who have sustained a single TBI compared to those with no history of

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TBI [11] had endured a single TBI found significantly more Alzheimer's disease pathology than what is observed in the general population [12]. The persistent effects of a single TBI have been shown to limit patients and reduce quality of life through their influence on cognition, and emotional processing, and physical functioning [13].

Cognition: The above observations regarding brain pathology help to explain the established link between TBI and dementia and why those who have sustained a TBI are 4 times more likely to develop dementia than those without TBI [13-15]. They may also help explain the increased risk of cognitive deficits in the face of TBI, among which are dysfunction of attention, memory, and executive functioning. These impairments can contribute to poor performance of complex cognitive functions and communication [16].

Emotional processing: In addition to cognitive difficulties, those with TBI are at heightened risk for affective disorders, including depression, anxiety, bipolar disorder, and mixed affective disorders. Difficulties with emotional processing likely contributes to these challenges [4,13].

Physical health: TBI increases the risk of somatic symptoms. For instance, those with TBI often complain of headaches, nausea, pain, sleep disturbances, vertigo, ringing in ears, tingling, and sensitivity to light and sound [13,17]. In addition to these unpleasant symptoms, TBI places people at higher risk for blood clots, stroke, and epilepsy [17,18].

Even a single mild TBI often leads to long-term adverse outcomes

While those with mTBI tend to recover more quickly and fully than those with more severe forms of TBI, approximately 15%to 20% of patients-deemed the miserable minority-suffer long-lasting symptoms in what is referred to as post-concussion syndrome [19]. Advanced imaging technologies are helping to identify brain abnormalities that can explain some of these persistent symptoms, as well as disorders that eventually develop in those with a history of a single TBI. Diffusion Tensor Imaging (DTI) can distinguish patients who have suffered a TBI from those who have not, even when the TBI was mild and regardless of how long it has been since the injury [20]. Similarly, Magnetic Resonance Spectroscopy (MRS) can detect changes in several metabolites following both single and repetitive mTBI that correlate with clinical symptoms [21]. These observations have helped to shift the paradigm from the belief that long-term health consequences from TBI require either moderate-to-severe TBI or repetitive mTBI. Previous techniques for identifying brain changes had substantially underestimated the damage produced by mTBI [9].

Because the chronic brain sequelae of single mTBI overlap significantly with those of repeat mTBI, people suffering one *vs.* repetitive head traumas often share neuropathological characteristics and symptoms [22]. For instance, in both cases, combinations of markers for neurodegenerative disease, such as amyloid, tau, lewy bodies, as well as the transcriptional repressor TDP-43, are observed. As a result, those with a history of single mTBI and those with a history of repetitive mTBI are sometimes diagnosed with the same disorders.

Neurodegeneration: Though the link between mTBI and neurodegenerative disease is stronger with multiple mTBIs, a single mTBI raises the risk [10,23-26]. The neurodegeneration that can occur following mTBI likely occurs in part due to the neuroinflammation that can persist for years following even a single TBI [27,28]

Cognitive dysfunction: TBIs of all severity levels increase the risk of cognitive impairments [16]. Recent data from a comprehensive review of 45 research studies have shown that despite prior assumptions that most people fully recover from concussions or mTBI within 3 months of their injury, roughly half of those with a single mTBI show long-term cognitive deficits [29].

Psychiatric illness: Even in patients with favorable Glasgow Outcome Scale scores, three quarters may suffer at least one neuropsychological deficit [30]. Several studies have also demonstrated a link between mTBI and Post-Traumatic Stress Disorder (PTSD) [19].

Reduced quality of life: Research on the persistence of symptoms following mTBI has shown that 82% of sufferers were still reporting symptoms a year after the mTBI [19]. Further, at 6 months and one year following the injury, 44.5% and 40.3% reported significantly lower scores on Satisfaction with Life Scale, respectively, than the general population, and 22.4% were not of full functioning status.

Reduced life expectancy: Individuals with mTBI have exhibited a s mall reduction in overall long-term survival compared to the general population [31].

DISCUSSION

A single moderate or severe TBI increases the risk of psychiatric and neurological conditions

Following severe TBI, a complex combination of factors related to the injury, demographics, and neuropsychology determine long-term outcomes [32]. For instance, with age as a factor, younger children who have suffered a severe TBI are more likely than older children to develop epilepsy [33]. A host of pathologies are identified in those who have sustained a single moderate-to-severe TBI. One study found exceptionally large lewy bodies, TDP-43 proteinopathy, and axonopathy following a single severe TBI [9].

Neurodegeneration: There is an abundance of research to suggest that a single moderate or severe TBI increases the risk of eventually developing clinical signs of neurodegeneration [26].

Alzheimer's disease: Tau pathology, which is a well-established characteristic of certain neurodegenerative diseases, such as Alzheimer's disease, develops in response to a single moderate or severe TBI more frequently than in those with no history of head injuries [34]. Further, meta-analysis data have demonstrated an association between head trauma that included loss of consciousness and Alzheimer's disease [15].

Parkinson's disease: While even those with mTBI are at heightened risk for Parkinson's disease, those with moderate-to-severe TBI are at a much higher risk for this particular disease [24]. For instance, it has been shown that while 0.31% of those with no TBI develop Parkinson's disease and 0.47% of those with mTBI develop Parkinson's disease, 0.75% of those with moderate-to-severe TBI develop the disease.

Chronic Traumatic Encephalopathy: It has long been thought that Chronic Traumatic Encephalopathy (CTE) occurs from repetitive TBI, but research into the risk of CTE for those who have sustained a single moderate or severe TBI is growing [10]. This research has helped substantiate the link between TBI and CTE but to also suggest that a single head trauma may increase risk for CTE [26].

Cognitive dysfunction: While cognitive dysfunction occurs more frequently in those with all levels of severity of TBI, the degree of dysfunction is often worse in those with moderate-to-severe injuries compared to those with mTBI. There thus appears to be a dose-dependent relationship between severity of TBI and cognitive outcomes with respect to learning, memory, and executive function [35]. However, some research suggests that while injury severity is associated with memory outcomes, emotional distress appears to be a better predictor of reasoning and executive function [30].

Psychiatric illness: Even more than a decade following their injury, people who have survived severe TBI are at an increased risk of significant psychiatric symptomology and for suffering from problems with family integration and social functioning [36,37]. They have relatively higher rates of depression and loneliness and display slower psychomotor skills.

Compromised cardiovascular systems: Even in the absence of major hemorrhage, TBI can derange blood pressure and heart rate [38]. Because clinicians are often unaware of this possibility, lack of intervention for cardiovascular instability may lead to long-term heart-related consequences.

Reduced life expectancy: Life expectancy is reduced in those who have suffered a single moderate or severe TBI. Even after inpatient rehabilitation, the life expectancy of people who have survived a moderate or severe TBI is 9 years shorter than those who have not suffered a TBI [1]. These TBIs enhance the risk of dying from several causes. Those with moderate-to-severe TBIs are 50 times more likely to die from seizures, 11 times more likely to die from drug poisoning, 9 times more likely to die from infections, and 6 times more likely to die from pneumonia than those without TBIs. Certain groups are more likely to die sooner, including older adults, men, the unemployed, those who are unmarried, those who have completed less education, and those who's TBIs were fall-related.

Enhanced Disability: People who have suffered a moderate to severe TBI are also at an increased risk for chronic health conditions that lead to a host of health and cost-related challenges of those who survive for 5 years after their TBI, nearly 60% are moderately or severely disabled, and 50% have returned to the hospital at least once. One out of 3 rely on others for help with everyday activities, 55% are no longer employed, and 29% are unsatisfied with their lives [7-9,39-41].

CONCLUSION

Research is helping to elucidate some of the risks faced by those who have endured TBI and to delineate the specific risks based on frequency and severity of TBI. While severity of symptoms and outcomes may be largely proportional to the severity of injury, evidence has accumulated to show that TBI is a chronic, evolving disease that often has long-term consequences. Because individuals with all levels of TBI severity can have a dysregulated immune response that leads to chronic inflammation and accelerated disease processes, many experts agree that TBI should be considered and treated as a chronic health condition. Given that there are few highly effective therapies for TBI, understanding the chronic effects of TBI is critical for clinical management. Regardless of TBI severity, clinicians should carefully consider the potential long-term effects described above.

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