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# Cognitive Changes and Dementia Risk after Traumatic Brain Injury: Implications for Aging Military Personnel

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## Abstract

Traumatic brain injury (TBI) is recognized as an important risk factor for the long-term cognitive health of military personnel, particularly in light of growing evidence that TBI increases risk for Alzheimer's disease and other dementias. In this article, we review the neurocognitive and neuropathologic changes after TBI with particular focus on the potential risk for cognitive decline across the life span in military service members. Implications for monitoring and surveillance of cognition in the aging military population are discussed. Additional studies are needed to clarify the factors that increase risk for later life cognitive decline, define the mechanistic link between these factors and dementia, and provide empirically supported interventions to mitigate the impact of TBI on cognition across the life span.

Previous studies suggest an association between depression and dementia in military veterans. The most likely biologic mechanisms that may link depression and dementia among military veterans include vascular disease, changes in glucocorticoid steroids and hippocampal atrophy, deposition of β-amyloid plaques, inflammatory changes, and alterations of nerve growth factors. In addition, military veterans often have depression comorbid with posttraumatic stress disorder or traumatic brain injury. Therefore, in military veterans, these hypothesized biologic pathways going from depression to dementia are more than likely influenced by trauma-related processes. Treatment strategies for depression, posttraumatic stress disorder, or traumatic brain injury could alter these pathways and as a result decrease the risk for dementia. Given the projected increase of dementia, as well as the projected increase in the older segment of the veteran population, in the future, it is critically important that we understand whether treatment for depression alone or combined with other regimens improves cognition. In this review, we summarize the principal mechanisms of this relationship and discuss treatment implications in military veterans.

**Keywords:** Alzheimer's disease; Traumatic brain injury; Risk factors; Military medicine; Dementia

## Introduction

There is growing evidence that a history of traumatic brain injury (TBI) places individuals at greater risk for developing neurodegenerative diseases such as dementia of the Alzheimer's type (DAT) and other dementias across the life span. Although much of the research has focused on the increased risk associated with moderate-to-severe brain injuries, emerging evidence suggests that mild head injuries, particularly repeated mild injuries, may also serve as a risk factor [1]. Both the Department of Defence (DoD) and the Department of Veterans Affairs (VA) have recognized the importance of better understanding this relationship, particularly given the incidence of TBI in the military resulting from combat exposures, the growing evidence of dementia risk after TBI, emotional disorders and other nonspecific factors, and concern for the implications of these factors on the aging service member [2].

The purpose of this article is to review neurocognitive and neuropathology changes after TBI, with a focus on the potential risk for cognitive decline across the life span in military service members with a history of TBI. We will begin by defining TBI and summarizing expected short- and long-term cognitive and behavioral outcomes. Next, we will summarize evidence for increased risk of dementia, particularly DAT and chronic traumatic encephalopathy (CTE), after a history of TBI. We will review TBI assessment protocols, outcomes, and lessons learned within the military and will end with a discussion of implications for monitoring and surveillance of cognition in the aging military population [3-4]. Given the current and projected growth of the older segment of the veteran population a better understanding of the link between depression and risk of dementia is important, especially for possible treatment and prevention. However, there are several challenges to understanding this link. For example, major depressive disorder is common among patients with dementia, occurring in up to 20% of patients with Alzheimer disease (AD) and up to 50% of patients with vascular dementia and, thus, disentangling which came first can be difficult. In addition, although depression and dementia are considered separate clinical entities, they share some common symptoms, such as impairment in attention and working memory, changes in sleep patterns, and a decrease in social and occupational function. Moreover, the concept of "pseudo dementia" highlights the blurriness of the distinction between depression and dementia [5]. Thus, the interrelationship of depression and dementia is complex and sometimes indistinguishable and this complicates the ability to determine the exact relationship of depression to dementia.

## Material and Methods

### TBI overview

Similar to the definition of TBI from the Centers for Disease Control and Prevention the VA/DoD define TBI as a traumatically induced structural injury and/or physiological disruption of brain function resulting from an 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 decreased

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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.); neurologic deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient; or intracranial lesion. Relevant to the military and veteran populations [6-7], this definition further specifies that external forces may include the head being struck by an object, the head striking an object, the brain experiencing acceleration/deceleration movement without external trauma to the head, a foreign body penetrating the brain, or forces generated from events such as a blast or explosion.

### Cognitive outcome after TBI

The effect of TBI on cognition and subsequent recovery varies as a function of injury severity. Individuals sustaining a mTBI will typically experience transient cognitive (e.g., mild confusion, difficulty maintaining attention, and forgetfulness), emotional (e.g., tearfulness, irritability), and physical symptoms (e.g., headaches, sensitivity to light, blurred vision) that begin immediately after the injury and improve over a period of days to weeks, as illustrated. Most available research shows that individuals with uncomplicated mTBI typically recover to baseline levels of cognitive functioning within 1 to 3 months after injury and are expected to have a favourable long-term outcome [8]. Prolonged recovery course has been associated with more severe acute injury indicators (e.g., unconsciousness, PTA, or initially more severe symptoms) and there is evidence that repeated mTBI or complicated mTBI may also place individuals at risk for a prolonged or atypical recovery course. Although persisting symptoms may remain in a minority of individuals outside of this window, evidence indicates that incomplete recovery from mTBI may be associated with or complicated by preexisting or comorbid psychiatric, medical, psychosocial, or litigation factors. The etiology of persistent complaints in some military service members after mTBI is poorly understood and will be discussed in more detail in Section.

### Effects of TBI in military

Most studies presented previously describe TBI in civilian populations. Given the high rates of TBI seen in veterans and military service members, the cognitive and behavioral sequelae of TBI among military personnel have been a primary focus of research in recent years. These studies build on the knowledge gained from civilian literature [9], while recognizing the unique characteristics of this special population who may have different injury mechanisms, risk factors, and comorbidities. Studies have examined both the acute and chronic symptoms of TBI as well as commonly occurring comorbid conditions.

## Conclusion

In summary, TBI is known to lead to transient or chronic effects on neurobehavioral and cognitive functioning, which vary according to severity, mechanics, and timing of injury. Growing research documents that a history of TBI may place some individuals at risk for dementia later in life, either because of genetic vulnerability or diminishing of cognitive reserve leading to earlier onset of neurodegenerative changes. Military service members are at particular risk for TBI, leading to significant implications for monitoring programs not only to detect these injuries and their effects at their onset but also for monitoring potential long-term effects across the life span. This article highlights research on the cognitive effects and risks for later life dementia from TBI in civilian and military populations [10]. Many lessons have been learned from current military TBI monitoring and management programs with significant implications for continued monitoring of aging service members and veterans. Increasing data supportive of the link of repetitive TBI with axonal injury and long term neurodegenerative consequence has had significant implications in sports which have already lead to changes in the rule and management of many popular sports. Understandably, resistance and refusal to accept the risk of TBI exist due to potential enormous financial repercussions, major change in the rule of the sports and even the possibilities of banning some high risk contact sports entirely or among children who are more susceptible to damage than adults.

Many unknowns related to the field will require clarification, including the risk of a single bout of TBI, other risk and protective factors, clinical diagnostic criteria, CSF, blood and radiological biomarkers, the precise pathophysiological cascade of events from TBI to CTE and potential therapeutic strategies. Prospective longitudinal studies along with clinic pathological evaluation would be the key in providing more information on the acute and long-term consequences of TBI in sport.

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### Conflict of Interest

None

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