



TBI and Cognitive Decline: Traumatic Brain Injury Increases Risks

What Is Already Known

There are an estimated 2.5 to 4 million cases of traumatic brain injury (TBI) per year, with a bimodal distribution based on age; the oldest and youngest individuals account for the greatest number of cases. The reasons for these injuries also vary by age group. Falls are the leading cause of emergency department visits for children aged 0 to 4 years and for adults aged 65 years and older. For older children and adolescents, being struck by or against an object is the leading cause of TBI, and for older adolescents to middle-aged adults, injuries are generally related to sports, motor vehicle accidents, and military service. Other causes of TBI at younger ages include adverse childhood experiences (ACEs) — potentially traumatic events that occur during childhood — and violence. Examples of ACEs include witnessing or experiencing violence, abuse, or neglect in the home or community. Greater exposure to ACEs earlier in life increases risk for future adverse experiences that place an individual at further risk for TBI, such as violence (e.g., domestic/intimate partner abuse and elder abuse). Regardless of when across the lifespan TBI events occur, they result in poorer overall health and can increase risk of experiencing cognitive decline or dementia in later life.

Background and Evidence Base

Evidence of an association between traumatic brain injuries and cognitive decline

TBI is typically associated with executive function, processing speed, and learning/memory-related functions. Injuries occurring in people younger than their early 20s affect the brain while it is still developing and therefore can potentially interfere with normal development, while older adults who experience injuries are less likely to recover fully from them. Additionally, it is not uncommon for people to experience more than one TBI. In fact, one of the greatest risk factors for TBI is history of a prior TBI. Depending on the severity of the TBI, risk for dementia is significantly increased later in life. The associations between TBI and the risk of specific dementia subtypes or neuropathological outcomes vary, but TBI occurring in older adults is associated with increased risk of dementia. While not a perfect dose-response

relationship, this elevated risk for dementia increases as the number of TBIs a person experiences increases.

The mechanisms underlying the relationship between TBI and later-life cognitive decline are not well understood. Leading potential mechanisms linking TBI and susceptibility to later-life cognitive decline include chronic neuroimmune activation, structural injury that results in cumulative neuronal and cellular dysfunction, and the disruption of the blood-brain barrier as a result of the injury

There is evidence to suggest that mild TBI (loss of consciousness or post-traumatic amnesia lasting 30 minutes or less) in early life may increase a person's risk of cognitive decline and dementia in later life, making further inquiry into such associations justifiable. Variations of the *APOE* gene have also been evaluated to assess how a genetic trait may relate to TBI and cognitive decline. So far, the evidence is mixed, although the presence of the $\epsilon 4$ allele may contribute in some populations to the risk of long-term symptomatology after TBI, especially cognitive impairment and fatigue. The *BDNF* gene (which involves the production of a protein that promotes the growth and maintenance of neurons) has been associated with various types of neurodegeneration. One variant of the gene (the *BDNF*^{Val66Met} allele) has been linked to an increased risk of experiencing TBI and is also being investigated for its association with memory deficits after TBI. In a study of a small group of military members, carriers of a different *BDNF* variant were found to have atrophy and less functional connectivity in the hippocampus after experiencing TBI compared with those who were homozygous for the typical form of *BDNF*.

Potential causes of traumatic brain injuries

ACEs

ACEs are potentially traumatic events that a child witnesses or experiences and can include abuse (emotional, physical, or sexual) and household challenges (such as intimate partner violence, substance abuse, mental illness, separation/divorce, and incarceration of a family member). More than 60% of adults have reported experiencing at least one type of ACE, and 1 in 6 have reported experiencing four or more types. Compared with other



groups, women and those from underrepresented racial/ethnic groups have a greater risk of experiencing four or more types of ACEs. ACEs can disrupt neurodevelopment and have a profound impact on health and well-being throughout the lifespan. They are associated with poor health outcomes, including heart disease, cancer, and diabetes. Some outcomes associated with ACEs, such as mental illness, homelessness, substance abuse, and violence, can increase a person's risk of experiencing TBI and thereby increase their risk of cognitive decline. Other outcomes, such as an increased risk of HIV/AIDS, toxic stress, and chronic health conditions, can directly increase a person's risk of cognitive decline in later life and potentially compound the adverse neurobiological effects of TBI.

Violence

TBI can also occur through physical violence to the head. In the United States, abusive head trauma is a leading cause of child abuse deaths in children under the age of 5. Domestic violence, intimate partner violence, and elder abuse are other forms of violence that can result in TBI, as the use of physical force can cause injury to the victim's head, neck (including through strangulation), and face. One study reported that 30% of domestic violence survivors reported losing consciousness at least once, and 67% reported residual problems that were potentially related to a head injury. Loss of consciousness can be associated with hypoxia and anoxia, potentially causing ischemic brain injury, as well as the release of brain-specific and neuroinflammatory molecules into the bloodstream, reflecting multiple brain injury processes. TBI may be underdiagnosed among survivors of domestic violence because symptoms can mimic those associated with mental illness, such as depression or anxiety. Additionally, survivors of domestic violence and TBI may appear to have behavioral issues, such as problems keeping appointments, and poor health.

Falls

People over the age of 75 are about twice as likely as people under the age of 75 to experience falls and associated complications. Additionally, about 10% to 25% of falls in this population cause fractures, with hip fractures being the most common. Individuals in this age group are more likely to fall indoors than outdoors, and the incidence of falls is even higher among certain populations, such as older adults living in institutions, those

recovering from a stroke, and those with diabetes or Parkinson's disease.

Implications for Public Health

Preventing TBI and its aftereffects can be achieved by targeting the circumstances precipitating a TBI event. Such prevention should be encouraged to preserve brain health in addition to overall general health. Targets must include children, young and middle-aged adults, older adults, and at-risk communities. Social-ecological models and approaches are needed for prevention to be effective in the public health space. Treatment for risk factors associated with TBI will have a large and compounding effect on preventing cognitive decline and impairment in older adulthood.

Discussion

TBI can occur in individuals of any age, and it can increase the risk for cognitive decline in older adulthood. Therefore, interventions to reduce the risk of cognitive decline associated with TBI should be focused on all age groups, with interventions targeted at the leading causes of TBI by age group. For example, to prevent injuries from accidents in children, playground surfaces should be safe, soft, and composed of appropriate materials (such as sand or wood chips). Children should also ride in appropriate car seats and booster seats. Adults and children of all ages should wear seatbelts and use helmets and other safety gear for recreational activities. The safety gear should be well maintained, age-appropriate, and worn consistently and correctly.

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