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A history of traumatic brain injury may be a key risk factor for developing cognitive impairment from Alzheimer's disease or a related neurocognitive disorder, according to new research.

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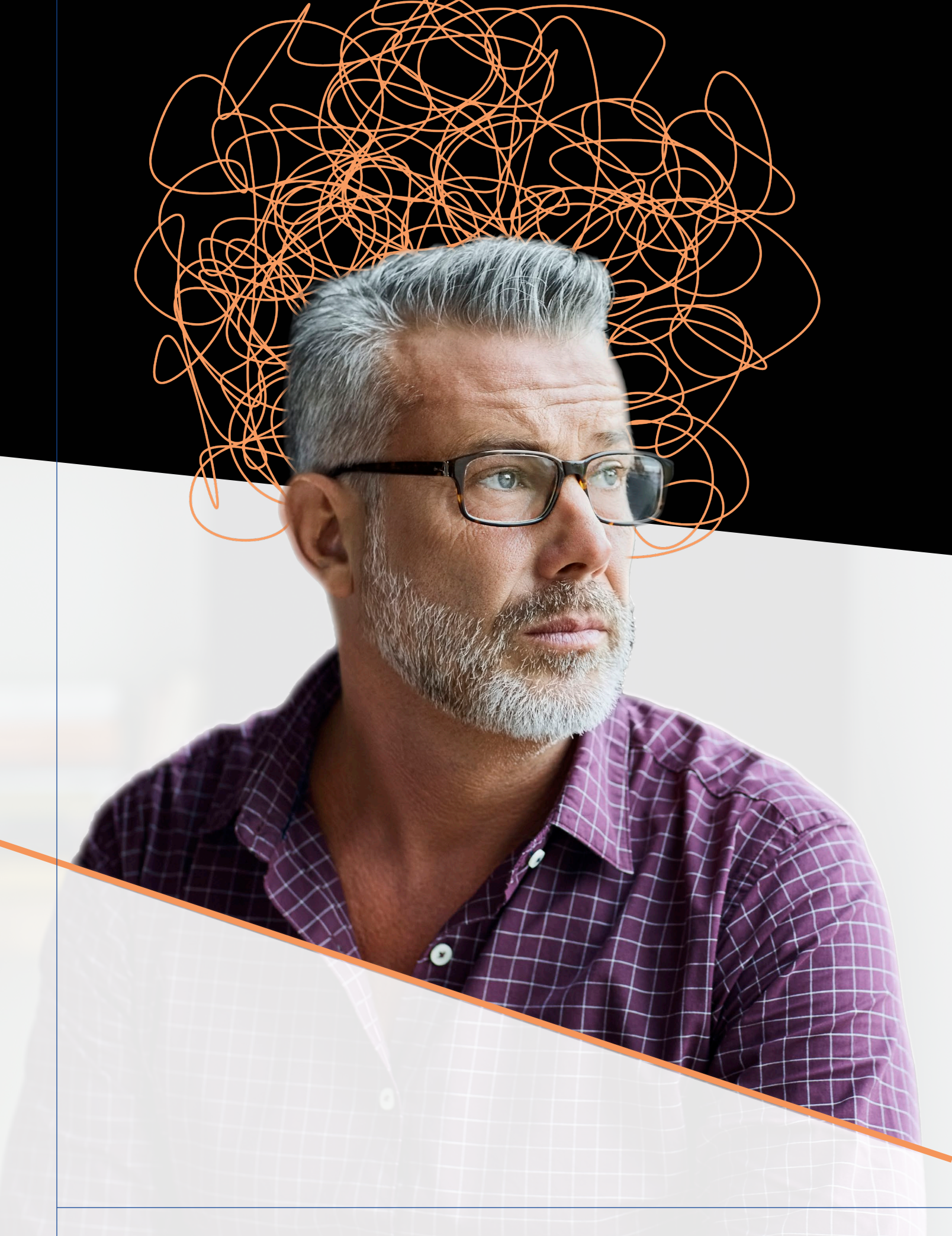

Head Trauma: Immediate and Long-Term Effects on Cognition

A history of traumatic brain injury may be a key risk factor for developing cognitive impairment from Alzheimer's disease or a related neurocognitive disorder, according to new research. BY KAREN GILBERT, DNP, MS, RN

The long-term effects of head trauma among professional athletes have long been a subject of concern. But football players are not the only demographic at higher risk of developing cognitive impairment due to head injuries. According to recent research, any head trauma—including from falls, car accidents, or military service—may increase a person's risk of dementia later in life.

Cognitive impairment is manifested by symptoms of dementia. In addition to problems with memory, dementia symptoms typically include difficulty with "executive functions," or the ability to think, understand, learn, analyze, and solve problems. Alzheimer's disease (AD) is said to be the most frequent cause of progressive and irreversible cognitive impairment and the consequent symptoms of dementia, accounting for an estimated 60% to 70% of those with symptomatic disease (World Health Organization, 2022).

There are modifiable and unmodifiable risk factors for developing AD. The **unmodifiable** risk factors include age, family history, gender, and genetics. Though one's risk of developing Alzheimer's disease is increased if the e4 version ("allele") of the APOE4 gene was inherited from one or both parents, it is now believed that lifestyle factors are significant determinants of whether symptomatic Alzheimer's disease will develop (Galvin, 2017). **Modifiable** lifestyle factors include (Alzheimer's Association, 2022):

- Smoking
- Sleep
- Socialization
- Diet
- Physical activity
- Hearing loss
- Type 2 diabetes
- High blood pressure (hypertension)
- Head protection

Additional modifiable lifestyle strategies include:

- Using one's non-dominant hand for everyday activities and tasks (Rose, 2019)
- Ongoing learning (Gupta, 2021)
- Maintaining dental health (Gupta, 2021)
- Finding meaning and purpose (Sutin et al., 2023)

To support one modifiable factor, head protection, one can wear seatbelts in vehicles and helmets when riding bicycles, motorcycles, or when skating, and observe precautions in using stepladders. However, a history of a head injury is clearly not modifiable.

Head injuries, or traumatic brain injuries (TBIs), are prevalent in people of all ages, and the incidence is substantial. According to the Centers for Disease Control and Prevention (CDC, 2022a), more than 64,000 deaths related to TBI occurred in the United States in 2020, equating to an average of more than 175 deaths per day.

The most common causes of TBIs include falls, firearm injuries, motor vehicle accidents, and assaults, with falls accounting for almost half of head injury-related hospitalizations, and suicide for most deaths by firearm (CDC, 2022a). Citing data for 2020, the CDC reports that adults older than 75 years of age accounted for most hospitalizations and deaths following head injury, representing 32% of hospitalizations and 28% of deaths (CDC, 2022b).

Types of Head Trauma

The most common TBI is concussion (Cleveland Clinic, 2021). Concussions commonly occur in contact and other sports, or result from falls, motor vehicle accidents, or assaults. Most concussions are said to impose no lasting effects (Moawad, 2022). If classified as moderate or severe, the greater degree of injury often requires care beyond the immediate post-injury period (CDC, 2022a).

Other types of head injuries include (Saling, 2022):

- **Contusion,** a bruise on the brain that may result in swelling and bleeding.
- **Hematoma**, resulting from bleeding within the skull, and formation of a blood clot.
- **Skull fracture**, referring to any break in the bones of the skull.

The Pathology of Concussions

Concussions may or may not involve loss of consciousness, and though commonly classified as mild traumatic brain injuries, the effects can manifest over the long term (Berry et al., 2020). Sustaining a concussion increases a person's vulnerability to another concussion, especially within a year of the event. A subsequent concussion may result from a lesser injury. The injured person may also experience a longer recovery period following a subsequent event (Allen, 2022).

The mechanism of concussion results from a blow to the head or trauma to the body that causes the head to shake or shift abruptly, and the brain to move quickly back and forth or bounce or rotate within the skull. For example, a concussion may result from an automobile accident even if the driver or passenger was restrained and did not sustain direct trauma to the head, but the head and body moved violently in the collision (CDC, 2019).

These traumatic movements of the brain stretch the brain's nerve cells (neurons) and disrupt the cell membrane of the neurons. This produces chemical changes that disturb the normal flow of calcium and potassium ions into and out of the neurons, damaging the neurons (UPMC HealthBeat, 2021). This abnormal flow of ions may also result in the abnormal accumulation of amyloid protein as plaques, and tau protein as neurofibrillary tangles, the pathology recognized as Alzheimer's disease. Associated inflammatory responses within the brain may convey secondary injury, potentially causing the death of neurons (Mallah et al., 2021).

A Spotlight on Concussions in Professional Football

The sports news in late December 2022 was dominated by reports about concussions sustained by Miami Dolphins quarterback Tua Tagovailoa. During a Christmas day game, Tagovailoa's head hit the ground during a tackle. He remained in the game, his performance obviously deteriorating in the second half. He was not placed on the National Football League's (NFL) concussion protocol until the following day after complaining of not feeling well. This concussion followed two similar episodes in games played four days apart in September 2022.

The way in which these injuries were addressed brought the controversy once again to the forefront of discussions regarding the dangers of football and other contact sports, focusing not only on the immediate ill effects of concussions, but also on concern for the latent, irreversible effects that may ensue years or even decades later, particularly related to repeated injuries.

The concerns for cognitive and physical health have been the subject of much discussion concerning college and professional football players. In 2017, pathologist Dr. Ann McKee performed autopsies on the donated brains of 111 former NFL players. All but one revealed chronic traumatic encephalopathy (CTE), a syndrome manifesting with symptoms of dementia, depression, and mood and behavioral aberrations. The

deceased players ranged in age from twenty-three to eighty-nine. Dr. McKee concluded that there could no longer be debate as to "whether or not there is a problem in football" (Ward et al., 2017).

Dr. McKee's concern is supported by the February 2023 announcement by The CTE Center of Boston University describing its findings of CTE in 345 out of 376 former professional football players. In sharp contrast, Boston University's 2018 study of 164 donated brains of both women and men from the general population revealed only one with CTE—and that brain belonged to a person who had played football in college (Boston University Chobanian & Avedisian School of Medicine, 2023).

The Experiences of Veterans

Modern conflicts in the Middle East have revealed "high rates of mild traumatic brain injury (mTBI) in U.S. service members and veterans" (Pattinson et al., 2019, p. 546). The authors studied the relationship between a history of TBI and the presence of post-traumatic stress disorder (PTSD). Noting that these disorders commonly occur concurrently in military personnel, this study suggests that both contribute to pathology of tau protein; that a TBI may impose an increased risk for developing PTSD; and that PTSD may also lead to the degeneration of neurons with or without TBI—culminating, in both cases, in a potentially increased risk of Alzheimer's disease in later life. Couch and Stewart (2022) also confirmed the long-term neurological consequences of TBIs related to military service, noting that symptoms such as dizziness and difficulty with balance and coordination were worse in those with a history of TBI prior to the service-related TBI, suggesting a "cumulative effect" from multiple injuries (p. 713).

A Long, Concerning History

With the recent attention on the short and long-term impacts of head injuries in athletes and military personnel, it could appear that awareness of the dangers of head trauma is a recent phenomenon; however, clinical manifestations and risks were identified well over one hundred years ago. Harrison (2014) writes of "The First Concussion Crisis," documenting what was known and discussed about trauma in football competitions in the late 1800s.

In 1928, Dr. Harrison Martland published a paper entitled "Punch Drunk" (a slang term previously associated with boxing) in which he documented tremors, movement disorders, confusion, and speech difficulties in boxers. This followed other physicians who, in 1924 and 1927, noted that small brain bleeds followed concussions, that these events were neither transient nor benign, and that they could be correlated with later degenerative changes. Dr. Martland performed autopsies on the brains of 309 people who had experienced head trauma. He found evidence of these small bleeds, or microhemorrhages, and theorized the connection between these bleeds and the symptoms seen in boxers who had sustained repeated head trauma. In 1937, Navy lieutenant J. A. Millspaugh reported on "dementia and disorientation" observed in naval boxers. He replaced the term "punch drunk" with the term *dementia pugilistica* to identify this phenomenon, a term familiar to this day (Changa et al., 2017).

Implications for Older Adults

Though studies of football players, boxers, jockeys, and other athletes focus on the repetitive nature of their TBIs, there is growing concern about how head injury from any source, at any time in life, whether repeated or not, impacts cognition later in life.

The National Alzheimer's Coordinating Center (NACC) was established in 1999 by the National Institute on Aging (one of the 27 Institutes of the National Institutes of Health) for the purpose of advancing research as part of a consortium of data-collecting organizations.

Iacono et al. (2021) studied the cognitive status of more than 600 subjects whose evaluations from their first assessment for cognitive decline were available from NACC's database. At the time of evaluation, 361 had a history of TBI, and 248 did not. Those with TBI may have experienced a single trauma or repetitive injuries and may or may not have experienced loss of consciousness with concussion. The cognitive impairment of the subjects was due to a variety of diagnoses in addition to Alzheimer's disease. These included mild cognitive impairment (MCI), Lewy body disease, vascular dementia, frontotemporal dementia, and Parkinson's disease, among other progressive cognitive disorders.

The results were remarkable in that subjects with a history of TBI were "significantly younger" than those without a history of TBI when first assessed with cognitive decline (Iacono et al., 2021). This "TBI age-lowering effect" for manifestations of cognitive impairment was noted in males and females, across races, in those with AD or a related disorder, among subjects with varying levels of education, and regardless of whether the APOE e4 allele was present (Iacono et al., 2021, p. 6). Across the various neurocognitive disorders, subjects with history of TBI exhibited greater frequency of neuropsychiatric symptoms, which include such manifestations as hallucinations, delusions, apathy, anxiety, motor skill problems, sleep disturbances, and disinhibition.

Consequences of a History of TBI

Along with the more dramatic and public discussions of traumatic brain injury in athletes, there is now evidence that head trauma can result in cognitive impairment years or even decades after the original injury. This has implications for everyone, throughout the lifespan. Vakhtin et al. (2021) explored the potentially delayed nature of TBI's impact on cognition in a study of veterans with "unexplained illnesses that may be deployment-related" (p. 31). A history of head injury was identified as either occurring before, during, or after concluding military service. While the authors reported that TBI history did not impact age-related changes in the brain, it did accelerate degeneration of the brain's white matter, the nerve fibers that communicate signals from and between the cell bodies of the brain's gray matter. Importantly, the time span between the injury and reported cognitive effects was greater than 17 years.

Implications for Evaluations of Adults Exhibiting Cognitive Impairment

A medical evaluation for symptoms of dementia should leave no stone unturned.

No assumption that a patient has Alzheimer's disease should be made based on age or symptomology. At any age, an adult can exhibit cognitive decline due to one or more of the treatable and/or modifiable causes discussed earlier.

Evaluation should be multidimensional and include laboratory testing for thyroid, kidney, and liver function, vitamin deficiencies (B12, D3), anemia, and testing for the presence of syphilis or the human immunodeficiency virus (HIV). Social history should include the type of work the person performed, as well as their habits and hobbies, any of which could have conveyed exposure to chemicals such as cigarette smoke, heavy metals such as lead, or pesticides (Elonheimo et al., 2021). Recreational activities may have resulted in one or more head injuries, which should be documented regardless of how recently or long ago they occurred, whether there was a single injury or multiple events, and whether or not the concussion resulted in loss of consciousness for any period.

There is much study regarding whether traumatic brain injury induces Alzheimer's disease. Commenting on the relationship between AD and TBI, Srinivasan and Brafman (2022) offer that prior studies support that a history of TBI doubles the risk of developing AD. They further conclude that—following the unmodifiable factors of age and the presence of APOE e4 genes—a history of TBI is "the strongest risk factor" linked to AD developing in those over age 65 (p. 2). Jacobsson and Lexell (2019) describe the need to know a person's "life situation," as more are living longer following a brain injury (p. 119).

Dams-O'Conner et al. (2021) note that the 2019 Alzheimer's Disease-Related Dementias Summit was the first to focus on traumatic brain injury and consequent risk of developing AD or a related disorder. The Summit produced the following draft recommendations for exploring this phenomenon:

- Encourage crosstalk and interdisciplinary collaboration between TBI and dementia researchers.
- Establish infrastructure to study TBI as a risk factor for AD and related disorders (ADRD).
- Promote basic and clinical research examining the development and progression of TBI AD/ADRD neuropathologies and associated clinical symptoms.
- Characterize the clinical phenotype of progressive dementia associated with TBI and develop non-invasive diagnostic approaches (p. 1).

As life span increases for many, a focus on the many modifiable lifestyle risk factors may impact the number of new diagnoses for symptoms of cognitive impairment and dementia. There is now ample evidence that a record of any head trauma, at any time in life, is a vital part of one's health history. Comprehensive history of modifiable and non-modifiable risk factors facilitates accurate diagnosis and early intervention. •CSA

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