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**BRAIN INJURY MAY MORE THAN DOUBLE DEMENTIA RISK IN  
OLDER VETERANS**

**- Additional Study Suggests that Former Athletes with Concussions have Increased Risk  
of Cognitive Impairment, with Earlier Onset -**

PARIS, July 18, 2011 – Older veterans who experienced traumatic brain injury showed a more than two-fold increase in the risk of developing dementia, according to new research presented today at the Alzheimer's Association International Conference 2011 (AAIC 2011) in Paris.

Another study reported at AAIC 2011 looked at former American (NFL) football players to gain insight into how sports-related head injuries might impact risk for Alzheimer's or cognitive decline. The athletes, some of whom had experienced concussions, were at elevated risk for mild cognitive impairment (MCI) or cognitive decline that resembled MCI.

A person with MCI has problems with memory, language, or another mental function severe enough to be noticeable to themselves or to other people and to show up on tests, but not serious enough to interfere with daily life. The best-studied type of MCI involves a memory problem and is called "amnestic MCI." While not everyone diagnosed with MCI goes on to develop Alzheimer's, research has shown that individuals with MCI have an increased risk of developing Alzheimer's over the next few years, especially when their main problem is memory.

"Head injury is common. However, in many cases it may be possible to protect against it by buckling your seat belt, wearing your helmet, and 'fall-proofing' your home," said William Thies, PhD, Chief Medical and Scientific Officer at the Alzheimer's Association. "There are other situations where head injury is much harder to avoid, such as in combat or in very physical sports."

According to Thies, more research is crucial to identify and verify risk factors for Alzheimer's disease, especially factors that people can modify to reduce their risk. This empowers people to take all possible health-promoting actions. Self-care and steps to reduce personal risk will always be important even after researchers discover better methods for early detection and more effective treatments.

“Looking at these studies, we must be thoughtful and take into account that elite athletes are an extraordinary group of people whose health issues are not necessarily representative of the general public or the population with Alzheimer’s disease or MCI,” Thies said. “That said, the relationship of brain and head injury to Alzheimer’s, and how those factors relate to and interact with other Alzheimer’s risk factors is a very interesting and important topic that deserves much more research attention.”

### **Increased Dementia Risk in Older Veterans with Brain Injury**

The relationship between traumatic brain injury (TBI) and risk of dementia remains unclear, with some studies suggesting an increased risk and others finding no association.

Kristine Yaffe, MD, Professor of Psychiatry, Neurology and Epidemiology at the University of California, San Francisco (UCSF) and Director of the Memory Disorders Program at the San Francisco VA Medical center, and colleagues believe that it is particularly important to clarify the association between TBI and dementia given the large number of soldiers experiencing TBI as part of current conflicts.

The researchers reviewed medical records of 281,540 U.S. veterans age 55 years and older who received care through the Veterans Health Administration and had at least one inpatient or outpatient visit during 1997–2000 and a follow-up during 2001–2007, and who did not have a dementia diagnosis at the start of the study. They searched the database for TBI and dementia diagnoses and investigated whether TBI of any type was associated with greater risk of dementia, while taking into account demographics and other medical conditions, including psychiatric disorders.

The risk of dementia was 15.3% in those with a TBI diagnosis compared with 6.8% in those without a TBI diagnosis ( $p < 0.001$ ). The adjusted hazard ratio for incident dementia in those with any TBI diagnosis was 2.3 (95% confidence interval: 2.1, 2.5) – a more than two-fold increase in the risk of developing dementia over seven years – and was significant for all TBI types. Approximately two percent of older veterans had a TBI diagnosis during the study period.

“This issue is important because TBI is very common,” said Yaffe. “About 1.7 million people experience a TBI each year in the United States, primarily due to falls and car crashes. TBI is also referred to as the ‘signature wound’ of the conflicts in Iraq and Afghanistan, where TBI accounts for 22 percent of casualties overall and 59 percent of blast-related injuries.”

“The data suggest that TBI in older veterans may predispose them toward development of symptomatic dementia. And they raise concern about the potential long-term consequences of TBI in younger veterans,” Yaffe said.

The researchers suggest that there are several potential mechanisms by which TBI could increase dementia risk. TBI is associated with swelling of axons, the long cell extensions that form connections among nerve cells in the brain. This swelling is accompanied by accumulation of proteins, including beta-amyloid, which is a hallmark of Alzheimer’s disease. In fact, according to the researchers, amyloid plaques similar to those found in the brains of people with Alzheimer’s are present in up to 30 percent of TBI patients who do not survive their injuries, regardless of age. It is possible that these injuries result in the death of axons and neurons, even after a single TBI. Loss of axons and neurons could result in earlier manifestation of Alzheimer’s symptoms.

“Our findings raise hope that early treatment and rehabilitation following TBI may help prevent long-term consequences such as dementia,” Yaffe said. “They also suggest that older adults who experience a TBI should be monitored for signs of cognitive impairment following their injuries.”

### **Mild Cognitive Impairment in Former NFL Football Players**

It has been suggested that retired American football players may be at increased risk for late-life cognitive disorders. This has not yet been definitively established. Christopher Randolph, PhD, Clinical Professor of Neurology at Loyola University Medical Center in Chicago and colleagues compared the likelihood of decline in cognitive function, including MCI, among retired American football players and older adults who had not played professional sports.

In 2001, all retired NFL players who belonged to the NFL Players' Association (n=3,729) were mailed a general health survey. In 2008, an additional survey specifically focusing on memory issues (including an Alzheimer's screening questionnaire known as the AD8) was sent out to all players over age 50 who responded to the first survey. A total of 513 follow-up surveys were returned with the AD8 completed by both the former player and his spouse. The mean age of all the players who responded was 61.

Just over 35 percent of respondents had an AD8 score that suggested possible dementia. By comparison, according to the Alzheimer's Association *2011 Facts and Figures* report, of Americans aged 65 and over, one in eight (13 percent) has Alzheimer's.

The researchers used this follow-up survey data to identify former players with probable MCI. After additional telephone screening interviews to confirm likely cognitive change, eligible respondents were brought in for extensive testing at the Center for the Study of Retired Athletes at the University of North Carolina, Chapel Hill.

The researchers compared the neuropsychological test results for the former athletes to those of two other groups with no background playing professional sports: (1) 41 demographically similar adults with no cognitive changes and (2) a clinical sample of 81 people diagnosed with MCI.

The researchers found that the former athletes were clearly impaired compared with the demographically similar nonathletes. Since the two groups were similar except for the athletes' professional sports background, this finding suggests that football may have played a role in the athletes' impairment.

The athletes with MCI had test results similar to the other adults with MCI, except the athletes were slightly less impaired. The athletes were also significantly younger, on average, than their nonathlete counterparts with MCI.

“It appears that there may be a very high rate of cognitive impairment in these retired football players, compared to the general population,” Randolph said. “These findings support the hypothesis that repetitive head trauma from many years of playing American football may result in diminished brain reserve, and lead to the earlier expression of age-related neurodegenerative diseases such as MCI and Alzheimer's. However, additional studies are necessary to confirm this conclusion. These results should be considered preliminary.”

### **About AAIC**

The Alzheimer's Association International Conference (AAIC) is the world's largest conference of its kind, bringing together researchers from around the world to report and discuss groundbreaking research and information on the cause, diagnosis, treatment and prevention of Alzheimer's disease and related disorders. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

### **About the Alzheimer's Association**

The Alzheimer's Association is the leading voluntary health organization in Alzheimer care, support and research. Our mission is to eliminate Alzheimer's disease through the advancement of research, to provide and enhance care and support for all affected, and to reduce the risk of dementia through the promotion of brain health. Our vision is a world without Alzheimer's. Visit [www.alz.org](http://www.alz.org) or call 800-272-3900.

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- Kristine Yaffe, MD, et al. Traumatic Brain Injury and Risk of Dementia in Older Veterans. (Funder: U.S. Department of Defense)
- Christopher Randolph, PhD, et al. Characterization of Mild Cognitive Impairment in Retired NFL Players. (Funders: Martek Bio Sciences, NFL Players Association)

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Session: Monday, July 18, 2011 Posters

Presentation: P2-117; 12:30-3:00 pm

### **Traumatic Brain Injury and Risk of Dementia in Older Veterans**

Presenting author: Kristine Yaffe, MD, University of California, San Francisco and San Francisco VAMC

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**Background:** The relationship between traumatic brain injury (TBI) and risk of dementia remains controversial, with some studies suggesting an increased risk and others finding no association. It is particularly important to clarify the association between TBI and dementia given the large number of soldiers experiencing TBI as part of current conflicts.

**Methods:** We performed a retrospective cohort study of 281,540 US veterans age 55 years or older who had at least one inpatient or outpatient visit during both the baseline (1997-2000) and follow-up (2001-2007) periods and did not have a dementia diagnosis at baseline. TBI and dementia diagnoses were determined using International Classification of Diseases - 9th edition codes. Cox proportional hazards models were used to determine whether TBI of any type was associated with greater risk of incident dementia, adjusting for demographics, medical comorbidities and psychiatric disorders.

**Results:** Veterans had a mean age of 67 +/- 8 years; 4% were women. Approximately 2% of older veterans had a TBI diagnosis during the baseline period. Diagnoses included intracranial injury (40%), unspecified head injury (34%), concussion (15%), post-concussion syndrome (12%) and skull fracture (5%), with 6% have more than one diagnosis. The risk of dementia was 6.8% in those without a TBI diagnosis compared to 15.3% in those with any type of TBI diagnosis (intracranial injury, 15.7%; unspecified head injury, 16.0%; concussion, 11.6%; post-concussion syndrome, 15.6%; skull fracture, 14.9%; all p<0.001). The adjusted hazard ratio for incident dementia in those with any TBI diagnosis was 2.6 (95% confidence interval: 2.4, 2.8) and was significant for all TBI types.

**Conclusions:** TBI diagnoses in older veterans are associated with nearly a 3-fold increase in the risk of developing dementia over seven years. Our findings suggest that TBI in older veterans may predispose toward development of symptomatic dementia and raise concern about the potential long-term consequences of TBI in younger veterans.

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Session: Tuesday, July 19, 2011 Posters

Presentation: P3-112: 12:30-3:00 pm

### **Characterization of Mild Cognitive Impairment in Retired NFL Players**

Presenting author: Christopher Randolph, PhD, Loyola University Medical Center, Chicago

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**Background:** It has been suggested that retired American football players may be at increased risk for late-life cognitive disorders, and there have been isolated findings of chronic traumatic encephalopathy (CTE) in athletes who have been exposed to repetitive head trauma.

**Methods:** The athletes were compared on a neurocognitive test battery to two groups; a demographically-matched cognitive intact cohort (N=41) and a clinical sample of patients with amnesic MCI (N=81).

**Results:** The prevalence of MCI within the sample of retired athletes appears to be higher than epidemiological studies would predict. The sample of athletes with MCI was clearly impaired relative to their demographically-matched cohort, confirming the presence of acquired impairment. The retired athletes were significantly younger than the clinical aMCI sample and slightly less impaired overall, but their neurocognitive profiles were highly similar to the clinical sample.

**Conclusions:** MCI may be more common in retired NFL athletes than in the general population, although more systematic studies are necessary to confirm this. The similarity of the neurocognitive profiles between the athletes and clinical cases suggests that the etiology of MCI in the retired players may be due to diminished cerebral reserve allowing the earlier clinical expression of MCI. Potential mechanisms are discussed.

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