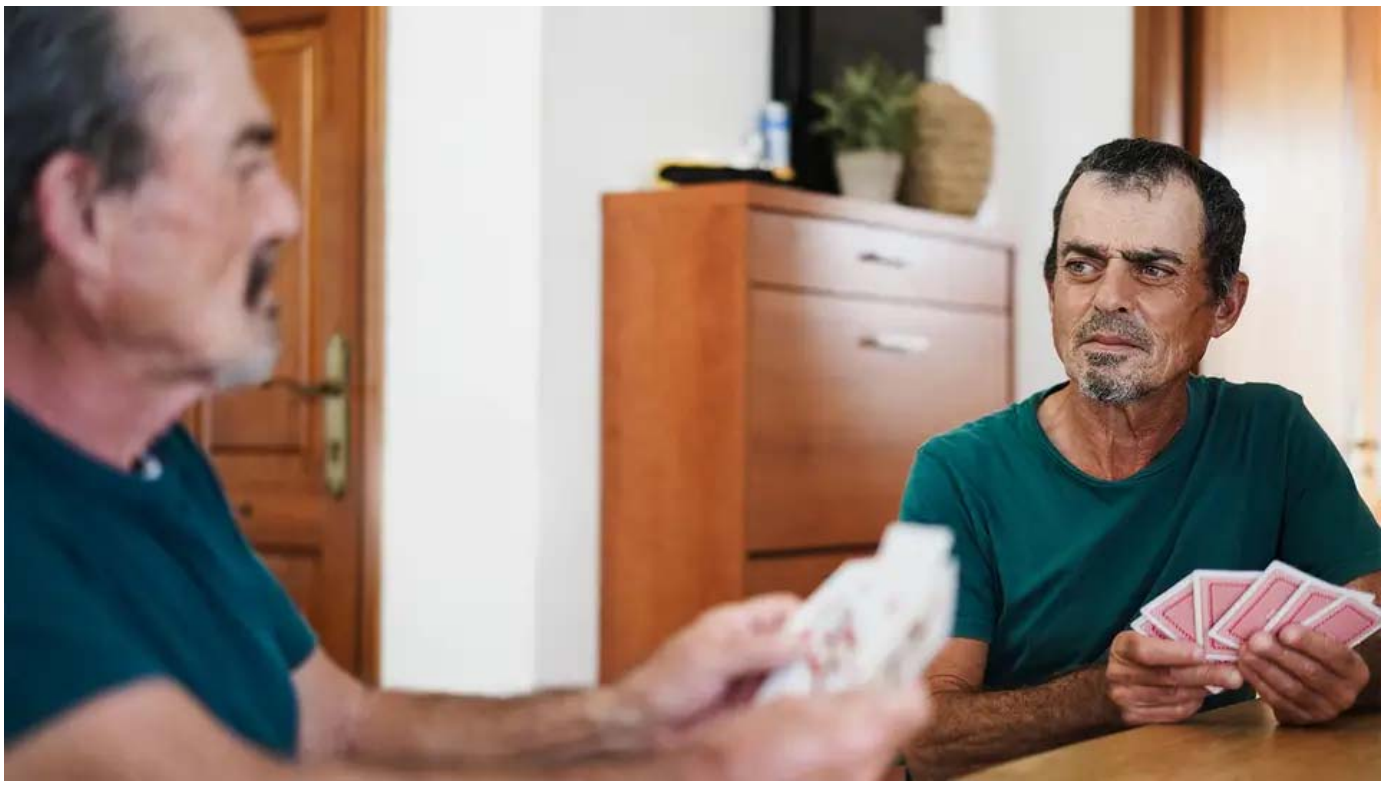
Twin Study Ties Cognitive Decline With Earlier Traumatic Brain Injuries

— Twins with TBI at age 25 or older had sharper drops in cognition as they aged

by Judy George, Deputy Managing Editor, MedPage Today September 7, 2023



Traumatic brain injury (TBI) earlier in life was linked with lower cognitive scores and a more rapid decline in cognition, a study of male twins showed.

Twins with a history of TBI were more likely to have lower cognitive test scores at age 70 than twins without TBI, reported Marianne Chanti-Ketterl, PhD, MSPH, of Duke University in Durham, North Carolina, and co-authors in *Neurology*.

Twins who had lost consciousness with TBI, had more than one TBI, or were 25 or older at injury had a faster drop in cognition than those without TBI in the 12-year study.

Relationships were stronger for monozygotic twin pairs. While effect sizes were modest, they showed how TBI may contribute to cognitive function after accounting for known covariates, the researchers said.

"These findings support an association on the impact of TBI on cognitive score and the rapidity of cognitive decline in later life," Chanti-Ketterl and colleagues wrote.

"The results in monozygotic pairs, who share all genes and many exposures particularly in early life, provide additional evidence of a causal relationship between TBI and poorer late-life cognitive outcomes," they added.

Traumatic brain injury is a known risk factor for dementia, accounting for an estimated 3.4% of dementia cases worldwide, according to the *Lancet* Commission. But teasing out variables that may confound this relationship -- like genetics and early environmental exposures -- has not been done in a study of twins before.

The findings leverage a novel population but should be interpreted with caution, observed Holly Elser, MD, PhD, and Andrea Schneider, MD, PhD, both of the University of Pennsylvania in Philadelphia, in an accompanying editorial.

Concordance rates in monozygotic twin pairs "vary across complex diseases," Elser and Schneider wrote. For example, concordance for Alzheimer's disease is an estimated 45% among male monozygotic twins, they pointed out.

Other research has revealed phenotypic differences due to underlying genetic differences in monozygotic twins, they noted. Moreover, early-life exposures may produce differences in DNA expression or epigenetic outcomes.

"[T]he observed difference in cognitive scores in monozygotic twin pairs discordant for TBI could still be explained in part by residual confounding from underlying differences, environmental factors, or gene-environment interactions leading to differences in epigenetic profiles," the editorialists wrote.

Chanti-Ketterl and colleagues evaluated 8,662 men in the National Academy of Sciences-National Research Center Twin Registry of World War II veterans. Of this group, 2,168 participants (25%) had a self-reported or proxy-reported history of TBI.

Over 12 years, participants were assessed up to four times with the modified Telephone Interview for Cognitive Status (TICS-m). TICS-m is a brief, standardized test of cognitive functioning modeled after the Mini-Mental State Examination (MMSE). It produces scores ranging from 0 to 50 that are highly correlated with MMSE scores.

Baseline age was defined as the age of first TICS-m score. Mean baseline age was 67 and mean baseline TICS-m score was 32.5. Twins with or without TBI did not differ by age or TICS-m score at baseline.

Differences emerged in both TICS-m scores at age 70 and in annual declines over 12 years:

- At age 70, twins with TBI had a TICS-m score 0.56 points lower than those without TBI
- TBI with loss of consciousness led to a TICS-m score that was 0.51 points lower at age 70 than those with no TBI
- Being 25 or older when TBI occurred led to a TICS-m score that was 0.66 points lower
- Compared with no TBI, TBI with loss of consciousness led to a faster rate of annual decline (0.03 points per year), as did more than one TBI (0.05 points per year) or being 25 or older when injury occurred (0.06 points per year)

Analyses of 1,195 twin pairs with known zygosity showed associations tended to be stronger in monozygotic compared with dizygotic pairs.

"Our twin study shows that TBIs, even decades prior to cognitive testing, led to lower cognitive levels and faster rates of cognitive decline in late-life, regardless of shared genetics and early-life exposures, and medical conditions," Chanti-Ketterl and colleagues wrote. "This association was stronger for those having a TBI at age 25 or later, suggesting that TBI both lowers cognitive reserve (level of cognition) and accelerates cognitive aging."

TBIs were self-reported, which may have led to bias, the researchers acknowledged. The cohort was exclusively male veterans and it's unclear whether findings apply to other populations. In addition, unmeasured confounders may have influenced

results.

Judy George covers neurology and neuroscience news for MedPage Today, writing about brain aging, Alzheimer's, dementia, MS, rare diseases, epilepsy, autism, headache, stroke, Parkinson's, ALS, concussion, CTE, sleep, pain, and more. Follow

Disclosures

This study was supported by the National Institute on Aging and the Department of Defense.

Researchers and editorialists reported no relevant disclosures.

Primary Source

Neurology

Source Reference: *Chanti-Ketterl M, et al "Associations between traumatic brain injury and cognitive decline among older veteran men - a twin study" Neurology 2023; DOI: 10.1212/WNL.0000000000207819.*

Secondary Source

Neurology

Source Reference: *Elser H, Schneider AL "Traumatic brain injury and cognitive decline: New insights and considerations from a twin study design" Neurology 2023; DOI: 10.1212/WNL.000000000020792.*

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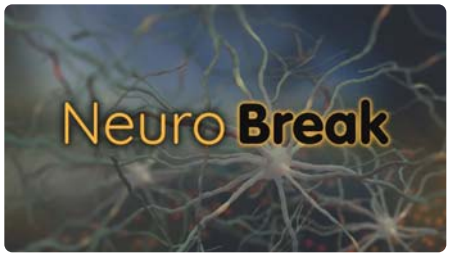

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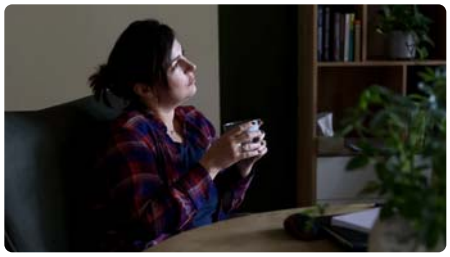

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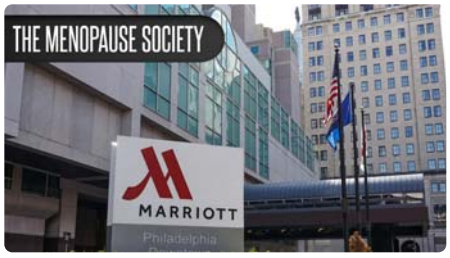

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