

Genetic variant may increase risk for CTE severity among older individuals with repetitive head impacts

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How could two individuals who both played football for 10 years and developed CTE have different disease severity? How could some

individuals develop dementia in their 50's while other never develop dementia at all? Perhaps the answer lies in their genes.

Repetitive head impact (RHI) exposure is the chief risk factor for [chronic traumatic encephalopathy](#) (CTE). However, the occurrence and severity of CTE varies widely among those with similar RHI exposure.

Now a new study from researchers from the BU CTE Center reveals that the genetic variant, *APOE*ε4 plays a major role in determining CTE severity and that having *APOE*ε4 makes an individual 2.34 times more likely to develop a more severe form of CTE.

"This study provides the most concrete evidence to date that *APOE*ε4 is a risk factor for CTE-related pathological and clinical outcomes. Understanding genetic underpinnings of CTE pathology may provide insights into disease mechanism and offers a precision medicine approach to harm reduction, including guiding decisions regarding contact sport play and providing a target for therapies," explains corresponding author Jesse Mez, MD, MS, director of the Boston University (BU) Alzheimer's Disease Research Center Clinical Core and a BU CTE Center investigator.

The researchers studied the brains of deceased individuals exposed to RHI through [contact sports](#) or [military service](#), 294 of whom developed CTE and 70 of whom did not. They then analyzed their neurological findings based on their *APOE* status and found that *APOE*ε4 carriers were 2.34 times more likely to have more severe CTE than those without. More severe CTE was determined by both CTE Stage (I through IV) and a quantitative analysis of abnormal *tau* protein burden.

"Our research team has shown that among [football players](#), an individual's odds of developing a more severe stage of CTE double every additional 4.4 years of play. Specifically, for football players over age

65, having *APOE*ε4 had an effect on CTE severity equivalent to playing an additional seven years of football, meaning it more than doubled risk," says Mez.

According to the researchers, these findings provide insight into how CTE progresses, which may provide new targets for developing treatments to slow or stop CTE progression.

These findings appear online in the journal *JAMA Neurology*.

More information: Association of APOE genotypes and chronic traumatic encephalopathy, *JAMA Neurology* (2022). DOI: [10.1001/jamaneurol.2022.1634](https://doi.org/10.1001/jamaneurol.2022.1634) , jamanetwork.com/journals/jaman.../fullarticle/2793575

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