

Dementia gene: Heading soccer balls increases brain risks for certain players

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Startling new evidence from medical investigators in New York suggests that "heading" a ball in soccer—in which players propel it with their heads—can lead to cognitive impairment in members of the sport who are endowed with a dementia-associated gene.

The findings are preliminary and require replication by other geneticists. But the emerging data build on a growing body of evidence that suggests ball heading increases the risk for adverse cognitive outcomes, particularly for certain members of the sport.

Soccer is played by more than 265 million people worldwide, and heading the ball is a key component of the game. Although usually not strong enough to cause a concussion, medical investigators are theorizing that heading has a cumulative effect on the brain. A new medical investigation involving players who had been in the game at least five years, revealed that verbal recall declined among those who frequently headed the ball and met a specific genetic profile. All participants in the investigation were tested for memory and recall. Evidence of cognitive impairment was strikingly apparent among study participants who headed the ball frequently, and for whom a dementia risk factor was indelibly inscribed in their DNA.

"Soccer is the most popular sport worldwide, and this research is part of a large, ongoing study conducted by our collaborators, namely the Einstein Soccer Study, which has already enrolled hundreds of participants over many years," said Dr. Yun Freudenberg-Hua, an assistant professor at the Feinstein Institutes for Medical Research on Long Island. The research division is part of the Northwell Health system, which has headquarters in New York.

"The goal of this study is to investigate whether the effects of repeated and long-term, routine heading interacts with a well-known genetic risk factor for dementia," Freudenberg-Hua told Medical Xpress.

That risk factor is the genotype, Apolipoprotein E ϵ 4, usually written in scientific shorthand as APOE ϵ 4. The research is a joint project of Albert Einstein College of Medicine in the Bronx, New York, and the Feinstein Institutes.

"Previous studies have shown that long-term heading is associated with abnormal white matter microstructure in the brain and with poorer neurocognitive performance," added Freudenberg-Hua, who is also an assistant professor of psychiatry and molecular medicine at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, also on Long Island.

"This study only looked at an association between heading and verbal learning performance, together with the specific genetic risk factor for dementia, APOE ϵ 4," she said.

Reporting in the *JAMA Neurology*, Freudenberg-Hua and her colleagues defined their study as one that focused on a group as soccer players who ranged between the ages of 18 and 55. All told, there were 379 participants who were allowed to take part in the research if they played for more than five years and were active in games more than six months a year. Each player was genotyped for the APOE ϵ 4 allele. Players also were asked to report heading exposure and to undergo a verbal memory assessment test.

"Participants were presented with a 12-item grocery shopping list at the beginning of the session and asked to recall that list at the end of the session, approximately 20 minutes later. The number of correct responses was recorded," Freudenberg-Hua said.

Carriers of the APOE ϵ 4 allele were more likely to have forgotten many of the items on the shopping list compared with fellow players without the genetic marker. Study participants who carry the gene performed

four times worse on the memory and recall task than players without the gene who rarely headed the ball.

"The APOE gene is a major risk gene for Alzheimer's disease and the APOE ϵ 4 allele is associated with a three-fold increased risk for Alzheimer's disease," Freudenberg-Hua explained.

What remains to be fully elucidated, she added, is precisely how ball heading exacerbates [cognitive impairment](#) with respect to the APOE ϵ 4 allele.

"The way APOE ϵ 4 allele confers this risk is not entirely clear yet, but likely involves multiple biological mechanisms, such as abnormal protein degradation, lipid metabolism, synaptic plasticity, spine integrity and neuroinflammation," she added. "This study shows that people who carry the APOE ϵ 4 allele and who had a high level of heading exposure may have greater risk of cognitive dysfunction."

As compelling as the research may seem, it has yet to be validated by other investigators, Freudenberg-Hua said, noting that reproducible findings define the gold-standard of scientific research. Nevertheless, she and her team advise players who know that they carry the gene to avoid aspects of the game that involve head impacts with the [ball](#).

"Genetic association results generally require replication in an independently collected group of participants," Freudenberg-Hua said.

"The larger the number of participants, the more confidence we have for our results.

"However, conducting any such study requires many years of labor-intensive community outreach, enrollment, data collection and data analysis. As geneticists, we always look to evaluate the effects of genetic variants across many traits," she said.

More information: Liane E. Hunter et al. Associations of Apolipoprotein E ϵ 4 Genotype and Ball Heading With Verbal Memory in Amateur Soccer Players, *JAMA Neurology* (2020). [DOI: 10.1001/jamaneurol.2019.4828](https://doi.org/10.1001/jamaneurol.2019.4828)

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