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Study Says Brain Trauma Can Mimic A.L.S.

By ALAN SCHWARZ

In the 71 years since the Yankees slugger Lou Gehrig declared himself "the luckiest man on the face of the earth," despite dying from a disease that would soon bear his name, he has stood as America's leading icon of athletic valor struck down by random, inexplicable fate.

A peer-reviewed paper to be published Wednesday in a leading journal of neuropathology, however, suggests that the demise of athletes like Gehrig and soldiers given a diagnosis of amyotrophic lateral sclerosis, commonly known as Lou Gehrig's disease, might have been catalyzed by injuries only now becoming understood: concussions and other brain trauma.

Although the paper does not discuss Gehrig specifically, its authors in interviews acknowledged the clear implication: Lou Gehrig might not have had Lou Gehrig's disease.

Doctors at the Veterans Affairs Medical Center in Bedford, Mass., and the Boston University School of Medicine, the primary researchers of brain damage among deceased National Football League players, said that markings in the spinal cords of two players and one boxer who also received a diagnosis of A.L.S. indicated that those men did not have A.L.S. They had a different fatal disease, doctors said, caused by concussionlike trauma, that erodes the central nervous system in similar ways.

The finding could prompt a redirection in the study of motor degeneration in athletes and military veterans being given diagnoses of A.L.S. at rates considerably higher than normal, said several experts in A.L.S. who had seen early versions of the paper. Patients with significant histories of brain trauma could be considered for different types of treatment in the future, perhaps leading toward new pathways for a cure.

"Most A.L.S. patients don't go to autopsy — there's no need to look at your brain and spinal cord," said Dr. Brian Crum, an assistant professor of neurology at the Mayo Clinic in Rochester, Minn. "But a disease can look like A.L.S., it can look like Alzheimer's, and it's not when you look at the actual tissue. This is something that needs to be paid attention to."

The finding's relevance to Gehrig is less clear. But the Yankees legend had a well-documented history of significant concussions on the baseball field, and perhaps others sustained as a battering-ram football halfback in high school and at Columbia University. Given that, it's possible that Gehrig's renowned commitment to playing through injuries like concussions, which resulted in his legendary streak of playing in 2,130 consecutive games over 14 years, could have led to his condition.

“Here he is, the face of his disease, and he may have had a different disease as a result of his athletic experience,” said Dr. Ann McKee, the director of the neuropathology laboratory for the New England Veterans Administration Medical Centers and the lead neuropathologist on the study.

Gehrig’s name does not appear in the paper; his case was discussed in interviews merely as an illustration of the new uncertainty surrounding cases resembling his, said Dr. Robert Stern, who serves with Dr. McKee as co-director of Boston University’s Center for the Study of Traumatic Encephalopathy. The cause of his disease will most likely never be determined because his remains were cremated, and now lie in Kensico Cemetery in Valhalla, N.Y.

More significantly, both doctors said, the finding solidifies a long-suspected connection between A.L.S.-like motor disease and head trauma experienced in collision sports and combat.

“People are being misdiagnosed clinically while they’re alive as having A.L.S. when in fact they have a different motor-neuron disease,” Dr. Stern said. He added, “Scientists will be able to get at a faster understanding of the disease in general, and therefore effective treatments, by knowing more about who’s at risk and who’s not.”

According to the A.L.S. Association, up to 30,000 people in the United States currently have A.L.S., an incurably fatal disease among primarily 40- to 70-year-old men that results in the swift and steady atrophy of all voluntary muscle control. Gehrig was its first prominent victim, dying two years after his 1939 diagnosis; some others, like the British physicist Stephen Hawking, now 68, can live for decades with fully functioning brains inside bodies that have wasted away.

The new finding could be double-edged for organizations fighting A.L.S.: it sheds some light on possible causes and research avenues, but also suggests that Gehrig might not have had it.

“It’s extremely interesting — it builds a more interesting picture, but what this all exactly means about how the disease plays out requires further investigation,” said Dr. Lucie Bruijn, the chief scientist for the A.L.S. Association. Dr. Bruijn described Gehrig as “an important fund-raising tool,” similar to the actor Michael J. Fox having Parkinson’s disease.

“It’s a name and a face that get people to understand what kind of a disease this really is,” she said. “It makes it more personal.”

A.L.S. in the N.F.L.

A link between professional football and A.L.S. follows recent discoveries of on-field brain trauma leading to dementia and other cognitive decline in some N.F.L. veterans. Dr. McKee and her group identified 14 former N.F.L. players since 1960 as having been given diagnoses of A.L.S., a total about eight times higher than what would be expected among men in the United States of similar ages.

However, the doctors cautioned, the existence of the increased number of A.L.S.-like cases should not create the same level of public alarm as the cognitive effects of brain trauma, which affect hundreds of

former professionals and perhaps thousands of boys and girls across many youth sports.

Recent epidemiological studies have suggested that brain trauma in sports can be a risk factor for A.L.S.; for example, a 2005 paper found that Italian professional soccer players had developed the disease at rates about six times higher than normal. Studies have also linked service in the United States military to higher risk for A.L.S., possibly because of battlefield collisions and blast injuries.

The study, to be published Wednesday on the Web site of the Journal of Neuropathology & Experimental Neurology, represents the first firm pathological indications that brain trauma results in motor-neuron degeneration, and that the resulting disease (at least in the three men studied) is actually not A.L.S. It is a different disorder with different markings, specifically a pattern of two proteins in the spinal cord that compromise nerve function.

Dr. McKee had already found 12 deceased N.F.L. veterans to have had chronic traumatic encephalopathy, a progressive disease in brain tissue that results in cognitive impairment and eventually dementia. Two of those men — Wally Hilgenberg, a longtime linebacker for the Minnesota Vikings in the 1970s, and Eric Scoggins, who played only three games at linebacker for the 1982 San Francisco 49ers — also had A.L.S. diagnosed by their physicians.

When Dr. McKee examined the spinal-cord tissue of those men, as well as a former boxer who had A.L.S.-like symptoms, she found dramatically high levels of tau and TDP-43, two proteins known to cause motor-neuron degeneration. She said that they would appear in the cord as a result of blows to the brain, with the proteins probably traveling down the spinal cord, rather than direct injury to the spinal cord itself.

Dr. McKee said that because she has never seen that protein pattern in A.L.S. victims without significant histories of brain trauma, she and her team were confident the three athletes did not have A.L.S., but a disorder that erodes its victims' nervous system in similar ways. McKee added that finding the distinctive pattern in all three men with A.L.S. symptoms was more than enough pathological evidence to make her conclusion.

"If we can create this in laboratory mice, which are easily genetically altered and breed quickly, we can learn about the pathogenesis of this disorder, and then provide treatment," Dr. McKee said. The consensus among experts is that brain trauma is almost certainly not solely responsible for diseases like this.

Those afflicted probably have genetic factors leading to susceptibility, with concussions serving as catalyst. In that regard, some doctors said, years from now athletes could be tested for the gene that leaves them vulnerable, not unlike how some today check for sickle-cell trait.

The Gehrig Mystery

More than any other American athlete, perhaps even the player who eventually broke his consecutive games streak, Cal Ripken Jr., Lou Gehrig has come to symbolize a commitment to playing every day, especially through injuries. That renown partly derives from well-documented incidents in which he sustained significant concussions but continued to play in ways now known to be dangerous.

The most notable came in June 1934, when, in an exhibition game, Gehrig was hit with a pitch just above the right eye and was knocked unconscious for what was described in news reports as five minutes. (He was not wearing a batting helmet; such protection was not meaningfully introduced in the major leagues until the 1940s or required until 1958.) He was removed from the game.

Despite a headache, a doctor's recommendation that he sit out and a bump on his head so large that he had to wear one of Babe Ruth's larger caps, Gehrig played the next day against the Washington Senators to continue his streak at 1,415 games. "A little thing like that can't stop us Dutchmen," Gehrig told a reporter, according to Jonathan Eig's definitive biography of Gehrig, "Luckiest Man."

In 1924, during a postgame brawl with the Detroit Tigers, Gehrig swung at Ty Cobb and fell, hit his head on concrete, and was briefly knocked out. While playing first base against the Tigers in September 1930, Gehrig was hit in the face and knocked unconscious by a ground ball. He was knocked out again by an oncoming runner in 1935.

Those are the four incidents in which Gehrig's being knocked unconscious was notable enough to be reported in newspapers. He most likely sustained other concussions that were never noticed or considered meaningful — for example, when he was hit in the head with a pitch during a 1933 game against Washington but continued playing — either in baseball or while serving as a halfback for Commerce High School in New York and later Columbia University.

"Obviously he played in the days before helmets, and he led with his head and with his shoulders, certainly on the football field," said Mr. Eig, adding that he found no record of brain injuries in news reports of Gehrig's football career. "On the baseball field he got knocked around a bit because he could be klutzy. Given the barnstorming he did in the off-season and his football career and style, there's no telling how many additional shots to the head he took."

Gehrig's handling of injuries inspired reverence among fans and the news media. Concussions then almost resembled cigarette smoking, in that what is now known to be harmful was in Gehrig's time considered benign, even charming. An advertisement for Camel cigarettes that filled the back page of Life magazine included various testimonials to "Larruping Lou's" playing through injuries, including the 1934 incident.

"Another time, he was knocked out by a 'bean ball,' yet next day walloped 3 triples in 5 innings," the ad reads. "Gehrig's 'Iron-Man' record is proof of his splendid physical condition. As Lou says: 'All the years I've been playing, I've been careful about my physical condition. Smoke? I smoke and enjoy it. My cigarette is Camel.'"

The End, and Legacy

Gehrig showed the first signs of degenerative motor disease in 1938, when his hands began to ache and his legs and shoulders gradually weakened. Gehrig's rickety spring training in 1939 indicated to even casual observers that something was quite wrong; after a poor April, on May 2, Gehrig told Yankees Manager Joe McCarthy that he would not play that day against Detroit, ending his streak at 2,130 games, dating back 14

seasons. He rested for a month before seeking some answers at the Mayo Clinic in June.

The diagnosis was amyotrophic lateral sclerosis, then a virtually unknown disease that doctors explained to the public as a form of "infantile paralysis" resembling polio. It had no known cause, and was not described as fatal. Gehrig's baseball career was immediately over, and two weeks later, on July 4, he was honored at Yankee Stadium in an on-field ceremony between games of a doubleheader.

Speaking through microphones to more than 60,000 hushed fans, Gehrig took the scene and called himself "the luckiest man on the face of the earth" — a remark that quickly symbolized his humility and, of course, just how unlucky the slugger truly was. Gehrig's once muscular frame, so seemingly perfect that only a few years before he had auditioned to play Tarzan in the movies, quickly deteriorated.

By the time Gehrig died two years later, A.L.S. was already commonly referred to as Lou Gehrig's disease, a disorder known as much for the player as for the seemingly arbitrary way in which he was chosen to die from it.

The Mayo Clinic retains Gehrig's medical records but has never disclosed them per institutional policy, a spokesman said. A neurologist who was allowed to inspect them years ago, Dr. Jay Van Gerpen of the Mayo Clinic in Jacksonville, Fla., was not permitted by the clinic to be interviewed for this article.

In considering how Gehrig's disease could be pinpointed, Dr. McKee of the Boston University group said that if Gehrig had been embalmed, rather than cremated, she theoretically could examine remaining tissue. He might have had A.L.S., like the more than hundreds of thousands of Americans who have had it since, and who have perhaps taken some solace in how such a famous and admirable man as Gehrig had it, too. Or, given his history of brain injuries, Gehrig might have been like Wally Hilgenberg and the growing number of athletes who, as science evolves, stand with increasing company as testimony to concussions' shocking cost.

"Lou Gehrig wanted to know everything possible about his own illness — he got to know his doctors, talked with scientists with obscure approaches, and volunteered himself as a guinea pig to find any way to combat the disease," Mr. Eig said. "He wouldn't stick his head in the sand and not want to hear about this. If he were around today, he would continue to have that same curiosity, and that burning desire, to help his situation, or to help others."