

# THE WAITING ROOM

THIS WAY IN

## Can Head Injury Cause Motor Neuron Disease?

BY KIERSTIN WESOLOWSKI

Is it possible that sustaining multiple head injuries, such as concussions, could result in the development of motor neuron disease? That's the provocative question posed in a study from the *Journal of Neuropathology and Experimental Neurology* in August. The study authors suggest that it is possible—and that some people diagnosed with amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease after the famous Yankees' baseball player, may not actually have the disease.

The study grabbed national headlines and ignited a firestorm of debate among ALS experts when study author Anne C. McKee, M.D., was quoted in the Aug. 17 *New York Times* speculating that Lou Gehrig may not have had ALS, which is the most common form of motor neuron disease. Dr. McKee, director of the neuropathology laboratory for the New England Veterans Administration Medical Center, made her remark based on the many concussions Gehrig sustained during his baseball career. However, nowhere in the study did the investigators present evidence to support this claim.

More than 30,000 people in the U.S. have ALS, according to The ALS Association. Many contacted their neurologist to ask if they had been inaccurately diagnosed with the disease. *Neurology Now* spoke with experts in the field to clear up the misconceptions presented in the media.

### On what evidence did the investigators base their findings?

Dr. McKee and colleagues studied the brains and spinal cords of 12 deceased, former athletes who had chronic traumatic encephalopathy (CTE), a progressive neurodegenerative disease caused by multiple head injuries. The disorder is characterized by the buildup of a toxic protein called "tau" throughout the brain.

People with the disease typically experience progressive loss of memory and other cognitive abilities. They also may also show personality changes, emotional instability, erratic behavior, inability to concentrate, and progressive loss of consciousness, according to the National Institute of Neurological Disorders and Stroke (NINDS).



**“A claim that head injury contributes to ALS cannot be based on findings seen in just three patients.”**

—ROBERT G. MILLER, M.D.

**SAFE... FROM SENSATION**  
There is no solid evidence to claim that Lou Gehrig's illness was not ALS.

Three of the 12 patients with CTE had also been diagnosed with motor neuron disease, which is a group of progressive neurologic disorders, including ALS, that destroy nerve cells called motor neurons. These nerve cells are involved in various muscle functions such as sleeping, walking, breathing, and swallowing, according to NINDS. Lucie Bruijn, Ph.D., chief scientist for The ALS Association, notes that the term “mo-

tor neuron disease” can refer to the impairment of the upper motor neurons (located in the brain) or the lower motor neurons (located in the brain stem and spinal cord) or both. For an ALS diagnosis, Dr. Bruijn says, both sets of motor neurons must be affected.

Recent studies have shown that the accumulation of the protein TDP-43 throughout the brain and spinal cord can cause ALS.

Dr. McKee and colleagues looked at the proteins tau and TDP-43 in the 12 athletes and compared their findings to a deceased “control group” comprised of 12 people who did not have neurologic disease and 12 others who had non-genetic (also called “sporadic”) ALS.

### What did the investigators observe in the patients?

The researchers found accumulations of tau throughout the brains and spinal cords of all nine athletes who had a diagno-

CONTINUED ON P. 12

CONTINUED FROM P. 11

sis of CTE prior to death. However, they did not find tau accumulations in any of the 24 controls. Researchers also noticed a buildup of TDP-43 in the brains and spinal cords of these nine athletes, which they also found in the 12 controls with ALS, but not in the 12 normal controls.

Robert G. Miller, M.D., program director of the Forbes Norris MDA/ALS Research Center at the California Pacific Medical Center, says finding TDP-43 accumulation in the CTE patients is an interesting discovery. "It raises the possibility that TDP-

43 buildup may be created by head injury," Dr. Miller says. Although TDP-43 had previously been found in the brains of people with ALS, he adds, "It hadn't been specifically related to brain trauma or injury."

The three athletes with CTE as well as motor neuron disease had different patterns of TDP-43 accumulation than did the people with sporadic ALS. The three athletes also had tau buildup, which was absent in the sporadic ALS patients and also the controls without neurologic disease.

## NEUROLOGY NEWS

# High-Dose Aspirin Cure for Migraine?

**A** new study in the journal *Neurology*, published by the American Academy of Neurology (AAN) suggests that intravenous (IV) aspirin use in high doses is safe, effective, and useful in managing severe headaches in hospitals. The British-based study focused on the use of IV aspirin for headaches resulting from withdrawal of other medications used to relieve pain, including acetaminophen, opioids, triptans, or serotonin receptor agonists. But its results are sparking interest in the potential use of IV aspirin treatments for severe migraine.

"This has the potential for helping a lot of people," notes Andrew Hershey, M.D., Ph.D., director of the Headache Center and associate director of research in the division of neurology at Cincinnati Children's Hospital, who was not involved in the study. "It gives us another form of IV treatment for use in emergency rooms and hospitals, and possibly wider use in doctor's offices."

In the five-year study, researchers looked at 168 patients—117 women and 51 men—who had been hospitalized for migraines or headaches and given aspirin through an IV for 15 days or more a month for three months. Based on interviews with and journals by the patients, 25 percent experienced a major drop in pain levels



(3 points on a pain scale of 10), while 40 percent felt a "moderate impact" of one or two points of pain reduction. Approximately six percent suffered minor side effects including nausea, vomiting, and trouble with the insertion of the IV. Two people dropped out of the study, one because of asthma and the other as a result of "needle phobia."

"The finding of pain improvement on hospital inpatients with headache given IV aspirin is plausible to me, given my own clinical experience," notes Gretchen E. Tietjen, M.D., chair of the neurology department and director of the Headache Treatment and Research Program at the University of Toledo Medical Center, who was not involved in the study. "However, this study was retrospective, uncontrolled, and confounded by the fact that many patients were prescribed more than one medication. Given the high cost of hospitalization and

patient's high expectations for pain relief in this setting, the overall finding of an average 1-point reduction on a 10-point pain scale tempers my enthusiasm."

Generally, retrospective studies are viewed as less reliable for several reasons. A retrospective study looks backward in time at information that has already been collected, instead of investigating the response of a group of patients to a particular treatment. Many experts believe that retrospective studies provide more opportunities for bias. Also, retrospective studies don't include what is considered a "gold standard" for clinical research: the comparison of a group receiving the experimental therapy versus a control group made up of subjects who receive either a placebo or alternative treatment.

Peter J. Goadsby, M.D., Ph.D., of the Headache Group at the University of California, San Francisco, acknowledges that the study has limitations, but says, "Our findings warrant more research into the use of IV aspirin for severe headache or migraine."

IV aspirin has not been readily available in the United States to date. The reason? The treatment is not FDA-approved, according to Crystal Rice, media representative at the U.S. Food and Drug Administration's Center for Drug Evaluation and Research.

"The next step would be to work through the FDA approval process," says Dr. Hershey.

"This study also demonstrates that migraine patients are not looking for sedation or addiction, they're looking for relief," Dr. Goadsby says. "If you can give them relief without those side effects, they'll be fine."

—Paul Smart

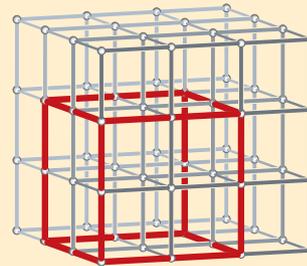
NEUROBICS

# Cubical Condos

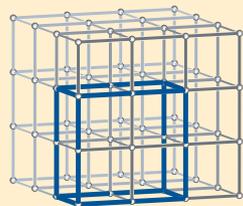
**T**his puzzle exercises your ability to visualize three-dimensional shapes.

Walking down the street one day you pass by Cubical Condos, a condominium complex under construction in which every room is a perfect cube. Below is the unfinished frame of the building showing the outlines of the rooms. There are twenty-seven rooms in the building: nine rooms on each of the three floors. Customers can order a custom-configured condo containing two to eight rooms.

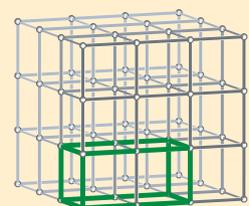
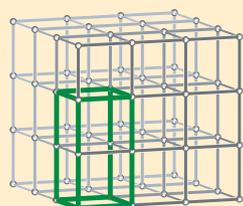
**1.** The red girders outline a luxury condo, which has eight rooms arranged in a two-story cube. How many different places could a luxury condo be configured within the twenty-seven room building?



**2.** The blue girders outline two different mid-range condos, which each have four rooms arranged in a square. Notice that mid-range condos can be one or two stories tall. How many different places could a mid-range condo be configured within the building?



**3.** The green girders outline two different economy condos, which each have two rooms arranged either side by side or one above the other. How many different places could an economy condo be configured within the building?



This puzzle was adapted from my 2011 *Mind Benders and Brainteasers Page-a-Day* calendar, published by Workman Publishing. — Scott Kim, [scott@scottkim.com](mailto:scott@scottkim.com)

ANSWERS ON P. 14

Since investigators found both proteins in different accumulation patterns than is typically seen in ALS, they concluded that head injury “results in motor-neuron degeneration, and that the resulting disease is not actually ALS. It is a different disorder... that compromises nerve function.”

**Is the evidence strong enough to suggest head injury can cause motor neuron disease?**

“The study authors are entitled to have any opinion they like regarding the study’s findings,” says Carmel Armon, M.D., professor of neurology at Tufts University School of Medicine and chief of the Division of Neurology at Baystate Medical Center. “My critique is that the data do not provide a factual foundation for the opinion.”

“To make a claim that head injury contributes to ALS—and may even cause ALS—cannot be based on findings seen in just three patients,” Dr. Miller says, adding that the majority of people who have been diagnosed with ALS don’t have a history of repeated head injuries.

“The number of patients I see who played professional [sports] or had repeated head injuries is infinitesimally small,” Dr. Miller says. “To select three patients who played professional sports and also had repeated head injuries, and to say on the basis of those three patients that this probably is the cause of ALS is ludicrous.”

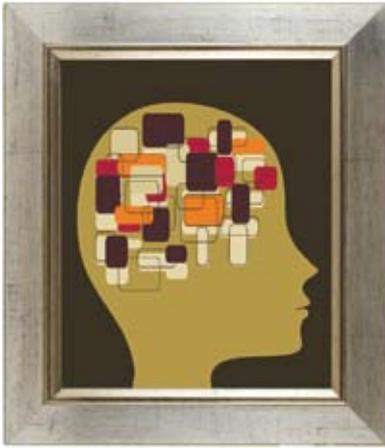
**Where can I go for more information?**

The sensationalized *Times* article outraged many neurologists and caused a significant amount of undue anxiety in people with and without ALS, says Dr. Buijn. Many people contacted The ALS Association with their concerns, from those who believed they had been misdiagnosed with ALS to those who were worried they might develop ALS due to a head injury.

The ALS Association released a Q&A on the article in an attempt to alleviate patients’ confusion and unease. Here are a few other resources to help you read health and science news with a critical eye.

 **CLICK AND CONNECT!** Access the links in this article by reading it on [neurologynow.com](http://neurologynow.com).

- ▶ **Lies, Damned Lies, and Science:** How to Sort through the Noise around Global Warming, the Latest Health Claims, and Other Scientific Controversies, Sherry Seethaler (FT Press, 2009)
- ▶ **Neurology Now,** “Miracle Drug! Or Not”: [bit.ly/963HoW](http://bit.ly/963HoW)
- ▶ **Neurology Today,** “Does Concussion Cause Motor Neuron Disease?: The Question Stirs Debate”: [bit.ly/9TF1dl](http://bit.ly/9TF1dl)
- ▶ **News and Numbers:** A Guide to Reporting Statistical Claims and Controversies in Health and Other Fields, Victor Cohn and Lewis Cope (Iowa State Press, 2001)
- ▶ **The ALS Association’s** Q&A on Head Trauma: [bit.ly/cZikU7](http://bit.ly/cZikU7)



## GET INVOLVED

### Donate Your Art to Help in the Fight to End Brain Disorders

Join us in the fight to end brain disorders by donating your artwork to the 2011 Art & Auction for Research, a fundraiser for the American Academy of Neurology Foundation. Donated art will be auctioned at the American Academy of Neurology's 63rd Annual Meeting, where more than 10,000 attendees are able to bid on your artwork.

Donate your art by visiting [aan.com/patients](http://aan.com/patients). The deadline is February 14, 2011.

## SHARE YOUR STORY

### Win up to \$1,000 and a trip to the 2011 Neuro Film Festival in Hawaii!

#### neuro film festival

SM Have you or a loved one been affected by a neurologic disorder? Do you have a story to share? Then submit

a short video to the 2011 Neuro Film Festival at [neurofilmfestival.com](http://neurofilmfestival.com).

The second annual Neuro Film Festival, presented by the American Academy of Neurology Foundation (AANF), aims to raise awareness about the need to fund research into the prevention, treatment, and cure of brain disorders such as Alzheimer's disease, stroke, autism, Parkinson's disease, and multiple sclerosis.

Winners of the 2011 Neuro Film Festival could win up to \$1,000 and a chance to attend the Neuro Film Festival in Hawaii on April 10, 2011, in conjunction with the AAN's 63rd Annual Meeting, which is the world's largest meeting of neurologists.

Last year's event was the first of its kind.

"The 2010 Neuro Film Festival exceeded our expectations, with more than 65 videos accepted into the contest," says Christine E. Phelps, deputy executive director of the AANF. "Because of the compelling and heartfelt stories submitted to the Neuro Film Festival, we're able to raise awareness about the need to donate to the American Academy of Neurology Foundation to support research, which may ultimately lead to treatments or cures for hundreds of devastating brain disorders."

You can view the entries on the Neuro Film Festival's YouTube channel, [youtube.com/neurofilmfest](http://youtube.com/neurofilmfest).

*Tracking Evan*, a 2010 winner, offers an inside look at how one family coped with their son's tuberous sclerosis and epilepsy by creating an online tool for logging seizures and medications. *CJD*, another 2010 winner, shares the experiences of a California physician whose wife developed Creutzfeldt-Jakob disease (CJD), a rare brain disease that causes dementia and other neurologic symptoms.

Video submissions to the Neuro Film Festival should be made at [neurofilmfestival.com](http://neurofilmfestival.com) by February 15, 2011. Videos should be



2010 Neuro Film Festival Storyteller Prize winner *CJD, A Personal Story* by Shenly Glenn of San Francisco, California

no more than five minutes in length. Each film must include the phrase, "Let's put our brains together to support brain research. Visit [www.neurofilmfestival.com](http://www.neurofilmfestival.com)."

A complete list of contest rules and a video showing how to submit to the Neuro Film Festival is available at [neurofilmfestival.com](http://neurofilmfestival.com), on the Neuro Film Festival's YouTube channel, and via the Neuro Film Festival page on Facebook®.

## NEUROBICS ANSWERS CONTINUED FROM P. 13

1. There are 8 places for a 2x2x2 luxury condo within the building — one touching each corner of the building.
2. There are 36 places for a 2x2x1 mid-range condo within the building — 4 for each of the 3 floors for a total of 12 one-story condos, and twice that number for two-story condos.  $12+24=36$ .
3. There are 54 places for a 2x1x1 economy condo within the building — 12 for each of the three floors, 9 that span the lower two floors, and 9 more that span the upper two floors.  $12+12+12+9+9=54$ .

ARTWORK: TOP: CHUWY/ISTOCKPHOTO; BOTTOM: JAYESH/ISTOCKPHOTO; FRAMES: TOP: DAVE WHITE/ISTOCKPHOTO; BOTTOM: ELIZA SNOW/ISTOCKPHOTO