

Fever-induced seizures cause brain changes

Convulsions triggered by high fevers strike up to 5 percent of infants and young children. Physicians generally regard such episodes as benign because they seldom lead to neurological problems in adulthood. A new study in rats, however, indicates that prolonged fever-induced convulsions, or febrile seizures, cause long-lasting changes in the brain, perhaps rendering it more prone to epilepsy.

"It's quite likely that if what we see in rats holds true in children, these fever-induced seizures lower the threshold for later seizures," says Ivan Soltesz of the University of California, Irvine, one of the study's investigators. Some researchers disagree with that interpretation of the findings, however.

Soltesz and his team used a procedure established by their Irvine coauthor Tallie Z. Baram to mimic a fever, or hyperthermia. By raising body temperatures in 10-day-old rat pups to about 41°C, comparable to children's high fevers, they stimulated seizures lasting at least 20 minutes. One week later, the researchers measured the chemistry of neurons in the hippocampus, the part of the brain involved in the most common form of adult epilepsy.

In the August *NATURE MEDICINE*, the team reports that the rat pups showed pronounced changes in communication between nerve cells in the hippocampus. These changes persisted even 10 weeks later, when the animals had reached maturity.

The rats showed long-lasting increases in an enzyme called protein kinase A, which in turn caused greater release of the chemical messenger GABA. When GABA floods the gaps, or synapses, between neurons, it inhibits activity in the hippocampus. Rats in a group that was not induced to have seizures showed no rise in protein kinase A or GABA.

The effects the scientists observed appear to be unique to heat-induced convulsions. When they gave another group of rat pups a drug that causes seizures, they later found no difference between animals that had had convulsions and those that hadn't. Similarly, pups that were exposed to heat but given a drug to prevent seizures exhibited no changes in brain activity.

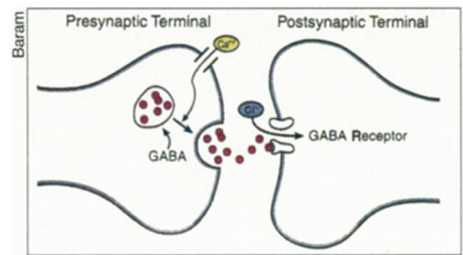
In an editorial accompanying the article, Matthew C. Walker and Dimitri M. Kullmann of University College London disagree with Soltesz's view that the changes caused by febrile seizures might make further seizures more likely. They suggest that febrile seizures may instead protect the brain. "Whether something is benign or malignant should be determined on the grounds of whether there's some evidence that the alterations have consequences for the health of the ani-

mal," Kullmann told *SCIENCE NEWS*.

Soltesz notes, however, that preliminary results of further experiments suggest that the pups that experienced heat-induced seizures may become more prone to seizures as adults. The researchers speculate that the GABA inhibition sets the stage for further seizures by priming cells in the hippocampus to fire simultaneously.

"It's a very interesting study because it shows that, at least in animals, febrile seizures can lead to long-lasting changes in neuronal excitability in the hippocampus," comments William H. Theodore of the National Institute of Neurological Disorders and Stroke in Bethesda, Md. "It's impossible to know, of course, whether you would see the same kinds of changes in humans, but one can certainly speculate that a similar mechanism might occur."

"The question of whether febrile seizures cause epilepsy has been incredi-



Inhibitory neurons release GABA (red) into the synapse between neurons in the hippocampus. After heat-induced seizures, rat pups release more GABA than control pups do. GABA, in conjunction with calcium and chloride ions, inhibits neuron activity.

bly controversial," says Baram. "We don't think all prolonged febrile seizures actually cause epilepsy. However, we can take a normal brain where there are no predisposing [abnormalities] and induce persistent changes in it with these seizures. We now need to know what those changes mean." —S. Carpenter

High-protein diets may help hearts

Much of the dietary advice directed in recent years at patients with heart disease has extolled the virtue of cutting down on fat by limiting consumption of meat and eating more vegetables.

Now comes a study that challenges the conventional wisdom. In terms of the heart, it finds, protein-rich meat may be healthier than those carbohydrate-rich veggies.

Since 1980, nutritional epidemiologists at the Harvard School of Public Health in Boston have been probing links between diet and health in female nurses. In their latest study, the researchers looked at protein consumption among 80,082 of the nurses, analyzing their diets at 2-to-4-year intervals through 1994. The survey sample included 658 nurses who had suffered heart attacks and another 281 who died from heart disease.

Women consuming the most protein—taking in some 24 percent of their calories in that form—faced just three-quarters of the heart-disease risk seen in the women deriving a mere 15 percent of their calories from protein. What's more, animal protein appeared as protective as protein derived from plants, report Harvard's Frank B. Hu and his team in the August *AMERICAN JOURNAL OF CLINICAL NUTRITION*.

A 1991 study at the University of Western Ontario in London switched 10 men and women at risk of heart disease between diets low or high in protein. During the high-protein phase, the participants' blood concentrations of triglycerides and low-density lipoproteins fell, while high-density-lipoprotein

concentrations climbed. All were changes that should reduce heart-disease risk, notes endocrinologist Bernard M. Wolfe, who headed that study.

A follow-up study in healthy people, due out soon in the *JOURNAL OF CLINICAL AND INVESTIGATIVE MEDICINE*, will report similar protein benefits. However, Wolfe notes, "in the healthy subjects, you don't see quite as big a change."

Such findings led Meir J. Stampfer, a coauthor of the new Harvard analysis, to expect that protein consumption would boost heart health in the nurses. "What did surprise me," he says, "was that the effect was so much stronger than I anticipated."

Alice H. Lichtenstein of Tufts University in Boston cautions that increasing the proportion of protein in the diet inevitably comes at the expense of fat and usually carbohydrates. So, teasing out whether any benefits trace to more protein versus less carbohydrate or fat becomes nearly impossible, she says.

Marion Nestle of New York University observes that there were major lifestyle and dietary differences between the high-protein and low-protein groups that may have contributed to the incidence of heart disease. For example, the high-protein group took more multivitamins and ate less red meat. Both she and Lichtenstein agree, however, that the provocative Harvard findings deserve to be investigated further.

Although the nurses in the study consumed most of their protein from animal sources, Stampfer says, "I still favor a low-meat diet for good health, particularly one with little red meat." —J. Raloff