THIS WAY IN

# New Research Into Epilepsy

BY PEGGY EASTMAN

New research is bringing hope to people who have seizures, according to speakers at a conference in Bethesda, MD, sponsored by the National Institute of Neurological Disorders and Stroke (NINDS), part of the federal National Institutes of Health.

"Progress in the last six years provides cause for optimism," said James O. McNamara, M.D., professor of neurosciences at Duke University School of Medicine, at the NINDS conference, called Curing the Epilepsies 2013: Pathways Forward. "I look at this glass today as half full and not half empty," he adds.

About 2.3 million Americans have epilepsy, a brain disorder characterized by a person's continuing tendency to have seizures. A seizure, which is caused by the abnormal or excessive activity of brain cells, can cause temporary loss of awareness or consciousness and disturbances of movement, sensation, mental function, or mood. Just as there are different forms of epilepsy, scientists say there are probably different causes of seizures. New clues to some of these causes are emerging.

## CHILDHOOD EPILEPSY LINKED TO HPV

In one tantalizing new finding reported at the NINDS conference, researchers have linked a widespread virus to a common form of childhood epilepsy. Researchers led by Peter Crino, M.D., Ph.D., professor of neurology at Temple University and Shriners Hospitals Pediatric Research Center in Philadelphia, PA, found human papillomavirus type 16 (HPV16) in the brains of children with focal cortical dysplasia, which is found in about half of people with epilepsy that doesn't respond to drug therapy.

HPV16 is also known to cause cervical cancer in women. Infection with HPV16 is thought to have been passed to the children's brains from their mothers during the babies' development in the womb. Dr. Crino found evidence of HPV16 in 50 brain tissue samples of patients with focal cortical dysplasia. Dr. Crino examined 36 brain tissue samples from patients who did not have focal cortical dysplasia, and none of the 36 samples tested positive for HPV16.

His finding does not prove that HPV16 *causes* this form of childhood epilepsy, Dr. Crino is quick to say. More research is needed. But, he notes, if further studies confirm his research, it may be possible to prevent focal cortical dysplasia. That's because two vaccines, Gardasil and Cervarix, protect against HPV16. "HPV infection is an epidemic, and it has prompted the medical community to recommend large-scale vaccination," he says.

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## RENEWED INTEREST IN KETOGENIC DIET

Other research presented at the NINDS conference offered a glimpse into how the high-fat, low carbohydrate ketogenic diet works to prevent seizures. "What is perhaps most intriguing about recent studies of the ketogenic diet is the evidence for its broad protective properties on nerve cells in the brain," says Jong Min Rho, M.D., professor of pediatrics and clinical neurosciences at the University of Calgary, Alberta, Canada. This protective effect seems to decrease seizures in some people, he notes. Although the mechanisms are not well defined, he notes that scientists be-

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lieve the protection results from reduced inflammation along with added reserves of energy for nerve cells.

The ketogenic diet is most effective in children, Dr. Rho tells *Neurology Now*, but staying on the diet is not easy. Because the ketogenic diet is extremely high in fat, and carbohydrates are nearly eliminated, it is very different from the typical American diet. In fact, the ketogenic diet mimics the biochemical changes that occur when people have limited access to food. Because maintaining this diet is a challenge, he cautions that a team of medical specialists, including a dietician, is necessary to help families implement it. "My experience is that whether the diet works or not is largely dependent on the dietician," Dr. Rho says.

Asked if there are any harmful side effects from the diet because it is high in fat, such as an increased risk of heart disease, Dr. Rho says there do not seem to be. According to a 24-week study of obese patients on the ketogenic diet, the level of total cholesterol (a risk factor for heart disease, if it is high) actually decreased. HDL cholesterol—the good kind—increased significantly, while triglycerides (a risk factor for heart disease, if they are elevated) fell. Although scientists and doctors have worked to improve the effectiveness and tolerability of the ketogenic diet, the ultimate goal—which has not yet been achieved—is creating a "ketogenic diet in a pill," Dr. Rho says.

### SURGERY FOR TREATMENT-RESISTANT SEIZURES

Antiepileptic drugs (AEDs) are effective in controlling seizures in more than two-thirds of people, and AEDs for specific seizure types have recently been approved. But medications fail to control seizures in about 30 percent of people with epilepsy. For these treatment-resistant seizures, surgery should be considered, according to some research presented at the NINDS conference.

Today, surgery is becoming less invasive, and improved imaging techniques are helping us map the brain to find the location of the seizures, notes Edward Chang, M.D., associate professor of neurological surgery and chief of epilepsy surgery at the University of California, San Francisco. Nevertheless, surgery is underused, according to Dr. Chang. Why? "Because many people think brain surgery is too dangerous. Actually, it is very safe overall," he says, adding that surgery should be considered as an option for people who have tried multiple AEDs without success.

### SUDEP

Researchers at the NINDS conference also shed light on sudden unexpected death in epilepsy (SUDEP). According to NINDS figures, about one person dies from SUDEP CONTINUED ON P. 14

MEMORY LANGUAGE AUDIO SPATIAL LOGIC NUMBER

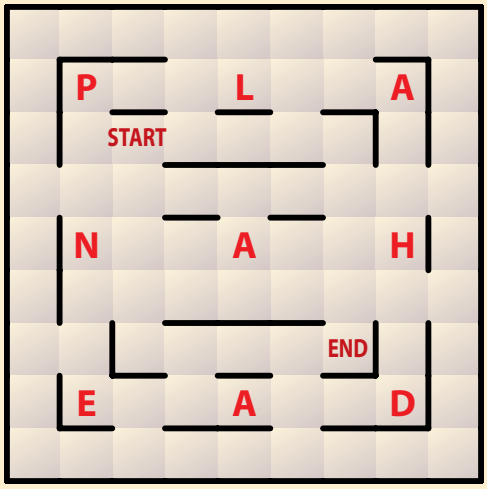
**NEUROBICS**

## Plan Ahead

**This maze will test your executive function.**

Most of the day, we don't think too hard about what we're doing. But when we encounter an unexpected or challenging situation, we have to think harder. The mental processes that allow us to plan ahead, change strategies, and evaluate possibilities are collectively called executive function.

Here is a maze that tests your ability to plan ahead.




**1** (BASIC CHALLENGE) Your goal is to draw a path that starts at START, passes through the letters L-A-H-D in order, and ends at END—without going through walls or visiting any square more than once.

**2** (INTERMEDIATE) Now draw a path that starts at START, passes through all nine of the big single letters, and ends at END—without going through walls or visiting any square more than once. There are many solutions, so find the path that makes the fewest number of turns. To solve this puzzle you will need to plan ahead.

**3** (CHALLENGING) Draw a path that starts at START, passes through the nine letters P-L-A-N-A-H-E-A-D in order, and ends at END—without going through walls or visiting any square more than once. To solve this puzzle you may have to change the strategy you used for #2.

**4** (BRAIN-BUSTING) Draw a path that starts at START, passes through the nine letters to spell two words different from PLAN AHEAD, and ends at END—without going through walls or visiting any square more than once. To solve this puzzle you will have to evaluate many different possibilities. Hint: the two words describe a healthy bear. —*Scott Kim*, scott@scottkim.com

ANSWERS ON P. 14

NEUROLOGY NEWS

# New Website Aims to Improve Patient-Doctor Dialogue


Four years ago, when neurologists Robert Cowan, M.D., and Alan Rapoport, M.D., sat down to talk shop, the subject of headache naturally came up. They are both headache specialists.

"At the time, there were 350 board-certified headache specialists in the United States but an estimated 60 million people living with headaches," recalls Dr. Cowan, clinical professor of neurology and neurological sciences at Stanford School of Medicine, president of the Headache Cooperative of the Pacific, and Fellow of the American Academy of Neurology (AAN). "The numbers didn't add up," he says. "How could 60 million people be adequately served by 350 specialists?"

The two friends wondered, "What if patients could provide their primary care doctors with the kind of detailed medical history used by headache specialists?"

## LAUNCHING PROMYHEALTH

Drs. Cowan and Rapoport set about developing a free, not-for-profit website called ProMyHealth (**promyhealth.org**) to provide this kind of medical history. By using decision-tree analysis (in which answers to questions determine the follow-up questions), ProMyHealth allows a patient to create a detailed report that can be printed, saved, and sent to a doctor, who can then store it as an electronic medical record. Doctors can also modify a report to include any additional information gathered during the visit.

The report is not meant to make a final diagnosis, Dr. Cowan stresses. "The idea is that a patient can go to the website and answer a series of carefully chosen questions—anywhere from about 80 to 340—and share it with his or her doctor. For example, one question might be, 'Do you have trouble sleeping?' If the patient answers yes, the next question might be, 'Do you have trouble falling asleep or staying asleep, or both?' The questionnaire also asks about exercise habits, any history of trauma, and various headache triggers for each individual patient, such as red wine, barometric changes, and menstrual cycle.

Most primary care doctors—and even many neurologists—don't have the hour or two that it would take to get this kind of detailed history, according to Dr. Cowan. He believes the model can "reduce wait time and the number of referrals, hopefully to a point where headache specialists don't have a nine-month wait to see patients."

## CAUTIOUS OPTIMISM

What's interesting about ProMyHealth is that it's geared towards patients, says Alison Weathers, M.D., medical director in the department of information services at Rush University Medical Center and member of the AAN. "Most of these kinds of tools for making a medical diagnosis are created with only the doctor in mind," she says.

However, it's important to be cautious about new healthcare technologies, she stresses; online tools such as ProMyHealth should never replace the face-to-face consultation. "A lot of how the patient tells their story is what guides us as neurologists, and if we're letting the computer get that story for us, we might miss something," Dr. Weathers says.

To listen to the extended interview with ProMyHealth cofounder Robert Cowan, M.D., visit: **http://bit.ly/AkhPNV**.

*—Olga Rukovets*

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per 1,000 people with epilepsy. Men younger than age 60 who have had epilepsy with no known cause for 15 years or more, who have frequent tonic-clonic seizures (formerly called grand mal), and who take multiple AEDs are at highest risk of SUDEP.

Scientists now believe that SUDEP in some people may be due to changes in breathing or heartbeat (see cover story, page 16), which raises the possibility of therapy with drugs that enhance breathing and implantation of cardiac devices to regulate the heart. "It is well known that seizures alter breathing and the activity of the heart," says George B. Richerson, M.D., Ph.D., chair of the Department of Neurology at the University of Iowa.

Because of new findings on SUDEP, Dr. Richerson recommends that all patients who have their brain activity studied for epilepsy should also undergo respiratory monitoring. During respiratory monitoring, a person wears a special device to determine whether there is any shortness of breath or difficulty in breathing.

## FOR MORE INFORMATION

For more *Neurology Now* coverage of epilepsy, go to **http://bit.ly/xMSLvd**.

## NEUROBICS ANSWERS

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