Researchers Testing New Electric Treatment for Migraines

By: **Morgen E. Peck**

4 October 2007—The brain's occipital lobe is usually the first to know when a migraine is coming. In desperation it frazzles the vision, smearing it with dark blotches, changing the perception of light intensity, sometimes even inserting things that aren't there. Only then does the pain come, radiating from the brain and into the rest of the body as fatigue and numbness.

Today, there are no fully satisfying treatments for migraine symptoms. But researchers at Beth Israel Deaconess Medical Center, in Boston, are testing a low-tech treatment that could shock migraine patients back to their senses and provide a cheap alternative to drugs. The technology involved—transcranial direct current stimulation (tDCS)—is simple: stimulate the brain with sudden, controlled bursts of electricity to interrupt and modify the brain circuits responsible for causing migraine pain.

The investigators, Dr. Felipe Fregni and Soroush Zaghi, both of Harvard Medical School, have recruited 24 patients who suffer migraine headaches at least 15 times per month. At scheduled intervals, which may or may not coincide with migraines, Fregni attaches electrodes to a subject's scalp and passes 2 milliamps of current through the brain, targeting the locus of pain. Two months into the study, he is encouraged by what he is seeing. "In the initial sample, the results went in the direction we predicted," he says.

Even if the trial succeeds, much more testing will have to be done in order for medical device regulators to allow a tDCS device to be sold as a migraine treatment in the United States.

At the moment, neuroscientists can only guess why jolting the brain would alleviate chronic migraine pain. "The short answer is that we don't know," Fregni says. One theory of migraines proposes that chronic pain happens when parts of the brain become hyperactive. Under this condition, the brain is less able to deal with the everyday barrage of sights, sounds, and smells. As the hyperactivity of one region spreads to others, it ultimately causes the blood vessels that cradle the brain to dilate (though no one is sure why), putting painful pressure on the organ.

Following that theory, what triggers migraines is just an extreme example of what causes ordinary headaches in the normal brain. "If you stay up all night, three days in a row, and there are loud sounds and bright lights, you're going to get a headache, too," Fregni says. For people with migraines it just takes much less stress because the baseline of activity in certain areas of the brain is much higher, he says.

Neurons, the cells that carry messages throughout the brain, are constantly receiving electrical inputs from surrounding cells. They integrate the voltage signals, and if the total is strong enough the neuron fires—sending a pulse of voltage out to other neurons to which it's connected.

During tDCS, the current hyperpolarizes the afflicted area of the brain, making the neurons less likely to fire. In the short term, the treatment usually staves off

an encroaching attack, but tDCS could have long-term benefits as well. Many studies have determined that when repeatedly exposed to a hyperpolarizing current, neurons eventually become less excitable, a process called long-term depression. The stimulation would take advantage of that phenomenon to prime the migraine-prone regions of the brain so that one great flash of light would not be enough to overload the whole system.

It's a way to "teach the brain to be in a better state," explains Alvaro Pascual-Leone, who directs research at the Behavioral Neurology Unit at Beth Israel.

If the tDCS treatment makes it through clinical trials, migraine sufferers may end up with a treatment safe enough to use without a physician present and whose only side effect would be a slight tingling sensation. Adding to the good news: "I can't see it costing more than $10," Zaghi says.

A similar device, using transcranial magnetic stimulation (TMS), has already been designed for consumers, and a company in Sunnyvale, Calif., called Neuralieve is slowly nudging it into the market. Within a year Neuralieve could be seeking approval from the U.S. Food and Drug Administration to sell the TMS device as a migraine therapy, says a member of the company's scientific advisory board.

A TMS device passes a magnetic field into the brain, producing an electric current in a small volume of brain cells. The current is strong enough to cause neurons to fire, but scientists are just beginning to understand magnetic stimulation's effects in the brain. In a report published in the 28 September issue of Science, University of California, Berkeley, scientists showed that whether TMS increases activity in a stimulated brain region depends on what that part of the brain was doing before the stimulation started.

When the Neuralieve device is applied to a person suffering from a migraine, the sudden excitation interrupts a wave of hyperactivity, recalibrating the brain before it can get out of control and lead to a migraine, says Dr. Yousef Mohammad, a neurologist at Ohio State University Medical Center who is testing the device in advanced clinical trials. "If you have a fire in the forest, the fire will spread from one tree to the other," he says. "What we're doing with TMS is cutting a few trees in the middle."

Because neurons are actually firing during TMS, the device will likely not have the same long-term therapeutic effect that tDCS seems to have; it probably will be useful only for interrupting the nascent tremors of a migraine.

Both tDCS and TMS are under investigation as treatments for depression and other psychiatric disorders.