Researchers connect electrical brain disturbances to worse outcomes following neurotrauma

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Electrical disturbances that spread through an injured brain like tsunamis have a direct link to poor recovery and can last far longer than previously realized, researchers at the University of Cincinnati Neuroscience Institute (UCNI) have found.

The disturbances, known as cortical spreading depolarizations, are short-circuits (electrical failures) that occur in a localized, or specific, area of injury and result in dampened brain waves. Because of their localization, the depolarizations are invisible in routine electroencephalography (EEG) exams. But they represent an extreme change in voltage—up to 10 times greater than any brain pattern that is normally present.

"Over the last several years we've learned how to measure and record spreading depolarization in the human brain, and we have known that these depolarizations occur in many patients who have suffered neurotrauma," says Jed Hartings, PhD, research assistant professor in UC's department of neurosurgery and director of clinical monitoring for the Mayfield Clinic. "But we didn't know what they meant or whether they were relevant. For the first time we now know that they relate to worse outcomes for patients who have suffered trauma to the brain."

That finding, Hartings adds, could eventually lead to new therapies. "If we can find a way to stabilize the brain's electrical activity and block spreading depolarizations, perhaps we can improve patients' outcomes."

An Advance Access, online version of the research, published April 7 by the neurology journal *Brain* appears online in its complete, paginated form today.

The observational, multi-site study of 53 patients represents the initial phase of a four-year, $1.96 million grant awarded by the Department of Defense (DOD). The topic of spreading depolarizations is of keen interest to the U.S. military because head injuries have emerged as the signature wounds of the wars in Iraq and Afghanistan.

Of the study's 53 participants, 10 had experienced the most severe form of depolarizations. All died or had severe disabilities six months after their injury.

"Spreading depolarizations, which occur in up to 60 percent of patients who have experienced serious neurotrauma, are electrical failures of the brain's local networks," explains Hartings, the study's principal investigator. "When these networks fail, brain waves can no longer be generated, and they become dampened, or depressed, in amplitude."

Hartings likens each brain cell, or neuron, to a battery. When spreading depolarization occurs, the cell discharges its electricity completely. "The neuron, once alive with electrical activity, stops working and has to be resuscitated with glucose and oxygen," Hartings says. "You could also liken it to a battery in your car. If it drains, then the car doesn't work."

Because networks of the brain's cortex are connected in a continuum, a depolarization triggered by an injury will spread across the cortex like a tsunami on the ocean. The wave of short-circuiting cells travels almost imperceptibly, at a speed of 1 to 5 millimeters per minute.

Previous studies had suggested that depolarizations would last no longer than two or three minutes. But Hartings and his team have shown that, after trauma, they can be very long-lasting.

"We found that 25 percent of the cortical spreading depolarizations lasted longer than three minutes, with durations that ranged up to 16 minutes," Hartings says. "These are the types of depolarizations that are typically observed with a developing brain infarction, or stroke. It was a surprise to see them in trauma."

To measure depolarizations, researchers placed a linear strip of electrodes on the surface of the brain, near the injured area, during neurosurgery at UC Health University Hospital. Only patients who required neurosurgery to treat their injuries were enrolled in the study. The electrode strip records computerized brainwaves similar to those of an EEG. But whereas EEG electrodes are placed on the scalp, spreading depolarization electrodes must be placed inside the skull, on the surface of the brain. The electrodes are removed three to seven days after implantation, without additional surgery.

New technology enabled the researchers not only to determine whether or not spreading depolarizations were occurring, but also—for the first time—to measure their duration. "A new signal-processing technique that we developed allowed us to measure exactly how long the cerebral cortex remains short-circuited, or depolarized," Hartings says. "This measurement—called the direct-current shift duration—is a direct index of how harmful the depolarization is, and of the brain's degree of injury."

The signal-processing technique is a computer program that Hartings and his colleagues published in 2009 in the *Journal of Neurophysiology*.

The spreading depolarization grant is being issued through the DOD's Psychological Health and Traumatic Brain Injury (PH/TBI) Research Program (formerly known as the Post Traumatic Stress Disorder/TBI

Research Program). Hartings' co-investigator at UC is Lori Shutter, MD, director of the Neurocritical Care Program at UCNI and associate professor of neurosurgery and neurology at UC. Also participating are researchers at the University of Miami, University of Pittsburgh, Virginia Commonwealth University and King's College Hospital in London.

UC began enrolling patients in early 2009. Patients in the study are not U.S. soldiers, but rather individuals who have suffered brain injury through falls, vehicular accidents, or other misfortunes.

More information: http://brain.oxfordjournals.org/

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