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Tsunami in the brain

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After a stroke, even unaffected areas of the brain are at risk – depolarization waves arise at the edges of the dead tissue and spread through the adjacent areas of the brain. If these waves are repeated, more cells die. This has previously been observed only in animal studies.

A clinical study at the university hospitals of Cologne and Heidelberg along with the Max Planck Institute of Neurological Research in Cologne has shown for the first time that this phenomenon occurs after a stroke in humans and is a warning sign that more nerve cells will die. The study, published in June 2008 in the renowned journal *Annals of Neurology*, may allow to translate more than 60 years of experimental research for the diagnosis and therapy of stroke patients.

More than 150,000 people a year in Germany suffer a cerebral stoke, the third most frequent cause of death in industrialized countries. When deposits clog vessels to the brain, some areas of the brain do not receive sufficient oxygen and the tissue dies. Depending on the size of the area affected, the patients may die or suffer permanent damage such as paralysis.

Spreading depolarizations first proven in stroke patients

The depolarization waves in the brain – known as cortical spreading depression (CSD) – have been studied only experimentally since the 1940s. Many features are thus known from animals – the waves of depolarization that can spread out at a speed of two to five millimeters

per minute are followed by silence – brain activity comes to a halt for a short time. In this time, the nerve cells recover. "The impact of these waves is several times greater for nerve cells than an epileptic seizure," says Professor Dr. Rudolf Graf from the Max Planck Institute of Neurological Research and co-founder of the international study group COSBID (Cooperative Study on Brain Injury Depolarisations).

"After the stroke, circulation in the tissue surrounding the affected area of the brain is initially poor, but it can still be saved," explained Dr. Christian Dohmen of the Neurology Department at Cologne University Hospital. The spreading depolarizations additionally impair the metabolism of the weakened nerve cells. "The more frequently such waves occur, the longer the nerve cells require to recover, until finally they die off entirely," says the main author of the study. To what extent the brain is damaged after a stroke depends thus on the number of these spreading depolarizations. This correlation is becoming apparent in humans as well.

Know-how from 60 years of research can now be used for treating stroke patients

The spreading depolarizations, which also occur after head injuries or hemorrhages, can be measured only on the surface of the brain. For this study, the physicians therefore selected 16 patients whose brain had to be partially exposed due to a life threatening swelling of brain tissue. Electrodes were applied to the surface of the brain around the affected tissue (electrocorticography), the incisions were closed, and brain waves were measured for five days. All patients were in an artificial coma during this period due to their serious condition.

"Our study puts an end to the discussion as to whether these waves also occur in a human brain following a stroke," says Dr. Oliver Sakowitz,

physician at the Department of Neurosurgery of the University of Heidelberg Hospital and co-author of the study. Now comes the question of how to prevent or at least contain them. "As they cause additional damage to the weakened tissue surrounding the stroke area, it is conceivable that we could prevent further damage by suppressing the waves," said the neurosurgeon.

In previous experimental studies on animals, a few therapy approaches were already developed which physicians can now apply. "The spreading depolarizations are a warning sign that other areas of the brain are at immediate risk and may be also useful as diagnostic measures," says Dr. Sakowitz. In a follow-up study on a larger number of stroke patients, the COSBID team under the direction of Dr. Christian Dohmen wants to clarify whether cortical spreading depression has an influence on the extent of sequelae such as paralysis.

Source: University Hospital Heidelberg