Brain's immune system may cause chronic seizures

July 6 2009

(PhysOrg.com) -- Chronic seizures caused by traumatic head injuries may result from chemicals released by the brain's immune system attempting to repair the injured site, according to a study led by the University of Colorado at Boulder.

The findings could help prevent one of the most common forms of adult epilepsy, called acquired epilepsy, which is often found in people who have suffered a brain injury or infection, according to CU-Boulder psychology and neuroscience Professor Daniel Barth, the study's chief author.

For decades researchers have focused on neurons as the culprits in seizures, which can be characterized as debilitating "electrical storms" in the brain.

However, recent research has shown that micro-glial cells may play a major role in seizures. Researchers have found that glial cells, which are supportive cells that also constitute a major part of the brain's immune system, cluster within areas in the brain when a severe brain injury has occurred.

"When there has been serious damage to the brain, such as a head injury or infection, the immune system is activated and tries to counteract the damage and repair it," Barth said. "These glial cells migrate to the damaged area and release chemicals called cytokines that, unfortunately, also profoundly increase the excitability of the neurons that they are

near.

"In our new study, we showed for the first time that glial cells moving in and secreting these cytokines cause the neurons in the area to become excitable enough to cause seizures."

The results of the study appear in the July issue of the journal *Brain*. Barth co-authored the paper with CU-Boulder professors of psychology and neuroscience Linda Watkins and Steven Maier, CU-Boulder graduate students Krista Rodgers and Alexis Northcutt and Professor Mark Hutchinson of the University of Adelaide in Australia. The National Institutes of Health funded the study.

Acquired epilepsy is one of the few forms of epilepsy that has the potential for being prevented, because known head injuries are often followed by latent periods when changes in the brain lead to the development of chronic seizures.

The findings are extremely promising, according to Barth, because if the brain's initial immunity reaction could be temporarily shut down, this could prevent the development of acquired epilepsy.

"After a traumatic brain injury, there is often a period of several months where nothing seems to be happening," Barth said. "And then suddenly the person may start having seizures, which often develop into chronic epilepsy."

What the research team believes is happening is that the initial immune response to the brain injury causes the first seizures. Then the adaptive immune system, which works on a longer-term basis, kicks in and makes structural changes in the brain, which could perpetuate epilepsy as a life-long condition, said Barth.

Drugs are available on the market that suppress the immune system temporarily, Barth said. Even more promising are drugs currently under Food and Drug Administration trials for human use that cross the blood-brain barrier, which in simple terms means patients can take a pill which will effectively suppress the glial cells and stop them from reacting.

"The thought is that maybe there is a window of opportunity where we could go in after an injury and administer one of these immune response inhibitors and stop a process that we think is going to lead to epilepsy," Barth said. "So instead of giving anti-seizure drugs, which have no effect in preventing or subsequently treating post-traumatic epilepsy, we could give some anti-immune drugs which may actually stop the process of developing epilepsy in the first place."

The research team came to its conclusions through a series of experiments with rats in which they applied a bacteria called lipopolysaccharide, or LPS, to the brain, activating the micro-glial cells. The glial cells very rapidly clustered around the area where the LPS was applied and created an immune reaction in that locale.

The glial cells then released their cytokines, causing the neurons to become excitable enough to cause seizures. By directly applying other drugs that either blocked the activation of glial cells or the effect of cytokines on neurons, all signs of increased brain excitability and seizures were abolished, Barth said.

Source: University of Colorado at Boulder (news : web)