

Brain inflammation may be friend, not foe, for Alzheimer's patients

June 1 2007

Inflammation in the brain may not be so bad after all when it comes to Alzheimer's disease. In the June 1 issue of the Journal of Clinical Investigation, a team of scientists from the University of Rochester Medical Center shows that a key inflammatory regulator, a known villain when it comes to parsing out damage after a stroke and other brain injuries, seems to do the opposite in Alzheimer's disease, protecting the brain and helping get rid of clumps of material known as plaques that are a hallmark of the disease.

While many scientists have assumed that inflammation as a result of disease or injury only adds to the brain's woes, the new findings show that the opposite may be true when it comes to Alzheimer's disease. Perhaps inflammation is playing the role of protector and is acting more like an ambulance crew helping at the site of a road wreck, not causing the crash.

The work suggests that doctors not rush in to turn off molecular events that scientists have widely considered to be detrimental in people with the disease. The findings could also renew efforts to develop a vaccine or other strategies against Alzheimer's by engaging the body's immune system.

The team expected to see the telltale clumps of material known as amyloid plaques, made up of the peptide amyloid beta, worsen. Instead, to the team's surprise, the brains of the mice with IL-1beta stuck in overdrive had only about half

“This work provides evidence that blocking all inflammatory responses in Alzheimer’s disease is not an ideal therapy,” added Shaftel. “This might hinder processes that are beneficial and part of the body’s adaptive response to fight plaques.”

The new findings hinge on a very special mouse that Shaftel spent three years creating with the guidance of his adviser, M. Kerry O’Banion, M.D., Ph.D., associate professor of Neurobiology and Anatomy. Shaftel genetically engineered a one-of-a-kind mouse that gives him pinpoint control over brain levels of a human molecule known as interleukin-1 beta, a well-recognized molecular kingpin in the realm of inflammation.

IL-1 beta, a signaling molecule that promotes brain inflammation, was one of the first molecules that scientists found in higher levels in the brains of people with Alzheimer’s disease compared to healthy people. It’s recognized as a critical player in bringing about much of the brain damage that follows a stroke and brain injury, so it’s no surprise that its presence in the brains of Alzheimer’s patients would be assumed to be part of the problem.

In the original development of his mouse, Shaftel worked closely with Stephanos Kyrkanides, D.D.S., Ph.D., associate professor in the Eastman Department of Dentistry and an expert on using a class of viruses known as lentiviruses for use in gene therapy. The team used a lentivirus to boost levels of IL-1 beta in select brain regions of its engineered mouse, then applied the technology in mice specially designed to develop Alzheimer’s disease.

The mice developed normally for six months. Then Shaftel raised the level of IL-1 beta in one part of the brain –the hippocampus, an area of the brain that specializes in memory and one of the first parts of the brain to be affected by the disease – and followed the mice for an

additional month, watching for effects in the brain regions that were awash in higher-than-normal levels of IL-1beta. It's the first use of an organism where scientists can boost IL-1beta in select areas and then watch what happens as the process unfolds.

The team expected to see the telltale clumps of material known as amyloid plaques, made up of the peptide amyloid beta, worsen. Instead, to the team's surprise, the brains of the mice with IL-1beta stuck in overdrive had only about half as many plaques as mice without the over-active IL-1beta.

Through extensive experiments, the team showed that the mice simply weren't making fewer plaques, but rather that the body was better at getting rid of the plaques. The team suspects the involvement of brain cells called microglia, the major immune cell that rushes to injury sites and helps repair and clean up wounds in the brain.

The work is the latest in a growing body of research that is trying to determine the exact role of inflammation in Alzheimer's disease.

O'Banion notes that some studies have found that taking medications to squelch inflammation, such non-steroidal anti-inflammatory drugs or NSAIDs, might help reduce a person's chances of getting Alzheimer's disease, while other studies, including a study of more than 2,100 people published in April, refute that notion.

"There is a great deal of evidence that inflammation plays a potentially negative role in Alzheimer's disease," said O'Banion. "But much of the evidence comes from experiments with cells in a dish or postmortem human tissue, not from living organisms in which disease progression is closely monitored.

"People have talked for a long time about a balance of 'good guys' and 'bad guys' within the inflammatory process, either causing harm or

alleviating the disease. The current work reinforces the idea that inflammation is not simply the bad guy that many people think it is.”

The work could have ramifications for the development of a vaccine or other strategy to protect against or fight off Alzheimer’s. Work on an Alzheimer’s vaccine has at times been promising, reducing the number of plaques in the brains of animals and a few people with the disease, but it’s also been fraught with difficulty, producing side effects such as encephalitis or severe brain inflammation in people with Alzheimer’s.

“The potential to treat Alzheimer’s disease by modulating the immune system is tremendous and is an area that has not been fully explored,” said O’Banion. “That said, people have to remember that the current findings are in mice, not people. We need to be cautious about how to interpret the results.”

Source: University of Rochester Medical Center

Citation: Brain inflammation may be friend, not foe, for Alzheimer's patients (2007, June 1) retrieved 9 April 2024 from <https://medicalxpress.com/news/2007-06-brain-inflammation-friend-foe-alzheimer.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--