Research identifies how inflammatory disease causes fatigue

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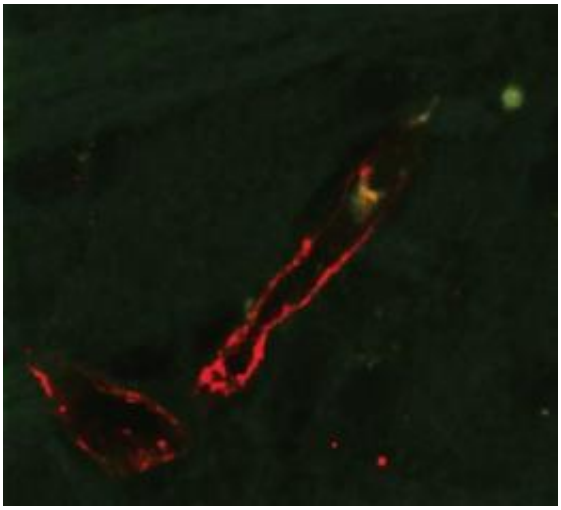

Image showing a brain blood vessel (outlined in red) and a monocyte within the blood vessel and adherent to the vessel wall (yellow), and a monocyte within the brain after being recruited from the blood (green) in a mouse with liver inflammation. Credit: The Journal of Neuroscience

New animal research in the February 18 issue of *The Journal of Neuroscience* may indicate how certain diseases make people feel so tired and listless. Although the brain is usually isolated from the immune system, the study suggests that certain behavioral changes suffered by those with chronic inflammatory diseases are caused by the infiltration of immune cells into the brain. The findings suggest possible new treatment avenues to improve patients' quality of life.

Chronic inflammatory diseases like rheumatoid arthritis, inflammatory bowel disease, psoriasis, and liver disease cause "sickness behaviors," including fatigue, malaise, and loss of social interest. However, it has been unclear how inflammation in other organs in the body can impact the brain and behavior.

The researchers found that in mice with inflamed livers, white blood cells called monocytes infiltrated the brain. These findings support previous research demonstrating the presence of immune cells in the brain following organ inflammation, challenging the long-held belief that the blood-brain barrier prevents immune cells from accessing the brain.

"Using an experimental model of liver inflammation, our group has demonstrated for the first time the existence of a novel communication pathway between the inflamed liver and the brain," said the study's senior author Mark Swain, MD, Professor of Medicine at the University of Calgary.

Swain and his colleagues found that liver inflammation triggered brain cells called microglia to produce CCL2, a chemical that attracts monocytes. When the researchers blocked CCL2 signaling, monocytes did not enter the brain despite ongoing inflammation in the liver.

Liver inflammation also stimulated cells in the blood to make an immune chemical (TNFα). When the researchers blocked the signaling of this immune chemical, microglia produced less CCL2, and monocytes stayed out of the brain.

In the mice with inflamed livers, preventing the entry of monocytes into the brain reduced sickness behaviors; mice showed more mobility and social interaction. These findings suggest that people with chronic inflammatory diseases may benefit from treatments that limit monocyte access to the brain.

"Sickness behavior significantly impacts quality of life. Our findings further our understanding and may generate potential new avenues for treatment of these often crippling symptoms," said Swain.

"The brain is the master coordinator of many of our bodies' defense responses, so it must be able to sense injury and inflammation in distant body organs. This study starts to explain the peripheral communication signals that activate the brain," said Nancy Rothwell, PhD, DSc, at the University of Manchester, an expert on brain inflammation who is unaffiliated with the study.

On the web: www.jneurosci.org/

Source: Society for Neuroscience