Study identifies source of fever

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With the finding that fever is produced by the action of a hormone on a specific site in the brain, scientists have answered a key question as to how this adaptive function helps to protect the body during bacterial infection and other types of illness.

Reported by researchers at Beth Israel Deaconess Medical Center (BIDMC), the study results appear today in Nature Neuroscience's Advance Online Publication.

"This study shows how the brain produces fever responses during infections," explains senior author Clifford Saper, MD, PhD, Chairman of the Department of Neurology at BIDMC and James Jackson Putnam Professor of Neurology and Neuroscience at Harvard Medical School. "Our laboratory identified the key site in the brain at which a hormone called prostaglandin E2 (PGE2) acts on a target, called the EP3 receptor, on neurons to cause the fever response."

During periods of inflammation, such as when the body is fighting an infection or illness, the body produces hormones known as cytokines. The cytokines, in turn, act on blood vessels in the brain to produce PGE2.

"PGE2 then enters the brain's hypothalamus, causing fever, loss of appetite, fatigue and general feelings of sickness and achiness," says Saper, explaining that these common symptoms of illness function as an adaptive response to enable the body to better fight infection.

“When body temperature is elevated by a few degrees, white blood cells can fight infections more effectively. Also, individuals tend to become achy and lethargic. Consequently,” he adds, “they tend to take it easy, thereby conserving their energy so that they can better fight the infection. That is why so many different types of illness result in more or less the same sickness behaviors.”

To this point, the specific neurons on which PGE2 was acting to produce fever were unknown. Saper and his colleagues created a knockout mouse in which the gene for the EP3 receptor – which registers the presence of PGE2 – could be removed in one part of the brain at a time.

“This was the first time that anyone has been able to remove the receptor at a single spot in the brain,” says Saper. “As a result, we are able to definitively say that this particular site in the brain – only a little bigger than the head of a pin – is where prostaglandins work to cause the fever response.

“We think that the other aspects of sickness behavior, such as the achiness caused by increased sensitivity to pain, also come from specific sites in the brain,” he adds. “We plan to use this same approach to dissect the brain’s response to inflammation, and find out why people feel the way they do when they are ill.”

Source: Beth Israel Deaconess Medical Center