# Researchers discover paradox about general anesthesia: It can increase post-surgical pain

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The general anesthesia that puts patients into unconscious sleep so they do not feel surgical pain can increase the discomfort they feel once they wake up, say researchers from Georgetown University Medical Center. They say their findings, the first to scientifically explain what has been anecdotally observed in the clinic, may lead to wider use of the few anesthetics that don't have this side effect, or to the development of new ones.

In the June 23rd issue of the Proceedings of the National Academy of Sciences (PNAS), the scientists report that "noxious" anesthesia drugs - which most of these general anesthetics are - activate and then sensitize specific receptors on neurons in the peripheral nervous system. These are the sensory nerves in the inflammation and pain pathway that are not affected by general anesthesia drugs that target the central nervous system – the brain and the spinal cord.

"The choice of anesthetic appears to be an important determinant of post-operative pain," says the study's lead investigator, Gerard Ahern, Ph.D., an assistant professor in the Department of Pharmacology at Georgetown University Medical Center. "We hope these findings are ultimately helpful in providing more comfort to patients."

It has long been known that general anesthetics cause irritation at the infusion site or in the airways when inhaled, Ahern says. And investigators have also known that while they suppress the central nervous system, they can activate so called "pain-sensing" or nociceptive

nerve cells on the peripheral nervous system – in fact, anesthesiologists often first use a drug to suppress inflammation and pain before delivering the anesthesia to put the patient to sleep.

But what has not been understood is the specific mechanism by which anesthetics affect sensory neurons, or that they can continue to cause pain and inflammation even as they are being used during surgery, he says.

The researchers tested the hypothesis that two specific receptor on the nerves cells (TRPV1 and TRPA1) which are often expressed together and which also react to other irritants, such as garlic and wasabi, were the ones activated by the noxious drugs.

"Plants produce chemicals such as capsaicin, mustard and garlic that were meant to stop animals from eating them. When they are eaten, the two main receptors that react to them are TRPV1 and TRPA1," he says. In fact, TRPA1 is more commonly known as the mustard-oil receptor, and is a principal receptor in the pain pathway, Ahern says.

Experiments showed that general anesthetics appear to regulate TRPA1 in a direct fashion, and are thus responsible for the acute noxious effects of the drugs. Perhaps the strongest evidence is that mice bred without TRPA1 genes demonstrate no pain when the drugs are administered and used, Ahern says. "Most general anesthetics activate the mustard oil receptor, and animals that don't have the receptor don't have irritation," he says.

The research team also found that nerve-mediated inflammation was greater when pungent (chemical irritants) versus non-pungent inhaled general anesthetics were used.

What both findings suggest is that sensory nerve stimulation throughout

the body just before and during surgery adds to the pain that is felt after the patient is awake, Ahern says. "This is a provocative finding in terms of the clinical setting, because it was not really recognized that use of these drugs results in release of lots of chemicals that recruit immune cells to the nerves, which causes more pain or inflammation."

Some general anesthetics do not activate the mustard-oil receptor, but they may not be as effective in other ways, Ahern says. "This tells us that there is room for improvement in these drugs."

Source: Georgetown University Medical Center