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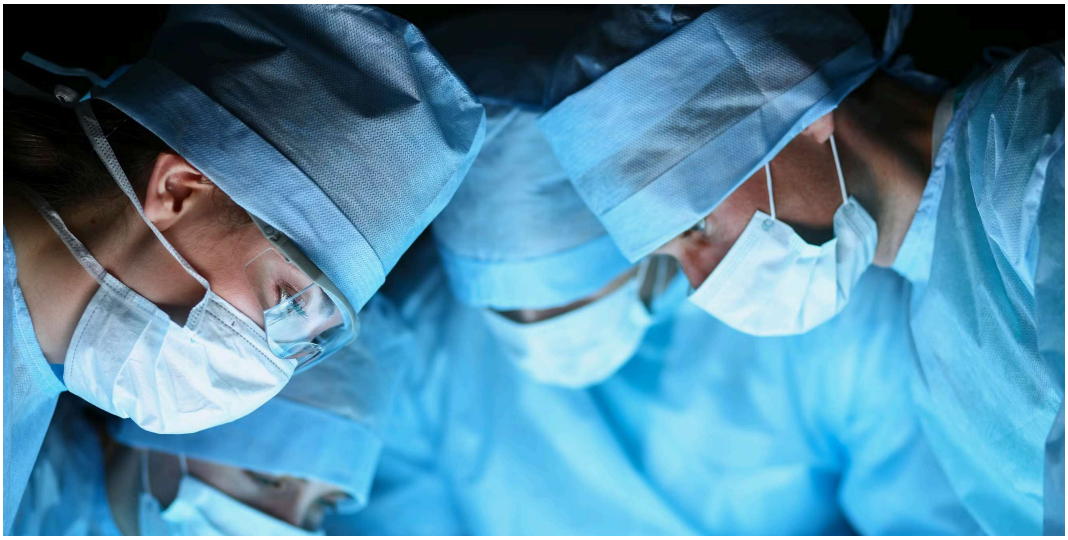

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First new non-opioid painkiller approved in the US for decades – here's how it works

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A new non-opioid painkiller, suzetrigine, has just been approved by the US drug regulator, the FDA. It is the first non-opioid painkiller the agency has approved in over two decades.

Because of their addictive nature, medical professionals have done a lot in recent years to minimise the use of opioids, especially the length of time they are taken for following surgery. Patients receiving opioids for longer than a week post-surgery were found to double their risk of using these drugs for more than a year.

In the US, a study showed that around 6% of all patients who underwent surgery became persistent opioid users, even if they had never taken opioids before. So the arrival of a relatively safe and effective non-opioid drug to treat acute pain without the risk of addiction is a huge deal.

Suzetrigine works by blocking the activity of proteins called sodium channels in nerve cells that send pain signals. This stops the pain signal in its tracks, before it reaches your brain and therefore before you experience it.

This is exactly how existing local anaesthetic drugs, such as lidocaine, work. Unfortunately, these drugs block all sodium channels throughout your body, including those that control the activity of your heart, your brain and your breathing. This is why, as their name implies, they can only be applied locally.

In dentistry, this is usually done using a syringe and accompanied by another drug (called a “vasoconstrictor”) to stop the anaesthetic from escaping into the bloodstream.

Targeting sodium channels to alleviate pain is a wonderful idea in principle. However, it is hampered by the widespread presence of these proteins – which initiate electrical signalling in almost all the cells of your body – and the consequent risks associated with blocking them. Not least the very real risk of sudden death.

In Japan, fugu, a dish made from puffer fish, is an exotic delicacy. At least part of its attraction is the slight tingle in the tongue that can be experienced when eating it. This tingling is caused by a poison, tetrodotoxin, that is a potent blocker of sodium channels. Too much tetrodotoxin is fatal. In Japanese restaurants, only qualified fugu handlers are permitted to prepare the dish.

Only specially trained fugu chefs are allowed to prepare the potentially deadly puffer fish. Roland Nagy / Alamy Stock Photo

So why is the discovery and development of suzetrigine so important? We have nine different genes that code for sodium channels (they run from Nav1.1 to Nav1.9). Each of these channels is present at different levels in the different cells and organs of your body. But only one of these channels, Nav1.8, is present in peripheral pain-sensing neurons and not in other parts of the body.

There is no evidence of Nav1.8 expression in either your heart or your brain. This selective expression suggests that this particular sodium channel might be a good target to alleviate pain.

This idea received further credence following the discovery that people with genetic mutations that increase the activity of this channel suffered nerve pain despite there being no obvious cause of the pain.

Highly selective

Over several years, Vertex Pharmaceuticals, the company that makes suzetrigine (brand name Journavx), screened many potential drugs to try to identify a safe, selective blocker of these channels that could be taken orally. Suzetrigine was found to be both a potent and very selective blocker of these channels. It is, staggeringly, at least 30,000 times more potent at blocking Nav1.8 channels than all the other types of sodium channels that we have.

In two clinical trials with over 1,000 patients in each, suzetrigine was found to be equally as effective as opioids at blocking acute pain following moderately painful surgery – either removal of bunions or a tummy-tuck.

Suzetrigine also produced far fewer side-effects than opioid treatment and had no risk of addiction. So far, however, there is no convincing evidence that suzetrigine is effective in chronic, long-term pain relief.

The discovery and approval for the use of suzetrigine opens up the possibility of treating acute pain by selectively blocking specific sodium channels, without the risk of addiction. More generally, selective targeting of the many different ion channels that underlie pain signalling may pave the way for new, non-addictive treatments for all forms of acute and chronic pain.

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