How lobed brain corals are helping solve the mystery of what general anaesthesia does to the brain

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Aequorea victoria is a bioluminescent jellyfish found in the Pacific Ocean. Credit: Shutterstock

Many of us will undergo general anesthesia at some point in our lives—losing consciousness so we can be operated on painlessly. But although humans have used general anesthesia for more than 150 years, we still don't fully understand how it affects the brain.

To find out, we turned to a genus of stony coral called lobed brain coral (*Lobophyllia*). Using a unique fluorescent molecule present in lobed brain coral, we managed to isolate an important target of general anesthetic drugs in fruit fly brains. Our findings could help develop safer anesthesia for humans.

Glow-in-the-dark coral

Lobed brain corals are bioluminescent, which means they can naturally produce and emit light. They're found in the Indian and Pacific oceans, alongside other similar scientifically valuable creatures such as the crystal jelly *Aequorea victoria*.

Bioluminescent ocean-dwellers have equipped researchers with a powerful toolkit of fluorescent molecules to study and track biological processes. They even inspired the Nobel Prize-winning discovery of the green fluorescent protein.

The fluorescent molecule found in the lobed brain coral, Eos, has a rather surprising feature: it can change color. This lets scientists observe the movement of proteins within living cells—something that was previously impossible.

Imagine you have a Christmas tree covered with lights but they were all lit the same color; the tree might appear a bit blurry from afar. If one of the lights were to switch to a different color, however, you'd spot it easily.

The same principles apply when scientists try to track moving proteins in cells. Proteins perform multiple vital tasks for a cell and tracking them can help us understand their function, but they're usually too small to see with regular microscopes.

Using the Eos molecule, we can develop super-resolution microscopes that reveal even the smallest elements within cells, including proteins.

A sleeping brain isn't 'inactive'

Anesthesia today generally involves injecting a patient's vein with a dose of a sedative drug and painkiller. For instance, the combination of propofol and fentanyl will make you unconscious and prevent you from feeling pain.

Sedative drugs, including sleeping pills, use your brain's natural ability to put you to sleep. They target the circuits in your brain that regulate wakefulness and stop them from being active.

However, the brain activity of a sleeping person is very different to that of someone under anesthesia. A sleeping brain performs many tasks and is quite active. A brain under anesthesia is largely unresponsive.

Why aren't we able to be woken up while under general anesthesia? To find out, scientists need to identify what else in the brain, apart from sleep pathways, is targeted by general anesthetic drugs.

Anesthesia stunts the brain's processing power

Neurons, the cells in the brain, communicate with each other through a process known as synaptic neurotransmission. This is the main way our brains process information.

For neurotransmission to occur, specialized proteins within neurons must release chemicals called neurotransmitters (such as dopamine or glutamate). Proteins are dynamic. They can move freely inside neurons and are often needed in different parts of the cell.

For our research, we took the Eos molecule and attached it onto a protein called "syntaxin1A"—which is responsible for facilitating neurotransmission—to see how general anesthetic drugs might affect its normal function in the brains of fruit flies.

We found syntaxin1A dynamics were altered with general anesthetic drugs such as propofol and isoflurane. The protein became trapped in clusters of proteins and its movement was therefore restricted.

This may have been what reduced the efficiency of neurotransmission, preventing the brain from processing complex information.

A goal to develop new, safer drugs

Many proteins apart from syntaxin1A are involved in neurotransmission. So it's likely others are also affected by anesthetic drugs.

This new way to observe individual protein behavior in intact brain tissue will hopefully uncover more drug targets and explain the precise mechanisms that underpin general anesthetics.

Consequently, this knowledge will aid in the development of safer drugs with fewer side effects. And targeted drug development could help prevent the abnormally long recovery times observed in some patients who undergo general anesthesia.

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