In recent decades, scientists have identified several chemical components of cannabis that suppress nausea and vomiting. The endocannabinoid system in the brain helps the body to control nausea and vomiting, as well as appetite, pain, and mood. While the endocannabinoid system is responsible for many of the effects of marijuana, the body also naturally produces its own cannabis-like chemicals that rely on this system. For example, the body produces two chemicals, called anandamide and 2AG, which bind to cannabinoid receptors (CB1, CB2) on brain cells and prevent them from sending chemical signals to other cells. Like plant-derived cannabinoids, naturally occurring 2AG has been shown to suppress nausea and vomiting in some animal species. The action of 2AG in the brain can be influenced in several ways. A chemical compound called JZL184 increases levels of 2AG in the brain by preventing it from being converted to its metabolic product, AA (arachidonic acid), while another drug, indomethacin, prevents AA from being broken down. Blocking the cannabinoid receptors CB1 and CB2 prevents 2AG from working.

The researchers examined the anti-nausea and anti-vomiting effects of 2AG by measuring the frequency of vomiting in shrews, and conditioned gaping (wide opening of the mouth in response to a nausea-paired flavour) in rats, since rats are unable to vomit. Both rats and shrews were given lithium chloride (LiCl) to cause nausea/vomiting. In the first experiment, the researchers evaluated whether blocking CB1 receptors could reverse the anti-vomiting effects of JZL184 in shrews. The second experiment looked at whether injecting 2AG directly could suppress conditioned gaping in rats. The third examined whether the suppression of conditioned gaping by 2AG or AA could be reversed by blocking CB1 or CB2 receptors, or an injection of indomethacin. Experiments four and five confirmed that 2AG selectively reduced nausea, and not learning per se, in rats.

The naturally occurring cannabinoid 2AG suppressed vomiting in shrews by attaching to the CB1 receptor. 2AG, along with its metabolite, AA, also suppressed nausea-induced conditioned gaping in rats, but this effect was largely independent of CB1 (or CB2) receptors.
What did the researchers find?
In shrews, increasing the levels of 2AG in the brain (with JZL184) suppressed vomiting, and this effect was reversed by blocking CB1 receptors. In rats, both 2AG and AA injections suppressed conditioned gaping to an illness-paired flavour, but unlike the anti-vomiting effects in shrews, this effect was not reversed by blocking either CB1 or CB2 receptors. It was reversed by indomethacin, however, suggesting that a metabolic product of AA (possibly prostaglandin E) may be directly responsible for the anti-nausea effects of 2AG in rats.

How can you use this research?
Neuroscientists can use this research to better understand how naturally occurring cannabinoids such as 2AG and AA regulate nausea and vomiting via the brain’s endocannabinoid system.

Pharmaceutical developers can use this research to develop drugs that suppress nausea and vomiting by increasing the levels of 2AG and/or AA in the brain.

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