We thought weight loss drug Ozempic worked in the gut. We were wrong.

When scientists first created the class of drugs that includes Ozempic, they told a tidy story about how the medications would work: The gut releases a hormone called GLP-1 that signals you’re full, so a drug that mimics GLP-1 could do the exact same thing, helping people eat less and lose weight.

In recent years, studies have shown that GLP-1 from the gut breaks down quickly and has little effect on our appetites. But the hormone and its receptors are naturally present in many parts of the brain too. These brain receptors are likely the reason the GLP-1 drugs can curb the desire to eat—but also, anecdotally, curb other desires as well. The weight-loss drugs are ultimately drugs for the brain.

A more refined understanding of how GLP-1 works in the brain could help improve the current injections. Nausea and vomiting are among the most common side effects and would seem to go hand in hand with a lack of appetite. But these symptoms appear to be governed by distinct systems in the brain, Scott Kanoski, a neuroscientist at the University of Southern California, told me. In fact, scientists have been able to find brain areas in rodents where GLP-1 analogues can suppress appetite without causing nausea, which hints at the possibility of developing drugs that do the same.

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