Science / Medicine

The Hormones Behind Our Gut Feelings

■ **Research:** Scientists are learning how the stomach and brain communicate. The lessons hold great promise for sufferers of many gastrointestinal problems.

By MARGIE PATLAK

In the early 19th Century, a young Canadian named Alex St. Martin suffered a gunshot wound that left a permanent opening in his stomach. This allowed his physician to make a striking observation—the man's angry feelings slowed the passage of food through his stomach and hampered secretion of various stomach juices which aid digestion.

More than 150 years after the case was detailed in a book by the physician, Dr. William Beaumont, "Experiments and Observations on the Gastric Juice and the Physiology of Digestion," researchers are making headway into understanding the chemical ties between the brain and the gut. These ties help explain how stress and emotional upsets can prompt a repertoire of common gastrointestinal complaints including ulcers, diarrhea and constipation. The research suggests new treatment avenues for gastrointestinal disorders, including drugs that work on the brain rather than the gut to relieve "gut feelings."

"We've made great strides in understanding how the brain and gut 'talk' to each other," said pharmacologist Cynthia Williams of the University of Texas in Houston. "There's really been an explosion of findings."

That explosion was brought about by the discovery, over the last 20 years, of more than 50 different compounds generated by the brain. About a dozen of these have a dramatic effect on the gut. "It's been a rumor for a long time that many GI [gastrointestinal] tract disorders are caused by stress or other emotions," said Williams, "but until we had these compounds to play around with, we had no way of systematically evaluating it."

□

One of the newer brain compounds to be discovered, corticotropin-releasing factor (CRF), plays a key role in wreaking the effects of stress on the colon, Williams' research suggests. Called a "master transmitter," CRF is released by the brain in response to stress and triggers a number of reactions in the body, including the boosting of heart rate and blood pressure and the suppression of food consumption and sexual activity.

Williams has shown that in rats, CRF propels food quickly through the colon, prompting excretion and, in high doses, diarrhea. The compound also slows the passage of food through the small intestine. The animals generated large amounts of CRF when they were stressed by being in a restraining harness. Other researchers have confirmed Williams' findings and shown that CRF also slows the emptying of stomach contents into the small intestine.

Eliminating food from the colon frees some of the body's blood supply so it can be used to enable a fast escape or a valiant fight. Slowing the passage of food through the small intestine and stomach makes an animal feel full so it will not have an urge to munch when faced with danger.

The type of stress these animals experienced in Williams' studies is not exactly akin to the stress a person experiences during rush-hour traffic or at work. Other studies have shown, however, that mental stress, such as that generated when undergoing a rigorous personal interview, prompts the same changes in the human colon that Williams saw in rats.

The cascade of hormones released in the human "fight or flight" response to stress appears to be universal among mammals. "When you're faced with a tiger in the woods," Williams explains, "you don't need your gastrointestinal functions. What you need, instead, is your heart pounding, sending a lot of blood to your muscles so you can quickly respond." Particularly promising is Williams' finding that when the rats were given a shot of a compound that partially blocks CRF's actions, it completely countered the effects of stress on the gut.

Williams and colleague Thomas Burks of the University of Arizona in Tucson currently have a patent pending for the use of this CRF blocker to treat patients with irritable bowel syndrome. The hallmarks of this syndrome are chronic diarrhea or constipation with abdominal pain. The disorder afflicts 15% to 20% of the population, according to epidemiologist James Everhart of the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Md.

□

No physical abnormalities explain the syndrome, although a number of studies link its occurrence to heightened stress. There currently is no effective treatment for the condition, which one gastroenterologist poetically called a manifestation of a "weeping colon."

Burks has recently shown that CRF boosts the number of contractions in the junction between the large and small intestines. This could explain the incapacitating pain experienced by irritable bowel syndrome patients, he said, as well as their constipation and diarrhea.

In other work, Yvette Taché of the UCLA Center for Ulcer Research and Education and her colleagues have uncovered two brain compounds that strongly influence whether animals develop stomach ulcers. Extremely small amounts of just one of these powerful chemicals, thyrotropin releasing hormone (TRH), have been shown to trigger a host of reactions in the gut, all of which foster ulcers. In four species of animals, for example, Taché and others have found that TRH boosts contractions and secretion of acid in the stomach, stems the stomach's production of bicarbonate, which neutralizes acid, and affects blood flow in the stomach, making it more susceptible to ulcers. When TRH is given to rats, they develop stomach ulcers within just two hours.

□

Although the links have not been proven conclusively, there is evidence to suggest that TRH is released in response to stress and can make animals more alert and responsive. It counteracts the depressant effects of certain drugs.

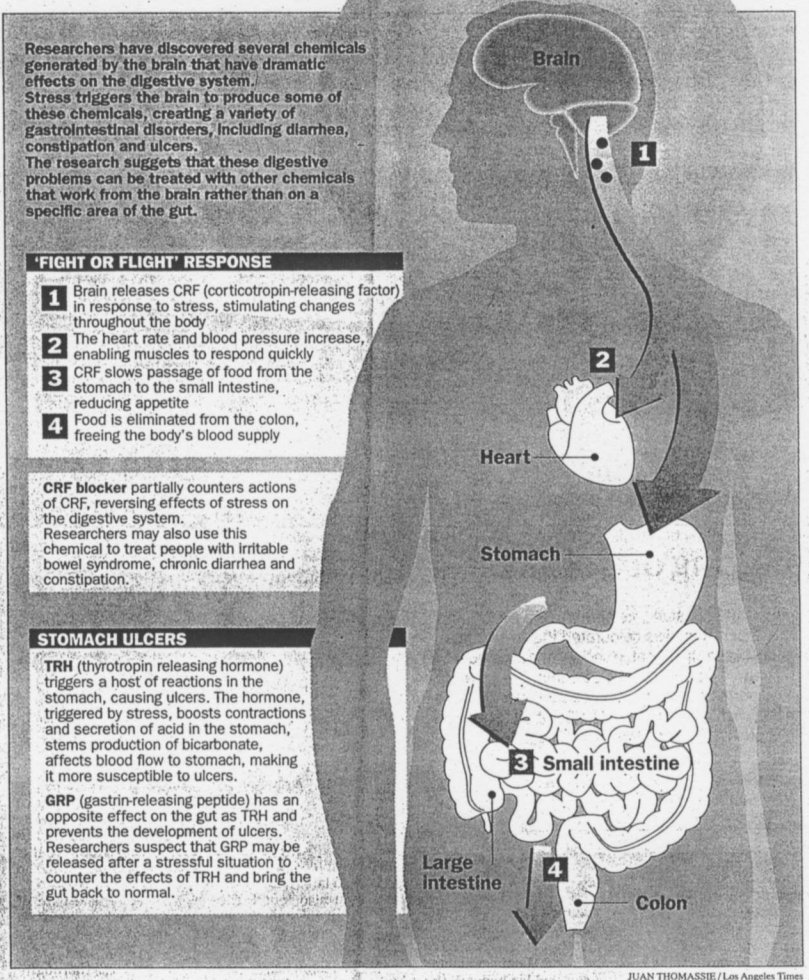
Fortunately for the stomach, brain cells also generate a compound called gastrin-releasing peptide (GRP), which has an opposite effect on the gut from TRH and protects animals from developing ulcers. Taché speculates that compounds such as GRP may be generated by the brain after a stressful situation to counteract the compounds induced by stress and bring the gut back to normal in most people.

A French company is currently pursuing GRP as an anti-ulcer drug.

"The beauty of our findings," said Taché, "is that from one small molecule working on just one site, you counter the gamut of response involved in ulcer formation. You could never get that kind of response by targeting a drug, as most current ulcer drugs do, to one aspect of ulcer formation. The cells that generate acid in the stomach, for example, don't also affect bicarbonate production."

"Manipulating the system from the top down," she said, "can be much more effective because it gives you the overall body response you want."

Patlak is a free-lance writer based in Elkins Park, Pa.



JUAN THOMASSIE / Los Angeles Times