The Gut Brain: Can it Think and Can it Learn?

The gut has a mind of its own, the enteric nervous system**.** Just like the brain in the head this system sends and receives impulses, records experiences and responds to emotions. Its nerve cells are bathed and influenced by the same neurotransmitters.

The gut's brain or enteric nervous system is located in the sheaths of tissue lining the esophagus, stomach, small intestine and colon. Considered a single entity, it is a network of neurons, neurotransmitters and proteins that zap messages between neurons, support cells like those found in the cranial brain as well as a complex circuitry that enables it to act independently, learn, remember and produce "gut feelings".

The gut brain is reported to play a major role in human happiness and misery. Just as the cranial brain affects the gut, the gut brain can talk back to the head. Most of the gut sensations that enter conscious awareness are negative things like pain and bloatedness. Many gastrointestinal disorders like colitis and irritable bowel syndrome appear to originate from problems within the gut brain. Victims of Alzheimer's and Parkinson's disease suffer from constipation. The nerves in their gut are as sick as the nerve cells in their cranial brains.

The enteric nervous system mirrors the central nervous system

Dr. Michael Gershon, professor of anatomy and cell biology at Columbia-Presbyterian Medical Center in New York, is one of the founders of a new field of medicine called neurogastroenterology. According to Dr. Gershon the enteric nervous system mirrors the central nervous system.

The gut contains 100 million neurons - more than the spinal cord. Major neurotransmitters like serotonin, dopamine, glutamate, norephinephrine and nitric oxide are found in the gut. Two dozen small brain proteins called neuropeptides are also there, as are major cells of the immune system along with enkephalins, a member of the endorphin family. The gut is also a rich source of benzodiazepines - the family of psychoactive chemicals that form the basis of drugs such as valium and xanax.

In evolutionary terms, it makes sense that the body has two brains, says Dr. David Wingate, professor of gastrointestinal science at the University of London and consultant at Royal London Hospital:

"The first nervous systems were in tubular animals that stuck to rocks and waited for food to pass by... As life evolved, animals needed a more complex brain for finding food and sex and developed a central nervous system. But the gut's nervous system was too important to put inside the newborn head with long connections going down to the body."

Offspring need to eat and digest food at birth. Therefore, nature seems to have preserved the enteric nervous system as an independent circuit inside higher animals. It is only loosely connected to the central nervous system and can mostly function independently, without instructions from the cranial brain.

Command neurons control the pattern of activity in the gut brain
Here is the embryological process as depicted by developmental biologists. A clump of tissue called the neural crest forms early on. One section turns into the central nervous system, while another section migrates to become the enteric nervous system. According to Dr. Gershon, it is only later that the two systems are connected via the vagus nerve.

The cranial brain sends signals to the gut by talking to a small number of command neurons, which in turn send signals to gut interneurons that carry messages up and down the pike. Both command neurons and interneurons are spread throughout two layers of gut tissue called the myenteric plexus and the submuscosal plexus. It is noteworthy that the command neurons control the *pattern* of activity in the gut, while the vagus nerve merely alters the *volume* by changing its rates of firing.

The two plexuses contain glial cells (see below) that nourish neurons, mast cells which are involved in immune responses and a 'blood-brain barrier' that keeps harmful substances away from important neurons. They also have sensors for sugar, protein, acidity and other chemical factors that monitor the progress of digestion, determining how the gut mixes and propels its contents.

(Glial cells are the most abundant cell types in the central nervous system. Types of glial cells include oligodendrocytes, astrocytes, ependymal cells, satellite cells, microglia and Schwann cells.)

As light is shed on the circuitry between the two brains, researchers are beginning to understand why people act and feel the way they do. When the cranial brain encounters a frightening situation, it releases stress hormones that prepare the body for fight or flight. The stomach contains many sensory nerves that are stimulated by this chemical surge - hence 'butterflies in the stomach'.

Fear also causes the vagus nerve to "turn up the volume" on serotonin circuits in the gut. Thus over-stimulated, the gut goes into a higher gear and diarrhea results. Similarly, people sometimes "choke" with emotion - when nerves in the esophagus are highly stimulated, people have trouble swallowing.

In cases of extreme stress, the cranial brain seems to protect the gut by sending signals to immunological mast cells in the plexus. The mast cells secrete histamine, prostaglandin and other agents that help produce inflammation. This is a protective reaction - the gut is now primed for surveillance. If the barrier breaks then the gut is ready to do repairs. These same chemicals also result in cramping and diarrhea unfortunately.

Interaction between the gut brain and pharmaceutical drugs.
According to Dr. Gershon, "when you make a drug to have psychic effects on the cranial brain, it's very likely to have an effect on the gut that you didn't think about." He also believes that some drugs developed for the cranial brain could have uses in the gut.

For example, the gut is loaded with the neurotransmitter serotonin. When pressure receptors in the gut's lining are stimulated serotonin is released, thus initiating the reflexive motion of peristalsis. 25 % of the people taking Prozac or similar antidepressants have gastrointestinal problems such as nausea, diarrhea and constipation. These drugs act on serotonin, preventing its uptake by target cells so that it remains more abundant in the central nervous system.

Gershon is conducting a study on the side effects of Prozac on the gut. Prozac in small doses can treat chronic constipation. Prozac in larger doses can *cause* constipation - the colon seems to "freeze up". Moreover, because Prozac stimulates sensory nerves, it can also cause nausea.

Some antibiotics like erythromycin act on gut receptors to produce ascillations, where people experience cramping and nausea. Drugs like morphine and heroin attach to the gut's opiate receptors, producing constipation. Both brains can be addicted to opiates.

Exploring gut brain and head brain interaction

A question has been raised: Why does the human gut contain receptors for benzodiazepine, a chemical that relieves anxiety? This seems to suggest that the body has its own internal source. Patients with liver failure fall into a deep coma. The coma can be reversed, in minutes, by giving the patient a drug that blocks benzodiazepine.

According to Dr. Anthony Basile, a neurochemist in the Neuroscience Laboratory at the National Institutes of Health in Bethesda, when the liver fails, substances usually broken down by the liver get to the brain. Some are bad, like ammonia and mercaptan, which are "smelly compounds that skunks spray on you". Another series of compounds is identical to benzodiazepine. "We don't know if they come from the gut itself, from bacteria in the gut or from food, but when the liver fails, the gut's benzodiazepine goes straight to the cranial brain, knocking the patient unconscious", says Dr. Basile.

Many people are allergic to certain foods like shellfish. This is because mast cells in the gut mysteriously become sensitized to antigens in the food. The next time the antigen shows up in the gut, the mast cells call up a program, releasing chemical modulators that try to eliminate the threat. The allergic person then experiences cramping and diarrhea. This leads researchers to believe that many autoimmune diseases like Krohn's disease and ulcerative colitis may involve the gut brain.

Two big questions remain: Can the gut brain think for itself and can it learn?

Dr. Gershon tells the story of a male nurse, an ex-army sergeant, in charge of a group of paraplegics. With their lower spinal cords destroyed, the patients would get impacted. "At 10 am every morning, the patients received enemas. Eventually the sergeant was rotated off the ward and his replacement decided to give enemas only after compactions occurred. At 10 the next morning however, everyone on the ward had a bowel movement at the same time - without enemas." Had the sergeant trained those colons?

Dr. R. King, Themes of the Times: General Psychology, 1996.