MedicalXpress

Digestive problems early in life may increase risk for depression, study says

May 12 2011

Depression and anxiety may result from short-term digestive irritation early in life, according to a study of laboratory rats by researchers at the Stanford University School of Medicine. The findings suggest that some human psychological conditions may be the result, rather than the cause, of gastrointestinal disorders such as irritable bowel syndrome.

"A lot of research has focused on understanding how the mind can influence the body," said Pankaj Pasricha, MD, professor and chief of gastroenterology and hepatology. "But this study suggests that it can be the other way around. Gastric irritation during the first few days of life may reset the brain into a permanently depressed state."

Clearly not all stomach upsets lead to lifelong psychological problems, however. The impact of the irritation may depend on when it occurs during development or the genetic makeup of the affected person, the researchers believe. In particular, the viscera, or internal organs, are particularly vulnerable early in development.

Pasricha is the senior author of the study, which will be published on May 12 in PLoS One. Research associate Liansheng Liu is the lead author of the research. The Stanford scientists collaborated with researchers from the University of California-San Francisco and the University of Kansas on the study.

About 15 to 20 percent of people experience what physicians call functional dyspepsia, or persistent or recurring pain in the upper

abdomen. Researchers like Pasricha have long noted that these people are also more likely than their peers to be anxious or depressed. Conventional wisdom has held that stress hormones associated with a patient's altered mood were responsible for his or her digestive disturbances.

However, there is another option. "The gut and the brain are hardwired together by the vagus nerve, which runs from the brain to the body's internal organs" said Pasricha. "In addition, the gut has its own nervous system that is relatively independent. So the communication between the gut and the adult brain is elaborate and bi-directional, and changes in the gut are signaled directly to the brain."

Because many of these patients date their gastrointestinal problems back to early childhood, before their psychological symptoms began, Pasricha and his colleagues wondered if the digestive disturbances could instead be causing the mood disorders. The possibility was bolstered by the fact that recent research by other groups has linked depression and anxiety in humans to changes in the composition of gut bacterial populations.

To test their hypothesis, the researchers used a laboratory model of functional dyspepsia they had developed years earlier. They subjected 10-day-old laboratory rats to mild stomach irritation daily for six days. They had previously shown that during the vulnerable newborn period such treatment, which causes a temporary inflammation or injury, results in hypersensitivity and functional abnormalities that persist long after the initial damage has been repaired.

"We hypothesized that this treatment might also be affecting the development of central nervous system, and driving the animals to anxiety and depression," said Pasricha.

Indeed, as the researchers assessed the behavior of the treated rats when

the animals were 8 to 10 weeks old, they found that those rats with early gastric irritation were significantly more likely than their peers to display depressed and anxious behaviors including a decreased consumption of sugar water, less-active swimming in a pool of warm water and a preference for dark rather than light areas in a maze.

The treated rats also exhibited increased levels of the stress hormones corticosterone and corticotrophin after an injection of saline, and had higher-than-normal resting levels of corticosterone and corticotrophin-releasing factor, or CRF. Blocking the animals' ability to perceive sensation from their gut with a drug did not affect their behavior, indicating that the rats were not responding to ongoing pain. In contrast, inhibiting the activity of CRF, which is known to be associated with depression in humans and animals, caused the treated rats to behave more normally in the tests.

"It seems that when the rats are exposed to gastric irritation at the appropriate point in time," said Pasricha, "there is signaling across the gut to the brain that permanently alters its function."

The researchers are now planning to investigate exactly how that signaling is initiated and acts in the brain, and whether it might be possible to develop new ways to treat depression and anxiety in humans.

"We'd like to know whether the vagus nerve is involved, and confirm what changes may occur in the brain in response to this signal," said Pasricha. "The vast majority of humans don't experience any long-lasting consequences from transient infections. But there may be subset of patients who are genetically predisposed to this effect by mechanisms we don't yet understand yet. Our hope is that this work will open another avenue for exploring, understanding and treating these very complex syndromes."

In particular, electrical stimulation of the vagus nerve has recently been approved by the Food and Drug Administration for treatment-resistant depression; this research may help researchers better understand and optimize this new approach.

Provided by Stanford University Medical Center