

Adult gut can generate new neurons

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The adult lower digestive tract can be stimulated to add neurons to the intestinal system, according to new mouse research in the August 5 issue of *The Journal of Neuroscience*. The study shows that drugs similar to the neurotransmitter serotonin increase the production of new neurons in the gut. This is the first research to confirm that an adult intestine can generate neurons in the enteric nervous system, the network of neurons in the gut's wall that controls the gastrointestinal system.

The findings suggest that drugs could be used to treat patients who suffer from intestinal disorders that may be caused by an absence or loss of neurons, which may be congenital or acquired. About 25 percent of adult Americans have some daily hindrance due to gastrointestinal disorders, and the number of employees who miss work because of these ailments is second only to the common cold.

"This is the first time that a treatment with a serotonin-related drug has been shown to add neurons to the adult enteric nervous system," said Mintsai Liu, DDS, and Michael D. Gershon, MD, at Columbia University, the study's principal authors. "Conceivably, treatment with compounds of this type can be used in the future to help repair a damaged or congenitally defective enteric nervous system without resorting to an invasive procedure."

While neuroscientists used to believe that neurogenesis — the formation of new neurons —occurred only in prenatal brains, it is now known to take place throughout adulthood, primarily in two brain regions. This study shows that neurogenesis also takes place in the enteric nervous



system.

For more than 40 years, researchers have known that human bowels contain high concentrations of serotonin (5-HT), a neurotransmitter used to regulate intestinal movements. A recently developed medication to treat constipation and <u>irritable bowel syndrome</u> targeted the serotonin receptor 5-HT₄. While that drug, tegaserod, was approved by the Food and Drug Administration in 2002, it was later withdrawn due to concerns it might cause heart attacks.

The study shows that the 5-HT₄ receptor and, by inference, serotonin play vital roles in the regulation of neurons created in the gut after birth. To prove this fact, the researchers compared the production of neurons in mice lacking that particular receptor with mice that had it. The mice without the receptor had a normal number of neurons at birth, but considerably fewer neurons added after birth.

In addition, when the authors gave the "normal" mice a drug that stimulated the activity of the 5-HT₄ receptor, the compounds promoted the generation of enteric neurons and also protected the neurons already there.

Arturo Alvarez-Buylla, PhD, at University of California, San Francisco, an expert in stem-cell neurobiology and developmental neuroscience who was not affiliated with the study, says the research helps to answer basic unresolved questions about the gastrointestinal system. "The finding not only suggests that new enteric neurons can be generated in the adult, but that activation of the serotonin receptor is required for this process," he said. "The enteric nervous system has a very large number of neurons, yet we know very little about their progressive loss during life and whether they can be regenerated."

More information: www.jneurosci.org/



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