

Serotonin 2C receptor regulates memory in mice and humans: Implications for Alzheimer's disease

June 28 2024



Credit: CC0 Public Domain

Researchers at Baylor College of Medicine, the University of Cambridge in the U.K. and collaborating institutions have shown that serotonin 2C receptor in the brain regulates memory in people and animal models.



The findings, <u>published</u> in the journal *Science Advances*, not only provide new insights into the factors involved in healthy memory but also in conditions associated with memory loss, like Alzheimer's disease, and suggest novel avenues for treatment.

"Serotonin, a compound produced by neurons in the midbrain, acts as a neurotransmitter, passing messages between brain cells," said cocorresponding author Dr. Yong Xu, professor of pediatrics—nutrition and associate director for basic sciences at the USDA/ARS Children's Nutrition Research Center at Baylor.

"Serotonin-producing neurons reach out to multiple <u>brain regions</u> including the hippocampus, a region essential for short- and long-term memory."

Serotonin communicates messages to brain cells by binding to receptors on the cell surface, which signal the receiving cell to carry on a certain activity.

In this study, the Xu lab, with expertise in basic and genetic animal studies, and the human genetics lab of co-corresponding author Dr. I. Sadaf Farooqi, professor of metabolism and medicine at the University of Cambridge, focused on <u>serotonin</u> 2C receptors, which are abundantly present in the brain's ventral hippocampal CA1 region (vCA1), investigating the role of the receptor in memory in humans and animal models.

"We had previously identified five individuals carrying variants of the serotonin 2C receptor gene (HTR2C) that produce defective forms of the receptor," Farooqi said. "People with these rare variants showed significant deficits on memory questionnaires. These findings led us to investigate the association between HTR2C variants and memory deficits in animal models."



The team genetically engineered mice to mimic the human mutation. When the researchers ran behavioral tests on these mice to evaluate their memory, they found that both males and females with the non-functional gene showed reduced memory recall when compared with the unmodified animals.

"When we combined the human data and the mouse data, we found compelling evidence connecting non-functional mutations of the serotonin receptor 2C with memory deficits in humans," Xu said.

The animal models also enabled the team to dig deeper into how the receptor mediates memory. They discovered a <u>brain circuit</u> that begins in the midbrain where serotonin-producing neurons are located. These neurons project to the vCA1 region, which has abundant serotonin 2C receptors.

"When neurons in the midbrain reaching out to neurons in the vCA1 region release serotonin, the neurotransmitter binds to its receptor signaling these cells to make changes that help the brain consolidate memories," Xu said.

Importantly, the researchers also found that this serotonin-associated neural circuit is damaged in a mouse model of Alzheimer's disease. "The neural circuit in the Alzheimer's disease animal model cannot release sufficient serotonin into the vCA1 region that would need to bind to its receptor in the downstream <u>neurons</u> to signal the changes required to consolidate a memory," Xu said.

However, it is possible to bypass this lack of serotonin and directly activate the downstream serotonin receptor by administering a serotonin analog, lorcaserin, a compound that selectively activates the serotonin 2C receptor in these cells.



"We tested this strategy in our animal model and were excited to find that the animals treated with the serotonin analog improved their <u>memory</u>," Xu said. "We hope our findings encourage further studies to evaluate the value of serotonin analogs in the treatment of Alzheimer's disease."

More information: Hesong Liu et al, Neural circuits expressing the serotonin 2C receptor regulate memory in mice and humans, *Science Advances* (2024). DOI: 10.1126/sciadv.adl2675. www.science.org/doi/10.1126/sciadv.adl2675

Provided by Baylor College of Medicine

Citation: Serotonin 2C receptor regulates memory in mice and humans: Implications for Alzheimer's disease (2024, June 28) retrieved 16 July 2024 from <u>https://medicalxpress.com/news/2024-06-serotonin-2c-receptor-memory-mice.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.