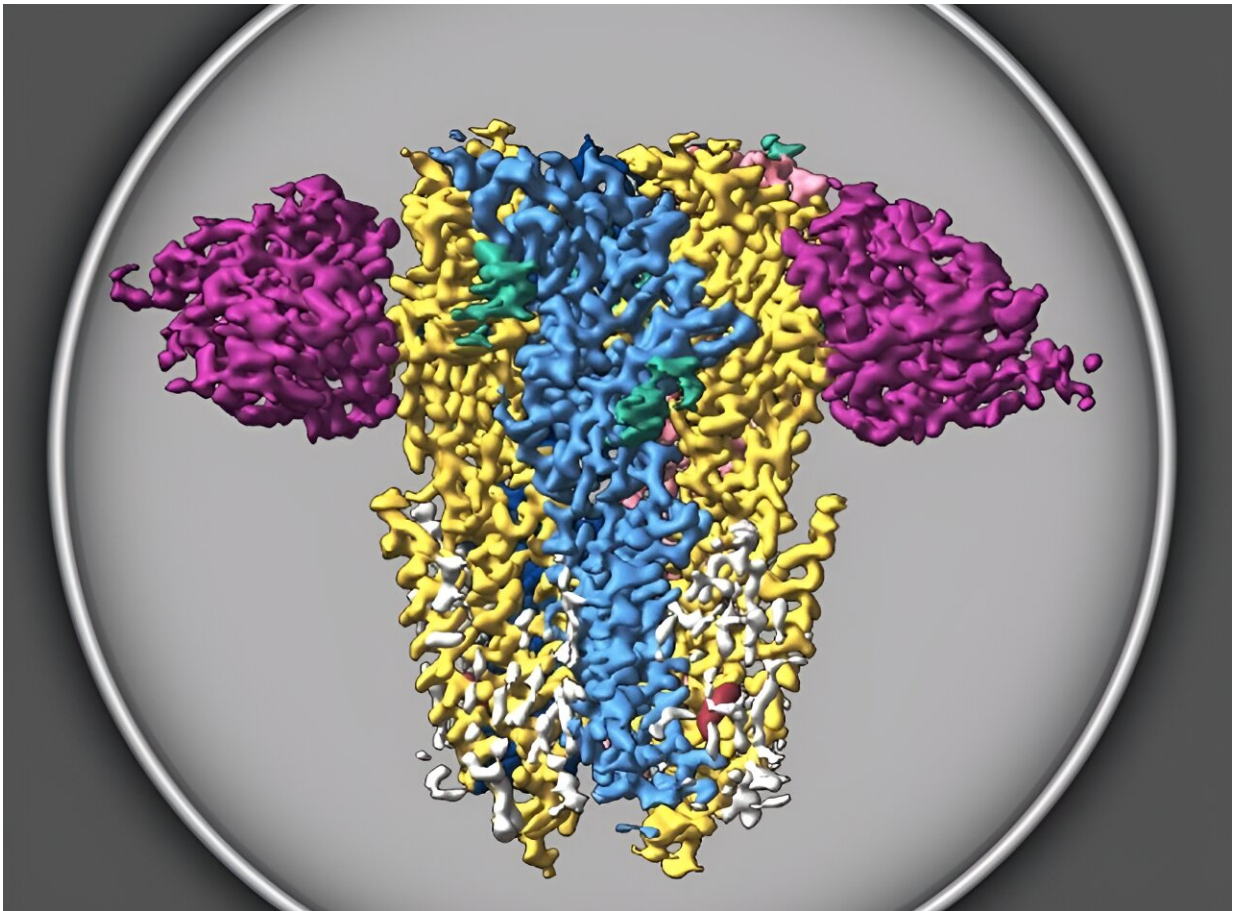


# Study reveals structure of crucial receptor in brain development and its function

September 20 2023, by Erik Robinson

---



Type A GABA receptors are targeted by pharmaceutical anesthetics, sedatives, and antidepressants because of their role in brain function. OHSU researchers uncovered the detailed molecular structure of the GABA receptor, which can lead to future development of improved therapies. Credit: OHSU

Scientists have revealed the molecular structure of a type of receptor that's crucial to brain development and function.

Known as Type A GABA receptors, these receptors are already targeted by pharmaceutical anesthetics, sedatives and antidepressants because of their important role in [brain function](#). The discovery, [published today in the journal \*Nature\*](#), reveals the dominant assemblies and states of the GABA receptor, a finding that could enable the development of new compounds that more specifically target a range of medical disorders.

"It is the main player that balances excitation and inhibition in the brain," said lead author Chang Sun, Ph.D., a postdoctoral researcher in the Vollum Institute at Oregon Health & Science University. "It affects all aspects of brain function, from motor function, to memory and learning, and also emotion and anxiety."

"Because the off switch is so crucial, GABA receptors are spread throughout the entire [brain](#)," added senior author Eric Gouaux, Ph.D., senior scientist in OHSU's Vollum Institute and an investigator with the Howard Hughes Medical Institute.

The receptor is defined by five-sided, or pentameric, assemblies derived from 19 different subunits, each of which give rise to a vast number of configurations that may or may not be clinically relevant. In this case, researchers painstakingly isolated native assemblies from mice and then infused them with common medications used to treat insomnia and postpartum depression.

They were then able to visualize three major structural populations of the receptor.

"This study shows the dominant assemblies and states of the GABA receptor," Gouaux said. "That's really the huge breakthrough—nobody

had been able to figure out which of the hundreds of thousands of these assemblies are most highly populated."

The discovery shows the GABA receptor in its native state as opposed to [tissue culture](#), as demonstrated in previous work, said co-author Sarah Clark, Ph.D., a former postdoctoral fellow in the Gouaux lab and now an assistant professor at Oregon State University. Researchers leveraged state-of-the-art cryogenic electron microscopy to reveal the structure in its natural state, rather than earlier techniques that required crystallizing vast quantities of identical molecules to form an artificial picture of their native structure.

"We used a combination of cryo-EM as well as single-molecule microscopy technique, which allowed us to count the subunits in each pentameric complex," she said.

Gouaux credited OHSU, as well as the Jennifer and Bernard Lacroute Endowed Chair in Neuroscience, for supporting this high-risk, high-reward research, along with the Howard Hughes Medical Institute, for providing the sustained support over more than three years to generate the discovery.

"This kind of work is difficult to fund because no one thinks it will work," Gouaux said.

**More information:** Eric Gouaux, Cryo-EM structures reveal native GABAA receptor assemblies and pharmacology, *Nature* (2023). [DOI: 10.1038/s41586-023-06556-w](https://doi.org/10.1038/s41586-023-06556-w).  
[www.nature.com/articles/s41586-023-06556-w](https://www.nature.com/articles/s41586-023-06556-w)

Provided by Oregon Health & Science University

Citation: Study reveals structure of crucial receptor in brain development and its function (2023, September 20) retrieved 28 April 2024 from <https://medicalxpress.com/news/2023-09-reveals-crucial-receptor-brain-function.html>

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.