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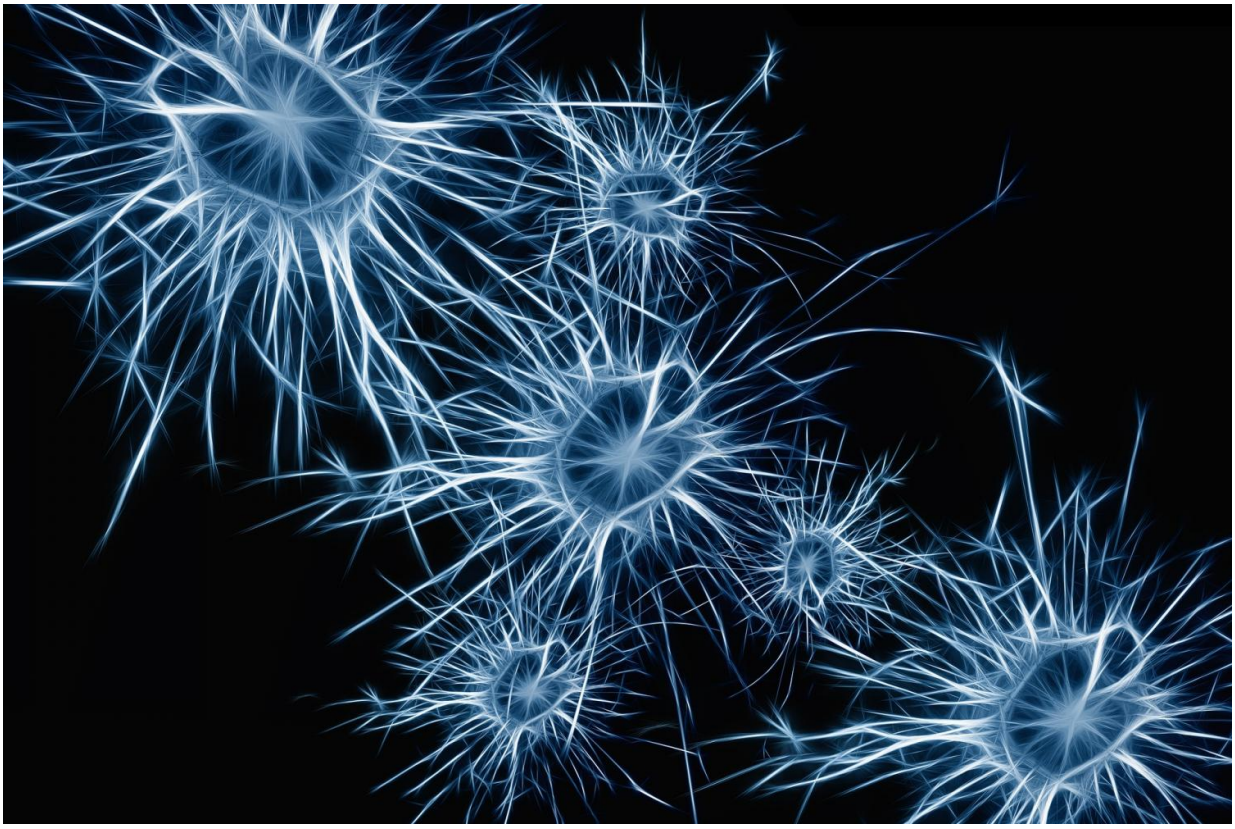
Researchers discover new binding partner for amyloid precursor protein

January 11 2019, by Bob Yirka



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An international team of researchers has discovered a new binding partner for amyloid precursor protein (APP)—a neurotransmitter called GABABR1a. In their paper published in the journal *Science*, the group

describes their study of a nonpathogenic version of APP and what they found. Martin Korte with Technische Universität Braunschweig has written a Perspective piece on the work done by the team in the same journal issue.

APP is well-known for the role it plays in the development of Alzheimer's disease—it is torn apart by an enzyme, resulting in the formation of amyloid β, which aggregates into the notorious clumps in the brain that that are the hallmark of the disease. As part of the study of neurological disorders, scientists have been working to understand what APP does in the brain prior to its role in Alzheimer's.

Prior research has shown that at least one version of APP is involved in balancing the firing of neurons by reducing the release of neurotransmitters sent between neurons. In this new effort, the researchers report discovering that APP works with a specific transmitter called GABABR1a as part of this process.

In their study, the researchers looked at a form of APP that resides in the membranes of neurons and another that is secreted by neurons. They note that GABABR1a belongs to the latter group. The team was specifically looking for APP binding partners in rat synapses (taken from the hippocampus). The process involved removing transmitters one at a time and watching changes in electrical output as they were introduced to APP. They found that when APP and GABABR1a were binding, there was a reduction in the release of the neurotransmitter. This suggested that the two are binding partners that play a role in the electrical firing involved with neuronal communications.

The team plans to continue their study of both APP and GABABR1a hoping to learn more about which cell types are typically involved and what brain parts. There is also more work to be done to determine the nature of other kinds of APP and what they do—and there also lies the

possibility of using new knowledge learned about APP to develop therapies for brain disorders.

More information: Heather C. Rice et al. Secreted amyloid-β precursor protein functions as a GABABR1a ligand to modulate synaptic transmission, *Science* (2019). DOI: 10.1126/science.aao4827

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