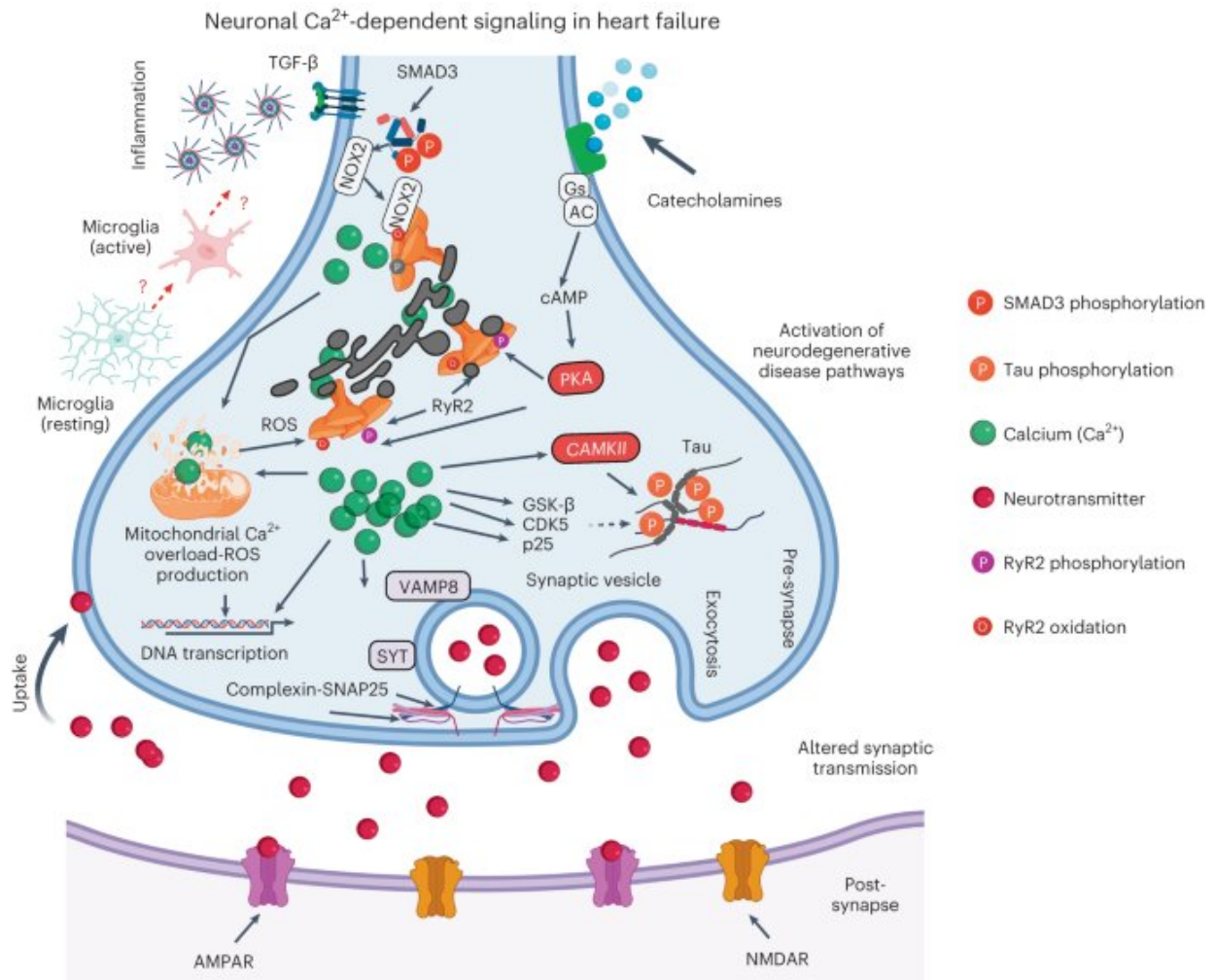


How heart failure leads to cognitive decline

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Neuronal Ca²⁺ signaling in heart failure. Credit: *Nature Neuroscience* (2023). DOI: 10.1038/s41593-023-01377-6

Heart failure may lead to cognitive decline by creating a tiny calcium leak inside the brain's neurons, according to a new study published in *Nature Neuroscience* by researchers at Columbia University. The finding could open the door to new treatments for the condition, called cardiogenic dementia.

"For many years, we've known that patients with [heart failure](#) tend to be cognitively impaired, but this was viewed as a coincidence. Only recently have studies suggested that heart failure causes the cognitive problems," says Andrew R. Marks, MD, chair of the Department of Physiology & Cellular Biophysics at Columbia University Vagelos College of Physicians and Surgeons, who led the research.

The Marks team hypothesized that a cellular calcium leak that contributes to heart failure may also contribute to cognitive decline in heart failure patients.

Within heart cells, calcium flows through a dedicated channel, but the channel can't close properly when it becomes overstimulated during the early stages of heart failure. As a result, calcium leaks through the channel, depriving heart cells of the calcium needed for contraction and further degrading the heart.

Because the same calcium channel is found in the brain, the researchers decided to see whether calcium leaks within brain cells could cause cognitive impairment.

Calcium leak within brain cells leads to cognitive impairment

They found that in mice with heart failure, calcium leaks in the brain's neurons led to cognitive impairment, but encouragingly, cognition could

be protected if the calcium leak was plugged with an experimental drug.

The brains of deceased patients with heart failure were also found to contain leaky calcium channels, suggesting the leak may also cause cognitive impairment in people.

The researchers have two hypotheses about how these leaks cause cognitive problems. One is that escaping calcium activates certain enzymes that prompt a reaction observed in patients with Alzheimer's disease. The other possibility is that the leaks cause abnormalities in parts of [neurons](#) required to transmit signals in the brain, Marks says.

Either way, the experimental drug designed by the Marks lab to plug the leak and slow the progression of heart failure may also be beneficial for the brain. The drug, called Rycals, is currently in clinical trials for people with heart and other muscle disorders caused by leaking calcium channels.

More information: Haikel Dridi et al, Heart failure-induced cognitive dysfunction is mediated by intracellular Ca²⁺ leak through ryanodine receptor type 2, *Nature Neuroscience* (2023). [DOI: 10.1038/s41593-023-01377-6](#)

Provided by Columbia University Irving Medical Center

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