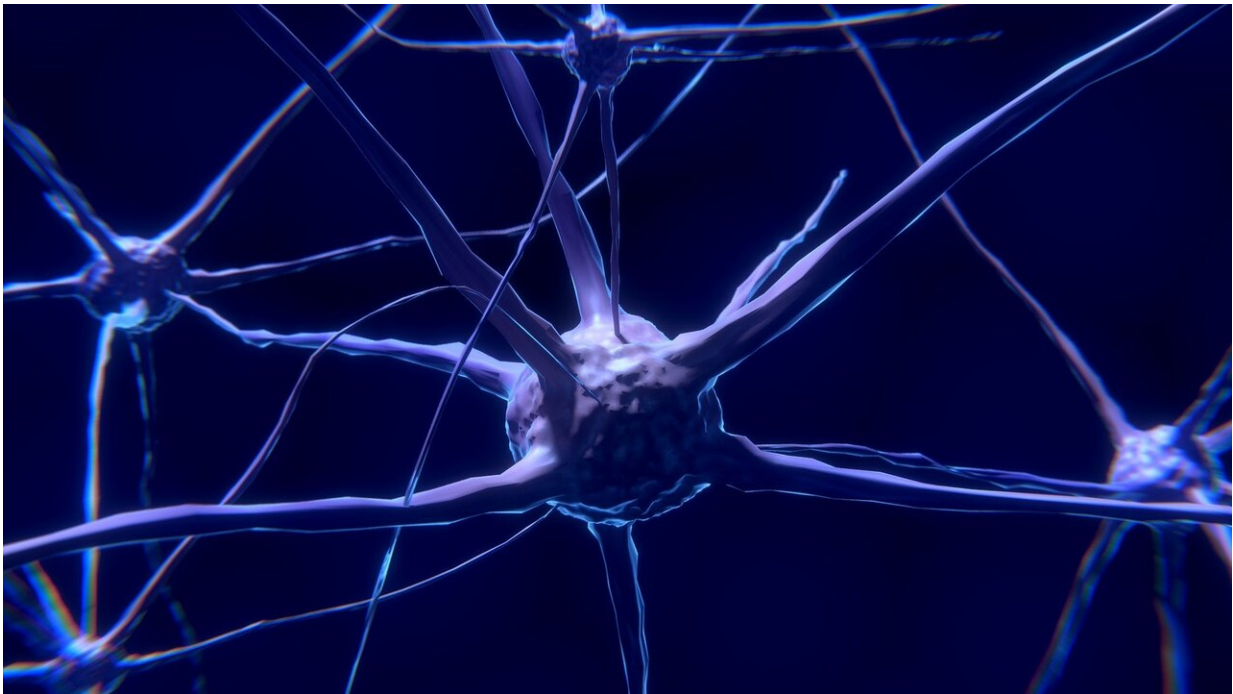


Researchers link brain memory signals to blood sugar levels

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A set of brain signals known to help memories form may also influence blood sugar levels, finds a new study in rats.

Researchers at NYU Grossman School of Medicine discovered that a peculiar signaling pattern in the [brain](#) region called the hippocampus, linked by past studies to memory formation, also influences metabolism,

the process by which dietary nutrients are converted into [blood sugar](#) (glucose) and supplied to cells as an energy source.

The study revolves around [brain cells](#) called neurons that "fire" (generate electrical pulses) to pass on messages. Researchers in recent years discovered that populations of hippocampal neurons fire within milliseconds of each other in cycles, with the firing pattern is called a "sharp wave ripple" for the shape it takes when captured graphically by EEG, a technology that records [brain activity](#) with electrodes.

Published online in *Nature* on August 11, a new study found that clusters of hippocampal sharp wave ripples were reliably followed within minutes by decreases in [blood sugar levels](#) in the bodies of rats. While the details need to be confirmed, the findings suggest that the ripples may regulate the timing of the release of hormones, possibly including insulin, by the pancreas and liver, as well of other hormones by the pituitary gland.

"Our study is the first to show how clusters of brain cell firing in the hippocampus may directly regulate metabolism," says senior study author György Buzsáki, MD, Ph.D., the Biggs Professor in the Department of Neuroscience and Physiology at NYU Langone Health

"We are not saying that the hippocampus is the only player in this process, but that the brain may have a say in it through sharp wave ripples," says Buzsáki, also a faculty member in the Neuroscience Institute at NYU Langone.

Known to keep blood sugar at normal levels, insulin is released by pancreatic cells, not continually, but periodically in bursts. As sharp wave ripples mostly occur during non-rapid eye movement (NREM) sleep, the impact of sleep disturbance on sharp wave ripples may provide a mechanistic link between poor sleep and high blood sugar levels seen

in type 2 diabetes, say the study authors.

Previous work by Buzsaki's team had suggested that the sharp wave ripples are involved in permanently storing each day's memories the same night during NREM sleep, and his [2019 study](#) found that rats learned faster to navigate a maze when ripples were experimentally prolonged.

"Evidence suggests that the brain evolved, for reasons of efficiency, to use the same signals to achieve two very different functions in terms of memory and hormonal regulation," says corresponding study author David Tingley, Ph.D., a post-doctoral scholar in Buzsaki's lab.

Dual role

The hippocampus is a good candidate brain region for multiple roles, say the researchers, because of its wiring to other [brain regions](#), and because hippocampal neurons have many surface proteins (receptors) sensitive to hormone levels, so they can adjust their activity as part of feedback loops. The new findings suggest that hippocampal ripples reduce blood glucose levels as part of such a loop.

"Animals could have first developed a system to control hormone release in rhythmic cycles, but then applied the same mechanism to memory when they later developed a more complex brain," adds Tingley.

The study data also suggest that hippocampal sharp wave ripple signals are conveyed to hypothalamus, which is known to innervate and influence the pancreas and liver, but through an intermediate brain structure called the lateral septum. Researchers found that ripples may influence the lateral septum just by amplitude (the degree to which hippocampal neurons fire at once), not by the order in which the ripples are combined, which may encode memories as their signals reach the

cortex.

In line with this theory, short duration ripples that occurred in clusters of more 30 per minute, as seen during NREM sleep, induced a decrease in peripheral glucose levels several times larger than isolated ripples. Importantly, silencing the lateral septum eliminated the impact of hippocampal sharp wave ripples on peripheral glucose.

To confirm that hippocampal firing patterns caused the glucose level decrease, the team used a technology called optogenetics to artificially induce ripples by re-engineering hippocampal cells to include light-sensitive channels. Shining light on such cells through glass fibers induces ripples independent of the rat's behavior or brain state (e.g. resting or waking). Similar to their natural counterparts, the synthetic ripples reduced sugar levels.

Moving forward, the research team will seek to extend its theory that several hormones could be affected by nightly sharp wave ripples, including through work in human patients. Future research may also reveal devices or therapies that can adjust ripples to lower blood sugar and improve memory, says Buzsaki.

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More information: David Tingley et al, A metabolic function of the hippocampal sharp wave-ripple, *Nature* (2021). [DOI: 10.1038/s41586-021-03811-w](https://doi.org/10.1038/s41586-021-03811-w)

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