Research on how dietary choline travels through the blood-brain barrier reveals pathway for treating brain disorders

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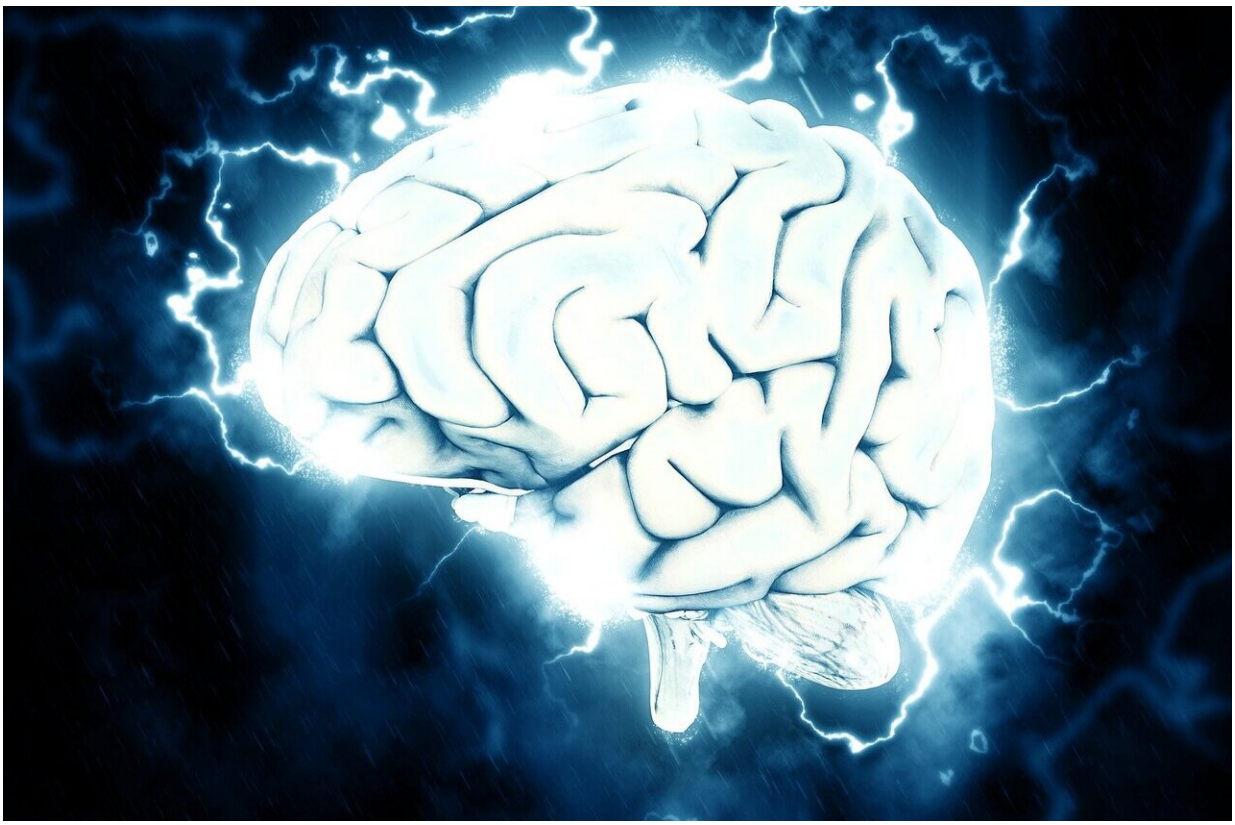

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A University of Queensland researcher has found molecular doorways that could be used to help deliver drugs into the brain to treat

neurological disorders.

Dr. Rosemary Cater from UQ's Institute for Molecular Bioscience led a team that discovered that an essential nutrient called choline is transported into the brain by a protein called FLVCR2. The research is published in *Nature*.

"Choline is a vitamin-like nutrient that is essential for many important functions in the body, particularly for brain development," Dr. Cater said.

"We need to consume 400–500 mg of choline per day to support cell regeneration, gene expression regulation, and for sending signals between neurons."

Dr. Cater said that until now, little was known about how dietary choline travels past the layer of specialized cells that separates the blood from the brain.

"This blood-brain barrier prevents molecules in the blood that are toxic to the brain from entering," she said.

"The brain still needs to absorb nutrients from the blood, so the barrier contains specialized cellular machines—called transporters—that allow specific nutrients such as glucose, omega-3 fatty acids and choline to enter.

"While this barrier is an important line of defense, it presents a challenge for designing drugs to treat neurological disorders."

Dr. Cater was able to show that choline sits in a cavity of FLVCR2 as it travels across the blood-brain barrier and is kept in place by a cage of protein residues.

"We used high-powered cryo-electron microscopes to see exactly how choline binds to FLVCR2," she said.

"This is critical information for understanding how to design drugs that mimic choline so that they can be transported by FLVCR2 to reach their site of action within the brain.

"These findings will inform the future design of drugs for diseases such as Alzheimer's and stroke."

The research also highlights the importance of eating choline-rich foods—such as eggs, vegetables, meat, nuts and beans.

More information: Filippo Mancia, Structural and molecular basis of choline uptake into the brain by FLVCR2, *Nature* (2024). DOI: 10.1038/s41586-024-07326-y.
www.nature.com/articles/s41586-024-07326-y

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