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# Research discovers key cause of restricted blood flow to the brain in vascular dementia

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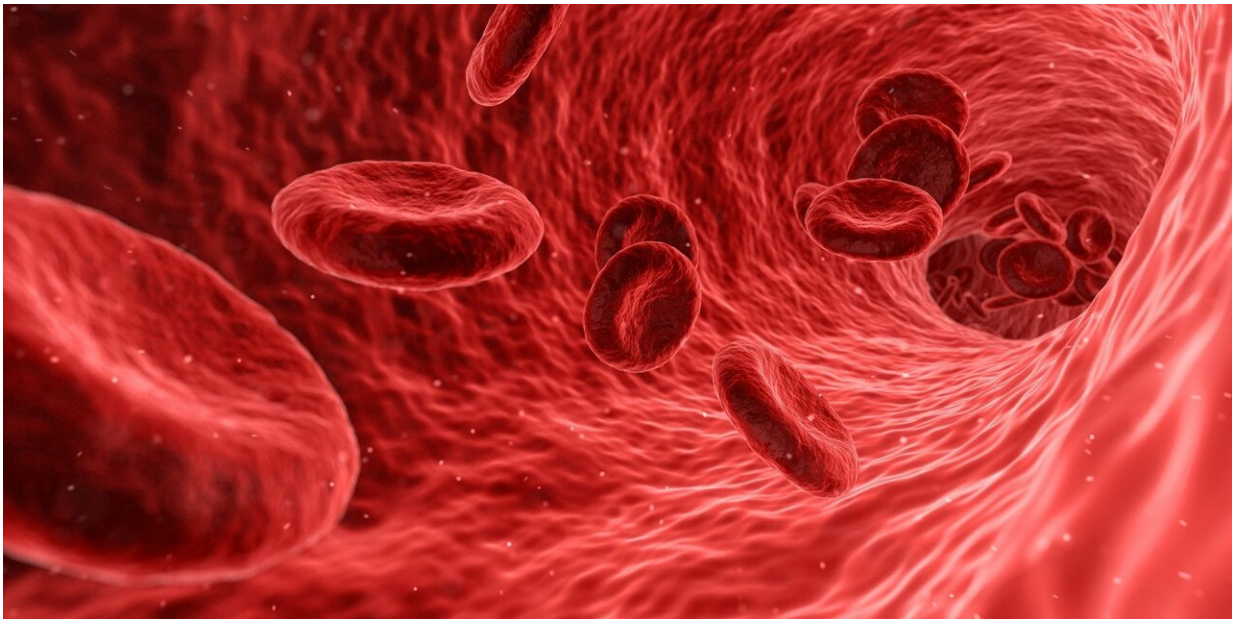

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Groundbreaking new research has uncovered a potential route to developing the first ever drug treatments for vascular dementia, that directly target a cause of the condition. The research, published in the *Proceedings of the National Academy of Sciences*, has shed light on how high blood pressure causes changes to arteries in the brain, a process that leads to the devastating condition.

High blood pressure is a main cause of vascular dementia, a condition characterized by poor blood flow to the brain. The reduced blood supply starves brain cells of nutrients and over time they become damaged and die. Symptoms of vascular dementia include loss of energy, lack of concentration and poor memory.

It's normal for the brain's arteries to narrow and widen in response to changes in blood pressure. However, consistently high blood pressure causes arteries to stay narrow and restrict the brain's blood supply. Until now, it was not known how.

The study, from researchers at the Geoffrey Jefferson Brain Research Centre at The University of Manchester, reveals that—in mice—high blood pressure disrupts messaging within artery cells in the brain. They found that this occurs when two cell structures, that normally help transmit messages that tell arteries to dilate, move further apart. This stops the messages reaching their target, which causes the arteries to remain permanently constricted, limiting blood flow to the brain.

By identifying drugs that could restore this communication, the researchers hope to soon be able to improve blood supply to affected areas of the brain and slow the progression of vascular dementia.

While the findings are yet to be confirmed in humans, the processes of blood vessel narrowing and widening are very similar in mice and humans. The researchers are now investigating drugs that could restore this signaling, which they hope, in future will lead to human studies that aim to restore healthy brain blood flow in vascular dementia.

Professor Adam Greenstein, a clinician scientist specializing in high blood pressure at the University of Manchester and one of the leaders of the research, said,

"By uncovering how high blood pressure causes arteries in the brain to remain constricted, our research reveals a new avenue for drug discovery that may help to find the first treatment for vascular dementia. Allowing blood to return as normal to damaged areas of the brain will be crucial to stopping this devastating condition in its tracks."

"Any drugs that are discovered to improve brain blood supply may also be able to open a new line of attack in treating Alzheimer's disease, which causes very similar damage to blood vessels as vascular dementia. Drugs to restore healthy blood flow could make current treatments, which focus on removing harmful amyloid plaques in the brain, more effective."

Professor Sir Nilesh Samani, Medical Director at the British Heart Foundation, said, "Vascular dementia affects around 150,000 people in the UK, and this number is going up. There are no treatments to slow or stop the disease, but we know that high blood pressure is an important risk factor. The incurable symptoms are hugely distressing for patients and those close to them."

"This exciting research reveals a specific mechanism by which high blood pressure might increase the risk of vascular dementia. Pinpointing how arteries remain permanently narrowed in vascular dementia could lead to the development of new effective treatments, raising hope that there may soon be a way to prevent this illness from destroying more lives."

**More information:** Taylor, Jade L. et al, Uncoupling of Ca2+ sparks from BK channels in cerebral arteries underlies hypoperfusion in hypertension-induced vascular dementia, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2307513120. doi.org/10.1073/pnas.2307513120

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