Potential new drug for incurable vascular dementia

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A drug already used to treat high blood pressure could be re-purposed as the first treatment to tackle a type of vascular dementia caused by damaged and 'leaky' small blood vessels in the brain, according to

research part-funded by the British Heart Foundation and published today in the *Journal of Clinical Investigation*.

High blood pressure is known to be the main risk factor in developing vascular dementia. However, the way that high blood pressure damages the small blood vessels, causing them to narrow and restrict blood flow to specific areas of the brain, has been unknown. The effectiveness of different types of blood pressure medication on these arteries has also never been directly tested.

Now, researchers at the University of Manchester working with colleagues in the USA have discovered that the blood pressure drug amlodipine could help treat vascular dementia or stop it in the early stages.

They looked at blood flow in the brains of mice with high blood pressure and vascular damage in the brain. Mice treated with amlodipine had better blood flow to more active areas of the brain. Their arteries were able to widen, allowing more oxygen and nutrients to reach the parts of the brain that needed it most.

The team also discovered for the first time that high blood pressure decreases the activity of a protein called Kir2.1 that is present in cells lining the blood vessels and increases blood flow to active areas of the brain.

Amlodipine was found to restore the activity of Kir2.1 and protect the brain from the harmful effects of high blood pressure. Researchers say that this protein could also be targeted by other drugs in the future, presenting a potential additional way to help fight the disease.

The team now hope to trial amlodipine as an effective treatment for vascular dementia in humans. If successful, it would be the first

clinically proven treatment for vascular dementia as a result of small vessel disease and could be used in those with early signs of the condition to prevent further progression.

Dr Adam Greenstein, Clinical Senior Lecturer in Cardiovascular Sciences at the University of Manchester, who led the Manchester team, says that "the way vascular dementia develops has remained a mystery until now, and there are currently no clinically proven treatments. Patients are presenting with symptoms of vascular dementia earlier than ever before, and with further research we could potentially offer those patients hope to prevent the progression of this life-changing disease."

Professor Metin Avkiran, Associate Medical Director at the British Heart Foundation says that "the way to better understand this devastating disease and find new treatments is through research. This study is a vital step forward towards finding new ways of stopping vascular dementia from progressing."

"These new discoveries highlight the major role that high blood pressure plays in developing the disease and shed light on how this occurs and might be prevented in the future. At present, the most important thing you can do to lower your risk of the disease is to keep your blood pressure within the healthy range. You can get your blood pressure checked for free at your GP or local pharmacy."

More information: Masayo Koide et al, Differential restoration of functional hyperemia by antihypertensive drug classes in hypertension-related cerebral small vessel disease, *Journal of Clinical Investigation* (2021). DOI: 10.1172/JCI149029

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