

**Changes in how cholesterol breaks down in the body may accelerate progression of dementia & alzheimer's disease**

*Study suggests that some cholesterol medications may impact signaling pathways in the Brain, particularly in men*

Cholesterol is impermeable to the blood brain barrier, yet high blood cholesterol is associated with increased risk of Alzheimer's disease and vascular dementia. However, the underlying mechanisms mediating this relationship are poorly understood. A study published in *PLOS Medicine* by Vijay Varma at National Institutes of Health, in Baltimore, Maryland, and colleagues suggests that disturbances in the conversion of cholesterol to bile acid (called cholesterol catabolism) may play a role in the development of dementia.

Little is known how high blood cholesterol may lead to an increased risk of Alzheimer's and dementia, yet understanding the contributing processes is critical to the development of effective Alzheimer's and dementia therapeutics. To investigate whether abnormalities in cholesterol catabolism through its conversion to bile acid is associated with development of dementia, researchers conducted a prospective cohort study of 141 aging individuals and 29 autopsy samples from older participants. The researchers tested whether cholesterol catabolism was associated with brain abnormalities typical of Alzheimer's and dementia. They next tested whether exposure to cholesterol medication that blocks bile acid absorption into the bloodstream was associated with an increased risk of dementia and if people with Alzheimer's disease tend to have altered levels of bile acids in their brains.

The authors found that the risk of dementia was higher among males using an increased number of bile acid blocking prescriptions, and that cholesterol catabolism and bile acid synthesis may accelerate the progression of dementia. However, additional studies are needed as the research was limited by the relatively small sample sizes of patients and autopsy samples, so future studies are needed.

According to the authors, "Our findings suggest that cholesterol catabolism and bile acid synthesis may impact dementia progression through sex-specific effects on signaling pathways in the brain. These results set the stage for experimental studies to test whether bile acid signaling in the brain may be a novel therapeutic target in dementia."

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