

DRUGS

## Viagra may lower the risk of Alzheimer's

BY ALICE PARK

VIAGRA IS BEST KNOWN FOR HELPING erectile dysfunction, but recent research suggests it might also lower the risk of Alzheimer's disease.

Viagra belongs to a group of drugs known as phosphodiesterase Type 5 inhibitors, which work by relaxing blood vessels and increasing blood flow in the penis. In a study published in *Neurology*, researchers found that the drugs were also associated with a lower risk of Alzheimer's disease.

The study analyzed the health records of nearly 270,000 men in the U.K. who were diagnosed with erectile dysfunction from 2000 to 2017. The researchers compared rates of Alzheimer's disease among men who had been prescribed drugs to treat their erectile dysfunction (primarily sildenafil, the generic name for Viagra) to those among men who had not been prescribed the drugs. In the U.K., lifestyle changes are the first line of treatment for the condition, and if those are not effective, then doctors prescribe medications. (In 2018, after the participants were enrolled, sildenafil

became available without a prescription at pharmacies in the U.K.)

Men who were prescribed a medication had an 18% lower risk of having Alzheimer's than those who were not. The reduction was greater among men who got 20 or more prescriptions over the study's five-year follow up period.

"We didn't have strong expectations and were thinking that surely there was no direct evidence between these drugs and reduced risk of Alzheimer's. But we definitely found a protective effect," says Ruth Brauer, lecturer at the University College of London's School of Pharmacy and senior author of the paper. "We feel these are excellent candidates for drug repurposing [for Alzheimer's]."

The study isn't the first to explore the connection between erectile dysfunction drugs and Alzheimer's risk. Two previous studies, both conducted in the U.S., reached conflicting conclusions: one found a 69% lower risk of Alzheimer's among users of the drugs, while the other found no association. Brauer points out, however, that one of those studies relied on insurance data, while her study included more detailed information from anonymized medical health records from the U.K.'s National Health Service. That allowed her team to better adjust for potential confounding factors that could affect either erectile dysfunction

or Alzheimer's risk, such as smoking, alcohol use, and other health conditions. Even after controlling for those factors, the connection between the drugs and a lower risk of Alzheimer's remained.

Erectile dysfunction treatments work by relaxing the blood vessels and increasing blood flow. That effect may extend to the brain, where improved circulation could help to clear the buildup of toxic proteins tightly linked to Alzheimer's disease. Based on animal studies, the drugs also indirectly increase levels of a brain chemical called acetylcholine, which is involved in memory, learning, and attention. (The first medications approved to address Alzheimer's symptoms increase brain levels of acetylcholine.)

Although the data don't establish a causal relationship between erectile dysfunction drugs and a lower risk of Alzheimer's, Brauer points to another piece of evidence that strengthens the association. When she broke down the data by age, the drugs had a stronger protective effect among men 70 years or older compared to men under 70. "The drugs seem to have a greater benefit among individuals at the greatest risk of Alzheimer's," she says. "We feel these promising results should justify taking these drugs further as candidates for repurposing."

One limitation of the study is that the scientists only had data on the number of prescriptions the men received, and could not verify if they filled the prescriptions or used the medications properly. They could also not account for the men's physical or sexual activity levels; it's possible, for example, that men with erectile dysfunction are more sexually and physically active than other men.

Brauer hopes that other researchers will further explore the potential of erectile dysfunction drugs by conducting trials to address these issues by including men without erectile dysfunction, along with women. If the connection remains strong, these drugs could potentially provide another way for people to protect themselves from the neurodegenerative disorder.

