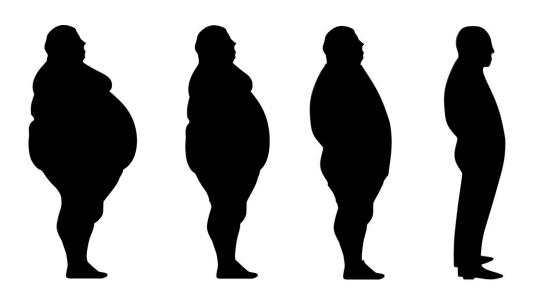


## Wegovy and Ozempic: Could the new weightloss drug also treat dementia?

May 19 2023, by Tim Viney and Barbara Sarkany



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Over <u>55 million people worldwide have dementia</u>. This mind-robbing condition has a huge impact on society and the economy, so scientists are working hard to find ways to treat or prevent it. One of the avenues being explored is the new weight-loss jab, Wegovy.

Although age is by far the greatest risk factor for <u>dementia</u>, obesity and type 2 diabetes are also major <u>risk factors</u> for developing the condition. This is where Wegovy and its sister drug, Ozempic, come into the picture. <u>Wegovy</u> and <u>Ozempic</u>, a drug to treat type 2 diabetes, both



contain the same active substance called semaglutide.

Semaglutide mimics the action of a hormone, GLP-1, that is normally released from the gut after a meal. The hormone latches on to receptors in the pancreas that stimulate the release of insulin, which helps <u>lower</u> <u>blood sugar levels</u>.

However, these receptors are also in "reward centers" of the <u>brain</u>, including in areas controlling eating. Given that semaglutide is able to <u>cross the blood-brain barrier</u> (the <u>protective layer</u> around the brain), it is likely to directly modify <u>brain activity</u> to make people feel less hungry.

A Danish study that followed people with type 2 diabetes for five years found those on semaglutide or liraglutide (another <u>diabetes drug</u>) had a lower incidence of dementia. Type 2 diabetes is more strongly associated with <u>vascular dementia</u> and not Alzheimer's disease (the most common form of dementia), so only certain forms of dementia might be reduced by semaglutide.

Nevertheless, <u>two clinical trials</u> which began in 2021 are testing whether daily oral doses of semaglutide will slow disease progress in people in the early stages of Alzheimer's. Since it takes a long time to develop the disease, trials are expected to be completed in 2026.

Alzheimer's disease is thought to originate in <u>specific regions of the</u> <u>cerebral cortex</u>—the region responsible for memories and spatial navigation. But receptors for GLP-1 were <u>not detected in the cortex</u>, making it unlikely that semaglutide directly activates memory networks. So how might the drug treat the disease?

The brains of Alzheimer's disease patients accumulate sticky plaques of amyloid-beta as well as clumps of tau proteins inside brain cells. These are thought to disrupt cognition.



<u>A clinical trial</u> is underway here at the University of Oxford that will specifically examine tau levels in people who have high levels of amyloid-beta but have not (yet) developed dementia. It is hoped that semaglutide will reduce cortical tau levels, leading to reduced rates of cognitive decline.

Drugs recently approved in the US to treat <u>Alzheimer's</u> target amyloidbeta plaques. But these drugs have proved controversial, with patients requiring hour-long infusions every two to four weeks.

These types of drug probably also target amyloid-beta around <u>blood</u> <u>vessels</u>, leading to potentially life-threatening <u>side-effects</u> such as bleeds in the brain. Alternative strategies are therefore desirable, and this is where semaglutide may shine.

## Inflammation

The key link between semaglutide and reducing Alzheimer's disease might be <u>neuroinflammation</u>—a state in which the <u>brain</u> is chronically inflamed.

Neuroinflammation <u>damages the blood-brain barrier</u>, which is disrupted in both Alzheimer's disease and vascular dementia. The <u>Oxford trial</u> examining tau is also looking at how semaglutide affects neuroinflammation (there are suggestions that <u>semaglutide is antiinflammatory</u> in people with obesity).

It also reduces neuroinflammation in the <u>brains of mice</u>, and restores <u>glucose transport</u> across the <u>blood-brain barrier</u> (something that is disrupted in people with Alzheimer's).

Another drug, memantine—originally developed to treat diabetes—was repurposed to ease symptoms of Alzheimer's disease, and is still



prescribed for that use <u>today</u>. Now we eagerly await the results of the next-generation of diabetes and weight-loss drugs to see if they can prevent or treat Alzheimer's disease.

In the meantime, there are lifestyle changes you can make to reduce your risk of <u>developing the condition</u>. These include keeping active, eating a <u>healthy diet</u>, maintaining a healthy weight, and quitting smoking.

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