

Nasal spray clears proteins linked to Alzheimer's, study finds

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Scientists in America have [developed](#) a nasal spray that can remove proteins in the brain associated with Alzheimer's disease—at least, in mice.

There are two proteins implicated in Alzheimer's: amyloid and tau. Most of the drugs—including those recently approved by the US Food and

Drug Administration (FDA)—focus on removing amyloid. To date, though, there has been little focus on removing tau "tangles." However, the new [nasal spray](#), developed by researchers at the University of Texas Medical Branch, focuses on this protein.

In a healthy brain, tau, among other things, helps to maintain the support structure of neurons ([brain cells](#)). In Alzheimer's and other neurodegenerative disease, these proteins accumulate inside cells, abnormally twist and form thread-like structures known as neurofibrillary tangles. These tangles are not efficiently cleared by the brain's normal waste removal processes, which causes cell damage and death. This leads to [memory loss](#).

So targeting tau may be an effective treatment for several [neurodegenerative diseases](#), including Alzheimer's, [frontotemporal dementia](#), Lewy body dementia and [progressive supranuclear palsy](#).

As mentioned above, Alzheimer's is not only associated with the accumulation of tau inside neurons but also with the build up of amyloid plaques between neurons, leading to their death.

So far, most treatments for Alzheimer's disease have targeted the removal of amyloid from the brain. These include the FDA-approved drugs [lecanemab](#) and [donanemab](#) (these drugs are not yet approved in the UK).

Lecanemab and donanemab have been effective in slowing the progression of cognitive decline in clinical trials; however, there are many limitations, including accessibility, price and the fact that they are only effective at an early diagnostic stage.

Some argue that the slowed disease progression is so slight, they would not be noticed by someone with early-stage Alzheimer's. And nobody

knows if the slowed disease progression is sustained in the long term.

Unfortunately, treatments targeting tau have proven less [effective](#) in human trials. Until recently, treatments targeting tau have struggled because of their limited ability to penetrate the parts of the neuron where tau is building up. Remember, amyloid accumulates outside of neurons, while tau accumulates inside them.

Effective in mice

The researchers at the University of Texas Medical Branch have developed an innovative nasal spray that has shown positive results in reducing the deadly tau protein build up and improving memory in aged [mice](#) models of neurodegenerative diseases.

The researchers first optimized antibodies (proteins created by the immune system) that latch onto the tau proteins and eliminate them. They achieved this by adding the antibodies into petri dishes containing human nerve tissue with tau proteins.

Once the most effective antibody for targeting tau was identified (called TTCM2), the researchers packaged the antibodies into tiny bubbles of fat (lipids). These are small enough to pass through the blood-brain barrier and enter neurons.

Breaking through the [blood-brain barrier](#) was the biggest challenge in targeting tau and tangles. Once in the brain, the outer layer of the bubble dissolved, releasing the antibodies and clearing the build up of tau.

For therapeutic purposes, this highly effective antibody was dissolved in a liquid solution and delivered using a nasal spray to mouse models of Alzheimer's disease.

The results showed that a single dose of this nasal spray in the old Alzheimer's mice significantly reduced tau accumulation in their brains. The same results were also discovered when applying the spray to human nerve tissue samples.

The nasal spray also showed significant improvements in memory and cognition in these mice. This was tested using the novel object recognition test, which tests whether the mice can identify a new object compared to a familiar object.

While all of this sounds very exciting, it's important to consider that this research is yet to be tested on humans. Although mice are valuable models for studying potential treatments, there are significant differences between mice and humans.

Around [70% of drugs](#) in the "preclinical phase" (before a treatment is tested in humans) do not make it to [human trials](#). The [success rate](#) at testing in humans, called [clinical trials](#), is even less optimistic, with [90% of drugs](#) failing to make it to market.

Having said that, this nasal spray method paves the way for non-invasive delivery of tau antibodies directly to the brain, offering promising potential for treating various neurodegenerative diseases affected by tau accumulation.

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