Novel treatment may restore memory in Alzheimer's, mouse study suggests

Written by Katharine Lang on August 15, 2024 — Fact checked by Jill Seladi-Schulman, Ph.D.

Could an experimental new drug help restore memory in Alzheimer's? Image credit: Chelsea Victoria/Stocksy.

- **Although Alzheimer's disease is the most common form of dementia, there is still no cure for the disease.**
- **New disease-modifying drugs have shown potential, but there are concerns about side effects of these treatments.**
- **In the search for new therapies, a study has developed a molecule that restores lost cognitive function in mice.**
- **The study authors suggest that, if similar results are seen in people, this could be the basis of a novel treatment for Alzheimer's.**

Some 55 million people worldwide have dementia. According to the Alzheimer's Association, 7 million people in the United States alone are living with Alzheimer's disease, the most common form of dementia. At present, there is no cure for the disease.

Current treatments can slow the progress of the disease, and alleviate symptoms, which may include:

- memory loss, especially taking in and remembering new information
- cognitive deficits, such as difficulty with reasoning, complex tasks and judgment
- recognising familiar objects and people
- problems with spatial awareness
- difficulties with speaking, reading and writing
- personality or behavior changes.

Newer monoclonal antibody drugs that clear the amyloid plaques characteristic of Alzheimer's disease were hailed as the first disease-modifying treatments for the condition, but research has raised concerns about their side effects.

Now, a new study has identified and synthesized a molecule that restores cognitive function in Alzheimer's disease model mice by increasing gamma oscillations.

The study, by researchers from The University of California, Los Angeles (UCLA), is published in *Proceedings of the National Academy of Sciences (PNAS)*.

Stefania Forner, PhD, Alzheimer's Association director of medical and scientific relations, not involved in this research, told *Medical News Today*:

> "It is an exciting time in Alzheimer's disease and dementia research with hundreds of potential therapies being tested at various stages of the research process, and many more being

> developed. This study, using a mouse model of Alzheimer's disease, explores a new approach to improving brain function related to cognition and memory."

Gamma oscillations are reduced in Alzheimer's disease

Gamma oscillations are high-frequency waves in the brain that play a role in many cognitive processes and working memory — the type of memory used when dialing a phone number you were just told, or remembering an address when being given directions.

Even in the early stages of Alzheimer's disease, these oscillations are reduced, and studies have suggested that aberrant gamma oscillations may be an early biomarker of Alzheimer's, detectable before amyloid plaques start to develop.

Some studies have improved cognitive ability in people with mild to moderate Alzheimer's disease using repetitive transcranial magnetic stimulation (rTMS), which has been shown to modify gamma oscillations.

In this study, the researchers aimed to enhance gamma oscillations by another method — using a molecule that targeted fast-firing nerve cells that are critical in generating gamma oscillations.

The molecule they identified — DDL-920 — acted on chemical receptors in these nerve cells that respond to the inhibitory chemical messenger known as GABA and reduce the gamma oscillations. DDL-920 led to more powerful gamma oscillations from the nerve cells.

Forner told *MNT*: "The study tests a small molecule called DDL-920, which boosts these gamma oscillations. Unlike current FDA-approved treatments that focus on removing beta-amyloid plaques, DDL-920 targets brain circuitry in a different way."

"While this approach offers a fresh perspective on enhancing cognitive function and memory in Alzheimer's, it's important to note that the

research is still in the early stages using mouse models," she noted.

Novel drug improves cognitive function in mice

Having established that DDL-920 increased gamma oscillations, the researchers then used an Alzheimer's disease mouse model to determine whether this resulted in improved cognitive function.

They gave DDL-920 orally twice a day to 3-month old Alzheimer's disease model mice. As a comparison, a similar number of AD model mice and wild-type mice were given a vehicle (inactive compound).

The mice were then tested in a Barnes maze — an elevated circular platform, with 20 holes, one of which leads to an escape tunnel — to assess their spatial learning and memory. After several days of training in a maze with an escape tunnel, the tunnel is closed. Learning and memory is then assessed by how long the mice spend in the region where the escape tunnel was.

Following treatment, the Alzheimer's disease model mice could recall the location of the escape hole at the same rate as the wild-type mice. Untreated Alzheimer's disease model mice took significantly longer.

Emer MacSweeney, MD, CEO and Consultant Neuroradiologist at Re:Cognition Health, also not involved in this research, explained that "[t]he study suggests that DDL-920 enhances memory and cognition by increasing gamma-oscillation power without affecting other brain functions or causing side effects."

However, she added a note of caution, pointing out that, "[s]ince the findings are based on a mouse model, further research is needed to evaluate the efficacy and safety of DDL-920 in humans."

Early findings suggest new approach to Alzheimer's treatment

The study authors suggest that if similar effects were seen in people, DDL-920 could form the basis of new treatments to revitalize memory and

cognition in Alzheimer's disease.

> "DDL-920 operates differently from monoclonal antibody (MAB) treatments like lecanemab, which target amyloid-beta plaques directly. Instead, DDL-920 enhances γ-oscillations, which may improve cognitive function, indirectly. This approach could have potential, especially if combined with MAB treatments, offering a complementary mechanism that targets neural activity and cognitive processes rather than amyloid burden alone. This could be particularly beneficial for patients who might not respond fully to amyloid-targeting therapies."
>
> – Emer MacSweeney, MD

Forner welcomed the results as "intriguing," but emphasized that animal models, while similar to the progression of Alzheimer's disease in people, cannot exactly replicate the condition. She also highlighted the importance of research into potential new treatments:

"Treatments that target Alzheimer's from all angles and all stages of the disease are essential, and that's why strategic research funding that works to diversify the therapies in the pipeline is so important. All evidence-based paths to treatment of Alzheimer's and all other dementia should be explored," she told us.

"The Alzheimer's Association envisions a future where there are many treatments available that address these diseases in multiple ways, and can be combined into powerful combination therapies, most likely in conjunction with brain-healthy lifestyle guidance," she added.

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