Alzheimer's disease, a new therapeutic target identified

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A new potential target for the treatment of Alzheimer's disease has been identified: PDE4B. Researchers from the University of Leeds and the University of Lancaster, in the United Kingdom, discovered this.

The results of the study, reported in Neuropsychopharmacology, open new avenues for the fight against Alzheimer's disease, which is the main cause of dementia and disability in old age in the world. As the number of people diagnosed with Alzheimer's disease is growing significantly, there is an urgent need for new treatments aimed at improving the quality of life of those affected.

The role of the PDE4B enzyme

PDE4B is an enzyme that, inside cells, breaks down a molecule, known as cyclic AMP, which regulates a series of cellular processes. Based on an Australian study that identified the PDE4B gene as a risk factor for the development of Alzheimer's disease, the British research team focused its investigation on understanding whether reducing PDE4B activity could protect against Alzheimer's and , consequently, represent a valid therapeutic approach.

To this end, scientists introduced a gene for reducing PDE4B activity into a mouse model of Alzheimer's disease, with amyloid plaques in the brain, a typical pathological feature of the disease. The researchers observed that Alzheimer's mice showed memory deficits in maze tests, but memory was not impaired in Alzheimer's mice with genetically reduced PDE4B activity. Using functional brain imaging, the research team found that the metabolism of glucose, the brain's

main energy source, was impaired in mice with Alzheimer's, as in patients with the disease. However, mice with genetically reduced PDE4B activity showed healthy levels of glucose metabolism in the brain.

The mouse experiment

To understand the mechanisms involved, the researchers then examined gene and protein expression levels in the brain. The scientists identified increased inflammation in the brains of Alzheimer's mice, like that found in patients with the disease, but the inflammation was less in Alzheimer's mice with genetically reduced PDE4B activity.

Similar effects have been observed for a number of other proteins involved in Alzheimer's pathology. Overall, the data suggest that reducing PDE4B activity could be a possible approach for treating Alzheimer's disease, although further research is needed to validate the use of drugs that target the enzyme.

Not just Alzheimer's

“Reducing PDE4B enzyme activity had a profound protective effect on memory and glucose metabolism in the Alzheimer's mouse model, although these mice showed no decrease in the number of amyloid plaques in the brain,” said Steven Clapcote , Principal Investigator at the University of Leeds. "This raises the prospect that reducing PDE4B activity may protect against cognitive impairment not only in Alzheimer's disease, but also in other forms of dementia, such as Huntington's disease," Clapcote continued.

“These findings offer real hope for the development of new treatments that will benefit Alzheimer's disease patients in the future,” said Neil

Dawson, from Lancaster University and co-author of the work. “It was interesting to find that reducing PDE4B activity by just 27% can dramatically rescue memory, brain function and inflammation in mice with the disease,” Dawson continued. “The next step is to verify whether drugs that inhibit PDE4B have similar beneficial effects in the Alzheimer's mouse model, so as to test their potential efficacy in the disease,” concluded Dawson.