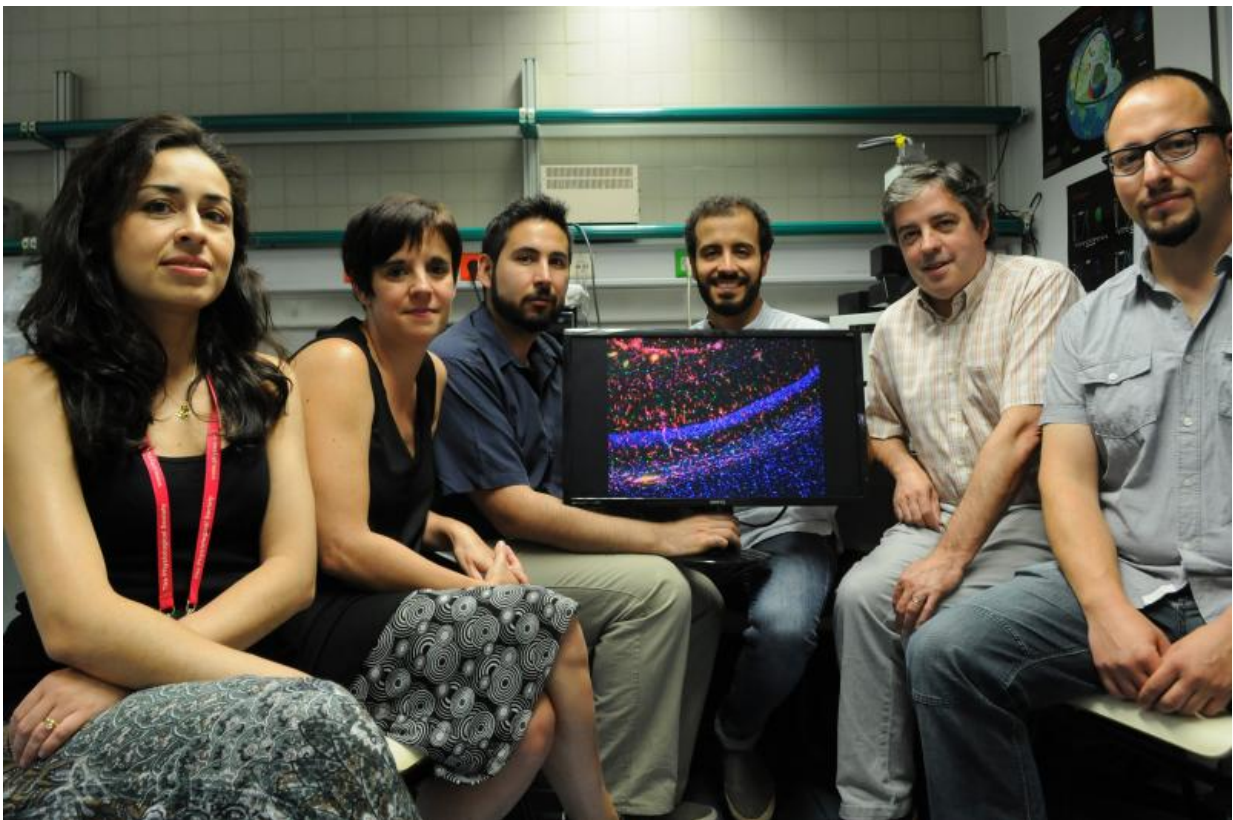


Researchers discovered new applications of the drug fingolimod to improve cognitive deficits in Huntington's disease

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University of Barcelona research team.

Fingolimod, a drug used to treat multiple sclerosis, restores hippocampal synaptic plasticity and improves memory function. This is the main

conclusion of a study developed by researchers at the University of Barcelona (UB) and the August Pi i Sunyer Biomedical Research Institute (IDIBAPS) in a mouse model of Huntington disease (HD). The study has been published in the journal *Human Molecular Genetics* and highlighted by the journal *Nature Reviews Neurology*.

"Preclinical results show an improvement of cognitive deficits in Huntington's disease. Given the safety profile of the [drug](#) and the fact that it can also rescue motor deficits in HD mice, the study suggests that fingolimod can be an effective drug to treat Huntington's disease. We believe it would be worthy to carry out clinical trials in the mid-term," says Professor Jordi Alberch, head of the Consolidated Research Group on Pathophysiology of Neurodegenerative Diseases of the UB, IDIBAPS researcher and leader of the study.

Huntington's disease is a progressive and irreversible neurodegenerative disorder that is caused by a mutation of the gene which codifies the protein huntingtin (HTT). In western countries, it affects between five and seven subjects out of 100,000. It is a rare hereditary disease which mainly affects basal ganglia and causes severe motor, cognitive and psychiatric disturbances. Remarkable advances have been done in basic research on Huntington's disease; however, an effective treatment has not been found yet.

Drugs with new applications

The Consolidated Research Group on Pathophysiology of Neurodegenerative Diseases of the UB, affiliated with the Centre for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), has studied the signalling pathways of brain-derived neurotrophic factor (BDNF) with receptors TrkB and p75NTR, a key factor in [synaptic plasticity](#) regulation, cognitive function and memory. In a previous study, the UB-IDIBAPS research team found that cognitive

and synaptic deficits of Huntington's disease patients linked to an imbalance between these two receptors.

The study proves that fingolimod influences BDNF receptors and re-establishes their normal balance, by increasing TrkB and reducing p75NTR simultaneously. From a cellular point of view, it attenuates over-activation of astrocytes and reduces neuroinflammation, ultimately leading to a better preservation of dendritic spines and [memory function](#).

In order to reliably assess the utility of the drug in the chronic treatment of Huntington's disease in a preclinical model, the drug was delivered to HD mice during 3 months, starting at presymptomatic stages. It was observed that memory deficits improved significantly in the long term and they perform better in spatial recognition tests.

"Findings constitute a significant step forward in understanding how fingolimod acts on brain cells; it has been proved that it can be an effective drug to treat diseases affecting the hippocampus, like Huntington's disease and Alzheimer's disease," says Andrés Minguez, researcher in the UB-IDIBAPS research group and first author of the paper. "Findings also open the door for studying cognitive function improvement in sclerosis multiple patients treated with fingolimod; this is an issue that has not been examined in detail yet even if it is estimated to occur in more than 50% of patients," concludes Miguez.

More information: "Fingolimod (FTY720) enhances hippocampal synaptic plasticity and memory in Huntington's disease by preventing p75NTR up-regulation and astrocyte-mediated inflammation". *Human Molecular Genetics*, June 2015. [DOI: 10.1093/hmg/ddv218](https://doi.org/10.1093/hmg/ddv218)

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