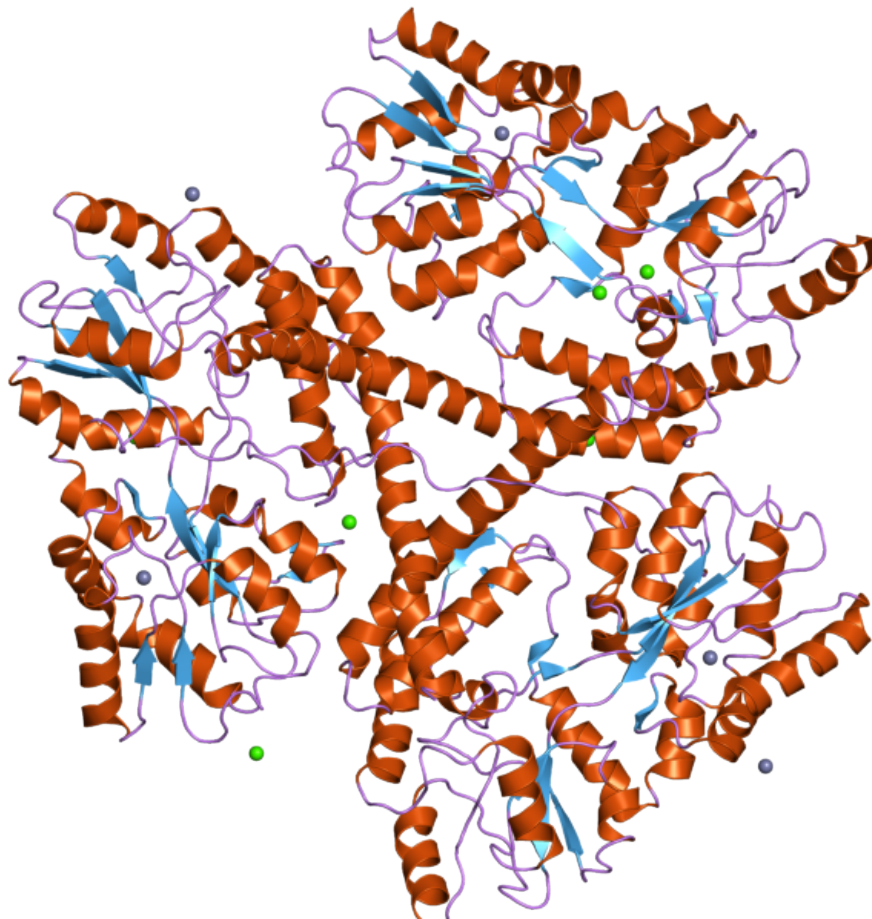


Blood pressure drug shows promise for treating Parkinson's and dementia in animal study

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Huntingtin. Crystallographic structure of the N-terminal region of the human Huntingtin protein with an artificially attached Maltose-Binding protein used for crystallographic purposes. Credit: Public domain

A prescribed drug to treat high blood pressure has shown promise against conditions such as Parkinson's, Huntington's and forms of dementia in studies carried out in mice and zebrafish at the University of Cambridge.

A common feature of these diseases—collectively known as [neurodegenerative diseases](#)—is the build-up of misfolded proteins. These proteins, such as huntingtin in Huntington's disease and tau in some dementias, form 'aggregates' that can cause irreversible damage to nerve cells in the brain.

In healthy individuals, the body uses a mechanism to prevent the build-up of such toxic materials. This mechanism is known as autophagy, or 'self-eating', and involves 'Pac-Man'-like cells eating and breaking down the materials. However, in neurodegenerative diseases this mechanism is impaired and unable to clear the proteins building up in the brain.

As the global population ages, an increasing number of people are being diagnosed with neurodegenerative diseases, making the search for effective drugs ever more urgent. However, there are currently no drugs that can induce autophagy effectively in patients.

In addition to searching for [new drugs](#), scientists often look to re-purpose existing drugs. These have the advantage that they have already been shown to be safe for use in humans. If they can be shown to be effective against the target diseases, then the journey to [clinical use](#) is much faster.

In a study published today in the journal *Nature Communications*, scientists at the UK Dementia Research Institute and the Cambridge Institute for Medical Research at the University of Cambridge have shown in [mice](#) that felodipine, a hypertension drug, may be a candidate for re-purposing.

Epidemiological studies have already hinted at a possible link between the drug and reduced risk of Parkinson's disease, but now the researchers have shown that it may be able to induce autophagy in several neurodegenerative conditions.

A team led by Professor David Rubinsztein used mice that had been genetically modified to express mutations that cause Huntington's disease or a form of Parkinson's disease, and zebrafish that model a form of dementia.

Mice are a useful model for studying [human disease](#) as their short life span and fast reproductive rate make it possible to investigate biological processes in many areas. Their biology and physiology have a number of important characteristics in common with those of humans, including similar nervous systems.

Felodipine was effective at reducing the build-up of aggregates in the mice with the Huntington's and Parkinson's disease mutations and in the zebrafish dementia model. The treated animals also showed fewer signs of the diseases.

Studies in mice often use doses that are much higher than those known to be safe to use in humans. Professor Rubinsztein and colleagues showed in the Parkinson's mice that it is possible to show [beneficial effects](#) even at concentrations similar to those tolerated by humans. They did so by controlling the concentrations using a small pump under the mouse's skin.

"This is the first time that we're aware of that a study has shown that an approved drug can slow the build-up of harmful proteins in the brains of mice using doses aiming to mimic the concentrations of the drug seen in humans," says Professor Rubinsztein. "As a result, the drug was able to slow down progression of these potentially devastating conditions and so

we believe it should be trialled in patients."

"This is only the first stage, though. The [drug](#) will need to be tested in patients to see if it has the same effects in humans as it does in mice. We need to be cautious, but I would like to say we can be cautiously optimistic."

More information: Siddiqi, FH et al. Felodipine induces autophagy in mouse brains with pharmacokinetics amenable to repurposing. *Nature Communications*; 18 April 2019; [DOI: 10.1038/s41467-019-09494-2](https://doi.org/10.1038/s41467-019-09494-2)

Provided by University of Cambridge

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