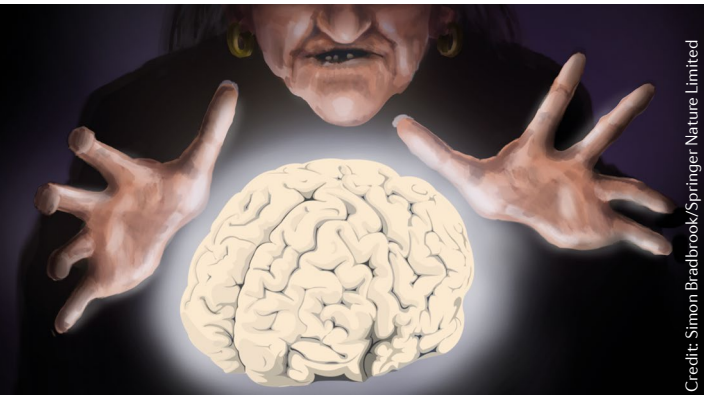
Credit: Simon Bradbrook/Springer Nature Limited

subsequent acceleration in cortical thinning and cognitive decline in early-stage de novo PD," conclude the authors. "Recognizing WMHs as early indicators of cognitive deficit, prior to onset of mild cognitive impairment or dementia, provides an opportunity for timely interventions."

Heather Wood

> a high WMH load at baseline was associated with increased cognitive decline

ORIGINAL ARTICLE Dadar, M. et al. White matter hyperintensities are linked to future cognitive decline in de novo Parkinson's disease patients. *Neuroimage Clin.* **20**, 892–900 (2018)
FURTHER READING Aarsland, D. et al. Cognitive decline in Parkinson disease. *Nat. Rev. Neurol.* **13**, 217–231 (2017)

be reversible," says first author Amber Southwell. "This is very encouraging in terms of developing treatments with the potential to profoundly impact patients' lives."

To assess the translatability of the findings, the team administered ASOs to cynomolgus monkeys via lumbar puncture, the route by which ASOs are currently administered to humans to target the brain. The ASOs reduced huntingtin expression in the cortical and limbic systems, suggesting this administration route could be effective.

Nevertheless, Hayden says there is more work to be done to make translation to the clinic successful. "The most important and pressing challenge is target engagement," he says. "A human phase III clinical trial beginning soon will help to determine what level of target engagement is needed to improve clinical features of HD and hopefully delay progression."

Ian Fyfe

> Administration to old mice after symptom onset reversed existing cognitive deficits

ORIGINAL ARTICLE Southwell, A. L. et al. Huntingtin suppression restores cognitive function in a mouse model of Huntington's disease. *Sci. Transl Med.* **10**, eaar3959 (2018)

MIGRAINE

Erenumab succeeds in alleviating migraine where other treatments fail

Treatment with erenumab reduces the number of migraine days in individuals for whom multiple conventional oral migraine treatments have failed, according to the results of a new phase III clinical trial published in *The Lancet*. The LIBERTY trial shows that therapy directed against the calcitonin gene-related peptide (CGRP) receptor could provide a well-tolerated and effective treatment option for an underserved population of patients with episodic migraine who do not respond to other therapies.

Conventional treatment of migraine consists of therapies that were not developed specifically for the condition. However, the efficacy and tolerability of these agents is poor. "About 75% of patients with migraine stop preventive migraine therapy within 6 months due to adverse effects or lack of efficacy," explains the lead author of the LIBERTY trial, Uwe Reuter. "These patients are considered difficult-to-treat due to a high level of frustration based on prior treatment failures. Often these individuals also suffer from comorbidities such as depression and anxiety."

In the past few years, new migraine-specific therapies have emerged. Several agents that target CGRP, a molecule upregulated during migraine attacks, have been found to be safe and effective in clinical trials. Erenumab, an antibody that targets the CGRP receptor, became the first of these disease-specific therapies to be approved for treatment of migraine in 2018.

In LIBERTY — a 12-week, double-blind, randomized, placebo-controlled trial — Reuter and colleagues investigated whether erenumab treatment might be an effective option in patients with difficult-to-treat episodic migraine whose condition previously failed to respond to between two and four other therapies. The team randomly assigned 246 individuals to receive either subcutaneous injection of erenumab or placebo once every 4 weeks for 12 weeks.

After 12 weeks, 30% of participants who received erenumab achieved the primary end point of a 50% or greater reduction in the number of monthly migraine days from baseline, compared with only 14% of those who received placebo.

> erenumab reduces the number of migraine days in individuals for whom multiple conventional oral migraine treatments have failed

As demonstrated by previous large clinical trials, erenumab was well tolerated and the frequency of adverse events seen with erenumab treatment was similar to that seen with placebo. More than 98% of participants completed 3 months of treatment with erenumab, whereas in trials of topiramate, an antiseizure medication also used to prevent migraine, ~25% of patients with migraine drop out by the same time point owing to adverse events.

"This patient group has never been studied before in a migraine prevention trial," remarks Reuter. As such, this study provides the first evidence that erenumab is an effective preventive treatment in individuals with episodic migraine who previously did not respond to multiple other treatments. Further investigation is now needed to examine the long-term adherence of these patients to erenumab beyond 12 weeks.

Charlotte Ridler

ORIGINAL ARTICLE Reuter, U. et al. Efficacy and tolerability of erenumab in patients with episodic migraine in whom two-to-four previous preventive treatments were unsuccessful: a randomised, double-blind, placebo-controlled, phase 3b study. *Lancet* https://doi.org/10.1016/S0140-6736(18)32534-0 (2018)