

## EPILEPSY

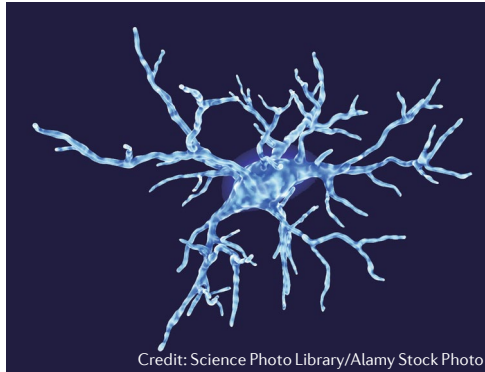
## Cortical thinning in epilepsy is linked to microglial activation

Cortical thinning in the brains of people with epilepsy correlates with the distribution of activated microglia, new research published in *Neuropathology and Applied Neurobiology* indicates. The study, conducted by the ENIGMA-Epilepsy Working Group, also showed that transient microglial depletion prevented seizure-associated cortical thinning in mice, suggesting a potential strategy to protect the cortex from seizure-induced damage.

“In the first ENIGMA study, which was published in 2018, Whelan et al. showed that epilepsy was associated with widespread and distinct patterns of cortical thinning,” explains co-corresponding author Sanjay Sisodiya. “In the current study, we have tried to identify the mechanisms of the thinning to determine if it might be prevented.”

By combining data on cortical thinning from the Whelan et al. study with gene expression data from the Allen Human Brain Atlas, the researchers found evidence that microglial and endothelial cell densities were increased in cortical regions that were vulnerable to thinning. Markers of activated microglia were particularly highly expressed in these regions, and post-mortem investigations confirmed the presence of large numbers of activated microglia in the brains of people with chronic epilepsy.

To further explore the relationship between microglial activation and cortical thinning, the authors examined the effects of transient microglial depletion, using the tyrosine kinase inhibitor PLX3397, in a mouse model of acquired epilepsy. This intervention was found to prevent cortical thinning in some regions but had no effect on the development of seizures, implying that these two processes



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are dissociable. “This is a really important finding and might help explain how outcomes in epilepsy can be poor even if seizures are controlled,” comments Sisodiya.

“Experiments in mice also showed that cortical thinning was associated with both neuronal cell loss and cognitive deficits on a behavioural test involving the entorhinal cortex — one area that undergoes thinning in epileptic mice and in humans with epilepsy,” adds co-corresponding author Annamaria Vezzani. “The animal data showed that microglia are involved in these effects in the early phases of epilepsy development.”

The researchers acknowledge that the cell types and mechanisms involved in epilepsy-associated cortical thinning require further investigation. The possible benefits of microglial manipulation in humans with epilepsy also remain to be explored: although PLX3397 has already been approved by the FDA for the treatment of tenosynovial giant cell tumour, the essential role of microglia in normal physiological responses to brain insults might limit the applications of this drug in the context of epilepsy.

Heather Wood

**ORIGINAL ARTICLE** Altmann, A. et al. A systems-level analysis highlights microglial activation as a modifying factor in common epilepsies. *Neuropathol. Appl. Neurobiol.* <https://doi.org/10.1111/nan.12758> (2021)

**RELATED ARTICLE** Whelan, C. D. et al. Structural brain abnormalities in the common epilepsies assessed in a worldwide ENIGMA study. *Brain* **141**, 391–408 (2018)

## IN BRIEF

## MULTIPLE SCLEROSIS

## Multiple sclerosis relapses not associated with mRNA COVID-19 vaccine

An mRNA COVID-19 vaccine does not increase the short-term risk of relapses in people with multiple sclerosis (MS), a new study indicates. Di Filippo et al. analysed data from 324 people with MS who received the Pfizer/BioNTech BNT162b2 vaccine and were followed up for  $\geq 2$  months after their first dose. The incidence of clinical relapses in the 2 months after vaccination did not differ significantly from that in the 2 months before vaccination. The results support the recommendation for people with MS to receive the COVID-19 vaccine.

**ORIGINAL ARTICLE** Di Filippo, M. et al. mRNA COVID-19 vaccines do not increase the short-term risk of clinical relapses in multiple sclerosis. *J. Neurol. Neurosurg. Psychiatry* <https://doi.org/10.1136/jnnp-2021-327200> (2021)

## NEURODEGENERATIVE DISEASE

## Deep learning distinguishes tauopathies

A deep learning-based model has been used to accurately differentiate and diagnose different tauopathies. The algorithm was trained to recognize different cortical tau lesions associated with Alzheimer disease, progressive supranuclear palsy, corticobasal degeneration and Pick disease. In testing and validation cohorts, the algorithm correctly diagnosed tauopathies with  $>95\%$  accuracy. The model could, therefore, have potential as a diagnostic tool in clinical practice.

**ORIGINAL ARTICLE** Koga, S., Ikeda, A. & Dickson, D. W. Deep learning-based model for diagnosing Alzheimer's disease and tauopathies. *Neuropathol. Appl. Neurobiol.* <https://doi.org/10.1111/nan.12759> (2021)

## MIGRAINE

## Hypothalamus loses control in migraine

Reduced hypothalamic control of the limbic system could be a cause of migraine attacks, according to new imaging research. Functional MRI was used to longitudinally assess hypothalamic connectivity and cortical perfusion during migraine cycles in 12 patients with episodic migraine. During the headache phase of migraine attacks, perfusion of the limbic system was high and hypothalamic connectivity to the limbic system was reduced relative to the interictal period. The research supports the idea that the hypothalamus is central to migraine pathophysiology and suggests that control of limbic circuits could be a novel therapeutic approach.

**ORIGINAL ARTICLE** Stankewitz, A. et al. Migraine attacks as a result of hypothalamic loss of control. *Neuroimage Clin.* **32**, 102784 (2021)

## DEMENTIA

## Early-onset dementia in autism spectrum disorder

Autism spectrum disorder (ASD) is associated with an increased risk of early-onset dementia, new research has shown. Vivanti et al. used US medical insurance records for  $>1.2$  million individuals aged 30–64 years to examine the prevalence of dementia over 5 years among people with a diagnosis of ASD, ASD with intellectual disability, intellectual disability alone or neither. The prevalence was highest among people with intellectual disability alone (7.10%), but was also considerably higher among people with ASD (4.04%) and people with ASD and intellectual disability (5.22%) than among the healthy population (0.97%). More research will be needed to understand the mechanisms that underlie this association.

**ORIGINAL ARTICLE** Vivanti, G. et al. The prevalence and incidence of early-onset dementia among adults with autism spectrum disorder. *Autism Res.* <https://doi.org/10.1002/aur.2590> (2021)