

## IN BRIEF

## CNS INFECTIONS

**High risk of epilepsy in children with Zika-related microcephaly**

Epilepsy is a frequent occurrence and is often difficult to treat in children with Zika-related microcephaly, according to new data published in *Epilepsia*. The study, which was conducted in Recife, Brazil, included 91 children born during the 2015–2016 Zika virus (ZIKV) epidemic, all of whom had congenital microcephaly associated with ZIKV infection. In the first 24 months of life in this cohort, the incidence of epilepsy was 71.4%, and only 46.1% of the affected children responded to antiepileptic drug treatment. Drug-refractory epilepsy has been widely reported in individuals with other types of brain malformation, such as lissencephaly, and the researchers propose that the seizures in children with Zika-related microcephaly could be related to structural brain abnormalities resulting from ZIKV infection.

**ORIGINAL ARTICLE** Carvalho, M. D. C. G. et al. Early epilepsy in children with Zika-related microcephaly in a cohort in Recife, Brazil: characteristics, electroencephalographic findings, and treatment response. *Epilepsia* <https://doi.org/10.1111/epi.16444> (2020)

## STROKE

**Trial casts doubt on tonic inhibition as a target in stroke treatment**

Despite success in preclinical studies, the GABA<sub>A</sub> α5 receptor antagonist S44819 does not improve outcomes in patients with ischaemic stroke, a trial recently published in *The Lancet Neurology* indicates. Previous research in rodent models of stroke showed that S44819 reversed tonic inhibition in the peri-infarct tissue, which resulted in improvements in motor recovery. The RESTORE BRAIN trial tested two different doses of S44819 (150 mg and 300 mg, administered twice daily) against placebo in 585 patients with ischaemic stroke, starting 3–8 days after stroke onset. Over a follow-up period of 90 days, no differences in clinical outcomes were observed between the S44819-treated patients and the placebo group. These findings raise questions about the influence of tonic inhibition on post-stroke recovery in humans versus rodents.

**ORIGINAL ARTICLE** Chabriat, H. et al. Safety and efficacy of GABA<sub>A</sub> α5 antagonist S44819 in patients with ischaemic stroke: a multicentre, double-blind, randomised, placebo-controlled trial. *Lancet Neurol.* **19**, 226–233 (2020)

## PARKINSON DISEASE

**Brain iron correlates with cognitive change in Parkinson disease**

Iron accumulation in the brain is an indicator of cognitive involvement in Parkinson disease (PD), a new neuroimaging study suggests. A team led by Rimona Weil at University College London, UK, performed quantitative susceptibility mapping (QSM) — an MRI technique that can measure the iron content of brain tissue — in 100 patients with early-stage to mid-stage PD and 37 age-matched controls. The researchers found that brain iron levels were elevated in the prefrontal cortex and putamen in patients with PD compared with controls. Within the PD group, the QSM signal in the parietal and prefrontal cortices correlated with the degree of cognitive impairment, as measured by the Montreal Cognitive Assessment. The results indicate that QSM can be used to track cognitive change in PD and could aid patient stratification and monitoring in clinical trials.

**ORIGINAL ARTICLE** Thomas, G. E. C. et al. Brain iron deposition is linked with cognitive severity in Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* <https://doi.org/10.1136/jnnp-2019-322042> (2020)

## STROKE

**Flood of cerebrospinal fluid causes oedema after stroke**

An influx of cerebrospinal fluid (CSF) causes brain oedema shortly after induction of ischaemia, according to a new study published in *Science*. The findings suggest that inhibition of glymphatic flow would benefit patients with stroke.

“Cerebral oedema is a serious complication of acute ischaemic stroke, but the treatment for oedema has not really changed over the last 60 years,” explains Maiken Nedergaard, who led the new study alongside Yuki Mori. “With new technology that we designed specifically for this study, we were able to visualize oedema development as it was happening.”

Nedergaard and colleagues injected macrospheres into mice to block the middle cerebral artery (MCA) in one hemisphere, leaving the contralateral hemisphere intact. The researchers also imaged CSF flow with a fluorescent tracer.

After MCA occlusion, CSF influx into the brain tissue was higher in the ischaemic hemisphere than in the contralateral hemisphere. This influx occurred in two waves (at ~11 s and ~5 min post-MCA occlusion) and was followed by a reduction in CSF volume in the ventricular system and an increase in the tissue water content of the ischaemic cortex. These observations suggest that CSF entering the brain tissue causes oedema shortly after stroke.

Post-stroke oedema was previously thought to be initiated by movement of Na<sup>+</sup> from the blood to the brain tissue, so Nedergaard and colleagues injected a radioactive form of Na<sup>+</sup> into the bloodstream of mice before MCA occlusion. The levels of radioactive Na<sup>+</sup> were the same in the ischaemic and contralateral hemispheres, suggesting Na<sup>+</sup> influx from the blood is not accelerated by ischaemia.

## DEMYELINATING DISEASE

**Vitamin B<sub>3</sub> promotes remyelination**

Vitamin B<sub>3</sub> promotes the remyelination of axons, according to a new study published in *Acta Neuropathologica*. The treatment acts by stimulating microglia and could be beneficial for individuals with demyelinating diseases such as multiple sclerosis (MS).

Loss of the myelin sheath can be caused by disease and is detrimental to axon function and health. Although remyelination of axons can occur, this process is often incomplete and becomes less efficient with age.

“We are very interested in finding clinically approved medications to promote remyelination,” explains Khalil Rawji, who led the new study at the University of Calgary alongside V. Wee Yong. “As such, we began this project to try to stimulate the ageing immune response to allow efficient myelin repair.”

Remyelination is thought to be facilitated by the clearance of myelin debris by microglia. Therefore, Adam Young and Robin Franklin,

collaborators of Rawji and Yong from the University of Cambridge, isolated primary microglia from young adult (6–8 weeks old) and aged (>15 months old) mice and analysed the phagocytic activity of these cells. Microglia from young mice took up a greater amount of myelin debris than microglia from aged mice.

Researchers from the Yong lab had previously screened a library of 1,040 drugs for those that could activate microglia and identified vitamin B<sub>3</sub> as the best candidate for clinical use.



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