IN BRIEF

CNS INFECTIONS

Severe impairment of motor function in congenital Zika syndrome

Zika virus infection during pregnancy is known to be associated with microcephaly and brain damage in the child. The clinical features of these children at birth have been well characterized, and by following the children's development, the course of congenital Zika syndrome (CZS) can be determined. In a new study by Adriana Melo and colleagues, motor function was assessed with the Gross Motor Function Measure (GMFM) in 59 children aged 5–29 months with CZS. The scores for 48 children placed them in level V of the Gross Motor Function Classification system, signifying severe motor impairment. Indeed, only four children could complete any tasks in the walking, running and jumping domains of the GMFM. A severe malformation of cortical development at birth was associated with a lower GMFM score, whereas a larger head circumference at birth and a higher per capita family income were associated with higher GMFM scores. These and other insights into the motor development of children with CSZ could form the basis of future therapeutic interventions.

ORIGINAL ARTICLE Melo, A. et al. Motor function in children with congenital Zika syndrome. *Dev. Med. Child Neurol.* https://doi.org/10.1111/dmcn.14227 (2019)

HEADACHE

Metabolite profiling links lipids to migraine

Altered metabolism of HDLs is associated with migraine and could offer a plasma-based biomarker, according to a new study by Gerrit Onderwater and co-workers. The researchers used a ^{1}H-NMR-based metabolics platform to analyse plasma samples from 2,800 patients with migraine and 7,353 controls. Low levels of apolipoprotein A1 and a low ratio of free cholesterol to total lipids were consistently associated with migraine. Analysis of the samples by sex also revealed that low levels of omega-3 fatty acids were associated with migraine in men but not in women. The findings suggest that migraine is associated with changes in HDL metabolism rather than with general dyslipidaemia. The authors propose that these alterations could contribute to the association of migraine with cerebrovascular and cardiovascular disease.

ORIGINAL ARTICLE Onderwater, G. L. et al. Large-scale plasma metabolome analysis reveals alterations in HDL metabolism in migraine. *Neurology* https://doi.org/10.1212/WNL.0000000000007313 (2019)

PERIPHERAL NEUROPATHIES

Gene therapy is effective for CMT in mice

Virus-mediated gene therapy has been used to treat a mouse model of Charcot–Marie–Tooth disease (CMT) type 4C in a recently published proof-of-principle study. Natasa Schiza and colleagues developed a lentiviral vector that was administered by intrathecal injection to mice in which the *Sh3tc2* gene — mutation or truncation of which causes CMT type 4C — was knocked out. At 8 weeks after the injection, motor performance was better in mice that had been treated with the gene therapy than in those that had been treated with a mock lentivirus. Nerve conduction velocity, myelin morphology and nodal molecular architecture were also all improved, and blood levels of neurofilament light — a marker of axonal degeneration — were reduced. The study indicates that viral gene replacement therapy that targets Schwann cells could be used to treat CMT type 4C and possibly other similar demyelinating neuropathies.

ORIGINAL ARTICLE Schiza, N. et al. Gene replacement therapy in a model of Charcot–Marie–Tooth 4C neuropathy. *Brain* https://doi.org/10.1093/brain/awz064 (2019)

NEURODEGENERATIVE DISEASE

Distinct tau filaments in CTE

The atomic structure of tau filaments that form in chronic traumatic encephalopathy (CTE) is distinct from that in Alzheimer disease (AD) and Pick disease, according to a new study. The work, published in *Nature*, was led by Sjors Scheres and Michel Goedert at the Medical Research Council Laboratory of Molecular Biology, UK, with collaborators at Indiana School of Medicine and the University of Kansas School of Medicine, USA.

"Aggregation of tau into amyloid filaments underlies multiple neurodegenerative diseases, known as tauopathies, of which AD is the most common," says Scheres.

In 2017, the researchers used cryo-electron microscopy to determine the atomic structures of tau filaments from the brain of a patient with AD. In 2018, they described the tau filament structure in Pick disease and found that it was very different from that in AD.

"CTE is also a tauopathy, and just like in AD, all six isoforms of tau aggregate in CTE," explains Scheres. "For this reason, some people expected the tau filaments from AD and CTE to be the same. Our observations with AD and Pick disease suggested that different tau structures might underlie the different tauopathies."

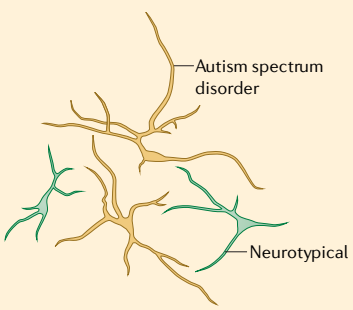
In their latest study, the researchers used cryo-electron microscopy to determine the structures of tau filaments from three individuals with CTE. Tau filament structures were the same in all three individuals, but differed from those from four patients with AD. "The same amino acids form the ordered core of the tau filaments in AD and CTE, but in AD the filaments are C-shaped, whereas the CTE filaments adopt a more open shape," notes Scheres. "The CTE tau filaments form a hydrophobic channel, which was

NEURODEVELOPMENTAL DISORDERS

Autism mutation produces hyper-connected neurons

A mutation in a synaptic scaffold protein that has previously been associated with autism spectrum disorder (ASD) causes neurons to form excessive connections, according to a new study published in *Nature Neuroscience*. The work opens up new possibilities for therapeutic intervention.

Induced pluripotent stem cell (iPSC) models of ASD, in which neuronal cultures are generated from iPSCs from patients, have produced evidence that synaptic function is reduced in severe genetic forms of the condition. However, variability between iPSC lines has hindered progress. In the new study, researchers led by James Ellis and Michael Salter used a novel approach to investigate neural connectivity in an iPSC model of ASD associated with mutations in *SHANK2*, which encodes a synaptic scaffold protein.



Credit: Philip Patenall/Springer Nature Limited

The researchers aimed to create a consistent culture environment by sparsely seeding differentially labelled mutant and control neurons onto an unlabelled neuron bed. "Our technique enabled mutant and control neurons to be co-cultured in the same environment and then single, fluorescently marked cells measured," explains Ellis. "This allowed neuronal phenotypes to be revealed that were not as reproducibly seen in monocultures."