IN BRIEF

PARKINSON DISEASE

Gene therapy boosts response to levodopa in patients with Parkinson disease

Virus-mediated delivery of a gene that encodes the dopamine-synthesizing enzyme L-amino acid decarboxylase (AADC) to the putamen can improve the response to levodopa therapy in patients with Parkinson disease (PD), according to research published in *Movement Disorders*. In many people with PD, AADC levels diminish over time, leading to loss of efficacy of levodopa. In a cohort of 13 patients with PD, John Nutt and colleagues observed improvements in motor responses to two different levodopa doses (0.6 mg/kg/h and 1.2 mg/kg/h) ~6 months after *AADC* gene therapy. The improvements were especially pronounced with the 0.6 mg/kg/h dose, suggesting that *AADC* gene therapy could enable the use of reduced levodopa doses, thereby making patients less susceptible to the adverse effects of this drug.

ORIGINAL ARTICLE Nutt, J. G. et al. Aromatic L-amino acid decarboxylase gene therapy enhances levodopa response in Parkinson's disease. *Mov. Disord.* https://doi.org/10.1002/mds.27993 (2020)

SPINAL CORD INJURY

Plexin B2 aids wound sealing and healing after spinal cord injury

After spinal cord injury (SCI), immune cells and glia are corralled to create a protective barrier around the lesion to prevent the spread of tissue injury and promote wound healing. A new study published in *Nature Neuroscience* has shown that this process depends on upregulation of the transmembrane receptor Plexin B2 in injury-activated microglia and macrophages (IAMs). The researchers found that in mice, Plexin B2 was induced in IAMs early after SCI and facilitated the formation of concentric rings of microglia and astrocytes around the necrotic core of the lesion. Ablation of Plexin B2 in myeloid cells impaired wound healing and motor–sensory recovery in a mouse model of SCI, further underlining the importance of this receptor for CNS repair.

ORIGINAL ARTICLE Zhou, X. et al. Microglia and macrophages promote corralling, wound compaction and recovery after spinal cord injury via Plexin-B2. *Nat. Neurosci.* **23**, 337–350 (2020)

ALZHEIMER DISEASE

Mitochondrial dysfunction manifests in the early stages of Alzheimer disease

Mitochondrial dysfunction in the parahippocampal region of the brain is an early occurrence in the course of Alzheimer disease (AD), a PET study recently published in *Neurology* indicates. The investigators used the PET radioligand ^{18}F-BCPP-EF to quantify the availability of mitochondrial complex I (MCI) — a measure of mitochondrial function — in the brains of patients with early-to-moderate AD and in cognitively healthy controls. The ^{18}F-BCPP-EF signal in the parahippocampus was found to be significantly lower in the patients with AD than in the controls, and this AD-associated reduction in MCI levels seemed to precede glycolytic impairments, as measured by ^{18}F-FDG–PET. The authors state that their study is the first to measure MCI availability quantitatively in the human brain, and the findings suggest that mitochondrial failure is an early event that represents a potential target for therapeutic intervention in AD.

ORIGINAL ARTICLE Terada, T. et al. In vivo mitochondrial and glycolytic impairments in patients with Alzheimer disease. *Neurology* https://doi.org/10.1212/WNL.0000000000009249 (2020)

MOTOR NEURON DISEASE

Konzo outbreak in Zambia linked to cassava-based diet

Konzo is an upper motor neuron disease that has been attributed to consumption of incorrectly processed cassava in the context of a protein-deficient diet. Writing in *Neurology*, Omar Siddiqi and colleagues present the first reported cases of konzo in Zambia, and their findings provide further evidence of a link with a cassava-based diet.

Cassava is an important staple food in Africa; however, in their unprocessed state, cassava roots can contain high levels of cyanogens, which are converted into the neurotoxin cyanide during digestion. At times of food insecurity, vital cassava-processing steps are often skipped, leading to widespread cyanide intoxication. Protein-rich foods provide a source of sulfur-containing amino acids that aid cyanide detoxification in the body.

"Cases of spastic paraparesis had been reported in the Western Province of Zambia as part of the routine polio surveillance activities by the Zambian Ministry of Health (MOH)," explains Siddiqi. "It took some time for health professionals to recognize that this cluster of cases represented a new entity requiring further investigation, because the cases occurred in very remote communities."

The new study was a collaborative effort involving the Zambian MOH, WHO, the Centers for Disease Control and Prevention and the University of Zambia School of Medicine. The researchers identified 32 cases that met the WHO criteria for konzo, namely, sudden-onset, symmetrical, non-progressive lower extremity paralysis.

The affected individuals had a high intake of cassava and consumed protein-rich foods less frequently than once a week on average. Children (aged 6–14 years) and breastfeeding

PARKINSON DISEASE

Exosomal α-synuclein as a biomarker for Parkinson disease

The amount of α-synuclein contained within brain-derived exosomes in the blood can provide a biomarker of early-stage Parkinson disease (PD), according to a new study published in the *European Journal of Neurology*. The finding could lead to earlier diagnosis of the disease.

In individuals with PD, pathological α-synuclein accumulation in the brain begins years before the symptoms of the disease become apparent. Increased α-synuclein concentration in the blood has been proposed as a biomarker of early PD pathology; however, α-synuclein is produced by many different tissues, so identifying changes in brain-derived α-synuclein in the blood is challenging.

Previous studies suggested that neurons can release α-synuclein packaged within membrane-bound vesicles known as exosomes. Exosomes originating from neurons can be identified by specific surface markers, so in the new study, Jun Liu, Wenyan Kang and colleagues aimed to establish whether measurements of levels of this exosomal α-synuclein in blood could provide a biomarker of PD.

The researchers isolated neuronal exosomes from the blood plasma of 36 individuals with early-stage PD, 17 individuals with advanced PD and 21 healthy controls. Levels of exosomal α-synuclein were higher in the groups of individuals with PD than in the controls. Exosomal α-synuclein levels also correlated with the severity of motor and non-motor symptoms of the disease. A receiver operating characteristic analysis indicated that brain-derived exosomal α-synuclein measurements could distinguish between individuals