IN BRIEF

ALZHEIMER DISEASE

Predicting progression to AD using a deep-learning model

Researchers have developed and validated a deep-learning time-to-event model to predict progression of mild cognitive impairment (MCI) to Alzheimer disease (AD) dementia using hippocampal MRI data. The model predicted progression to AD dementia with a concordance index of 0.762 in a group of 439 patients with MCI (follow-up duration 6–78 months) and a concordance index of 0.781 in a different group of 40 patients with MCI (follow-up duration 18–54 months). The model performed better than models based on anatomical features such as hippocampal volume and shape. Predictive performance improved further when the deep-learning-based model was combined with baseline clinical measurements. The model was also able to identify subgroups of patients with different timings of progression to AD dementia.

ORIGINAL ARTICLE Li, H. et al. A deep learning model for early prediction of Alzheimer's disease dementia based on hippocampal magnetic resonance imaging data. *Alzheimers Dement.* https://doi.org/10.1016/j.jalz.2019.02.007 (2019)

HUNTINGTON DISEASE

Different clinical profiles in Huntington disease show distinct patterns of brain alterations

A new study has identified relationships between interindividual differences in brain structure and the prominence of the different types of symptoms (motor, cognitive and psychiatric disturbances) in patients with Huntington disease (HD). Garcia-Gorro et al. investigated the relationship between HD symptom domains and grey and white matter structural alterations measured by different neuroimaging modalities in 43 HD gene carriers. Cognitive and motor symptoms were associated with a pattern of reductions in grey matter, cortical thickness and white matter integrity in cognitive and motor networks, indicating a common neurobiological basis. By contrast, depressive symptoms were associated with a component mainly characterized by reduced cortical thickness in limbic and paralimbic regions. The authors say that their findings are relevant to clinical trials as they could be used to define specific biomarkers for symptom profiles even before clinical signs appear.

ORIGINAL ARTICLE Garcia-Gorro, C. et al. Specific patterns of brain alterations underlie distinct clinical profiles in Huntington's disease. *Neuroimage Clin.* https://doi.org/10.1016/j.nicl.2019.101900 (2019)

AMYOTROPHIC LATERAL SCLEROSIS

Antibiotic use might increase risk of ALS

Repeated antibiotic use might be associated with an increased later risk of amyotrophic lateral sclerosis (ALS), say researchers in Sweden. Sun and colleagues performed a nested case–control study involving 2,484 patients diagnosed with ALS (cases) and 12,420 age-matched and sex-matched controls. Patients with ALS were more likely than controls to have taken antibiotics during the year before diagnosis. After excluding antibiotic prescriptions within the year before ALS diagnosis (to account for the usual diagnostic delay of 10–12 months), any antibiotic use was associated with an increased risk of ALS (ORs 1.06, 1.13 and 1.18 for 1, 2–3 and ≥4 prescriptions, respectively). The authors speculate that an altered gut microbiome might be involved in such an association, but further studies are needed before any causal relationship can be inferred.

ORIGINAL ARTICLE Sun, J. et al. Antibiotics use and risk of amyotrophic lateral sclerosis in Sweden. *Eur. J. Neurol.* https://doi.org/10.1111/ene.13986 (2019)

NEURODEGENERATIVE DISEASE

Drug reduces excess iron in ultra-rare neurodegenerative disease

The iron-chelating drug deferiprone reduces excess iron in the brains of people with pantothenate kinase-associated neurodegeneration (PKAN) and might slow progression of the disease, according to a new study published in *Lancet Neurology*. The study is the first randomized controlled trial of any treatment for PKAN and demonstrates the feasibility of such trials in ultra-rare disorders.

PKAN is an ultra-rare hereditary disorder caused by mutations in the gene that encodes pantothenate kinase 2. The condition is characterized by high concentrations of iron in the brain, which are thought to be toxic. The symptoms of PKAN, which include progressive dystonia and parkinsonism, begin in childhood and no disease-modifying treatments are currently available.

The new study, led by Thomas Klopstock from the University of Munich, Germany, was designed to build upon previous case reports and pilot trials that suggested that the iron chelator deferiprone benefited individuals with PKAN. Klopstock and colleagues enrolled close to 10% of all the patients with PKAN in the USA and Europe. The team randomly assigned the 88 patients to receive either deferiprone or placebo for 18 months. This period was followed by another 18-month open-label study with the drug only.

Iron concentrations in the globus pallidus decreased in the group that received deferiprone but not in the placebo group. In addition, worsening of dystonia during the study period was less pronounced in the patients who received deferiprone than in those who received placebo, although this difference only reached statistical significance in the subgroup of patients with the later onset form of PKAN. This observation suggests

TRAUMATIC BRAIN INJURY

Predicting treatment response in post-TBI cognitive impairment

Imaging of dopamine transporter (DAT) activity enables stratification of patients for treatment of cognitive impairment after traumatic brain injury (TBI), according to a new study. The work also illustrates the value of biomarker-driven stratification in trials.

Cognitive impairment is a major cause of disability in patients with TBI, and treatment options are limited. Damage to the dopaminergic system can cause this impairment, and some evidence suggests that treatment with methylphenidate — which increases levels of noradrenaline and dopamine — helps. However, responses vary, probably in relation to the degrees of damage to the dopaminergic system.

In their new study, Peter Jenkins and colleagues aimed to determine which patients are most likely to benefit from methylphenidate treatment. They first used ^{123}I-ioflupane single-photon emission computed tomography (SPECT) to assess DAT activity, which changes with synaptic dopamine levels, in 40 patients with TBI. They then conducted a randomized placebo-controlled trial of methylphenidate in these patients to assess how DAT activity related to treatment response. "We tested the hypothesis that patients with low caudate DAT, indicating a hypodopaminergic state, would show greater cognitive improvement following administration of methylphenidate," the investigators write.

Patients were randomly assigned to receive methylphenidate or placebo for 2 weeks, followed by the other treatment for a further 2 weeks. Each patient served as their own control. Patients were classified as having low or normal DAT activity.