Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

could be used in future biomarker studies of treatment outcomes or genetic research.

For more on the **European Epilepsy Brain Bank** see https://epi-care.eu/diagnostics/6-neuropathology

The European Epilepsy Brain Bank, a virtual database of neuropathology results from 37 centres across 18 European countries, reported on data from 9147 patients for whom seizure outcomes were available in 8191 (89·5%) at 2 years, and 5577 (61·0%) at 5 years.[10] These data showed histopathological diagnosis, age at surgery, and duration of epilepsy to be important predictors of outcome, with children more likely to be seizure free without medication at age 5 years.

Taken together, phenotypic and genotypic insights have made major strides towards a mechanistic approach in the treatment of monogenic epilepsies, whereas big data and data sharing are changing the way we undertake research and will have implications for epilepsy care.

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Movement disorders in 2020: clinical trials, genetic discoveries, and COVID-19

With 2020 hindsight, this has been an extraordinary year not just for patients with movement disorders but also for every individual around the world, due to the impact of the COVID-19 pandemic. Several studies investigating the effect of COVID-19 on individuals with Parkinson's disease have suggested that parkinsonian symptoms worsened among those who were infected, that those with more advanced Parkinson's disease were at increased risk of pulmonary compromise, that hospitalised patients with Parkinson's disease and COVID-19 appeared to have a heightened mortality rate, and that patients with Parkinson's disease showed more stress, depressive symptoms, and anxiety during the lockdown period than before this period.[1] A case report linking severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection with new-onset Parkinson's disease has led to an increased awareness of this potential association and also its underlying biological plausibility.[2]

Amid the pandemic, several clinical safety and proof-of-concept trials have taken small steps towards identifying disease-modifying therapies. Targeting α-synuclein, either through active or passive immunisations, gained considerable attention in the past few years for its potential for slowing down neurodegeneration, as dysfunction of the protein is a major driver of neurodegeneration. In a first-in-human phase 1 randomised study of subcutaneous immunisations with PD01A (ie, an active immunotherapy using a short peptide directed at oligomeric α-synuclein), 21 of the original 24 patients completed all the initial and booster immunisations over more than 4 years of follow-up.[3] The immunisation led to an increase in antibody titres with neither imaging evidence of neuroinflammation nor significant clinical adverse effects, providing impetus for investigators to proceed to the next phase of the study.

Loss-of-function mutations in the glucocerebrosidase gene that encodes lysosomal β-glucocerebrosidase

(GCase) represent an important risk factor for Parkinson's disease, and can lead to α-synuclein accumulation. Ambroxol, a secretolytic agent used in the treatment of respiratory diseases, increases GCase activity and hence reduces α-synuclein. In an open-label study using an escalating dose of oral ambroxol, 18 of the 23 patients with moderately severe Parkinson's disease completed the study.[4] Ambroxol was well tolerated and detected in the CSF, with an increase in CSF GCase activity. Although an improvement in the clinical motor scores was suggested with the drug, future randomised controlled trials will be required to show its effect on motor progression.

Subcutaneous injection or infusion of apomorphine (a non-selective dopamine agonist) via mini pumps has been used in patients with advanced Parkinson's disease to relieve off states. Alternative routes of delivery of apomorphine have now been investigated. A multicentre, randomised, double-blind study in patients with Parkinson's disease and more than 2 h off time per day compared an effective dose of apomorphine sublingual film individually titrated to 10–35 mg with a placebo (54 *vs* 55 patients).[5] There was a significantly better improvement in the Movement Disorder Society-Unified Parkinson Disease Rating Scale motor scores (from predose to 30 min post-dose) at week 12 in participants receiving apomorphine than in those receiving placebo. 31% of participants who were on the drug reported mild-to-moderate oropharyngeal side-effects, with 17% discontinuing the treatment. The long-term safety and efficacy of this apomorphine formulation as an on-demand therapy for off episodes in patients with Parkinson's disease still needs to be further evaluated.

Repurposing of drugs continues to attract interest as this strategy can potentially reduce the time frame and cost and improve regulatory support for successful clinical translation. Nilotinib has been used to treat chronic myeloid leukaemia. In a single-centre, double-blind, placebo-controlled phase 2 trial, 75 patients with moderately severe Parkinson's disease were randomised into placebo, nilotinib (150 mg), or nilotinib (300 mg) groups (daily oral administration for a year).[6] Although there were more adverse side effects in the nilotinib groups than in the placebo group, the drug was generally safe and detectable in CSF. The concentrations of some metabolic markers and specific proteins (such as α-synuclein oligomers and hyperphosphorylated tau) in CSF were altered in those on nilotinib, raising the possibility that these can be used as potential biomarkers of drug response in future phase 3 trials.

Next generation sequencing approaches to unravel underlying genetic causes of rare movement disorders can provide definitive diagnosis and facilitate pathophysiological studies to identify novel therapeutic targets. To unravel the monogenic causes of dystonia (a clinically and genetically heterogeneous disease), whole exome sequencing was done in 764 patients with dystonia and 346 healthy parents in an international collaborative study involving 33 centres.[7] The authors managed to identify causative or probable causative gene variants in 135 (19%) of the 728 families, and diagnostic variants in 11 genes not previously linked to dystonia. Most of the identified variants are in genes that are linked to neurodevelopmental disorders. In essence, the application of exome sequencing in a collective large number of patients with dystonia improves diagnosis, facilitates genotype–phenotype correlation, potentially guides genetic testing, and improves the clinical management of patients with dystonia.

Repeat expansion disorders have been linked to a wide clinical phenotype. One study examined 100 genetically confirmed carriers of cerebellar ataxia with neuropathy and vestibular areflexia syndrome, which is due to biallelic repeat expansions in *RFC1* (replication factor complex subunit 1).[8] The investigators found that a dry spasmodic cough is commonly associated with repeat expansion disorders, and that sensory neuropathy was the only manifestation in some patients,[8] although other investigators have reported *RFC1* mutations in multiple system atrophy.[9] Similarly, GGC repeat expansions in *NOTCH2NLC*, which causes neuronal intranuclear inclusion disease, have now been reported in patients with Parkinson's disease and essential tremor who do not show cognitive dysfunction or imaging evidence of intranuclear inclusion disease.[10] A high index of suspicion and awareness is needed for appropriate genetic testing in patients who present with movement disorders.

I declare that I have received honoraria from Elsevier and Wiley for editorial duties.

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Multiple sclerosis in 2020: *un bon cru*

The landscape of multiple sclerosis is changing, with new insights on prognosis, the emergence of artificial intelligence in brain imaging, technological advances challenging knowledge on disease pathogenesis, and the identification of novel therapeutic pathways. However, 2020 will certainly be remembered for the spread of the COVID-19 pandemic. In this context, the possibility of an increased susceptibility to severe COVID-19 in patients with multiple sclerosis has rapidly become an important question. Higher age, an Expanded Disability Status Scale score of 6 or more, and obesity were identified as independent risk factors for severe COVID-19 in a French multicentre observational cohort.[1] Whereas in this study, which included 347 patients, there was no significant association between disease-modifying treatment exposure and COVID-19 severity, some evidence is now emerging that therapies targeting CD20 might be linked to an increased risk of severe COVID-19, and several studies aiming to establish whether this is the case are ongoing.

How to manage individuals with radiologically isolated syndrome—people with brain MRI scans compatible with CNS inflammation but without neurological symptoms—remains challenging because the long-term outcome after this diagnosis is unknown. The multicentre Radiologically Isolated Syndrome Consortium study,[2] the largest and longest study to date, included 277 individuals with radiologically isolated syndrome. The cumulative probability of a clinical event at 10 years was 51·2%. Consistent with previous publications, young age and spinal cord lesions were identified as independent predictors of a first clinical event. The novelty here is the identification of two additional risk factors—the presence of oligoclonal bands or elevated IgG index in the CSF and infratentorial lesions—with a stepwise increase of risk associated with the number of factors (probability ranging from 29% for individuals with at least one risk factor to 87% for those with four risk factors). Nevertheless, in the absence of results from ongoing trials of potential disease-modifying drugs (TERIS [NCT03122652] and ARISE [NCT02739542]), there is no recommendation to treat individuals with radiologically isolated syndrome.

Artificial intelligence has opened new avenues for medical imaging in general. In multiple sclerosis, one example is a deep learning approach applying convolutional neural networks,[4] evaluating the possibility of predicting brain lesion activity without the need for contrast injection. In this study, conventional MRI data from 519 patients with a total of 1390 enhancing lesions were used to train and test network performance. Participants with enhancing lesions were classified with 70% accuracy. Similarly, a method proposed by Wei and colleagues[4] could offer an alternative to PET scanning to predict myelin content changes by using multisequence quantitative MRI. Myelin imaging with ^{11}C-PIB PET allows quantification of myelin content changes in vivo, but is invasive, with injection of a radioactive tracer, and is poorly suited to multicentre studies. The deep learning approach used by Wei and colleagues[4] allowed generation of synthetic images predicting myelin content changes in a longitudinal analysis of patients with multiple sclerosis. By providing MRI-based algorithms, deep learning methods are likely to modify, in the near future, the management of patients with multiple sclerosis, as well as the design of therapeutic studies.

With regard to disease pathogenesis, single-cell RNA-sequencing methods have revealed heterogeneity