IN BRIEF

MIGRAINE

First genome-wide association study in migraine without aura identifies two susceptibility loci

The first genome-wide association study in patients with migraine without aura—the most common form of migraine—has revealed susceptibility loci for this disorder. Comparing genomes of 2,326 German and Dutch patients with those of 4,580 controls, the researchers identified single nucleotide polymorphisms associated with the disorder, which were then carried forward to replication studies in large, independent cohorts. Two susceptibilty loci were identified: one at 1q22, in the *MEF2D* gene, and one at 3p24, near the *TGFBR2* gene.

Original article Freilinger, T. *et al.* Genome-wide association analysis identifies susceptibility loci for migraine without aura. *Nat. Genet.* doi:10.1038/ng.2307

MOVEMENT DISORDERS

Novel myoclonic disorder identified in Canadian family

Russell *et al.* investigated a four-generation Canadian family presenting with adult-onset cortical myoclonus without seizures, in order to determine the phenotype of this disorder. Genetic sequencing revealed a nonsense mutation in the gene encoding nucleolar protein 3 (NLO3), which led to altered post-translational modification of the protein in all affected individuals. The authors name this novel movement disorder 'familial cortical myoclonus', and suggest that investigation into the role of NLO3 will provide insight into the pathophysiology of myoclonus and related disorders.

Original article Russell, J. F. *et al.* Familial cortical myoclonus with a mutation in NLO3. *Ann. Neurol.* doi:10.1002/ana.23666

NEURO-ONCOLOGY

Prognostic model enables accurate prediction of survival in patients with brain metastases from breast cancer

A prognostic model, combining a novel nomogram and the breast-specific graded prognostic assessment index, enables accurate prediction of survival in patients with brain metastases from breast cancer, according to recent findings. The model developed by Ahn *et al.*, which incorporates treatment effects of trastuzumab and other biological features specific to breast cancer, enabled accurate discrimination of median survivial time (P <0.0001) in individuals with brain metastases.

Original article Ahn, H. K. *et al.* Prediction of outcomes for patients with brain parenchymal metastases from breast cancer (BC): a new BC-specific prognostic model and a nomogram. *Neuro-Oncology* doi:10.1093/neuonc/nos137

NEURODEGENERATIVE DISEASE

Cholesterol as therapy for Pelizaeus–Merzbacher disease?

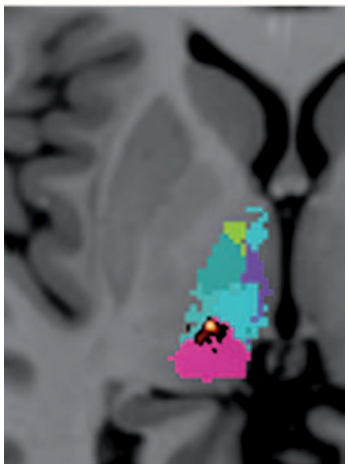
Pelizaeus–Merzbacher disease is a fatal leukodystrophy caused by duplication of the gene encoding proteolipid protein (PLP), with subsequent overexpression of the protein. Saher *et al.* previously observed co-accumulation of PLP and cholesterol in oligodendrocytes in a mouse model of the disease, prompting an investigation into the role of cholesterol in disease pathology. A cholesterol-enriched diet increased myelin content and improved motor function in the mice. Furthermore, initiation of this diet before onset of clinical symptoms slowed disease progression.

Original article Saher, G. *et al.* Therapy of Pelizaeus-Merzbacher disease in mice by feeding a cholesterol-enriched diet. *Nat. Med.* doi:10.1038/nm.2833

PAIN

MRI might identify patients at risk of post-stroke thalamic pain

Researchers at the Technische Universität München in Munich, Germany have identified thalamic areas consistently involved in the generation of post-stroke pain. After a thalamic stroke, ~7% of patients develop severe, distressing neuropathic pain, typically accompanied by sensory disturbances, and characterized by thalamic lesions. "Our aim was to determine if the location of these lesions could be used to predict if a particular patient was at high risk of developing thalamic pain," explains Till Sprenger, lead author of the study.



Mapping post-stroke thalamic-pain risk: the highest risk is with lesions at the border of the ventral posterior nucleus (light green) and the pulvinar (pink). Image courtesy of T. Sprenger.

The research team compared structural MRI scans from 10 patients with post-stroke thalamic pain and 10 pain-free control patients who had experienced a thalamic stroke >2 years previously. The application of nonlinear deformations to map each volumetric structural MRI image into standard stereotactic space facilitated voxel-by-voxel analysis of the thalamic volumes of interest. Odds ratios were also created for each individual voxel, to create a high-resolution risk map for post-stroke pain.

Control patients tended to have medial lesions; by contrast, nine of the patients with post-stroke thalamic pain had lesions affecting a region bordering the ventral posterior thalamic nucleus and pulvinar, coinciding with the ventrocaudalis portae nucleus (the remaining patient had a lesion adjacent to, but not including this area). "Lesions in this area produce exceedingly high odds of developing thalamic pain," Sprenger notes.

Although the patients with thalamic pain typically had significantly larger lesions than controls, Sprenger and colleagues consider the precise lesion location to be the principal determinant of the risk of post-stroke pain. As Sprenger points out, specific pain and temperature relay neurons are indeed thought to be located in an area overlapping the ventrocaudalis portae nucleus.

Whether at-risk patients can be identified using these MRI features awaits investigation in prospective studies. The team also hope to clarify the pathophysiological mechanisms underlying thalamic pain. "The study of brain plasticity in these patients would be of great interest," Sprenger says, "as reshaping of the functional network probably ultimately produces the pain."

The pain-free interval after a thalamic lesion might also offer an important time window for preventive treatment. The authors speculate that drugs such as antidepressants, anticonvulsants or *N*-methyl-D-aspartate receptor antagonists could be tested in at-risk patients to see whether they can prevent the onset of symptoms. "Early interventions may be necessary and we believe that such strategies can now be tested," Sprenger concludes.

Ellen Bible

Original article Sprenger, T. *et al.* Assessing the risk of central post-stroke pain of thalamic origin by lesion mapping. *Brain* doi:10.1093/brain/aws153