

EDITOR'S CHOICE

A new prion disease with a terrible name

Just when we were beginning to relax over variant CJD in the UK, a new prion disease has been described in the US: 'protease-sensitive prionopathy'. 11 cases (10 autopsy, 1 biopsy) were seen at the National Prion Disease Pathology Surveillance Centre. Clinically, these patients had a rather distinct phenotype: a mean age of 62 years, presenting with behavioural, cognitive and psychiatric abnormalities, then developing ataxia and parkinsonism and surviving only 20 months. 6/10 had a family history of 'dementia'. No tests proved helpful: EEG did not show periodic complexes and CSF 14-3-3 was nondiagnostic. MRI showed diffuse atrophy with no changes on diffusion weighting. Uniquely, protease-resistant PrP was not found in the neocortex; instead the abnormal prion protein found in the brain of these patients was sensitive to proteases and formed distinctive plaques in the cerebellum. All of the patients were homozygous for valine at codon 129 of the prion protein gene; this is the rarest genotype found in only 12% of healthy people, and in two forms of regular sporadic CJD (VV1 and VV2) that differ from these cases in other ways. None had a mutation in the PrP gene ORF that is characteristic of Gerstman-Straussler-Scheinker disease, although the family histories clearly suggest a genetic cause. This type of prion disease accounted for 3% of referrals to the US National Prion Disease Pathology Surveillance Centre, so it is not vanishingly rare. And it is possible that more exist, currently misdiagnosed as having Alzheimer's, fronto-temporal dementia or Lewy Body disease. But, as well as that practical point, there are some more intriguing questions. As with Gerstman-Straussler-Scheinker, we have to ask whether this new 'prion disease' is transmissible, a necessary characteristic of Pruisner's original 'prion hypothesis'. And why is this accumulate prion protein protease-sensitive? The relevant animal experiments are on-going.... – *AJC*

Gambetti P, Dong Z, Yuan J, Xiao X, Zheng M, Alshekhlee A, Castellani R, Cohen M, Barria MA, Gonzalez-Romero D, Belay ED, Schonberger LB, Marder K, Harris C, Burke JR, Montine T, Wisniewski T, Dickson DW, Soto C, Hulette CM, Mastrianni JA, Kong Q, Zou WQ.

A novel human disease with abnormal prion protein sensitive to protease.

ANNALS OF NEUROLOGY

2008 Jun;63(6):697-708.

EPILEPSY: injuries and Range Rovers

The Canadian Health Study identified patients with epilepsy from a door-to-door survey of 130,882 individuals over the age of 12 years, across Canada and representative of 98% of the Canadian population. 835 people with epilepsy (PWE) were found and were asked if they had suffered an injury in the last 12 months. Injuries sufficient to limit activity had occurred in 13.3% of controls and 14.9% of PWE. There was no increase fractures or sprains but a trend towards more burns and scalds (6.9% v 3.9%) in PWE. Controls were a little more likely to have injuries whilst engaged in sports, perhaps reflecting a reluctance of patients with epilepsy to undertake sport. Even though many people were sampled, the number of injuries in PWE was only 121, which means that the power of the study to identify differences between groups was limited, especially when looking at subdivisions of injuries. The study did not look at Range Rover driver behaviour. This is otherwise known as risk compensation, where those who feel at risk (Trabant drivers, who perceive themselves as vulnerable) behave in a risk averse fashion, whereas those in black Range Rovers with dark tinted windows embrace risk, as they perceive themselves as safe. It seems likely that epilepsy patients will be more risk averse than controls. Most other studies point to a slight excess risk of injury amongst patients with epilepsy and I suspect this is closer to the truth. Of course Canada is so icy in Winter that perhaps everyone is falling and breaking something so that differences are hard to detect. – *MRAM*

Tellez-Zenteno JE, Hunter, G, Wiebe S.

Injuries in people with self-reported epilepsy: A population-based study.

EPILEPSIA

2008;49:954-61.

CHRONIC FATIGUE SYNDROME: shrinking brains

This Dutch group have previously shown that people with chronic fatigue syndrome (CFS) have reduced grey matter volume in the lateral prefrontal cortex. They now go on to ask whether this is cause or consequence of the illness. They first showed that grey matter volume was most reduced in those CFS patients with lower physical activity and slower cognition (perhaps supporting that rather annoying dictum 'if you don't use it, you lose it'). They then followed 22 women with CFS as they had 16 sessions of cognitive behavioural therapy and graded exercise programs over 6-9 months. The expected improvements in health status, physical activity and cognitive performance followed. This correlated with an increase in lateral prefrontal cortex grey matter volume, ('pain and gain?') less marked in older patients. This increase amounted to only 12% of the difference between CFS patients and controls, raising the possibility that some of the deficit of CFS is irreversible. But much more interesting is the mechanism of the increase in grey volume.... for which the authors offer speculations only. They argue that, as neocortical neurogenesis is rare or absent from adult brains, that an increase in volume is likely to arise from increased dendritic growth or synaptogenesis.

de Lange FP, Koers A, Kalkman JS, Bleijenberg G, Hagoort P, van der Meer JW, Toni I.

Increase in prefrontal cortical volume following cognitive behavioural therapy in patients with chronic fatigue syndrome.

BRAIN

2008 Aug;131(Pt 8):2172-80.

NEURODEGENERATION: emerging new treatments

To complement the conference review by Tom Foltynie I perused the abstracts (all 1200 of them!!) of the recent Movement Disorder meeting in Chicago to find those of particular interest for restorative treatments of movement disorders. So here goes!

- Marks et al (A96) report on the 24 month efficacy of the safety and efficacy of AAV2 virus - neurturin in 12 patients with Parkinson's disease. The result is very encouraging with 8 out of the 12 having a major response of greater than 50% in the UPDRS off score without any significant adverse effects being reported.
- In contrast Frank et al (A568) show that there is no long term survival and efficacy of porcine striatal xenotransplants for Huntington's disease. Only 2 patients are still alive out of the original 12 and none showed any significant benefit with two patients having no surviving cells of porcine origin at post mortem.
- Watts et al (A598) provide an update on the Spheramine trial in patients with moderately advanced Parkinson's disease. Spheramine consists of human retinal pigmentary epithelial cells, attached to a microcarrier support of matrix cells, which are capable of synthesising dopamine. Six patients receiving transplants of these cells and matrix have shown no major adverse events but there again at 60 months there have been no major improvements either.

So at the moment gene therapy with neurotrophic factor delivery is winning over novel cell therapies for neurodegenerative disorders but the full publication of these studies will ultimately help us decide on the merits or otherwise of these studies. – *RAB*

All abstracts from MOVEMENT DISORDERS (2008) 23: Supplement 1

EPILEPSY: More than two syndromes

Some neurologists, and we all know who they are, are funny diseases doctors. They can remember all the weird and wonderful eponymous syndromes. I was never one of those and as middle age slips its tentacles ever deeper between my synapses, the chances of my ever remembering the clinical characteristics of 28 types of spinocerebellar ataxia is – well you can guess. So adult epilepsy is a great specialty for me; just two conditions to remember, focal epilepsy and generalised epilepsy. But I always knew it was too easy. It has never been realistic to think that all forms of focal epilepsy are the same, that the mechanism of the epilepsy is the same whatever the aetiology and this is one of a really small number of studies that has looked systematically at the differences. The authors studied 119 consecutive patients with refractory focal epilepsy, defined as failing two AED's. Where the cause remained cryptogenic after detailed MRI, the chances of a one year remission was 40%. Those with pathologies usually considered for surgical treatment, such as hippocampal sclerosis or dysplasia, achieved a remission of 11% and 27% of those with other forms of focal epilepsy achieved remission. Numbers were too small to analyse individual pathologies, but previously it has been demonstrated that hippocampal sclerosis carries a poor prognosis, especially if there is dual pathology. We know that dysplasia exhibits spontaneous EEG spikes and electrographically appears different from other causes and per-

