PANDORA'S BOX

Pandora searches the world literature for evidence, news and other sources on matters of interest (doesn't shy away from controversy) to bring to the reader. She welcomes comments and suggestions (via ip@rcpsych.ac.uk)

### *Lewy body dementia – you can diagnose it in no time at all!*

If you have been struggling with the differential diagnosis of dementia you can now rest assured that at least Lewy body dementia should not be a challenge anymore. A recent study claims to make its diagnosis quick and easy through the use of a tool called the Lewy Body Composite Risk Score (LBCRS), which can distinguish Lewy body dementia from other forms of dementia.

It is a simple test that takes no more than a few minutes and consists of ten questions that cover motor symptoms (slowness of movement, balance problems, falls and resting tremor) and non-motor symptoms (sleep, illogical thinking, staring spells, visual hallucinations, acting out dreams and orthostatic hypotension). The answers are 'yes' or 'no' and three or more 'yes' responses suggests that Lewy bodies are the cause of the dementia, according to the author. Simple!

Galvin, J. E. (2015) Improving the clinical detection of Lewy body dementia with the Lewy body composite risk score. *Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring*, **1**, 316–324.

### *Is it all to do with the prions?*

Are Alzheimer's disease and Parkinson's disease in fact prion disorders? A review in *Science* gathers recent evidence to argue that the scope of prion diseases should be extended beyond Creutzfeldt–Jacob disease (CJD), kuru and scrapie and include other neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease. This could make one cringe but there are good arguments in favour of this view.

Alzheimer's disease is characterised neuropathologically by brain atrophy and the accumulation of extracellular Aβ plaques and intraneuronal neurofibrillary tau lesions.

The term 'prion' (proteinaceous infectious particle), previously known as 'slow virus', was introduced in order to make a distinction between protein pathogens (replicating without nucleic acid) and viruses. Prions were at first thought to be limited to a group of diseases such as CJD in which glycolipid anchored sialoglycoprotein adopts a conformation rich in β-sheet. However, as similar conformations have been observed for Aβ, tau and α-synuclein upon assembly, it is argued that the prion concept should also apply to Alzheimer's disease and Parkinson's disease.

An argument against the expansion of the concept is that, unlike CJD and kuru, there is no evidence of transmission between individuals with Alzheimer's disease or Parkinson's disease. However, the author argues, human prion diseases are not easily communicable or contagious; only 1% of cases of CJD are acquired, while 99% are sporadic or inherited. In order to confirm this there needs to be evidence that a large increase in the titre of 'infectivity' is observed in assembled Aβ, tau and α-synuclein, as occurs after injection of misfolded prion protein in the brain.

The review concludes that trans-cellular propagation of protein pathogens, reminiscent of the spread of viruses, represents an unprecedented concept of disease and claims that it is now known to extend beyond CJD, to include Alzheimer's disease and Parkinson's disease. At present there is no effective treatment for neurodegenerative disorders. Understanding the molecular processes that lead to the formation of inclusions, where they begin to behave like prions, and their routes of transneuronal spread as well as the role of glial cells in the latter may be critical to the development of therapies that can tackle these conditions.

Goedert, M. (2015) Alzheimer's and Parkinson's diseases: the prion concept in relation to assembled Aβ, tau, and α-synuclein. *Science*, **349**, doi: 10.1126/science.1255555.

### *Are we overdiagnosing ADHD in children?*

Eleven per cent of children in the USA are diagnosed with attention-deficit hyperactivity disorder (ADHD) and the numbers are rising. The investigators present data from a 2014 nationally representative survey that was sponsored by the Centers for Disease Control and Prevention's National Center for Health Statistics. Households providing data for this report all had children aged 2–15 years. About 31% of the children were diagnosed before the age of 6 years and as many as 76% of the diagnoses were made before the age of 9 years. The ADHD diagnoses were made by paediatricians in 39% of the children, by other primary care physicians in 14%, by psychologists in 14%, psychiatrists in 18% and neurologists in 5%, with the remainder of the diagnoses made by other types of providers.

The conclusion was that in the USA, non-psychiatrists and non-psychologists make most of the diagnoses, irrespective of the child's age, and that the assessment may not be fully in keeping with guidelines. Hopefully the UK National Health Service is doing better in this respect?

Visser, S. N., Zablotsky, B., Holbrook, J. R., *et al* (2015) Diagnostic experiences of children with attention-deficit/hyperactivity disorder. *National Health Statistics Report*, **3**, 1–7.

### *PTSD treatment breakthrough!?*

Post-traumatic stress disorder (PTSD) is here to stay, as we humans, with our unique ability to create conflict among ourselves, ensure we have a constant supply of sufferers. Can we prevent its spread? Possibly, if we could work together, but we can't – Pandora's box remains open! Can we treat those affected? There are psychological and pharmacological methods and there is EMDR (eye movement desensitisation and reprocessing), all of which have shown some efficacy.

Dr Eugene Lipov, an anaesthesiologist and the medical director of the Global Post-traumatic Stress Injury Foundation in the USA, claims to have found a much more effective treatment. He has shown that blockade of the stellate ganglion, a method used for many years in the treatment of migraine and chronic pain, is also effective in


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a method used for many years in the treatment of migraine and chronic pain, is also effective in PTSD. He claims that 70% of 2200 people with PTSD in seven US military hospitals were successfully treated with this method. Horner's syndrome (a droopy eyelid) is an unwanted side-effect, but that is a small price to pay for peace of mind free of flashbacks! A group of doctors recently presented data showing evidence of its effectiveness on positron emission tomography, at the American Society of Anesthesiologists' meeting in San Diego, California. Perhaps we should wait to see the published results?

Alkire, M. T., Hollifield, M., Khoshar, R., *et al* (2015) Neuroimaging suggests that stellate ganglion block improves post-traumatic stress disorder (PTSD) through an amygdala mediated mechanism. At http://www.eugenelipovmd.com; the author has featured in a number of television programmes talking about his findings (http://globalptsifoundation.org/videos).

### *Lithium good for the brain and bad/not bad for the kidney?*

Lithium remains the 'gold standard' in the treatment of bipolar disorder and the recent finding that it increases grey matter in the brain has given more confidence in its use. However, the fear of long-term damage to the kidneys has been lurking in the background, at least in the minds of the treating clinicians.

The findings of a study carried out in Scotland and published in October 2015 in *Lancet Psychiatry* offer some reassurance. This was a retrospective, population-based cohort study in patients aged 18–65 who had started maintenance treatment with lithium between 2001 and 2011 and they were compared with a group of patients who had been treated with quetiapine, olanzapine and semi-sodium valproate. The primary outcome was the change in eGFR (estimated glomerular filtration rate) per year, adjusted for age, gender and baseline eGFR; the data were analysed by random coefficient models.

The researchers found no differences between the lithium and non-lithium group and concluded that stable lithium maintenance treatment with levels within therapeutic range is not associated with nephrotoxicity in the absence of acute intoxication.

Clos, S., Rauchhaus, P., Severn, A., *et al* (2015) Long-term effect of lithium maintenance therapy on estimated glomerular filtration rate in patients with affective disorders: a population-based cohort study. *Lancet Psychiatry*, **2**, 1075–1083.

### *Stress can lead people to make unhealthy food choices!*

Many people will have made New Year's resolutions about eating more healthily! But we'd be advised to stay away from food when stressed. Maier and colleagues investigated the neural mechanisms involved in how stress may influence self-control. In a study in humans using functional magnetic resonance imaging (fMRI) they found that acute stress made the participants opt for tastier food even if this was less healthy and against their self-imposed diet, compared with the non-stressed control group. This choice pattern was associated with increased functional connectivity between the ventromedial prefrontal cortex (VMPFC) and the amygdala and striatal regions that encode taste. Furthermore, stress was associated with reduced connectivity between the VMPFC and dorsolateral prefrontal cortex, regions linked to self-control. The authors conclude that stress may compromise self-control by enhancing the impact of immediately rewarding attributes and at the same time reducing the efficacy of regions promoting behaviours which are consistent with long-term goals.

Maier, S. U., Makwana, A. B. & Hare, T. A. (2015) Acute stress impairs self-control in goal-directed choice by altering multiple functional connections within the brain's decision circuits. *Neuron*, **87**, 621–631.

### *To be or not to be?*

The right to be helped to end one's life has been debated for many years and continues to be a hot potato for many countries. The Netherlands, Belgium, Switzerland and others, including some states in the USA, have decriminalised assisted suicide. Many others, such as the UK, continue to debate the issue, which is kept alive as it is repeatedly brought to the public's attention, mostly by people with terminal illness taking their case to court in their wish to prepare for the possibility of euthanasia when the time comes. Euthanasia remains a criminal act for the time being in the UK.

Germany has recently passed a law which brings the subject of assisted suicide to the forefront again. 'Passive euthanasia', such as withholding treatment, has been 'generally accepted' in Germany and there are a number of organisations that provide lethal medications to people who are terminally ill. However, the German parliament has now taken a firm stance and in early November 2015 it voted for a law that criminalises 'commercial euthanasia'. This means that any agency which offers assisted suicide for a fee will be prosecuted. What about assisted suicide offered free of charge? The German law needs to be clarified.

What about the rest of us – should we be free to choose to be 'euthanased' or not? The debate goes on…

### Correction

In the November 2015 issue of *BJPsych International* (vol. 12, no. 4), the surname of the fifth author of the Chile country profile (p. 95) should have been spelt Vanegas (not Venegas). The online version has been corrected, post-publication and in deviation from print.


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