

# CARPHOLOGY by A Fo Ben



Pract Neurol 2009; 9: 252

## More evidence to avoid valproate in pregnancy

What advice should we offer women wishing to become pregnant but taking valproate for epilepsy? IQ differences in offspring were detected as early as aged 3 years in this prospective study of 309 pregnant women taking monotherapy carbamazepine, lamotrigine, phenytoin or valproate. Mean IQ was 100 (2) on the first three medications but nine points lower (95% CI 3.1 to 14.6;  $p = 0.009$ ) on valproate compared with lamotrigine. These are not randomised data (of course) but the neuropsychologists were blinded to the mothers' drugs and attempted to control for a wide number of appropriate confounders. The IQ differences appear to be dose related so the advice should be that where valproate is essential, target the lowest effective dose.

*N Engl J Med* 2009;**360**:1597–605.

## Parental age is important too

New parents in the western world are getting older. Using the Collaborative Perinatal Project data, a large birth cohort of more than 50 000 children born between 1959 and 1965 in the USA and tested before aged 7 years, McGrath *et al* identified lower intelligence scores (controlled for parental mental health and socioeconomic status) in children born to fathers aged 50 years (IQ 103) compared with those aged 20 years (IQ 105). More surprising, though, was the linear rise in cognitive performance with increasing maternal age.

*PLoS Med* 2009;**6**:e10000040.

## Religion and end of life care

Do religious coping mechanisms allow people with terminal cancer to accept their prognosis, find strength to face the inevitable and plan for their last days? Not according to a study of a primarily Christian US population. People rated with high levels of religious coping were more likely than those with low levels to be

artificially ventilated (adjusted odds ratio (AOR) 2.81) and to have intensive life prolonging care during the last week of life (AOR 2.90). The study was well powered ( $n = 345$ ) and attempted to adjust for abstract confounders such as "preference for heroics". Faith may support the dying but may also foster unrealistic expectations and paradoxically give a poorer quality death.

*JAMA* 2009;**301**:1140–7.

## A bright cold day in April, and the clocks were striking 13

Orwell's 1984 describes the "herd effect" of false memories (fuelled by strict censorship) when Winston Smith's Oceania was waging war, oscillating between Eurasia and Eastasia. An Italian team have described memory persistence, centred on a stopped clock showing 10:25 following the Bologna station bomb blast in 1980, which killed 85 and wounded 200. In fact, the clock had been quickly repaired and had functioned normally for 16 years before being reset permanently to 10:25 as a memorial in 1996. Of 180 people familiar with the station (remarkably these included all 21 railway employees), 92% stated that the clock had always been broken. When "flash bulb" memories (emotionally charged and highly retained memories—eg, JFK's assassination) become distorted they confer an exceptionally high degree of confidence.

*Cortex* 2009;**45**:686–7.

## PML risk with more monoclonals

The FDA has issued a warning concerning one possible and three confirmed cases of progressive multifocal leukoencephalopathy (PML) in patients taking efalizumab, the anti-psoriasis agent. The European Medicines Agency recommended in February 2009 that efalizumab's benefits no longer outweighed its risks. Neurologists specialising in demyelination are already familiar with PML following natalizumab in clinical trials; two of 1869

patients with multiple sclerosis and one of 1043 with Crohn's disease. Although still unclear who is most risk, clinicians must consider PML in those taking monoclonal antibodies modulating T cell immunity.

*JAMA* 2009;**301**:1423–4.

## A step towards describing stroke genes

Twin studies suggest an inheritability of stroke risk but the important genes involved remain unknown. Although not the first genome-wide association study in stroke, a prospective cohort of 19 602 participants, all white, and with 1164 ischaemic strokes over 11 years, identified a locus at 12p13 ( $p < 5 \times 10^{-8}$ ). Three single nucleotide polymorphisms (SNPs) were identified, two in close proximity to *NINJ2*, encoding ninjurin2, a member of the "nerve injury induced protein" family. One SNP increased the risk of all strokes (and ischaemic stroke in particular) with a hazard ratio of 1.33 (95% CI 1.21 to 1.47) and a population attributable risk of 12%. This SNP was also replicated in two independent samples of North American black persons and Dutch white persons.

*N Engl J Med* 2009;**360**:1718–28.

## Amnesia in memoriam

Henry Molaison (HM) 1926–2008, became a neuropsychological cause célèbre following bilateral hippocampectomy for epilepsy in 1953. Scofield and Milner were the first of HM's 100 published investigators in their 1957 *J Neurol Neurosurg Psychiatry* paper, "Loss of memory after bilateral hippocampal lesions". HM had worked on a Connecticut assembly line following high school graduation. Postoperatively, and despite preserved topographical memory, he acquired no new memory or vocabulary and had retrograde amnesia to age 16 years. His obituary reports that he enjoyed television and crosswords, showed no interest in sexual relationships yet appeared content and almost never complained.

*BMJ* 2009;**338**:b968.