Carphology by A Fo Ben

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WhaTS new? It's cleverolimus

Children and adults with tuberous sclerosis (TS) can have a particularly challenging focal epilepsy to treat. A phase III randomised, double-blind, placebo-controlled trial enrolled 366 people aged 2–65 years to either everolimus or placebo. Everolimus has been studied in the context of reducing lesion growth but not yet as an anti-epilepsy agent. The primary outcome was 50% (or more) reduction in seizure frequency. Responses were 15% for the placebo group, 28% for those on low-dose everolimus and 40% for those on a high dose. Fourteen per cent of those on the drug had a serious adverse event, as did 3% on placebo. All normal caveats apply about a short duration of follow-up and that everolimus was an adjunctive therapy to standard antiepileptic drugs, but this agent, in this context, may be truly disease modifying as well as an effective seizure treatment.

Lancet 2016;S0140-6736:31419–2.

IN RUDE HEALTH

You are part of an intensive care team working on a neonate with necrotising enterocolitis—what do you need? What you don't need is an international expert watching you and criticising your resuscitation and denigrating healthcare in your entire country. This was the set-up for a randomised trial of rudeness, where a team exposed to hostile comments was compared with one that was not. Did the barbs from the expert spur the team on to greater things? Not in the slightest —diagnostic and procedural performance was poorer in the team exposed to rudeness.

Pediatrics 2015;136:487–95.

HOW LOW CAN YOU GO?

What should we do to blood pressure following acute cerebral haemorrhage? Patients were randomised to either a target of 110–139 mm Hg or 140–179 mm Hg. Intravenous nicardipine was administered within 4.5 hours of onset. The primary endpoint was death or disability, using the modified Rankin scale. One thousand participants were enrolled and then, because of an interim analysis, recruitment was halted, that is, there was no difference in outcome between the groups. Those who were aggressively treated did have significantly more renal problems at 7 days (9% vs 4%, p=0.002). (Incidentally, the trial was called ATACH-2—which makes A Fo Ben want to shout *Gesundheit!*)

N Engl J Med 2016;375:1033–43.

BIG IS BEAUTIFUL

'Big Brain' does seem like the name given to the bumper Christmas annual of *A Journal of Neurology*—but it is the interactive digital resource created from a brain of a 65-year-old man (figure 1). The brain was embedded in paraffin and sectioned in 7404 coronal histological sections, 20 μm across and then stained for cell bodies. The high-resolution histological section is a thing of true beauty.

Science 2013;340:1472–5.

TRIAL AND ERROR

The intricacies of the rise and fall of the PACE trial of the benefits of graded exercise in chronic fatigue syndrome (CFS) are too nuanced to be explained in full here. This was a significant, £5 million trial, and the outcomes were subsequently embedded in National Institute for Health and Care Excellence (NICE) guidance. Many people with CFS argued that the trail design was skewed in favour of finding a benefit for 'the researchers' preferred approaches.' The major concerns were reporting of conflicts of interest, recruitment of trial participants and how the data were analysed and presented. The 2011 *Lancet* paper was the subject of an unprecedented freedom of information request and a tribunal ruled that anonymised trial data should now be released. A reanalysis suggests that recovery outcomes were inflated fourfold. A Fo Ben suggests that this controversy will never tire.

Lancet 2011;377:823–36.

Competing interests None.

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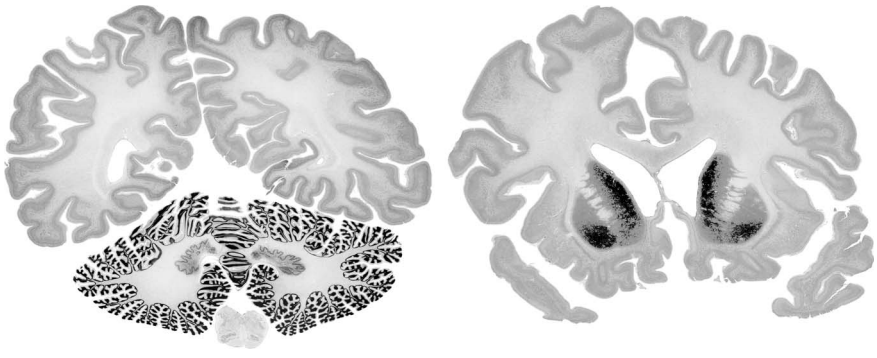

Figure 1 High-resolution coronal sections (Courtesy of the BigBrain project, McGill University).