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AN OLDIE BUT A GOODIE

Typically, you wait 14 years for a follow-up for the seminal SANAD study and then two open-label, non-inferiority, multicentre, phase IV, randomised controlled trials come along at once.

Children and adults with focal epilepsy were randomised (1:1:1) to lamotrigine, levetiracetam or zonisamide for initial monotherapy. Patients were followed up for 2.0–7.5 years. At 2 years, 5% fewer participants had a remission on levetiracetam compared with lamotrigine. Lamotrigine was also better tolerated; compared with lamotrigine, there were 16% more treatment failures on levetiracetam and 23% more treatment failures on zonisamide at 2 years; the majority of these were due to adverse effects. This means that, despite the slower titration of lamotrigine, the median time to 12-month remission was 516 days for lamotrigine, 588 for levetiracetam and 530 for zonisamide.

In the study of genetic generalised epilepsy (levetiracetam vs valproate), levetiracetam was found to be neither clinically effective nor cost-effective. At a year, 9% fewer patients had entered 12-month remission on levetiracetam; the two drugs were similar with regards to adverse events. This is a ringing endorsement for valproate which also ‘came out on top’ against lamotrigine and topiramate in the 2007 SANAD trial—but in practical terms a major clinical concern because of the potential for valproate to be such a significant physical and cognitive teratogen. For men—it is valproate, for women it is problematic.

Lancet. 2021;397(10282):1363–1374.

Lancet. 2021;397(10282):1375–1386.

BUNNY HOP

A team of geneticists have identified why a strain of rabbits (*sauteur d’Alfort*) walk on their ‘hands’ like a circus performer. Mutations in the gene *RORB* cause aberrant protein production, which impairs inhibitory spinal cord interneurons. *RORB* produces a transcription factor, meaning it controls the activity of many other genes. With these interneurons missing, the rabbits flex certain muscles excessively, which lifts their hind legs off the floor and over their heads. They conclude that *RORB* is required for the performance of saltatorial locomotion in rabbits, which is bunny hopping to you and me.



The abnormal posture of the sauteur rabbits. Photo adapted from R. Cavignaux, *PLoS Genet.* 2021;17(3):e1009429.

LUMA? TICK

The novel antipsychotic, lumateperone, is thought to exert effects via three neurotransmitter pathways: serotonin, dopamine and glutamate. A total of 450 people with an acute exacerbation of schizophrenia were randomised to lumateperone or placebo. Those receiving the drug had symptom relief without more motor, cardiometabolic or endocrine adverse effects than placebo. Sedation (17.3% vs 4.0%), somnolence

(12.7% vs 5.4%), fatigue (5.3% vs 1.3%) and constipation (6.7% vs 2.7%) were seen more commonly with the drug than with placebo.

JAMA Psychiatry. 2020;77(4):349–358.

LADY GABA

Don’t blame it on the sunshine, don’t blame it on the moonlight, don’t blame it on good times, blame it on the high titres of glutamic acid decarboxylase 65-IgG. Among the most curious of the reflex epilepsies may be musicogenic epilepsy—a form of temporal lobe epilepsy where songs trigger seizures. Nine of 16 people with musicogenic epilepsy were tested for GAD65 serum antibodies and all were positive, with titres above 100 times the normal range. A tantalising report that needs replication, and then a study of treatments: Cure vs Placebo? (As far as A Fo Ben is aware there is not a popular beat combo called ‘intravenous immunoglobulin’, but they would be a death metal band).

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