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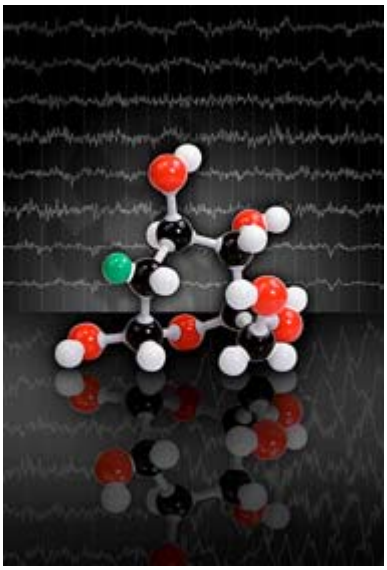

Sugar threat.
2DG (in forefront) supresses epileptic seizures in rats (as shown by the electroencephalogram in background).

Credit: Avtar Roopra

Ban the Sweets, Stop the Shakes

By Prashant Nair
*Science*NOW Daily News
17 October 2006

Scientists have found a way to suppress epileptic seizures in rats by inhibiting the animals' ability to break down sugars. If the approach works in humans, it could herald a novel class of antiepileptic drugs.

Epilepsy arises when brain neurons fire in an uncontrolled frenzy, causing seizures. Most current treatments are aimed at decreasing neuronal activity, but these approaches have side-effects, such as drowsiness and cognitive difficulties.

Neurobiologists Thomas Sutula and Avtar Roopra at the University of Wisconsin, Madison, decided to tackle epileptic seizures from a different angle. Scientists have long known that seizures can sometimes be kept at bay when people with epilepsy steer clear of sugars and other carbohydrates--the so-called ketogenic diet. In addition, removing glucose from slices of the hippocampus--the brain region activated in epilepsy--leads to a dip in neuronal firing in animal studies.

Sutula and Roopra focused on an inhibitor of sugar breakdown--or glycolysis--known as 2DG. When rats predisposed to epileptic seizures were given 2DG, the amount of electric current needed to set off a seizure in these animals was significantly higher than that in animals not given the drug. Furthermore, treated rats required twice as many electric discharges than untreated ones to produce seizures. An analysis of the hippocampus of treated rats revealed that 2DG was blocking the action of a protein complex that drives the expression of seizure-related genes. The activity of this complex is dependent on the end products of glycolysis, the team reports in the October issue of *Nature Neuroscience*.

Although no side effects were seen in rats treated with 2DG for up to 6 months, designing clinical trials for humans will be difficult, says Sutula. One concern, he says, is working out factors such as dosage and administration time. The length of time for which humans can be safely exposed to inhibitors of sugar breakdown is yet

to be determined. Another issue is designing a trial around a drug that modulates gene expression in a chronic fashion, because conventional epilepsy drugs and anticonvulsants act directly on molecules that cause neurons to fire.

The study provides a significant insight into the molecular pathways that could be harnessed to protect the brain from epilepsy, says neuroscientist Dimitri Kullmann at University College London. However, he cautions that because the team had to induce epilepsy with electrical charges, the results may not be applicable to the naturally occurring disorder.

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