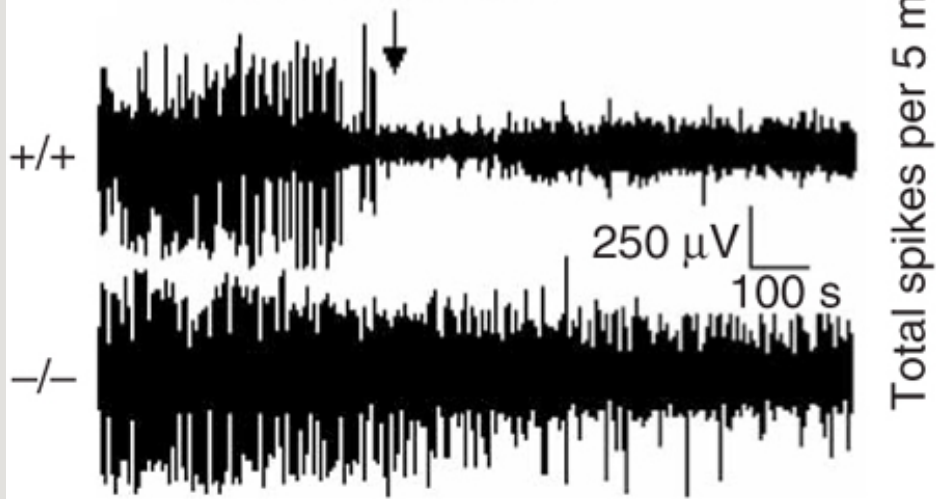


Spike attenuation



Rapid recovery.

ASIC1a ion channels help mice bring seizure-related brain activity under control (*top*). Mice lacking the channels suffer more prolonged and severe attacks (*bottom*).

Credit: Ziemann *et al.*, *Nature Neuroscience*, Advance Online Publication (8 June 2008)

To Stop a Seizure

By Elsa Youngsteadt
ScienceNOW Daily News
9 June 2008

Sometimes seizures become a nightmare without end. Roughly 15% of epileptics will, at some point, experience status epilepticus, a medical emergency in which convulsions can only be stopped with strong anesthetics. Now researchers have found a piece of cellular machinery--an acid-activated ion channel-- that helps bring seizures under control. They hope the discovery will lead to new drugs that could stop these deadly events.

For decades, researchers have suspected a link between brain acidity and seizures. In 1929, doctors noted that patients breathing CO₂ had shorter seizures; the gas boosts the acidity of blood reaching the brain.

Even without intervention, brain pH can drop during a seizure due to changes in breathing and metabolism. John Wemmie, a psychiatrist at the University of Iowa in Iowa City and colleagues wondered if an ion channel called ASIC1a might play a role, as it is known to activate neurons by pumping calcium and sodium across the cell membrane when the brain becomes acidic.

Wemmie's team compared normal mice with those that were genetically engineered to lack the channel.

When they injected these knockouts and controls with chemicals that cause epilepsy-like seizures, the normal mice fared much better than the ones without ASIC1a. A compound called kainate produced serious whole-body convulsions in all seven knockout mice, whereas the six normal mice had only minor seizures in their heads and fore-limbs. A second group of knockouts injected with a different drug, PTZ, had longer seizures than control mice--and those seizures were several times more likely to become deadly tonic-clonic whole-brain seizures (formerly known as "grand mal" seizures). In contrast, mice genetically engineered to have double the normal number of ASIC1a channels had shorter and less severe seizures than wild-type mice, the team reports online this week in *Nature Neuroscience*.

Wemmie and his colleagues have begun to investigate whether ASIC1a also has a role in epileptic humans. If it does, Wemmie hopes that new drugs may help turn the channels on and stop seizures in patients who go into status epilepticus--perhaps without the side effects of large doses of currently available anticonvulsants, which can also cause patients to stop breathing or experience kidney failure.

Jeffrey Noebels, a neurologist at Baylor College of Medicine in Houston, Texas, says any insight into status epilepticus is "welcome news," adding that the discovery may help clinicians understand why some people are more likely than others to experience the condition. Epileptologist Douglas Coulter of the University of Pennsylvania School of Medicine in Philadelphia agrees that the study is "compelling," but he notes that much more work is needed to understand exactly how the channel exerts its beneficial effects.