

# A step towards gene therapy against intractable epilepsy

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By delivering genes for a certain signal substance and its receptor into the brain of test animals with chronic epilepsy, a research group at Lund University in Sweden and colleagues at University of Copenhagen Denmark has succeeded in considerably reducing the number of epileptic seizures among the animals. The test has been designed to as far as possible mimic a future situation involving treatment of human patients.

Many [patients](#) with [epilepsy](#) are not experiencing any improvements from existing drugs. Surgery can be an alternative for severe epilepsy, in case it is possible to localise and remove the epileptic focus in the brain where seizures arise.

"There is a period between the detection of this focus and the operation when the [gene therapy](#) alternative could be tested. If it works well, the patient can avoid surgery. If it doesn't, surgery will go ahead as initially planned and the affected part will then be removed. With this approach, the experimental treatment will be more secure for the patient", says Professor Merab Kokaia.

He and his group are working on a rat model that mimics [temporal lobe epilepsy](#), the most common type of epilepsy. The test animals are given injections of the epilepsy-inducing substance, kainate, in the temporal lobe of one the cerebral hemispheres. Most of the animals had seizures of varying degrees, whereas some had no seizures, which Merab Kokaia considers a good result, as it is similar to the situation among people.

Brain damage resulting from various accidents has very different consequences for different patients, as some develop epilepsy, whereas others do not.

The rats that developed epilepsy were then given gene therapy in the part of the brain in which the kainate had been injected, and where the seizures arose. Genes were delivered for both the signal substance (neuropeptide Y) and one of its receptors. The idea was that the combination would create a larger effect than only delivering the gene for the signal substance itself. Neuropeptide Y can bind to several different receptors and in the worst case it binds to a receptor that promotes increase in the number of seizures instead of decrease.

The study results have so far been positive. The increase in the frequency of seizures that has been seen among the control animals that were treated with [inactive genes](#) was halted after the treatment with combination of active genes, and for 80 % of the animals the number of [seizures](#) was reduced by almost half.

"The test must be repeated in more animal studies, so that the possible side effects, on memory for example, can be studied. But, we regard this study as promising proof of concept, a demonstration that the method works," states Merab Kokaia.

He expects that the first gene therapy treatments will be carried out on patients who have already been selected for surgical procedures. In the long term, however, gene therapy will be of the greatest benefit to those patients who cannot be operated on. There are patients with severe epilepsy whose epileptic focus is so badly placed that an operation is out of question since it can impair e.g. speech or movement. These patients can therefore never undergo a surgical procedure, but could be helped by gene therapy in the future.

**More information:** Litsa Nikitidou Ledri et al. Translational approach for gene therapy in epilepsy: Model system and unilateral overexpression of neuropeptide Y and Y2 receptors, *Neurobiology of Disease* (2016).

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