New research provides insight into epilepsy

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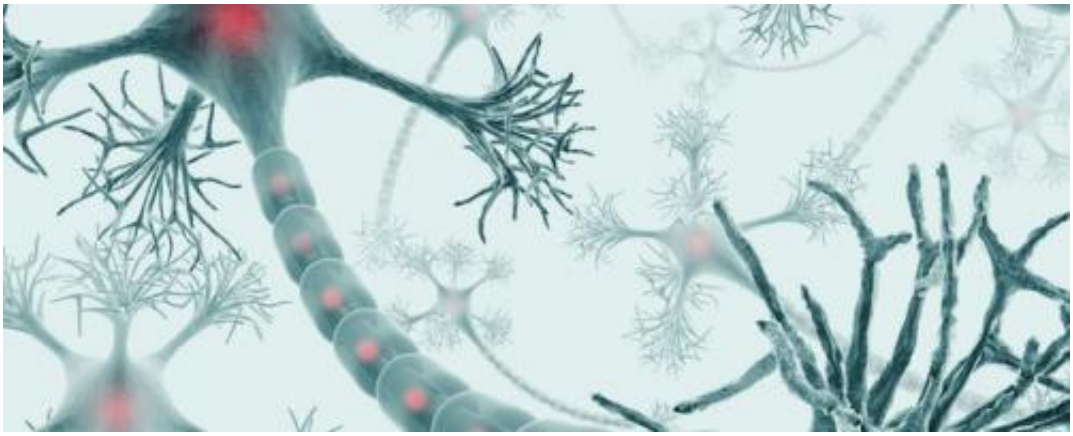

Experiments using mice have led to new research results showing that the amount of microRNA-128 has a great impact on the musculoskeletal system. If the level of microRNA-128 is increased, it leads to lower neuron activity and can thereby help reduce uncontrolled movements in connection with epilepsy or Parkinson's disease. MicroRNA-128 can similarly be decreased to boost the neuron activity.

Jørgen Kjems and Morten Trillingsgaard Venø, Department of Molecular Biology and Genetics and the Interdisciplinary Nanoscience Centre (iNANO), contribute to an article on microRNA-128 just published in *Science*. In the experiments on mice, it was possible to control the amount of microRNA-128 in specific neurons that react to the signal substance dopamine. "If microRNA-128 is kept down in these

neurons in neonatal mice, it results in a strong phenotype," explains Morten T. Venø. "It leads to a higher level of activity, which means the mice move more, develop epilepsy and finally die of the seizures," he clarifies.

Morten T. Venø, postdoc. at the Department of Molecular Biology and Genetics, has worked with the leader of the project Anne Schaefer during his PhD degree programme.

Here he worked on an advanced technology, where it is possible to see how microRNA binds to the mRNA.

MicroRNA works by binding to so-called Ago proteins and guiding these proteins to specific locations on the mRNA. The mRNAs are the copies of the DNA's genes, which are translated directly into protein.

The Ago proteins bind to both the microRNA and the mRNA at the same time, which either means that the mRNAs are broken down, or that the so-called translation into protein is otherwise hindered.

Morten T. Venø and Anne Schaefer worked with special mice, which had been genetically modified to produce a special type of Ago protein in the brain's neurons.

This special Ago protein, together with the RNA that was bound to it, could be purified from the brain tissue of the mice with the help of an antibody. The researchers were thus able to determine where the different microRNA in the neurons bind.

MicroRNA-128 turned out to be the microRNA that controls the greatest number of mRNAs in the brains of the mice - more specifically in the neurons!

Experiments on mice

Together with his former supervisor Jørgen Kjems, the young researcher has continued to collaborate with Anne Schaefer on microRNA-128 and its function in neurons.

Experiments on mice show that you can check the amount of microRNA-128 in neurons that respond to dopamine, and thus also check how it affects a wide variety of gene expression in these neurons, which results in an altered activation of the neurons. "A large volume of microRNA-128 results in a lower neuron activity and can help to hamper the degree of activation in the musculoskeletal system.

Such a strong reaction to a change of the microRNA level is seen extremely rarely.

The reason for the intense effect of the microRNA 128 reduction in neurons must probably be found in the fact that microRNA 128 regulates a lot of the mRNAs (and, thus, many gene expressions) ", explains Morten T. Venø.

Mice are the first step - humans are the next

The new research is not yet transferable to humans, but Morten T. Venø and Jørgen Kjems are involved in a five-year EU project, where the role of microRNA in epilepsy is being examined with a view to future treatment.

In addition to microRNA 128, microRNA 134 also has an impact on epilepsy, particularly under the microscope.

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