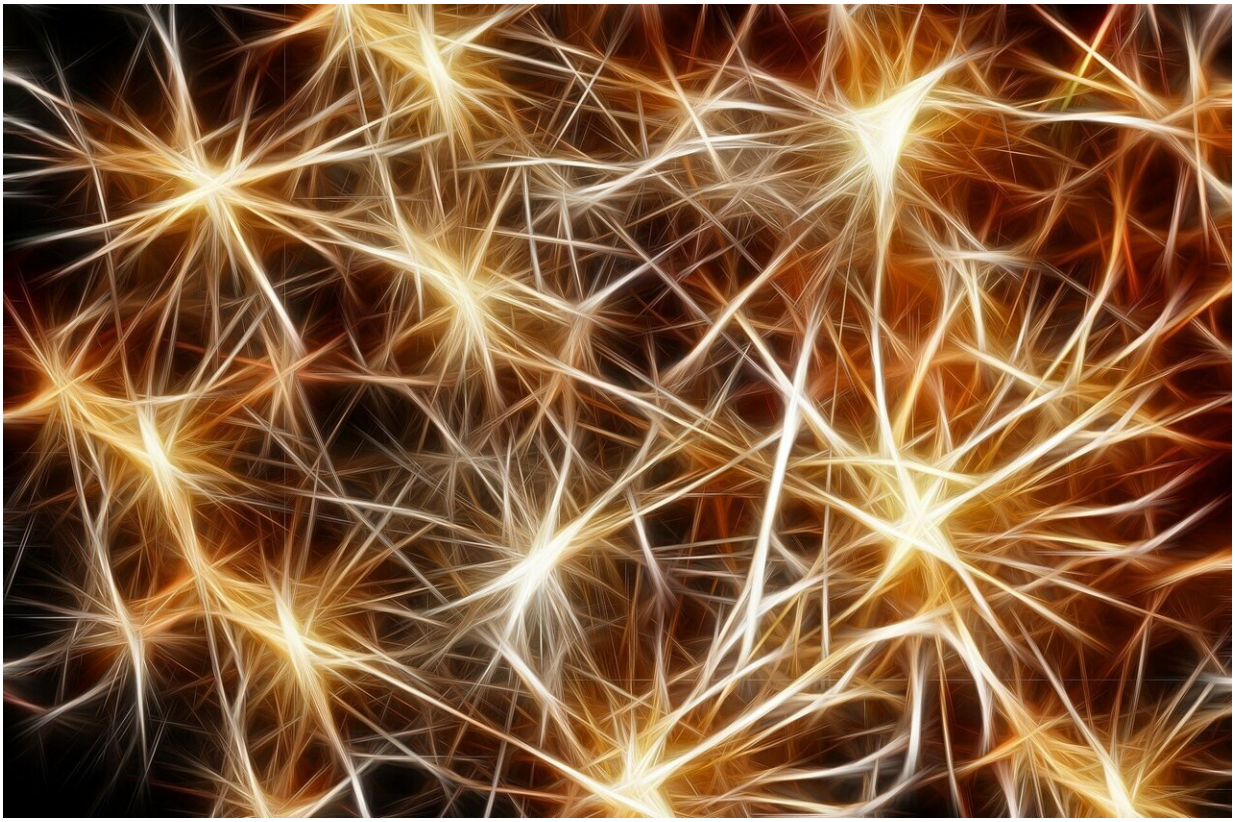
Reprogramming glial cells into neurons reduces the rate of epileptic seizures in mice

September 30 2021



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A new study from researchers at the French National Institute of Health and Medical Research (INSERM), in collaboration with the Institute of Psychiatry, Psychology, & Neuroscience (IoPPN) at King's College

London, has found that cellular reprogramming can help to reduce epileptic seizures in mice.

The study, published today in *Cell Stem Cell*, demonstrates that by reprogramming brain-resident glial cells into what's known as 'interneurons' (i.e. inhibitory neurons that help keep the neural network excitation at bay), chronic seizure activity in the brain can be dampened in a pre-clinical mouse model of epilepsy. The investigators now hope that this offers a potential cell-based means of combatting seizures in drug-resistant epilepsy.

The research focussed specifically on mesial temporal lobe epilepsy (MTLE), the most common form of 'focal epilepsy' that is characterized by spontaneous recurrent seizures. Unfortunately, it is also among the most treatment resistant forms of the illness, with anti-seizure medication and resective surgery both proving ineffective for many patients in the long term.

The investigators hypothesized that regenerating neurons via a process known as 'in vivo lineage reprogramming' could help to reduce the occurrence of these drug-resistant seizures.

Over the course of the study, researchers demonstrated that glial cells could be efficiently reprogrammed within the brain of epileptic mice into 'induced neurons' that effectively took on the identity of interneurons, and formed synaptic connections in the brain. These induced interneurons were shown to reduce the occurrence of spontaneous recurrent seizures in the mice studied.

Reprogramming glial cells into clinically-relevant induced neurons is an emerging strategy for treating abnormal brain functioning. To be of therapeutic value, it is crucial that the induced neurons can promote functional recovery in the brain, in order to restore lost brain functions

and/or correct functional deficits.

Dr Christophe Heinrich, the study's lead author from INSERM said, "Our study uncovers glia-to-neuron reprogramming as a cell-based strategy to regenerate lost interneurons in epilepsy and to combat therapy-resistant seizures. We believe that glia-to-neuron reprogramming could serve as an innovative strategy also in the context of other devastating neurological disorders."

The researchers now hope to refine the process of glia-to-neuron reprogramming towards improved functional restoration, with the ultimate hope of translating the findings to benefit people experiencing epilepsy.

More information: Célia Lentini et al, Reprogramming reactive glia into interneurons reduces chronic seizure activity in a mouse model of mesial temporal lobe epilepsy, *Cell Stem Cell* (2021). DOI: 10.1016/j.stem.2021.09.002

Provided by King's College London