**////Title: Rewiring the Brain: How a Small-world Network Structure Mimics Spontaneous Synchronisation in Epileptic Seizures**

**////Stand-first**:

Epilepsy is a chronic, long-term disease in which abnormal activity in the brain leads to repeated seizures, and it affects nearly 70 million people worldwide. The exact mechanisms behind epileptic seizures are still poorly understood. However, we do know that epilepsy can be caused by changes in the network structure of our brains and that seizures may be a result of spontaneous excessive brain synchronisation. Professor Eckehard Schöll [Ekke-hard Shull] and his Master student Moritz Gerster [Mo – ritz Ger-ster] together with colleaguesare using computer simulations to better understand the interplay of network structure and network synchronisation in epilepsy.

**////Body text:**

Our brain network consists of brain areas and neuronal interconnections between these areas. Each brain area contains up to billions of neurons. Many neurons within a brain area fire electrical signals at the same time, in synchrony, and even neurons across different areas of the brain may synchronise. These are known as synchronous clusters.

The collective firing of neurons in synchronous clusters is assumed to create brainwaves, also known as neural oscillations. This synchronised firing is essential to memory and learning processes as well as fundamental physiological processes. Neural oscillations can be measured using electroencephalography [uh lek trow en·seh·fuh·lo·gruh·fee] recordings, otherwise known as EEG recordings, which measure the electrical activity of the brain using multiple electrodes fixed across the scalp.

EEG recordings of brain waves from subjects with epilepsy have shown that during epileptic seizures, there can be spontaneous episodes of excessive synchrony. But unfortunately, the mechanisms behind these spontaneous episodes are not well understood.

A major question for researchers is why these spontaneous episodes of excessive brain synchrony start (termed self-initiation) and why they end (self-termination). It is also unclear how the changes in the network structure of our brains can lead to epilepsy.

In a novel collaboration between physicists and neurologists, Professor Eckehard Schöll, Moritz Gerster, and their colleagues set out to create a dynamic computer model of the network connections and neural oscillations in the brain that is capable of mimicking electrical activity in the brain and simulating epileptic seizures.

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To begin, the researchers constructed a realistic brain network using magnetic resonance imaging. Then they simulated the dynamics of the neurons using a mathematical model which consisted of coupled FitzHugh-Nagumo [Fitz-juh-Nagumo] oscillators that behave just like ensembles of neurons.

Using this model of the human brain, the researchers then compared simulated and real-life measured seizures and found that their simulations using the coupled FitzHugh-Nagumo oscillator model could accurately reproduce the excessive synchronisation patterns observed in EEG recordings during generalised epileptic seizures in humans.

Next, the researchers used their model to perform experiments that can only be accomplished in the computer: They rewired the network structure of the brain to explore the role of coupling structure in spontaneous synchronisation. During the rewiring process, they were especially interested in the role of the so-called clustering coefficient. If two independent brain areas are both connected to a third brain area, there is a given probability that these two brain areas are also connected. This probability is quantified by the clustering coefficient, and it is different for different network topologies. We should note here that the clustering coefficient describes how densely the different nodes – or areas of the brain – are connected.

When comparing their various simulations, Professor Schöll and his colleagues found that networks with intermediate clustering best mimic the real structural connectivity of the human brain.

Furthermore, they observed that there was no consistent seizure-like spontaneous synchronisation in the simulations using the other network topologies where seizure phenomena either did not take place or the level of synchrony remained too high throughout the simulation.

This finding suggests that some form of balance between the regularity of high clustering and randomness of low clustering must be involved in the self-initiation (start) and self-termination (end) of the synchronisation process during an epileptic seizure.

To further explore this observation, Professor Schöll, Moritz Gerster and their colleagues used their model to randomly rewire all the brain connections, resulting in a model with a low number of clusters in the network – and ultimately destroying the original structure of the brain.

Intriguingly, what they found was that seizures still occurred but unlike in real seizures they tended to be more frequent and shorter. They also identified that the average level of brain synchrony is much higher in their random model, even during the healthy state between spontaneous seizures. This indicates that random network structures actually increase overall brain synchronisation.

Next, the researchers tested the other extreme, a simulated brain network with a high number of clusters. This time the brain was found to synchronise fully, leading the simulation to create a prolonged 3-hour seizure with no self-termination and no healthy brain activity.

From these simulations, it became clear that both highly clustered, regular networks as well as networks with low clustering and high randomness increase brain synchrony. This led Professor Schöll and colleagues to the conclusion that a healthy brain network needs a delicate balance between clustering and randomness.

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Overall, Professor Schöll and his colleagues found that if the network structure in the brain is too random or too ordered, there is a greater chance of spontaneous synchronisation occurring.

The researchers speculate, based on their simulations, that subjects with epilepsy may have brain networks that are either too strong (highly clustered) or too weak (more random) in their network clustering. This would suggest that epilepsy is a condition that results from a disruption of the typical network clustering structure. A healthy human brain, on the other hand, lies somewhere between these two extremes.

These insights into the interplay of network structure and network synchronisation in epilepsy could help to further improve treatment methods which aim to change the network structures of epileptic brains.

This SciPod is a summary of the paper ‘FitzHugh–Nagumo oscillators on complex networks mimic epileptic-seizure-related synchronization phenomena’, by Moritz Gerster, Rico Berner, Jakub Sawicki, Anna Zakharova, Antonín Škoch, Jaroslav Hlinka, Klaus Lehnertz [Klaʊ̯s Leː - nɛrt͜s] and Eckehard Schöll, published in Chaos 30, 123130 (2020), <https://doi.org/10.1063/5.0021420>.

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