Mimicking brain cells to understand Parkinson's

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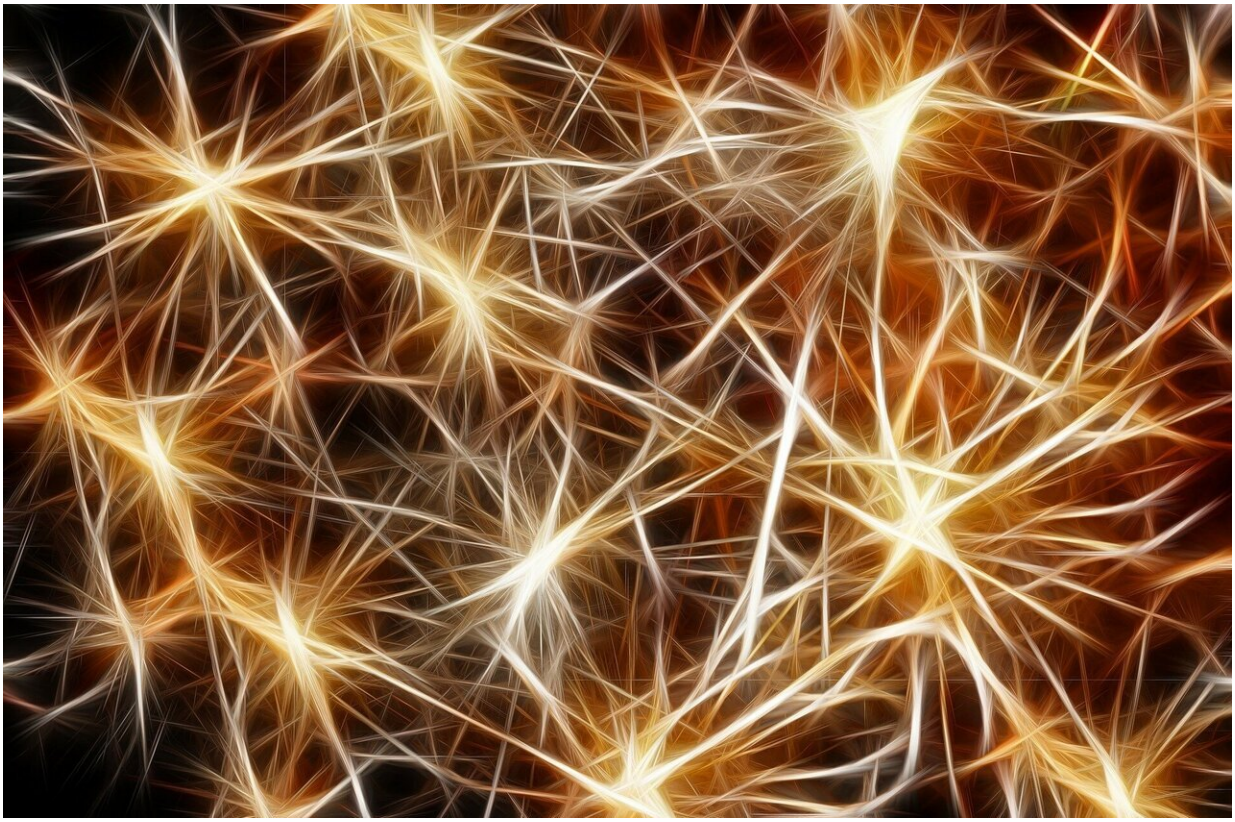

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A device that mimics the brain cells affected by Parkinson's disease could help find new treatments for the condition. The device is described in the Elsevier journal *Organs-on-a-Chip*. "We have created

human neurons that are in an environment, more similar to the one of the human brain. These can help us get closer to understanding what happens in Parkinson's disease and develop more effective treatments," says lead author Jens Schwamborn of the University of Luxembourg.

From organs-on-a-chip to neurons-on-a-chip

The device developed by Schwamborn's team is an example of an organ-on-a-chip. These are being developed by biomedical researchers across the globe to simulate the activities and workings of organs and organ systems. By testing drugs and therapies on these devices, it is hoped that animal testing can be reduced, drug development accelerated and personalized medicine advanced.

Organ-on-a-chip devices are typically made of a clear polymer or glass with small channels containing living cells. Fluids flow though the channels to mimic the environment of the organ. Specifically, Schwamborn's device is a neurons-on-a-chip. Neurons are the cells in the brain affected in Parkinson's disease.

The team have adapted existing technology to create a three-dimensional (3-D) artificial neuron in which fluid flows continually for an extended period of time. Schwamborn notes: "Cell cultures for chip devices have typically been grown in 2-D. To get closer to the real situation in the brain, the neurons need to be in a 3-D environment."

The introduction of a continuous flow is thought to grow more authentic neuronal cells in channels, whilst also creating an environment that is more like that in the real neurons of the brain. These adaptations make the device compatible with systems that will allow automated experiments to be carried out. This enables multiple experiments to be done in parallel, saving time and money and accelerating biomedical research.

Understanding Parkinson's

Parkinson's disease affects more than 10 million people worldwide. People with the disease experience damage to the central nervous system. Many neurons die, including those that release dopamine. The death of these dopaminergic neurons is the main reason that Parkinson's patients exhibit the diseases' characteristic and debilitating physical symptoms.

To study what really happens in Parkinson's disease, dopaminergic neurons need to be recreated. This is now possible thanks to a technique that creates stem cells that can differentiate into many different types of human cell. From this method, a protocol was developed to recreate the dopaminergic neurons affected in Parkinson's. Schwamborn and his team rely on this protocol to cultivate the dopaminergic neurons that line the channels of their neuron-on-a-chip.

Mimicking the neurons in the brain

Schwamborn's team redesigned a commercially available and automatable organ-on-a-chip product called the OrganoPlate. They used a series of modeling techniques to optimize the size of the medium channels so that they can receive a continuous flow for a long time period. This enables the neuronal cell culture to grow (as per the protocol mentioned previously) and mimics blood flow in the human brain better than other methods used to make chip devices.

Once manufactured, the team demonstrated the device's biological compatibility by using it to successfully cultivate human dopaminergic neurons. As they are cultured with a continuous flow, the conditions are now optimized to mimic those of the normal and diseased human brain. It is hoped that this technique can also be applied to optimize chip design

so that other types of cell can be cultured.

More information: Khalid I.W. Kane et al. Passive controlled flow for Parkinson's disease neuronal cell culture in 3D microfluidic devices, *Organs-on-a-Chip* (2020). DOI: 10.1016/j.ooc.2020.100005