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Study finds that human neuron signals flow in one direction

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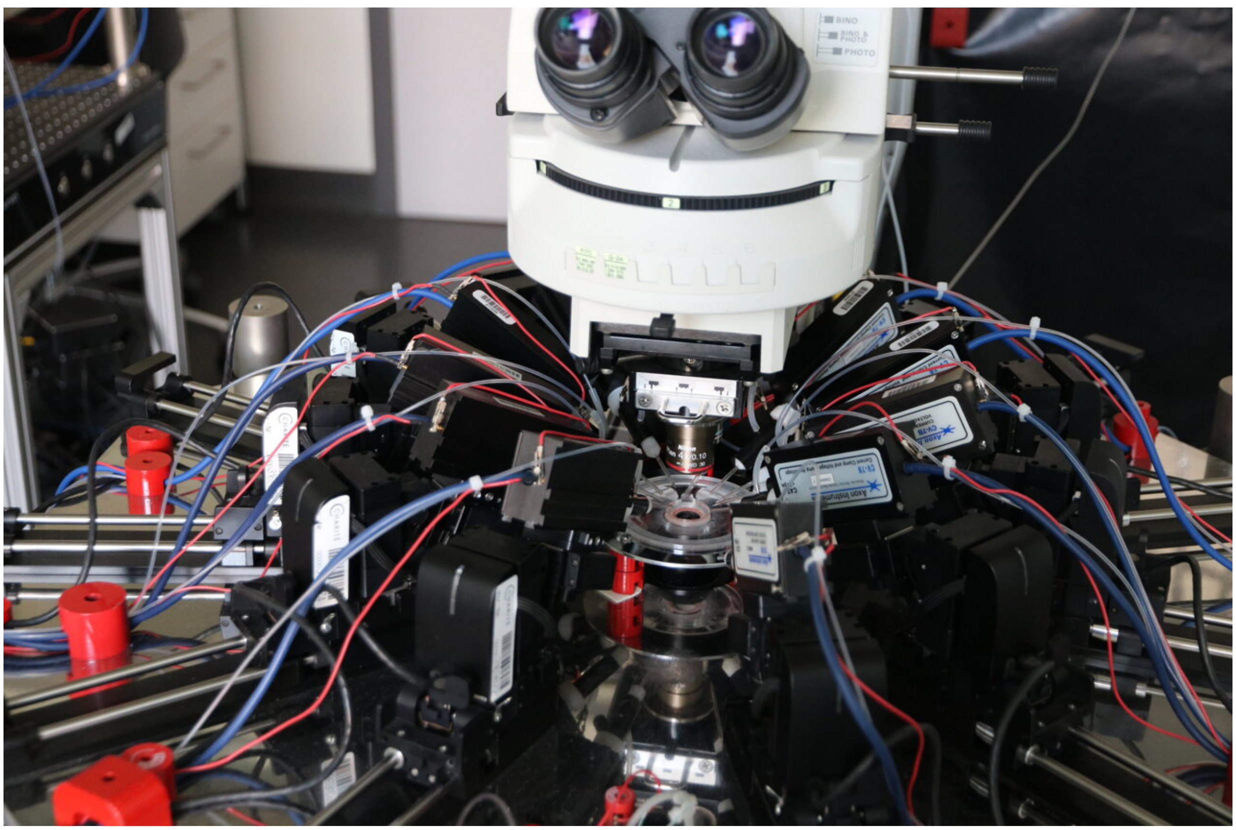

Experimental setup for multi-patch experiments that record the activity of up to ten neurons. Credit: Charité | Yangfan Peng

Contrary to previous assumptions, nerve cells in the human neocortex are wired differently than in mice. Those are the findings of a new study conducted by Charité-Universitätsmedizin Berlin and published in the journal *Science*. The study found that human neurons communicate in one direction, while in mice, signals tend to flow in loops. This increases the efficiency and capacity of the human brain to process information. These discoveries could further the development of artificial neural networks.

The neocortex, a critical structure for human intelligence, is less than five millimeters thick. There, in the outermost layer of the brain, 20 billion neurons process countless sensory perceptions, plan actions, and form the basis of our consciousness. How do these neurons process all this complex information? That largely depends on how they are "wired" to each other.

More complex neocortex, different information processing

"Our previous understanding of neural architecture in the neocortex is based primarily on findings from animal models such as mice," explains Prof. Jörg Geiger, Director of the Institute for Neurophysiology at Charité. "In those models, the neighboring neurons frequently communicate with each other as if they are in dialogue. One neuron signals another, and then that one sends a signal back. That means the information often flows in recurrent loops."

The human neocortex is much thicker and more complex than that of a mouse. Nonetheless, researchers had previously assumed—in part due to lack of data—that it follows the same basic principles of connectivity. A team of Charité researchers led by Geiger has now used exceptionally rare tissue samples and state-of-the-art technology to demonstrate that this is not the case.

A clever method of listening in on neuronal communication

For the study, the researchers examined brain tissue from 23 people who had undergone neurosurgery at Charité to treat drug-resistant epilepsy. During surgery, it was medically necessary to remove brain tissue in order to gain access to the diseased structures beneath it. The patients had consented to the use of this access tissue for research purposes.

To be able to observe the flows of signals between neighboring neurons in the outermost layer of the human neocortex, the team developed an improved version of what is known as the "multipatch" technique. This allowed the researchers to listen in on the communications taking place between as many as ten neurons at once.

As a result, they were able to take the necessary number of measurements to map the network in the short time before the cells ceased their activity outside the body. In all, they analyzed the communication channels among nearly 1,170 neurons with about 7,200 possible connections.

Feed-forward instead of in cycles

The team found that only a small fraction of the neurons engaged in reciprocal dialogue with each other.

"In humans, the information tends to flow in one direction instead. It seldom returns to the starting point either directly or via cycles," explains Dr. Yangfan Peng, first author of the publication. He worked on the study at the Institute for Neurophysiology and is now based at the

Department of Neurology and the Neuroscience Research Center at Charité. The team used a computer simulation that they devised according to the same principles underlying the human network architecture to demonstrate that this forward-directed signal flow has benefits in terms of processing data.

The researchers gave the artificial neural network a typical machine learning task: recognizing the correct numbers from audio recordings of spoken digits. The network model that mimicked the human structures achieved more correct responses to this speech recognition task than the one modeled on mice. It was also more efficient, with the same performance requiring the equivalent of 380 neurons in the mouse model, but only 150 in the human one.

An economic role model for AI?

"The directed network architecture we see in humans is more powerful and conserves resources because more independent neurons can handle different tasks simultaneously," Peng explains. "This means that the local network can store more information. It isn't clear yet whether our findings within the outermost layer of the temporal cortex extend to other cortical regions, or how well they might explain the unique cognitive abilities of humans."

In the past, AI developers have looked to biological models for inspiration in designing artificial neural networks, but have also optimized their algorithms independently of the biological models. "Many artificial neural networks already use some form of this forward-directed connectivity because it delivers better results for some tasks," Geiger says. "It's fascinating to see that the human brain also shows similar network principles. These insights into cost-efficient information processing in the human neocortex could provide further inspiration for refining AI networks."

About the study

The work was done in close cooperation between the basic research and clinical departments of Charité. Under the leadership of the Institute of Neurophysiology, the following were involved: the Department of Neurosurgery, the Department of Neurology with Experimental Neurology, the Institute of Integrative Neuroanatomy, the Department of Neuropathology, the Neuroscience Research Center, and the NeuroCure Cluster of Excellence, with support from the University Clinic for Neurosurgery at Evangelisches Klinikum Bethel and the Institute of Neuroinformatics at ETH Zurich.

About the method

When surgery is performed to treat drug-resistant (refractory) epilepsy, it is often medically necessary to remove brain tissue. The explicit consent of patients was required in order to examine this valuable tissue for the study that has just been published. The research group is profoundly grateful to the patients for their consent. The authors used what is known as the "patch-clamp" method to analyze synaptic communication between neurons.

In this technique, an ultra-thin glass pipette is attached to a single neuron under a microscope to measure or stimulate the cell's electrical activity. The study utilized an advanced form of this technique in which multiple of these micropipettes simultaneously record the activity and connectivity of up to ten neurons (the "multipatch" method).

To be able to position the pipettes precisely, the device is equipped with robot arms that enable movements in the nanometer range. The measurement process is highly challenging and labor-intensive. Using two devices in parallel allowed the team to study several hundred connections between the nerve cells for each tissue sample. The brain tissue can be preserved for up to two days outside the body in an artificial nutrient solution before activity ceases.

More information: Yangfan Peng et al, Directed and acyclic synaptic connectivity in the human layer 2-3 cortical microcircuit, *Science* (2024). DOI: 10.1126/science.adg8828.
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