Brain cell network supplies neurons with energy

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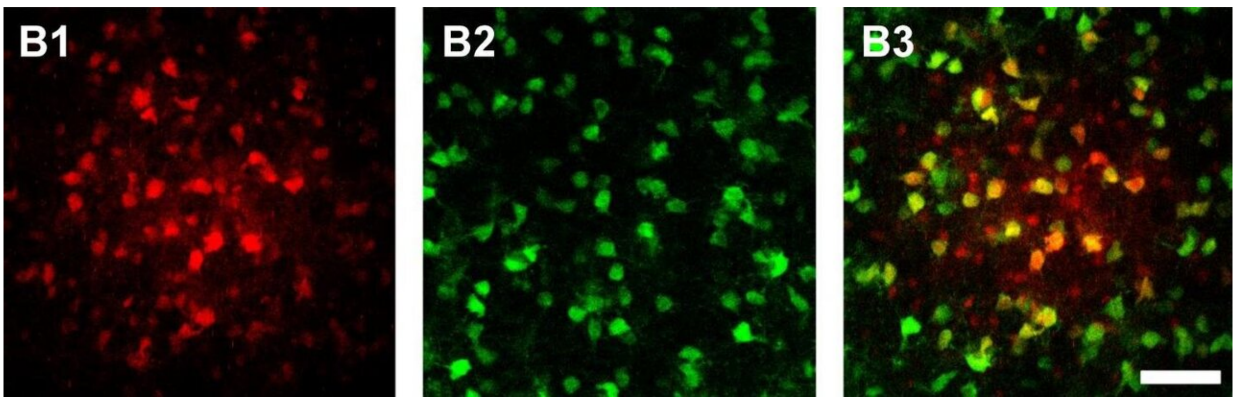

When an astrocyte in the thalamus is filled with a dye, it diffuses into neighboring cells of the network (red). These include many oligodendrocytes (green), as shown by the overlay (B3, yellow). Credit: © Group Steinhäuser; from: Cerebral Cortex, January 2018;28: 213-222; doi: 10.1093/cercor/bhw368

The human brain has about as many neurons as glial cells. These are divided into four major groups: the microglia, the astrocytes, the NG2 glial cells, and the oligodendrocytes. Oligodendrocytes function primarily as a type of cellular insulating tape: They form long tendrils, which consist largely of fat-like substances and do not conduct electricity. These wrap around the axons, which are the extensions through which the nerve cells send their electrical impulses. This prevents short circuits and accelerates signal forwarding.

Astrocytes, on the other hand, supply the nerve cells with energy: Through their appendages they come into contact with blood vessels and absorb glucose from these. They then transport it to the interfaces between two neurons, the synapses. Before that, they partially convert the sugar into other energy-rich molecules. "We have now been able to show that oligodendrocytes play an important role in the distribution of these compounds," explains Prof. Christian Steinhäuser from the Institute of Cellular Neurosciences at the University of Bonn (Germany). "This is apparently especially true in a particular brain region, the thalamus."

Huge supply network

The thalamus is also called the "gateway to consciousness." The sensory signals it receives include those from the ears, eyes, and skin. It then forwards them to the respective responsible centers of the cerebral cortex. Only then do we become aware of this information, for instance the sound of an instrument.

It has long been known that astrocytes can form close connections: They build intercellular networks through tunnel-like coupling. Molecules can migrate from one cell to another through these "gap junctions." A few years ago, Steinhäuser and his colleagues were able to show that there are also oligodendrocytes in these networks in the thalamus, about as many as astrocytes. The cells form a huge network in this way, which neuroscientists also call a "panglial network" ("pan" comes from Greek and means "comprehensive"). In other regions, however, the networks consist predominantly of coupled astrocytes. "We wanted to know why this is different here," explains Dr. Camille Philippot of Steinhäuser's research group, who conducted much of the work. "Our results demonstrate that the high-energy compounds travel through this network from the blood vessels to the synapses," Philippot emphasizes. "And oligodendrocytes seem to be indispensable in this process."

The researchers were for instance able to demonstrate this in mice, in which the oligodendrocytes are unable to participate in the network because they lack the appropriate tunnels. In these mice, energy molecules no longer reached the synapses in sufficient quantities. The same was true if the astrocytes lacked the appropriate connecting links. "The thalamus apparently requires both cell types for transport," Steinhäuser concludes.

Starved neurons cannot communicate

The researchers were also able to show the consequences of such a disrupted energy supply for neuronal information processing. The synapses are where two neurons meet—a sender cell and a receiver cell. When a pulse from the sender cell arrives at the synapse, it releases messenger molecules into the synaptic cleft. These neurotransmitters dock onto the recipient cell and trigger electrical signals there, the postsynaptic potentials. When these signals are generated, potassium and sodium ions pass through the membrane of the recipient cell—sodium ions inward, potassium ions outward. These, like the neurotransmitters, must then be pumped back again. "And for that, the neurons need energy," explains Steinhäuser, who is also a member of the Transdisciplinary Research Area "Life and Health" at the University of Bonn. "When energy is lacking, pumping activity ceases." In the experiments, "starved" neurons were therefore no longer able to generate postsynaptic activity after just a few minutes.

More information: Camille Philippot et al, Astrocytes and oligodendrocytes in the thalamus jointly maintain synaptic activity by supplying metabolites, *Cell Reports* (2021). DOI: 10.1016/j.celrep.2020.108642

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