Brain works more chaotically than previously thought

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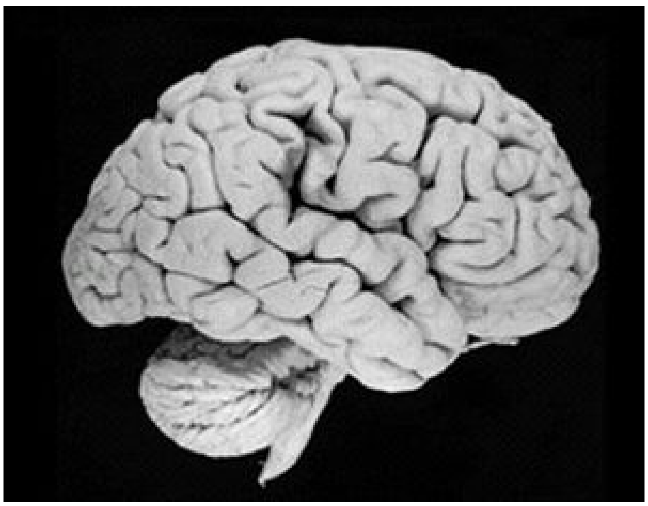

Modern human brain. Image source: Univ. of Wisconsin-Madison Brain Collection.

The brain appears to process information more chaotically than has long been assumed. This is demonstrated by a new study conducted by scientists at the University of Bonn. The passing on of information from neuron to neuron does not, they show, occur exclusively at the synapses, i.e. the junctions between the nerve cell extensions. Rather, it seems that the neurons release their chemical messengers along the entire length of these extensions and, in this way, excite the neighbouring cells.

The findings of the study are of huge significance since they explode fundamental notions about the way our brain works. Moreover, they might contribute to the development of new medical drugs. The study is due to appear shortly in the prestigious academic journals *Nature Neuroscience* and has already been posted online (doi:10.1038/nn1850).

Until now everything seemed quite clear. Nerve cells receive their signals by means of little "arms", known as dendrites. Dendrites pass on the electrical impulses to the cell body, or soma, where they are processed. The component responsible for "distributing" the result is the axon. Axons are long cable-like projections of the cell along which the electrical signals pass until they meet, at a synapse, the dendritic arm of another neuron. The synapse presents an insurmountable barrier to the neuron's electrical pulses. The brain overcomes this obstruction by means of an amazing signal conversion: the synapse releases chemical messengers, known as neurotransmitters, which diffuse to the dendrites. There, they dock onto specific receptors and generate new electrical impulses. "It was previously thought that neurotransmitters are only released at synapses," points out Dr. Dirk Dietrich at Bonn University. "But our findings indicate that this is not the case."

The messenger attracts insulating cells

Together with his colleagues Dr. Maria Kukley and Dr. Estibaliz Capetillo-Zarate, Dietrich has conducted a careful examination of the "white matter" in the brain of rats. This substance contains the "cable ducts" linking the right and left halves of the brain. They consist essentially of axons and ancillary cells. There are no dendrites or even synapses here. "So it is not a place where we would expect to see the release of messengers," the neuroscientist explains.

Yet it is in the white matter that the scientists have made a remarkable discovery. As soon as an electrical impulse runs through an axon cable, tiny bubbles containing glutamate travel to the axon membrane and release their content into the brain. Glutamate is one of the most important neurotransmitters, being released when signal transmission occurs at synapses. The researchers were able to demonstrate that certain cells in the white matter react to glutamate: the precursor to what are known as oligodendrocytes. Oligodendrocytes are the brain's "insulating cells". They produce the myelin, a sort of fatty layer that surrounds the axons and ensures rapid retransmission of signals. "It is likely that insulating cells are guided by the glutamate to locate axons and envelope them in a layer of myelin," says Dirk Dietrich.

As soon as the axons leave the white "cable duct" they enter the brain's grey matter where they encounter their receptor dendrites. Here, the information is passed on at the synapses to the receptor cells. "We think, however, that on their way though the grey matter the axons probably release glutamate at other points apart from the synapses," Dietrich speculates. "Nerve cells and dendrites are closely packed together here. So the axon could not only excite the actual receptor but also numerous other nerve cells."

If this hypothesis is correct, the accepted scientific understanding of the way neurons communicate, which has prevailed for over a hundred years, will have to be revised. In 1897 Sir Charles Sherrington first put forward the idea that chemical messengers are only released at "synapses", a term he coined. According to the founder of modern neurophysiology this means that nerve cells can only communicate with a small number of other nerve cells, i.e. only with those with which they are connected via synapses. This concept is the basis of the notion that neuronal information in the brain, somewhat like electricity in a computer, only spreads directionally in the brain, following specific ordered circuits.

Too much glutamate is the death of cells

There is, however, also an aspect to the research team's discovery that is of considerable medical interest. It has long been known that in the event of oxygen deficiency or a severe epileptic fit, large numbers of insulating cells in the white matter are destroyed. The trigger for this damage is our old friend, the neurotransmitter glutamate. "Nobody knew until now where the glutamate actually comes from," says Dr. Dietrich. "Our results might open the door to totally new therapeutic options." After all, drugs have already been developed that prevent glutamate bubbles from discharging their load into the brain. Indeed, Bonn's neuroscientists now know precisely which receptors of the insulating cells are stimulated by the neurotransmitter – another starting point for developing new drugs.

Yet, why can glutamate sometimes be so dangerous? When an epileptic fit occurs, the nerve cells "fire" very rapidly and fiercely. In this event so many impulses run through the axons that large quantities of glutamate are released all at once. "In these concentrations the neurotransmitter damages the insulating cells," says Dietrich. "It's the dosage that makes it harmful."

Source: University of Bonn