

The balance of learning

Study of the hippocampus shows: inhibitory synapses vary in stability at dendrites and the axon head

Our brain must be able to learn new things without losing previously stored information or the stability of its networks. Researchers at the Leibniz Institute for Neurobiology (LIN) in Magdeburg, together with partners in Bielefeld and Zurich, have investigated how this balance is achieved. They show that learning alters the stability of inhibitory synapses in opposite ways depending on their position on the same nerve cell.

On the dendrites – the input side of the nerve cell – inhibitory synapses are reorganised more frequently following learning. At the axon hillock, where the cell generates its own electrical signal, they become more stable. This spatial division of labour could help to process new information whilst ensuring that learned information remains reliably accessible. The study has now been published in Nature Communications.

Input and output react differently

Nerve cells receive and process signals from other cells via their branched extensions, the dendrites. At the start of the axon, it is determined whether this results in the nerve cell generating and transmitting its own electrical signal. Inhibitory synapses regulate this flow of information and can therefore intervene in the processing at different points, depending on their position.

The researchers observed that learning alters these synapses differently depending on their position: on the dendrites, they were reorganised more frequently, whilst at the start of the axon they remained more stable. Their total number hardly changed.

The study thus points to a spatial division of labour within the same nerve cell: whilst the inhibitory connections on the input side become more flexible, they remain more stable on the output side.

“It is surprising that inhibitory synapses within the same nerve cell do not respond uniformly to learning,” says Alessio Attardo from the LIN. “Their exact position appears to help determine whether they are remodelled or stabilised. This gives us a new insight into how a neural network can remain both plastic and stable at the same time.”

Monitoring the same synapses over 13 days

For the study, the researchers observed inhibitory synapses in the hippocampus of 23 mice over a period of 13 days. Using two-photon microscopy, they were able to return repeatedly to the same nerve cells and synaptic contacts. This allowed them to track directly which synapses persisted, which disappeared and where new ones formed.

In total, the team recorded more than 1,100 inhibitory synapses on dendrites, cell bodies and at the axon initial segment. During the study period, the animals completed a learning task: they learnt to associate a sound and a specific environment with an aversive stimulus that followed later. The hippocampus plays a key role in this form of learning.

The repeated scans revealed how the same inhibitory synapses changed before and after learning. The key factor was not a significant change in their total number, but their varying stability at different locations on the nerve cell.

The model narrows down possible mechanisms

The study combines experimental and theoretical approaches. The learning experiments, long-term recordings and data analyses were carried out in close collaboration between the research groups led by Alessio Attardo and Stefan Remy at the LIN. Researchers from the Universities of Bielefeld and Zurich contributed to the project with mathematical modelling and specialised image analysis.

The mathematical model of a neural network showed the same basic pattern as the experimental data: greater reorganisation at the dendrites and greater stability at the axon head. Furthermore, it helps to narrow down which groups of inhibitory neurons might mediate the changes in the different regions of the neuron. It thus provides concrete starting points for further experiments.

The study investigates fundamental mechanisms of learning in mice. Further research is needed to clarify whether comparable processes also play a role in humans.

Further information

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Project partners

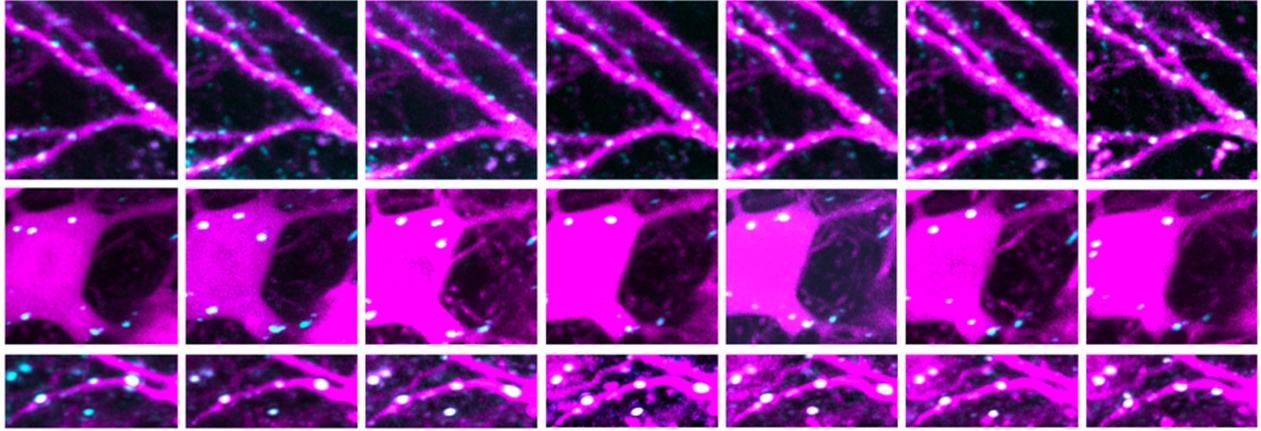
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About the LIN

The Leibniz Institute for Neurobiology (LIN) in Magdeburg conducts research into the fundamentals of learning, memory and behaviour. Researchers from various disciplines investigate how the brain processes, stores and retrieves information – from molecular processes to the interaction of neural networks. In doing so, they lay the foundations for a better understanding of disorders affecting these processes and for the development of new approaches in medicine and technology.

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Time series from the hippocampus of living mice: images taken at two-day intervals show inhibitory synapses (cyan) on nerve cells (magenta). Top: dendrites; centre: cell bodies; bottom: axon terminals. Whilst the structure of the nerve cells remains stable, the inhibitory synaptic contacts change to varying degrees over time, depending on the region of the nerve cell.