

Researchers identify a region of the brain as a key source of signals encoding past experiences in the neocortex

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The brain encodes information collected by our senses. In order to perceive and interact with the environment, however, these sensory signals must be interpreted in the context of past experiences stored in the brain and the individual's current aims. A team led by Prof. Dr.



Johannes Letzkus, Professor at the Faculty of Medicine of the University of Freiburg and Research Group Leader at the Max Planck Institute for Brain Research in Frankfurt am Main, has now identified a key source of this experience-dependent so-called top-down information. The scientists have published their results in the journal *Science*.

The neocortex is the largest and most powerful area of the human brain. All of its important cognitive functions are made possible by the convergence of two distinct streams of information: a "bottom-up" stream, which represents signals from the environment, and a "top-down" stream, which transmits internally generated information about past experiences and current aims. The question of how and where exactly this internally generated information is processed is still largely unexplored, says Letzkus. This motivated him and his team to search for the sources of these top-down signals. The scientists succeeded in identifying a region of the thalamus, a brain area embedded deep within the forebrain, as a key candidate region for such internal information.

Based on this, Dr. M. Belén Pardi, postdoctoral fellow in the Letzkus laboratory, developed a strategy to measure the responses of individual thalamic synapses in the neocortex of the mouse before and after a learning paradigm. "Whereas neutral stimuli without relevance were encoded by small and transient responses in this pathway, learning strongly boosted their activity and made the signals both faster and more sustained over time," explains Pardi. "We were really convinced when we compared the strength of the acquired memory with the change in thalamic activity: This revealed a strong positive correlation, indicating that inputs from the thalamus prominently encode the learned behavioral relevance of stimuli," says Letzkus.

In further experiments and computer modeling, which were conducted together with the team of Dr. Henning Sprekeler from the Technische Universität Berlin, the researchers discovered a previously unknown



mechanism that can finely regulate this information and identified a specialized type of neuron in the outermost layer of the neocortex that dynamically controls the flow of these top-down signals. This confirms the scientists' assumption that the thalamus' projections to the sensory neocortex act as a key source of <u>information</u> about previous experiences associated with sensory stimuli. "Such top-down signals are disrupted in a number of <u>brain</u> disorders like autism and schizophrenia," Letzkus explains. "Our hope is that the present results will also enable a deeper understanding of the maladaptive changes underlying these severe conditions."

More information: M. Belén Pardi et al. A thalamocortical top-down circuit for associative memory, *Science* (2020). DOI: 10.1126/science.abc2399

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