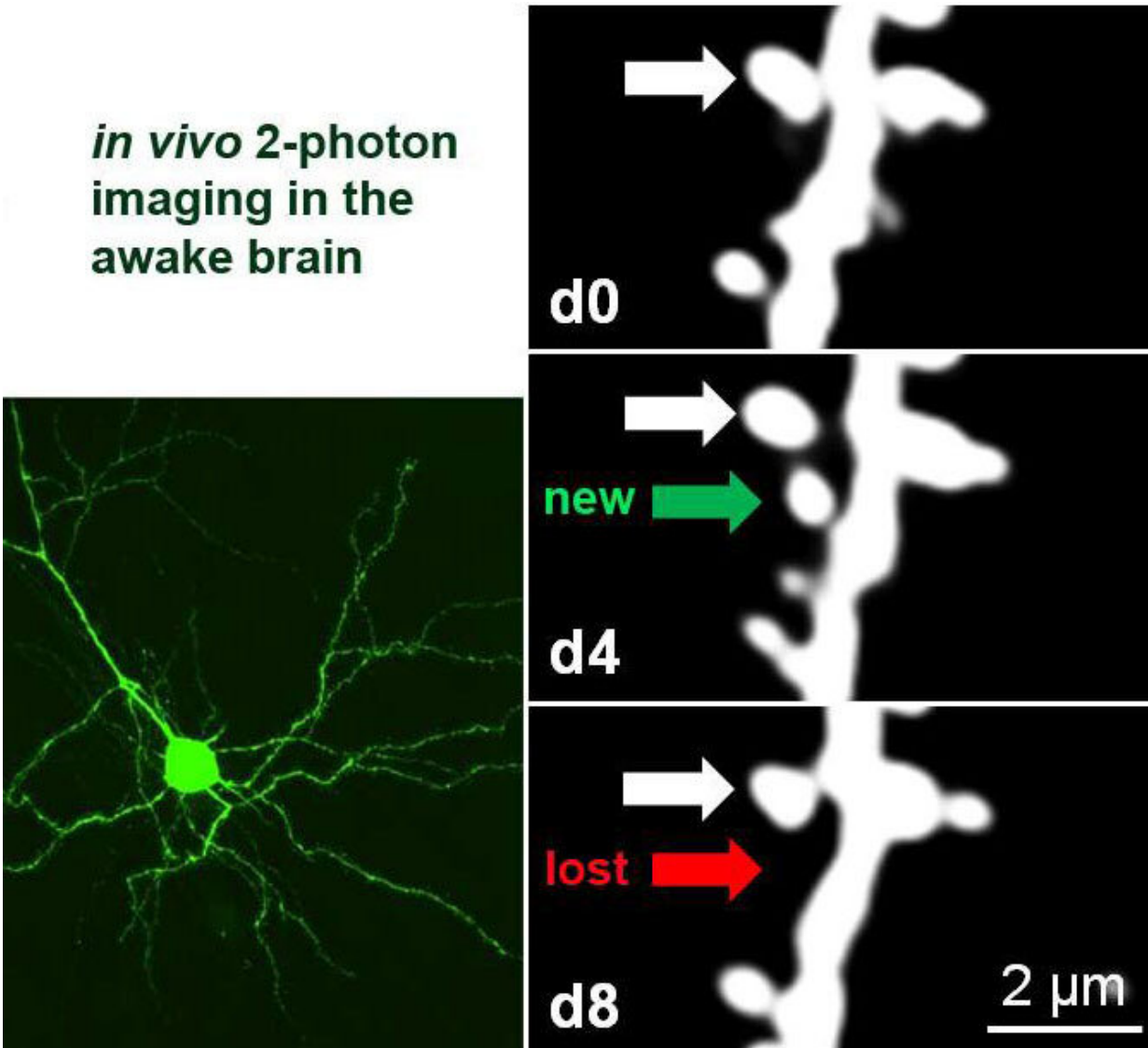


# Watching the brain learn

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Chronic 2-photon imaging of fluorescently labeled visual cortical neurons in the living adult mouse brain: within the first 4 days of imaging, from day 0 (d0) to day 4 (d4), one dendritic spine (white dendritic protrusion) was newly formed

(green arrow); after selective visual stimulation over the next 4 days (until d8), the spine was eliminated (red arrow). White arrow points to a stable spine. Dendritic spine elimination in this paradigm is usually only seen in juvenile mice, but also observed in adult PSD-95 deficient neurons, indicating that PSD-95 is necessary for synapse maturation and stabilization. Credit: S Löwel

Understanding the cellular and molecular mechanisms underlying brain plasticity (how the brain can learn, develop and reorganize itself) is crucial for explaining many illnesses and conditions. Neuroscientists from the University of Göttingen and University Medical Center Göttingen (UMG) have now managed to repeatedly image synapses, the tiny contact sites between neurons, in awake adult mice. They are the first to discover that adult neurons in the primary visual cortex with an increased number of 'silent synapses' (ie newly formed synapses that are inactivated), lacking a certain protein (PSD-95), display structural changes that were previously only reported in young mice. This research by the Collaborative Research Centre CRC889 was published in *PNAS*.

It is well known that during [early brain development](#), there are critical periods during which the brain is particularly plastic and individual experiences can trigger reorganization and adaptation in neuronal circuits. In developing brains, silent synapses are common and they help to functionally optimize the connections between principal neurons. The research teams of Professor Siegrid Löwel (University of Göttingen) and Professor Oliver Schlüter (UMG) had already discovered that the maturation of silent synapses requires postsynaptic density protein-95 (PSD-95) and closes early critical periods. However, the specific processes that govern whether synaptic connections are kept or removed depending on experience were largely unknown.

To investigate this, the researchers imaged neurons from the mouse

visual cortex with a two-photon microscope while the animal was awake before and after a particular visual experience. As first author Rashad Yusifov from the University of Göttingen explains, "Previous studies have generally used anesthetized mice but we now know that anesthesia itself can influence neuronal plasticity, which is why we did the current study in awake animals." Yusifov goes on to say, "This challenging technique, which entails repeatedly locating and imaging very tiny structures—around one-thousandth of a millimeter—known as [dendritic spines](#), can only be carried out in a few laboratories in the world".

Researchers discovered that adult neurons deficient in PSD-95 display increased experience-dependent spine removal, an effect in the past only observed in young animals. Building on their previous discoveries, this collaborative research shows that PSD-95 deficient neurons display both functional and structural hallmarks of plasticity associated with a critical period. This means that neurons lacking PSD-95 keep a juvenile ability to restructure cortical connectivity even into adulthood. Senior author Professor Löwel adds, "Answering these key questions will not only help to understand the rules underlying [brain](#) development, functioning and learning, but will also open up new avenues to develop clinically relevant concepts to promote regeneration and rehabilitation for diseased and injured brains."

**More information:** Rashad Yusifov et al, Spine dynamics of PSD-95-deficient neurons in the visual cortex link silent synapses to structural cortical plasticity, *Proceedings of the National Academy of Sciences* (2021). [DOI: 10.1073/pnas.2022701118](https://doi.org/10.1073/pnas.2022701118)

Provided by University of Göttingen

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