Media Release

Roska group researchers find: When unconscious, the brain is anything but ‘silent’

The cerebral cortex is thought to be the seat of conscious processing in the brain. Rather than being inactivated, specific cells in the cortex show higher spontaneous activity during general anesthesia than when awake, and this activity is synchronized across those cortical cells. Improving our understanding of the neuronal mechanisms of general anesthesia could lead to better anesthetic drugs and improved surgical outcomes.

Basel, May 12, 2022 In a paper recently published in *Neuron*, researchers from the group of Botond Roska at IOB reveal how different cell types in cortex change their activity during general anesthesia, helping to understand how unconsciousness may be induced.

You are lying on the operating table. The doctor tells you to count to 5, and places an anesthetic mask on your face. By the count of 4, you’ve lost consciousness. You will not wake up until after the surgery. What happened in your brain during this time?

One would probably assume that your brain has been silent. Especially your cortex, the brain area thought to be the seat of conscious processing. However, for close to 100 years, it has been known that some cells in the cortex are active and that cortex alternates between periods of high and low activity during general anesthesia. Using EEG electrodes attached to the scalp is one of the few tools available to measure this activity, but electrodes don’t allow one to identify the cells underlying this activity. Therefore, the question has remained: which cells contribute to the rhythmic activity in the cortex, and how might that contribute to the loss of consciousness during general anesthesia.

Cortex is composed of different cell types, each with different functions. Different general anesthetics act on different receptors, located on different types of neurons, distributed throughout the brain. Yet, all general anesthetics lead to the loss of consciousness, and so “we were interested in finding if there is a common neuronal mechanism across different anesthetics”, says Martin Munz from the IOB Central Visual Circuits Group.

In this *Neuron* publication, the researchers used modern genetic tools, in combination with mouse lines labeling individual cortical cell types to address this question. They found that in contrast to what had previously been suspected, only one specific cell type within cortex, layer 5 pyramidal neurons, showed an increase in activity when the animal was exposed to different anesthetics.

“Each anesthetic induces a rhythm of activity in layer 5 pyramidal neurons. Interestingly, these rhythms differed between anesthetics. Some were slower, and some were faster. However, what was common across all anesthetics was that they all induced an alignment of activity. That is, when they were active, all layer 5 pyramidal neurons were active at the same time”, says Arjun Bharioke from the same IOB group, “We called this ‘neuronal synchrony’”.

Layer 5 pyramidal neurons serve as a major output center for the cerebral cortex and also connect different cortical areas to each other. Thus, they communicate both between different cortical areas, as well as from the cortex to other areas of the brain. Therefore, a synchronization of activity across layer 5 pyramidal neurons restricts the information that the cortex can output.

“It seems that instead of each neuron sending different pieces of information, during anesthesia all layer 5 pyramidal neurons send the same piece of information”, says Arjun Bharioke, “One could think of this as when people in a crowd transition from talking to each other, for example before a soccer or basketball game, to when they are cheering for their team, during the game. Before the game starts, there are many independent conversations. In contrast, during the game, all the spectators are cheering on their team. Thus, there is only one piece of information being transmitted across the crowd”.

Prior work has proposed that loss of consciousness occurs through the disconnection of cortex from the rest of the brain. The results of the IOB team suggest a mechanism by which this may occur – by the transition to lowered information output from cortex, during anesthesia.

Alexandra Brignall, a third member of the group and a veterinarian by trade says: “Anesthetics are very powerful, as anyone who has been in a surgery can attest to. But they are also not always easy to use. During a surgery, one has to continuously monitor the depth of the anesthetic to ensure that the patient is not too deep or too shallow. The more we know how anesthetics work and what they do in the brain, the better. Maybe this will help researchers develop new drugs to more specifically target the cells in the brain associated with unconsciousness.”

“Our findings are highly relevant for medicine, since anesthesia is one of the most frequently performed medical procedures. Understanding the neuronal mechanism of anesthesia could lead to better anesthetic drugs and improved surgical outcomes”, says Botond Roska, corresponding author and director of the IOB Molecular Research Center.

Original Publication:

General anesthesia globally synchronizes activity selectively in layer 5 cortical pyramidal neurons

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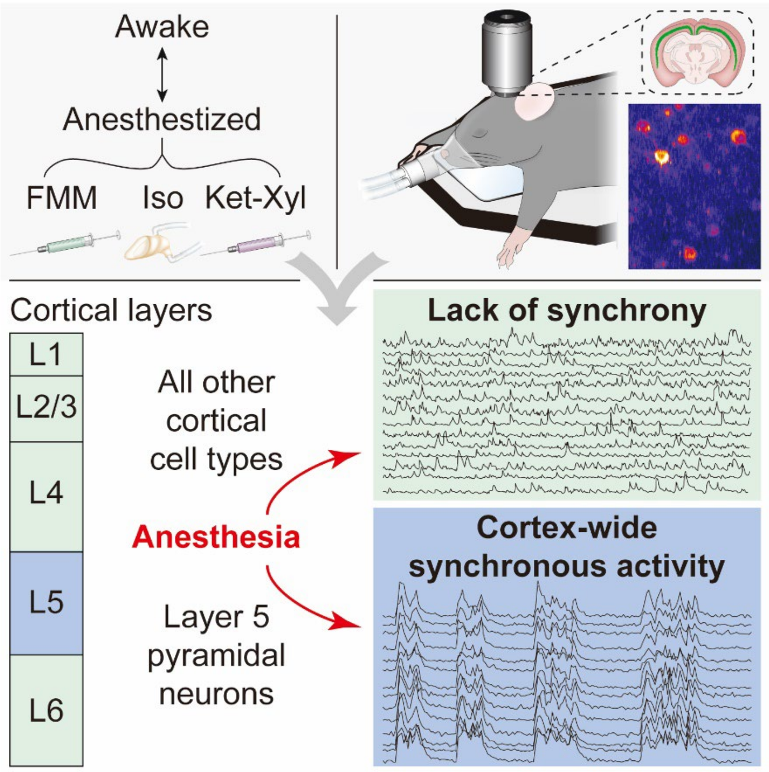
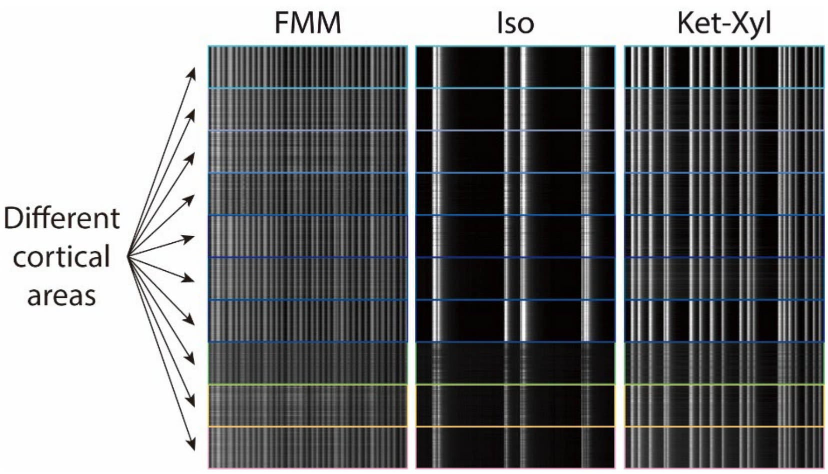
Link to paper:

All images and media can be found at:
https://drive.google.com/drive/folders/1C9oe0IQAYHWvRggHZLnXjvFtBhPXSU5S?usp=sharing

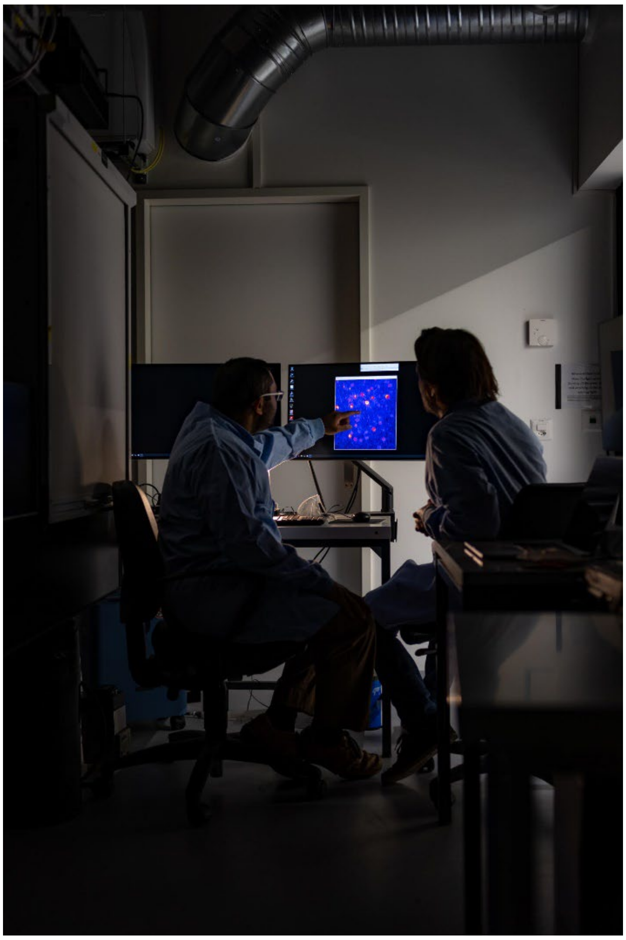
Images



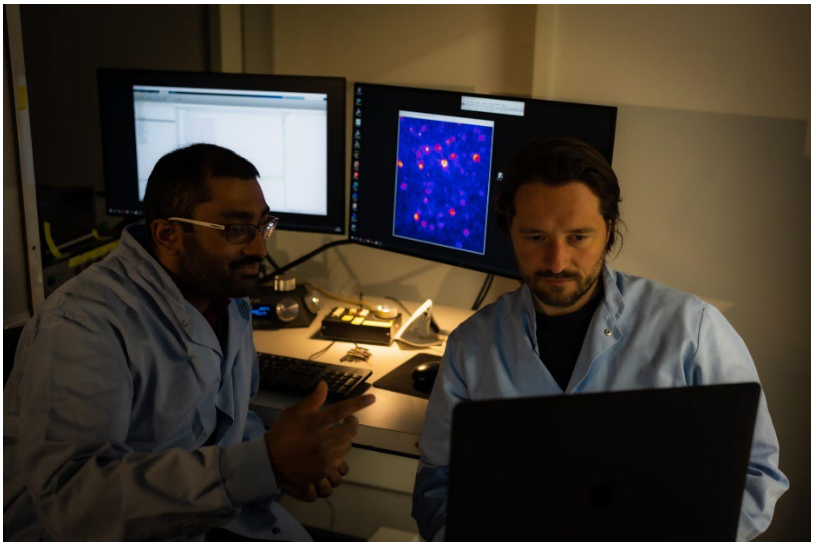
Imaging from individual cell types in the mouse cortex, and comparing their activity while awake and anesthetized, the authors find that only layer 5 pyramidal neurons show synchronous activity.



Synchronous activity is a global effect across cortex, spreading across millimeters of space, and functionally distinct cortical areas, including visual areas, motor areas, and even areas performing higher order processing.



Arjun Bharioke (left) and Martin Munz (right) discussing a recording of layer 5 neuronal activity.



Arjun Bharioke (left) and Martin Munz (right) discussing analysis of cortical recordings.

Institute of Molecular and Clinical Ophthalmology Basel


Martin Munz (left) and Arjun Bharioke (Right)

Other Media:
Isoflurane anesthesia (GIF / Video)
Layer 5 pyramidal neurons imaged under isoflurane anesthesia show synchronous activity.

About IOB
At the Institute of Molecular and Clinical Ophthalmology Basel (IOB), basic researchers and clinicians work hand in hand to advance the understanding of vision and its diseases, and to develop new therapies for vision loss. IOB started its operations in 2018. The institute is constituted as a foundation, granting academic freedom to its scientists. Founding partners are the University Hospital Basel, the University of Basel and Novartis. The Canton of Basel-Stadt has granted the institute substantial financial support.
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