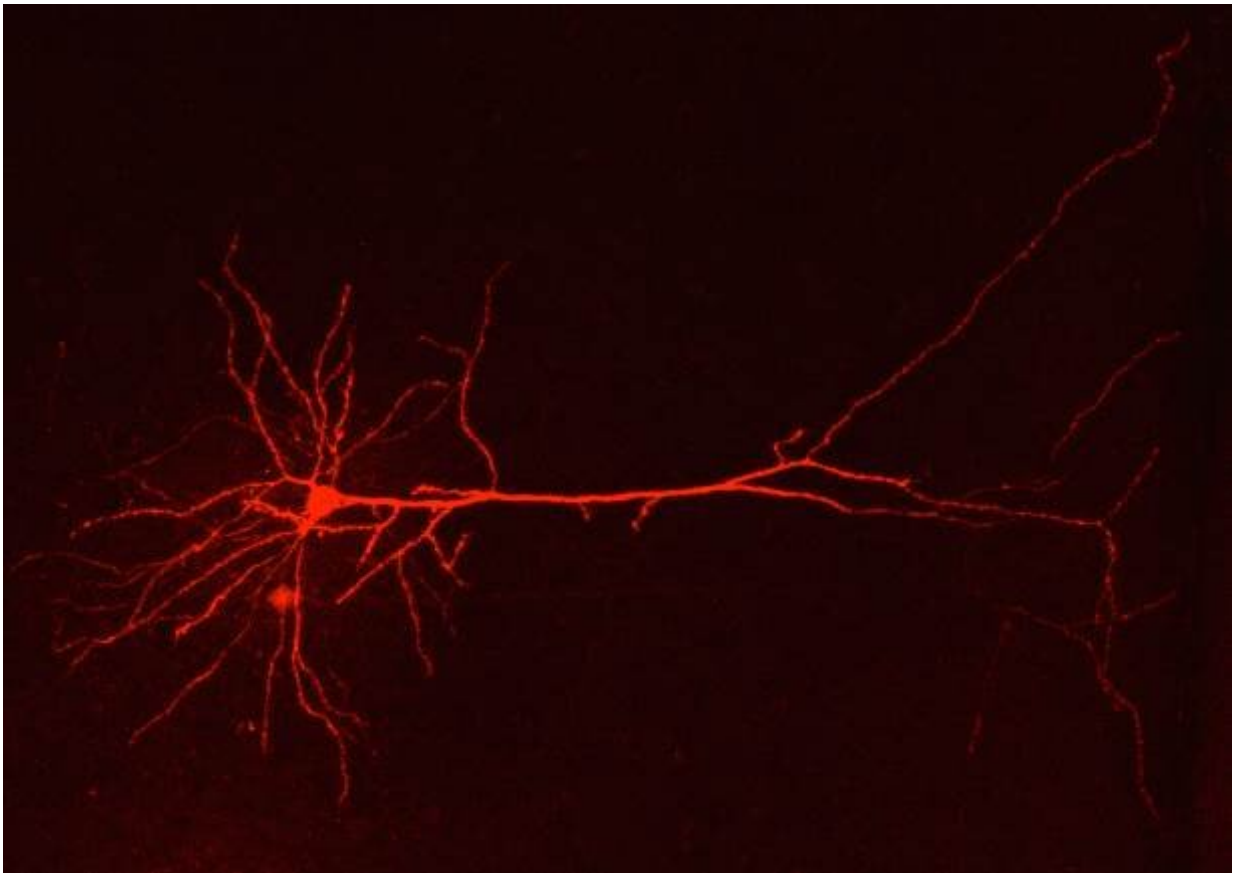


Genetic malfunction of brain astrocytes triggers migraine

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Morphological reconstruction of a neuron of the cingulate cortex in a migraine episode. Credit: UZH

Neuroscientists of the University of Zurich shed a new light on the

mechanisms responsible for familial migraine: They show that a genetic dysfunction in specific brain cells of the cingulate cortex area strongly influences head pain occurrence.

Migraine is one of the most disabling disorders, affecting one in seven people and causing a tremendous social and economic burden. Several findings suggest that [migraine](#) is a disease affecting a large part of the central nervous system and characterized by a global dysfunction in sensory information processing and integration, which also occurs between migraine episodes (interictal period). For example, patients with migraine exhibit increased cortical responses to sensory stimuli during the interictal period. At present, the cellular mechanisms responsible for these alterations are largely unknown.

Malfunction of astrocytes in the cingulate cortex

A team of neuroscientists led by Mirko Santello at the Institute of Pharmacology and Toxicology of the University of Zurich, in collaboration with the University of Padua, has identified a new mechanism implicated in a special form of migraine caused by genetic mutation. They report that this familial hemiplegic migraine type 2 (FHM2) causes a malfunction of astrocytes in the cingulate cortex, a brain region that is involved in the feeling of pain. Astrocytes, specific star-shaped [brain cells](#), are essential contributors to neuronal function and have a strong impact on brain circuits and behavior.

"Despite their abundance, astrocytes have been relatively overlooked by neuroscientists," says Mirko Santello, last author of the study. Yet these cells are extremely important to clear transmitters released by neurons. In their study the researchers were able to show that in familial migraine the astrocytes cannot remove excessive transmitters released by neurons. "The impairment in astrocytic glutamate uptake in the cingulate cortex strongly enhances cortical dendritic excitability and thus enhances firing

of the neurons," Santello says.

Less migraine occurrence due to genetic manipulations

Furthermore, the study reported that the malfunction of the cingulate cortex also influences migraine occurrence. In a [mouse model](#) the researchers showed that the mice displayed increased sensitivity to head pain triggers. "By manipulating astrocytes in the cingulate cortex, we were able to reverse their dysfunction. This prevented an increase in head pain in mice carrying the genetic defect," says Jennifer Romanos, first author of the study.

Migraine is a complicated disorder that affects part of the nervous system. "Our results provide a clear example of how [astrocyte](#) dysfunction produced by a [genetic defect](#) affects neuronal activity and sensitivity to head pain triggers," explains Mirko Santello. The findings help to better understand migraine pathophysiology and suggest that the cingulate [cortex](#) may represent a critical hub in the disease. The demonstration of the link between dysfunction of astrocytes in the [cingulate cortex](#) and familial migraine could help in devising new migraine treatment strategies.

More information: Jennifer Romanos et al. Astrocyte dysfunction increases cortical dendritic excitability and promotes cranial pain in familial migraine, *Science Advances* (2020). [DOI: 10.1126/sciadv.aaz1584](#)

Provided by University of Zurich

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