Compound shown to reduce brain damage caused by anesthesia in early study

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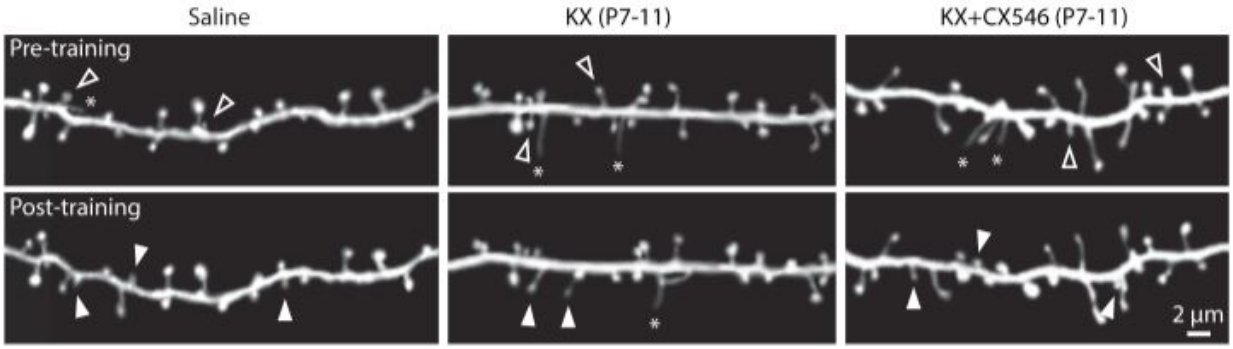

In vivo time-lapse imaging of dendritic spines before and 2 days after rotarod motor training in the primary motor cortex of 1-month-old mice that received saline, anesthesia (ketaminexylazine [KX]), and anesthesia with an AMPAkine drug (CX546). Credit: L. Huang et al., *Science Translational Medicine* (2016)

An experimental drug prevented learning deficits in young mice exposed repeatedly to anesthesia, according to a study led by researchers from NYU Langone Medical Center and published June 22 in *Science Translational Medicine*.

The study results may have implications for children who must have several surgeries, and so are exposed repeatedly to general anesthesia. Past studies have linked such exposure to a higher incidence of learning disabilities, attention deficits and hyperactivity.

Specifically, the research team found that the experimental drug CX456, part of the AMPAkine class in clinical trials for several neurological conditions, counters for the dampening effect of anesthesia on nerve signaling. The treatment bolstered nerve cell activity as well as learning ability in mice recovering from repeated exposure to general anesthesia.

"Each year, in the United States alone, more than a million children under age four undergo surgical procedures that require anesthesia, and the numbers are growing," says the study's senior investigator Guang Yang, PhD, assistant professor of anesthesiology at NYU Langone. "There are currently no effective treatments to combat potential toxicity linked to repeated anesthesia, and we would like to change that."

Yang's group took advantage of genetically engineered young mice that have protein markers which glow in response to changes in nerve function. Researchers then used advanced microscopy to visualize activity in their brains, comparing nerve signaling activity in those exposed to anesthesia to those who were not.

The research team found that anesthesia exposure resulted in a prolonged reduction of signal transmission among nerve cells following anesthesia. They also observed that CX456 treatment enhances this transmission, along with learning and memory in mice exposed to anesthesia.

The team studied the anesthetic ketamine, which blocks NMDA (N-methyl-D-aspartate) receptor proteins that enable charged particles like calcium to flow into nerve cells, like electric switches that trigger and shape messages. In contrast, CX546 increases nerve cell activity and calcium influx into nerve cells by enhancing the activity of proteins called AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors.

"We were able to counter anesthesia-induced deficits in the formation of connections between nerve cells and related learning problems," says Yang. "This work is an important proof-of-principle study, and opens the door to a new direction for preventing long-term neurocognitive deficits."

More information: "Post-anesthesia AMPA receptor potentiation prevents anesthesia-induced learning and synaptic deficits," *Science Translational Medicine*, DOI: 10.1126/scitranslmed.aaf7151

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