Asthma drug found to rejuvenate older rat brains

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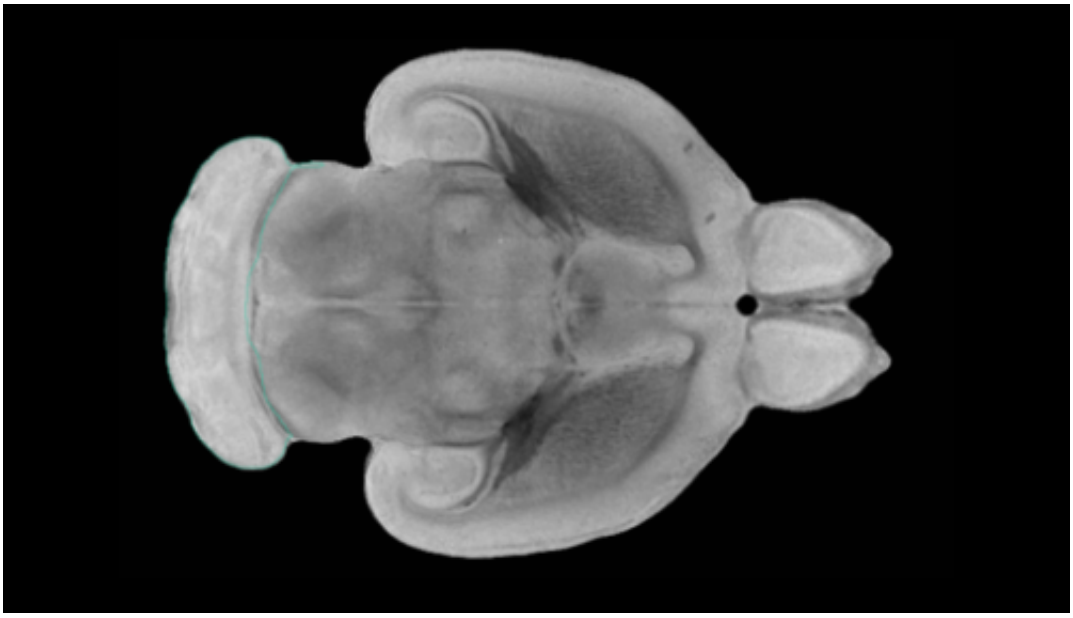

Cerebellum of CIVM postnatal rat brain atlas. Credit: Neurolex

(Medical Xpress)—A European team of researchers working in Austria has found that a drug commonly prescribed to treat asthma can lead to rejuvenation in an older rat brain. In their paper published in the journal *Nature Communications*, the group describes their study that involved giving the drug to rats and then testing them on their cognitive and memory abilities.

As people grow older, cognitive abilities diminish, along with a decline

in memory skills—that that has driven scientists to study aging and the brain and has led to the discovery that most of the decline is due to inflammation in the brain, which comes about when certain receptors are activated. In this new effort, the researchers looked at the drug montelukast because it lessens the problems associated with asthma by reducing inflammation in the lungs. They thought it might do the same for the brain.

To find out, they gave a small group of 20 month-old (analogous to 65 years in humans) test rats the drug for six weeks and then compared their cognitive abilities against 4 month-old rats, by testing both groups to see how well they were able to learn a new task—in this case, to look for an underwater platform. The older rats were selected as average representatives—they did not suffer from a neurodegenerative disease, just the loss of abilities as part of the normal aging process. In studying the results, the researchers found that the older rats were nearly as able to learn the new task as the younger mice, unlike other untreated rats of the same age.

When they tested the same rats two weeks later, they found that the treated rats were just as capable of remembering what they had learned as the younger rats, again, unlike untreated rats.

The team then dissected the brains of the treated rats and found new neural growth, which was uncharacteristic of rats their age—there was also less inflammation. The team also found that the blood-brain barrier had less seepage than rats normally would at their age, another indicator of a reduction in inflammation.

In a separate study, the team also studied mouse cells that had been genetically modified to generate less of the receptors that have been identified as causing inflammation in the brain, and found that the results were very similar to the rats that had been given montelukast,

suggesting the drug worked in similar ways.

While the results by the researchers are promising, it is still not clear if the same results could be found in humans—that will have to await the results of clinical trials.

More information: Julia Marschallinger et al. Structural and functional rejuvenation of the aged brain by an approved anti-asthmatic drug, *Nature Communications* (2015). DOI: 10.1038/ncomms9466

Abstract
As human life expectancy has improved rapidly in industrialized societies, age-related cognitive impairment presents an increasing challenge. Targeting histopathological processes that correlate with age-related cognitive declines, such as neuroinflammation, low levels of neurogenesis, disrupted blood–brain barrier and altered neuronal activity, might lead to structural and functional rejuvenation of the aged brain. Here we show that a 6-week treatment of young (4 months) and old (20 months) rats with montelukast, a marketed anti-asthmatic drug antagonizing leukotriene receptors, reduces neuroinflammation, elevates hippocampal neurogenesis and improves learning and memory in old animals. By using gene knockdown and knockout approaches, we demonstrate that the effect is mediated through inhibition of the GPR17 receptor. This work illustrates that inhibition of leukotriene receptor signalling might represent a safe and druggable target to restore cognitive functions in old individuals and paves the way for future clinical translation of leukotriene receptor inhibition for the treatment of dementias.