

## Runner's high linked to cannabinoid receptors in mice

October 6 2015, by Bob Yirka

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Credit: Martha Sexton/public domain

(Medical Xpress)—A team of researchers from several institutions in Germany has found a link between cannabinoid receptors in mice and what is commonly known as "runner's high." In their paper published in *Proceedings of the National Academy of Sciences*, the team describes their study with lab mice and why they now believe cannabinoid

receptors are a vital part of the phenomenon.

Most people who run or exercise regularly have experienced runner's high—it is characterized by a reduced level of anxiety and a higher tolerance for pain. In the past, some have attributed it to raised levels of  $\beta$ -endorphins which are a type of opioid peptide. In this new study, the researchers noted that such endorphins are too large to pass through the [blood-brain barrier](#) and thus are likely not the cause of the associated symptoms. Instead, they suspected the cause was more likely tied to cannabinoid receptors in the brain—the same ones that respond when a person smokes marijuana. To find out, they conducted a study with [lab mice](#).

The [mice](#) in the study were first conditioned to run on a treadmill, then were separated into two groups. One group did nothing, while the other group ran on a treadmill for five hours. Afterwards, both groups were tested for reduced anxiety (via light-dark test) and a higher tolerance for pain (exposure to a hotplate). The team found that the group that ran experienced roughly the same symptoms as human exercisers. To find out the source, the team conducted the same experiment but the second time around administered endocannabinoid and endorphin antagonists—they block the effects normally associated with them. This time, the team found that despite running, the mice did not become less anxious or able to better withstand pain. The same held true when mice were genetically engineered to not respond to endocannabinoid [receptors](#).

These findings, the team reports, strongly suggest that runner's high is very likely associated with [cannabinoid receptors](#), though it may not be the whole story—they were not able to test another symptom often associating with [runner's](#) high, euphoria, because of its subjective nature—it was not possible to ask the mice how they were feeling and get a measureable response.

**More information:** A runner's high depends on cannabinoid receptors in mice, Johannes Fuss, [DOI: 10.1073/pnas.1514996112](https://doi.org/10.1073/pnas.1514996112)

## Abstract

Exercise is rewarding, and long-distance runners have described a runner's high as a sudden pleasant feeling of euphoria, anxiolysis, sedation, and analgesia. A popular belief has been that endogenous endorphins mediate these beneficial effects. However, running exercise increases blood levels of both  $\beta$ -endorphin (an opioid) and anandamide (an endocannabinoid). Using a combination of pharmacologic, molecular genetic, and behavioral studies in mice, we demonstrate that cannabinoid receptors mediate acute anxiolysis and analgesia after running. We show that anxiolysis depends on intact cannabinoid receptor 1 (CB1) receptors on forebrain GABAergic neurons and pain reduction on activation of peripheral CB1 and CB2 receptors. We thus demonstrate that the endocannabinoid system is crucial for two main aspects of a runner's high. Sedation, in contrast, was not influenced by cannabinoid or opioid receptor blockage, and euphoria cannot be studied in mouse models.

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