

Go for a run or eat chocolate: A choice dictated by the cannabinoid receptors

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Physical inactivity is a common factor in lifestyle diseases—and one that is often linked to the excessive consumption of fatty and/or sugary foods. The opposite scenario of excessive physical activity at the



expense of caloric intake can also be harmful, as cases of anorexia nervosa illustrate. These data therefore point to the crucial need to research the neurobiological processes that control the respective motivations for exercise and food intake. A study by Inserm and CNRS researchers published on March 7, 2019 in *JCI Insight* reveals that the cannabinoid type 1 (CB1) receptors play an essential role in the choice between running and eating chocolatey food.

The authors of this paper had previously reported that the cannabinoid type-1 (CB1) receptors, present on several types of neurons, play a key role in performance during physical activity in mice. A conclusion based on the performances achieved by animals with <u>free access</u> to an <u>exercise</u> wheel—a model in which it was not possible to distinguish the mechanism involved (motivation, pleasure...). Given that the motivation for a reward can only be estimated by measuring the efforts that the individual—whether human or animal—is prepared to make to get that reward, the researchers devised a model in which each access to the wheel was conditional on a prior effort. This involved the animal repeatedly introducing its snout into a recipient, an essential prerequisite for unlocking the wheel. After a training period during which the level of effort required to unlock the wheel remained the same, the mice were confronted with a test in which the effort required was gradually increased. When exposed to this test, the mice lacking CB1 receptors showed an 80 % deficit in the maximum effort they were prepared to make to unlock the wheel, and without a decrease in performance during their access to it. This finding indicates that the CB1 receptors play a major role in controlling motivation for exercise. The use of other genetically-modified mice also enabled the researchers to demonstrate that these CB1 receptors controlling motivation for exercise are located on GABAergic neurons.

The researchers then examined whether the CB1 receptors in the GABAergic neurons control the motivation for another reward:



chocolatey <u>food</u> (like humans, mice love it even when they are otherwise well-fed). While the CB1 receptors also play a role in motivation for food—albeit to a lesser extent than in motivation for exercise—the CB1 receptors located on the GABAergic neurons are not implicated in the motivation for eating chocolatey food.

In our <u>daily life</u>, we are faced with an ongoing choice between various rewards. A fact which has encouraged the researchers to develop a model in which following a learning period the mice had the choice—in return for the efforts described above—between exercise and chocolatey food. The motivation for exercise was greater than that for chocolatey food, with the exception of the mice lacking CB1—whether generally or just on GABAergic neurons—whose preference was for the food.

In addition to these findings indicating that the cannabinoid receptor is essential for the motivation for exercise, this study opens up avenues for researching the neurobiological mechanisms behind pathological increases in this motivation. One illustration is provided by anorexia nervosa which often combines the decreased motivation to eat with an increased <u>motivation</u> to exercise.

More information: Carolina Muguruza et al, The motivation for exercise over palatable food is dictated by cannabinoid type-1 receptors, *JCI Insight* (2019). DOI: 10.1172/jci.insight.126190

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