Cannabis and its effects on the brain

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The psychotropic effects of cannabis are due to a family of molecules called cannabinoids. Surprisingly, the brain produces its own cannabinoids, and the effects of cannabis on the brain are caused by the activation of an endogenous system (endocannabinoid) in most animals which evolved long before the appearance of the Cannabis sativa plant on earth.

AN ANCIENT SYSTEM

One of the basic principles of pharmacology is that a substance must necessarily interact with a molecular target to trigger a biological response. In other words, if a substance such as cannabis is able to provoke psychotropic effects, this must be because its principal constituents (cannabidiol [CBD] and Δ9-tetrahydrocannabinol [THC]) specifically bind to certain receptors (targets) naturally present within the brain, and can thereby trigger a biological response.

The discovery of these receptors, called CB1 and CB2, provided evidence for the presence of an endocannabinoid system, not only in humans, but also in most other animals, even those that are very distant from us from an evolutionary perspective (fish, birds and reptiles). In fact, this suggests that the first cannabinoid receptors originally appeared about 400 million years ago, thus long before the cannabis plant first made its appearance on earth about 35 to 65 million years ago. These receptors are part of a basic mechanism involved in brain function which appeared very early during the evolution of animal life.

ENERGY MANAGEMENT

The two endocannabinoids that have been best studied are anandamide (arachidonoylethanolamine) and 2-arachidonoylglycerol (2-AG), two molecules derived from a fatty acid present in the membranes of our cells, arachidonic acid. These two endocannabinoids are neurotransmitters which play very important roles in the control of metabolism, particularly anything which affects the consumption of food (stimulation of appetite) and the storage of calories[1]. The blood levels of endocannabinoids vary considerably over the course of a day, with the highest concentrations being reached around midday and the lowest levels during sleep, which allows synchronizing appetite with the waking cycle. This important role of endocannabinoids in the control of appetite also explains why activation of the CB1 receptor by THC in cannabis is generally associated with a notable increase in hunger (the famous 'munchies') in people who have consumed the drug.

ENDOCANNABINOIDS AND EXERCISE

Several studies have found that physical exercise increases the blood levels of endocannabinoids. Aside from reflecting the central role played by these molecules in the control of metabolism, these recent results suggest that this mobilization could also contribute to the sense of well-being that accompanies physical activity, which is commonly referred to as runner's high[2]. The researchers found that physical activity provoked an important increase in anandamide, and that this molecule was responsible for the anxiolytic and analgesic effects of exercise. For example, when animals were treated with medications to block endocannabinoid receptors, the post-exercise "buzz" disappeared completely, whereas anti-endorphin medications had no effect. In other words, the soothing effect of exercise is much more due to endogenous cannabis than to endogenous opioids.

These positive effects of endocannabinoids make a great deal of sense from an evolutionary point of view: to survive, our ancient ancestors had to walk and run over long distances, routinely up to 20 km per day, and it is likely that the secretion of these molecules allowed them to continue to move despite injury or discomfort. Not to mention that light euphoria felt after a busy day certainly represented a good motivation to start again the next day.

(1) Hillard CJ. Circulating endocannabinoids: from whence do they come and where are they going? Neuropsychopharmacology Rev. 2018; 43: 155-172.

(2) Fuss J et al. A runner's high depends on cannabinoid receptors in mice. Proc. Natl Acad. Sci. USA 2015; 112: 13105-13108.

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