Endocannabinoid system, a target to improve cognitive disorders in models of Down syndrome
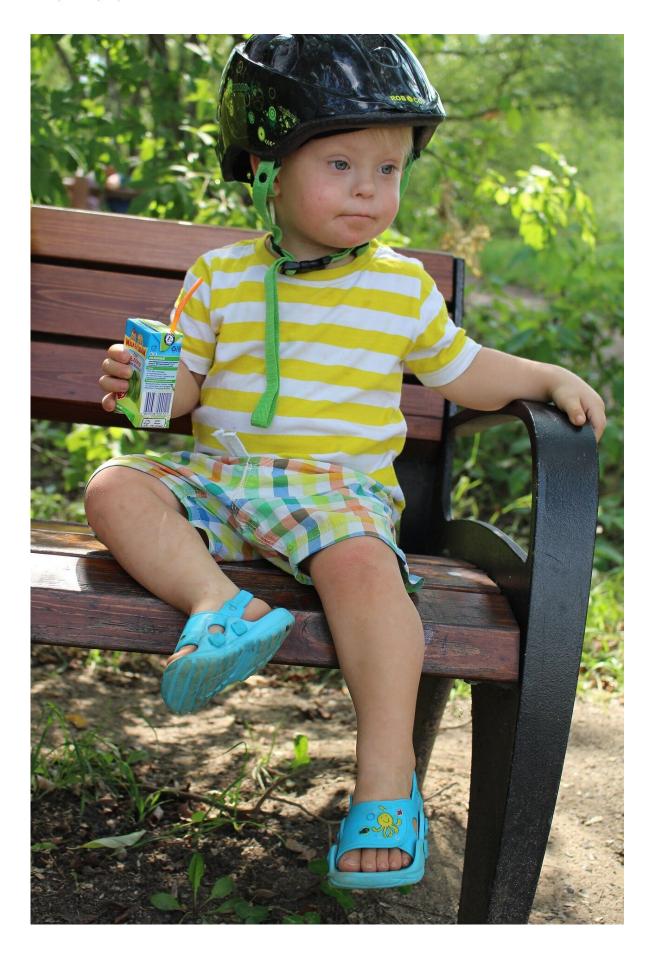
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A study by the Neuropharmacology Laboratory-NeuroPhar of the Department of Experimental and Health Sciences (DCEXS) at UPF reveals the involvement of the endocannabinoid system in cognitive disorders in mouse models of Down syndrome. The work, led by Andrés Ozaita and Rafael Maldonado, which has been published in the journal *Neurobiology of Disease*, also identifies cannabinoid receptor type-1 (CB1) as a potential treatment target.

Down syndrome is the most common genetic cause of mental disability. It is caused by the total or partial trisomy of chromosome 21 and affects one in every 700-1000 live births.

"The endocannabinoid system is involved in many functions, including learning and memory processes. However, until now the role of the system in the cognitive deficits of Down syndrome had not been explored," explains Alba Navarro-Romero, first author of the paper.

The researchers studied two rodent models that mimic the genetic alterations observed in individuals with Down syndrome. "In these models, we have found that CB1 receptor has a higher expression and is also more active in a brain area with a key role in memory as is the hippocampus," Andrés Ozaita explains.

Their results show that the increased expression of the CB1 receptor would be associated with the memory problems encountered by these mice such as, for example, to recall objects they have previously explored.

In fact, the inhibition of CB1 receptors both via genetic blockade techniques and via pharmacological approaches, improved the memory problems observed in model mice of Down syndrome for both sexes. This combination of beneficial effects reaffirms the role of CB1 receptors as a potential target for exploring.

"In addition, we noted that the pharmacological approaches normalized both the synaptic plasticity that is altered in models of Down syndrome and cell proliferation processes in areas of the brain responsible for creating new neurons," Anna Vazquez-Oliver points out.

"Our data show the CB1 receptor as a new target that could improve cognitive abilities in individuals with Down syndrome. Although this is our working hypothesis, our study is the first step of many others that will be needed to confirm this hypothesis," Andrés Ozaita concludes.

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