

Boosting natural marijuana-like brain chemicals treats fragile X syndrome symptoms

UCI study points to role endocannabinoids play in common genetic cause of autism

American and European scientists have found that increasing natural marijuana-like chemicals in the brain can help correct behavioral issues related to fragile X syndrome, the most common known genetic cause of autism.

The work indicates potential treatments for anxiety and cognitive defects in people with this condition. Results appear online in *Nature Communications*.

Daniele Piomelli of UC Irvine and Olivier Manzoni of INSERM, the French national research agency, led the study, which identified compounds that inhibit enzymes blocking endocannabinoid transmitters called 2-AG in the striatum and cortex regions of the brain.

These transmitters allow for the efficient transport of electrical signals at synapses, structures through which information passes between neurons. In fragile X syndrome, regional synapse communication is severely limited, giving rise to certain cognitive and behavioral problems.

Fragile X syndrome is caused by a mutation of the FMR1 gene on the X chromosome. People born with it are mentally disabled; generally experience crawling, walking and language delays; tend to avoid eye contact; may be hyperactive or impulsive; and have such notable physical characteristics as an elongated face, flat feet and large ears.

The researchers stress that their findings, while promising, do not point to a cure for the condition.

“What we hope is to one day increase the ability of people with fragile X syndrome to socialize and engage in normal cognitive functions,” said Piomelli, a UCI professor of anatomy & neurobiology and the Louise Turner Arnold Chair in the Neurosciences.

The study involved mice genetically altered with FMR1 mutations that exhibited symptoms of fragile X syndrome. Treated with novel compounds that correct 2-AG protein signaling in brain cells, these mice showed dramatic behavioral improvements in maze tests measuring anxiety and open-space acceptance.

While other work has focused on pharmacological treatments for behavioral issues associated with fragile X syndrome, Piomelli noted that this is the first to identify the role endocannabinoids play in the neurobiology of the condition.

Kwang-Mook Jung and Nicholas DiPatrizio of UCI; Marja Sepers, Olivier Lassalle, Daniela Neuhofer, Henry Martin, Melanie Ginger and Andreas Frick of INSERM; and Christopher Henstridge and Istvan Katona

of the Hungarian Academy of Sciences contributed to the study, which received support from INSERM and the U.S. National Institute on Drug Abuse (grant number DA-012447). Italian Institute of Technology researchers also participated in the study.

About endocannabinoids: Endocannabinoid compounds are created naturally in the body and share a similar chemical structure with THC, the primary psychoactive component of the marijuana plant, Cannabis. Endocannabinoids are distinctive because they link with protein molecule receptors — called cannabinoid receptors — on the surface of cells. For instance, when a person smokes marijuana, the cannabinoid THC activates these receptors. Because the body's natural cannabinoids control a variety of factors — such as pain, mood and appetite — they're attractive targets for drug discovery and development. Piomelli is one of the world's leading endocannabinoid researchers. His groundbreaking work is showing that this system can be exploited by new treatments to combat anxiety, pain, depression and obesity.

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