

Cannabis' Potential Exciting Researchers in Treatment of ALS, Parkinson's Disease - URB597

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A Legal Mood Lifter: Researchers are investigating a new antidepressant and pain reliever that works like cannabis (marijuana), without the illegal side effects.

A decade ago, when Daniele Piomelli went to scientific conferences, he was often the only researcher studying cannabinoids, the class of chemicals that give marijuana users a high. His work often drew snickers and jokes, but no more. At the annual Society for Neuroscience conference this month, scientists here delivered almost 200 papers on the subject.

Why the attention? Many scientists believe cannabis-like drugs might be able to treat a wide range of diseases, far beyond the nausea and chronic pain typically treated with medical cannabis. Researchers here presented tantalizing evidence that cannabinoid drugs can help treat amyotrophic lateral sclerosis, known as ALS or Lou Gehrig's disease, Parkinson's disease and obesity. Other researchers are studying whether the compounds can help victims of stroke and multiple sclerosis.

Although the chemicals work on the same area of the nervous system, the new drugs are much more refined and targeted than cannabis, with few of its side effects. "Cannabinoids have a lot of pharmaceutical potential," said Piomelli, a neuroscientist at the University of California at Irvine. "A lot of people are very excited."

Although the federal government opposes the use of medical marijuana, it generally doesn't restrict cannabinoid research, most of which doesn't involve the cannabis plant itself. Scientists who use Marinol, a legal but tightly regulated marijuana-like drug, do need government permission. Because the cannabinoid system wasn't discovered until the late 1980s, decades after serotonin, dopamine and other neurotransmitters, researchers still know relatively little about how it works. Like all neurotransmitter networks, the cannabinoid system consists of a series of chemical pathways through the brain and nervous system.

Cannabis produces its effects by activating this pathway, primarily through the effects of tetrahydrocannabinol, or THC, the drug's main active ingredient. Over the past decade, researchers have been following these abundant trails to determine their real purpose. "You don't have them there to get stoned. So, there must be internal reasons," said Andrea Giuffrida, a neuroscientist at the University of Texas Health Sciences Center in San Antonio.

Researchers have learned that endogenous cannabinoids, internal brain chemicals that activate the system, play a role in tissue protection, immunity and inflammation, among other functions. The cannabinoid system also appears to exert wide influence, modulating the release of dopamine, serotonin and other neurotransmitters. Giuffrida and others believe cannabinoids can treat degenerative disorders such as Parkinson's disease and ALS. At the conference, Giuffrida announced that a cannabinoid drug wards off Parkinson's-like effects in mice.

The disorder, which afflicts more than 1 million Americans, destroys neurons in a key part of the brain, causing patients to lose control over movement.

Giuffrida, with colleagues David Price and James Roberts, injected mice with a chemical called MPTP, which mimics Parkinson's damage. When some of the animals subsequently received a drug that blocks cannabinoid receptors, their nerve cells suffered far less damage than did the cells of the other mice. This was the first demonstration that a cannabinoid drug can have this effect. Although he is not sure how the anti-cannabinoid compound works, Giuffrida suspects it protects neurons by reducing inflammation, a key component in Parkinson's. Cannabinoids might also slow down ALS, which destroys neurons that control muscles until victims become paralyzed, unable to breathe on their own.

Neuroscientist Mary Abood first became interested in cannabinoids after hearing about ALS patients who got some relief from smoking cannabis. So she began animal experiments at the California Pacific Medical Center in San Francisco. In her study, mice with a variant of ALS were given a combination of THC and cannabidiol, another compound found in cannabis. Both substances are cannabinoid agonists, chemicals that activate the cannabinoid system. Abood measured the course of the ailment by testing how long the mice could stand on a rod that was slowly rotating.

The treatment delayed disease progression by more than seven days and extended survival by six days. In human terms, this would amount to about three years. That's a significant improvement over the only existing ALS drug, riluzole, which extends life by two months. "I was very excited when I got my initial results," Abood said.

Also at the conference, researchers at the Institute of Neurology in London announced results that corroborated her findings. Cannabinoids have also helped some human ALS patients in one small trial, and Abood is trying to get funding

for a larger one. If cannabinoids can shield human neurons from harm, researchers say, they might prove useful against other neurological diseases, including mental illness. Scientists are looking at whether cannabinoids can treat multiple sclerosis, epilepsy and Huntington's disease, while Giuffrida is beginning a study of their effect on schizophrenia.

Advocates of medical cannabis have long argued that the drug can be useful for treating many conditions, particularly chronic pain, nausea and glaucoma (in the latter, cannabis works by temporarily decreasing pressure around the eye). Although they don't dispute this view, most researchers believe there are better, more precise ways to stimulate the cannabinoid system. They believe cannabis has too many negatives to be a truly effective drug, with side effects that include memory problems, decreased immunity and possibly addiction. (Some researchers dispute this.)

Cannabis has another drawback. From a scientific standpoint, Giuffrida says, it's "a very dirty drug." It contains more than 300 compounds, 60 of which affect the cannabinoid system. Scientists don't understand what most of these substances do or how they work together. This complexity makes it hard for researchers to pinpoint cannabis' effects.

One cannabinoid, Marinol, is available legally. The compound, which contains THC in a pill form, is usually prescribed for nausea and for appetite loss among AIDS patients. But Marinol has the same psychoactive effects as cannabis. "So the key", Piomelli says, "is getting the effects without the side effects."

To that end, Piomelli has developed a compound called URB597, which doesn't flood the body with cannabinoids, as Marinol and cannabis do. Instead, it slows the breakdown of the cannabinoids in the system. He thinks the drug may help treat pain, anxiety and even depression without making patients stoned and forgetful. He and others are testing it on animals.

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Currently called URB597 -- it raises levels of endocannabinoids, the brain's own cannabis-like chemicals that trigger feelings of well-being. The drug balances mood- and stress-regulating brain chemicals such as serotonin as effectively as existing antidepressants -- and doesn't cause intoxication.

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<http://sev.prnewswire.com/magazines/20060705/NYW08205072006-1.html>

<http://en.wikipedia.org/wiki/URB597>