A LOOK INTO THE BENEFITS OF CANNABIS FOR ALZHEIMER'S DISEASE

JOSH KAPLAN

Alzheimer's disease (AD) is the most common form of dementia and accounts for approximately 30 million cases worldwide. Because of the increasing global life expectancy, this prevalence is expected to nearly quadruple by 2050.

With these numbers on the rise, researchers are looking for novel approaches to prevent and treat the disease—and cannabis is among those being considered. But how far has research come in proving its utility?

What Characterizes Alzheimer's?

Alzheimer's usually begins by attacking the brain's hippocampus, a critical brain region in memory processing. This causes memory and cognitive impairments that define the initial stages of the disease. It also contributes to the anxiety, depression, and agitation from which AD patients also suffer. As the disease progresses through the rest of the brain, additional symptoms develop that impair normal functioning.

Only relatively recent and limited attention has been given to cannabinoids for Alzheimer's. And these studies hold unique promise.

Eventually, patients may become so impaired that they have trouble coughing, swallowing, and breathing. They become more susceptible to aspirating food, pneumonia, and other infections, making Alzheimer's the sixth leading cause of death in the US.

There are three hallmark characteristics of the AD brain:

- The buildup of amyloid-ß (Aß) plaques

- Tangles of fibers inside brain cells called neurofibrillary tangles
- The activation of support cells in the brain called microglia

Additionally, abnormally high levels of free radicals have been regarded as a common pathological feature of Alzheimer's. The accumulation of Aß plaques and neurofibrillary tangles causes brain inflammation and increases free radicals that lead to the progression and worsening of the disease. These processes cause the release of the brain chemical, glutamate, from microglia. This elevates glutamate to toxic levels, killing neurons which serve as the primary signaling brain cells. They also reduce another brain chemical, acetylcholine, which leads to the initial impairments in memory and cognitive function.

Based on the origin and progression of AD, some treatment approaches could be to:

- Reduce Aß plaques and tangles
- Soak up the excess free radicals
- Reduce inflammation and prevent the activation of microglia to dampen the toxic release of glutamate that kills neurons

Of course, scientists have considered these for decades, and obviously their attempts to cure AD have been unsuccessful. But only relatively recent and limited attention has been given to cannabinoids. And these studies hold unique promise.

How Cannabinoids Affect Alzheimer's Disease

Much research energy was spent devising ways of getting rid of Aß plaques because it was thought that if you get rid of the plaques, you prevent AD. Unfortunately, the proteins that form these plaques have other important contributions to brain cell function, so if you get rid of the proteins, there are severe consequences. So that's a no-go.

THC and CBD are potent antioxidants and have anti-inflammatory properties. These are important qualities because brain inflammation is thought to be a major contributor to Alzheimer's.

An alternative approach could be to limit the harmful consequences of having plaques. Mainly, neutralize the damaging free radicals and reduce the harmful inflammatory processes. Fortunately, the prominent cannabinoids, THC and cannabidiol (CBD), are good at both.

THC and CBD are potent antioxidants and have anti-inflammatory properties. These are important qualities because brain inflammation is thought to be a major contributor to AD. So it's not surprising that anti-inflammatory drugs, like non-steroidal anti-inflammatory drugs (NSAIDs; e.g., ibuprofen) reduce risk for developing AD. But these drugs, especially their chronic use, can damage the kidneys. CBD and limited amounts of other cannabinoids have been widely used with limited side effects, and are largely considered safe for adult and senior use.

Important CBD Targets in Alzheimer's Treatment

Numerous studies using mouse models of AD reveal that CBD blunts the ability of Aß plaques to induce inflammation, thereby limiting their toxic effects on brain cells. But importantly, CBD can also reduce the plaquesthemselves by activating one of its many targets, the PPAR-γ receptor, which improves brain cell survival. This PPAR-γ receptor seems to be an important target for CBD's treatment benefits in AD. Indeed, a phase II clinical trial found that an activator of PPAR-γ successfully improved cognition and memory in AD. This is in contrast to CBD and THC's effects on CB2 receptors, which prevent Aß plaques buildup, but don't seem to improve cognitive function or prevent neurofibrillary tangles.

CBD may also protect against the development of neurofibrillary tangles in cases where Aß plaques underlie their pathology.

CBD Protects Brain Cells

The benefits of CBD on memory and cognition result largely from its ability to protect the brain's hippocampus from toxins and disease. One important way CBD seems to protect these brain cells is by reducing the activation of microglia.

Combination therapies involving both THC and CBD in mouse models of Alzheimer's effectively reduce microglia activation and improve Alzheimer's symptoms.

Microglia make up 10% of the cells in the brain. They're similar to neurons and are "activated" following injury or in disease. Although the purpose of microglia is to protect other brain cells, their chronic activation leads to more harm than good. Activated microglia release glutamate, cytokines, and other harmful substances which, over time, kill neurons.

Not surprisingly, activated microglia are a prevalent feature in the AD brain that contribute to the disease. Some of the current strategies to block the release of harmful chemicals from microglia have serious side effects which preclude their clinical use. Cannabis, however, presents a well-tolerated strategy to dampen the activation of these microglia.

How Does Cannabis Consumption Affect the Brain?

Combination therapies involving both THC and CBD in mouse models of Alzheimer's effectively reduce microglia activation and improve AD symptoms. These treatments are most effective when given early in the disease process.

The Future of Cannabis in Alzheimer's Prevention

Despite cannabis' exciting potential from pre-clinical studies, we're still a long way from using cannabis to treat or prevent Alzheimer's in humans. For one, seemingly promising AD treatment strategies that work in rodents haven't translated well to humans or have severe side effects. But even more limiting, humans take a lot longer to age than

rodents. We can obtain data on the effectiveness of cannabis in rodent models of AD within a year, but humans require decades.

Cannabis has also been shown to generally improve quality of life for AD patients by improving sleep, reducing agitation, and increasing food intake in Alzheimer's patients.

Nonetheless, cannabis has been effective at treating some of its challenging symptoms. In a small trial of 10 patients with Alzheimer’s, a four-week treatment with cannabis oil reduced some of the cognitive symptoms of AD. Cannabis has also been shown to generally improve quality of life for AD patients by improving sleep, reducing agitation, and increasing food intake in AD patients.

Despite the dearth of long-term studies, if AD runs in your family, you may choose not to wait. Increased access to legal cannabis allows people to take control of their own healthcare, and it may be worth having a conversation with your physician about the benefits of cannabis-based preventative treatment strategies.