

Alzheimer's Disease

Alzheimer's disease (AD) is a neurological disorder of unknown origin that is characterized by a progressive loss of memory and learned behavior. Patients with Alzheimer's are also likely to experience depression, agitation and appetite loss, among other symptoms. Over 4.5 million Americans are estimated to be afflicted with the disease. No approved treatments or medications are available to stop the progression of AD, and few pharmaceuticals have been FDA-approved to treat symptoms of the disease.

A review of the recent scientific literature indicates that cannabinoid therapy may provide symptomatic relief to patients afflicted with AD while also moderating the progression of the disease.

Writing in the February 2005 issue of the *Journal of Neuroscience*, investigators at Madrid's Complutense University and the Cajal Institute in Spain reported that the intracerebroventricular administration of the synthetic cannabinoid WIN 55,212-2 prevented cognitive impairment and decreased neurotoxicity in rats injected with amyloid-beta peptide (a protein believed to induce Alzheimer's). Additional synthetic cannabinoids were also found to reduce the inflammation associated with Alzheimer's disease in human brain tissue in culture. "Our results indicate that ... cannabinoids succeed in preventing the neurodegenerative process occurring in the disease," investigators concluded.[1] Follow up studies by investigators demonstrated that the administration of the nonpsychotropic plant cannabinoid cannabidiol (CBD) also mitigated memory loss in a mouse model of the disease.[2]

Investigators at The Scripps Research Institute in California in 2006 reported that THC inhibits the enzyme responsible for the aggregation of amyloid plaque — the primary marker for Alzheimer's disease — in a manner "considerably superior" to approved Alzheimer's drugs such as donepezil and tacrine. "Our results provide a mechanism whereby the THC molecule can directly impact Alzheimer's disease pathology," researchers concluded. "THC and its analogues may provide an improved therapeutic [option] for Alzheimer's disease [by]... simultaneously treating both the symptoms and the progression of [the] disease." [3]

More recently, investigators at Ohio State University, Department of Psychology and Neuroscience, reported that older rats administered daily doses of WIN 55,212-2 for a

NORML

Working to Reform Marijuana Laws

period of three weeks performed significantly better than non-treated controls on a water-maze memory test. Writing in the journal *Neuroscience* in 2007, researchers reported that rats treated with the compound experienced a 50 percent improvement in memory and a 40 to 50 percent reduction in inflammation compared to controls.[4]

Previous preclinical studies have demonstrated that cannabinoids can prevent cell death by anti-oxidation.[5] Some experts believe that cannabinoids' neuroprotective properties could also play a role in moderating AD.[6] Writing in the September 2007 issue of the *British Journal of Pharmacology*, investigators at Ireland's Trinity College Institute of Neuroscience concluded, "[C]annabinoids offer a multi-faceted approach for the treatment of Alzheimer's disease by providing neuroprotection and reducing neuroinflammation, whilst simultaneously supporting the brain's intrinsic repair mechanisms by augmenting neurotrophin expression and enhancing neurogenesis. ... Manipulation of the cannabinoid pathway offers a pharmacological approach for the treatment of AD that may be efficacious than current treatment regimens."[7]

In addition to potentially modifying the progression of AD, clinical trials also indicate that cannabinoid therapy can reduce agitation and stimulate weight gain in patients with the disease. Most recently, investigators at Berlin Germany's Charite Universitatmedizin, Department of Psychiatry and Psychotherapy, reported that the daily administration of 2.5 mg of synthetic THC over a two-week period reduced nocturnal motor activity and agitation in AD patients in an open-label pilot study.[8]

Clinical data presented at the 2003 annual meeting of the International Psychogeriatric Association previously reported that the oral administration of up to 10 mg of synthetic THC reduced agitation and stimulated weight gain in late-stage Alzheimer's patients in an open-label clinical trial.[9] Improved weight gain and a decrease in negative feelings among AD patients administered cannabinoids were previously reported by investigators in the *International Journal of Geriatric Psychiatry* in 1997.[10]

Additional study assessing the use of cannabinoids for Alzheimer's would appear to be warranted.

REFERENCES

[1] Ramirez et al. 2005. Prevention of Alzheimer's disease pathology by cannabinoids. *The Journal of Neuroscience* 25: 1904-1913.

[2] Israel National News. December 16, 2010. "Israeli research shows cannabidiol may slow Alzheimer's disease."

[3] Eubanks et al. 2006. A molecular link between the active component of marijuana and Alzheimer's disease pathology. *Molecular Pharmaceutics* 3: 773-777.

[4] Marchalant et al. 2007. Anti-inflammatory property of the cannabinoid agonist WIN-55212-2 in a rodent model of chronic brain inflammation. *Neuroscience* 144: 1516-1522.

[5] Hampson et al. 1998. Cannabidiol and delta-9-tetrahydrocannabinol are neuroprotective antioxidants. *Proceedings of the National Academy of Sciences* 95: 8268-8273.

[6] Science News. June 11, 1998. " Marijuana chemical tapped to fight strokes."

[7] Campbell and Gowran. 2007. Alzheimer's disease; taking the edge off with cannabinoids? *British Journal of Pharmacology* 152: 655-662.

[8] Walther et al. 2006. Delta-9-tetrahydrocannabinol for nighttime agitation in severe dementia. *Physcopharmacology* 185: 524-528.

[9] BBC News. August 21, 2003. " Cannabis lifts Alzheimer's appetite."

[10] Volicer et al. 1997. Effects of dronabinol on anorexia and disturbed behavior in patients with Alzheimer's disease. *International Journal of Geriatric Psychiatry* 12: 913-919.