# Cannabis and the Brain:
## A User's Guide

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Preclinical data recently published in the *Journal of Clinical Investigation* demonstrating that cannabinoids may spur brain cell growth has reignited the international debate regarding the impact of marijuana on the brain. However, unlike previous pseudo-scientific campaigns that attempted to link pot smoking with a litany of cognitive abnormalities, modern research suggests what many cannabis enthusiasts have speculated all along: ganja is good for you.

**CANNABINOIDS & NEUROGENESIS**

"Study turns pot wisdom on its head," pronounced the *Globe and Mail* in October. News wires throughout North America and the world touted similar headlines -- all of which were met with a monumental silence from federal officials and law enforcement. Why all the fuss? Researchers at the University of Saskatchewan in Saskatoon found that the administration of synthetic cannabinoids in rats stimulated the proliferation of newborn neurons (nerve cells) in the hippocampus region of the brain and significantly reduced measures of anxiety and depression-like behavior. The results shocked researchers -- who noted that almost all other so-called "drugs of abuse," including alcohol and tobacco, decrease neurogenesis in adults -- and left the "pot kills brain cells" crowd with a platter of long-overdue egg on their faces.

While it would be premature to extrapolate the study's findings to humans, at a minimum, the data reinforce the notion that cannabinoids are unusually non-toxic to the brain and that even long-term use of marijuana likely represents little risk to brain function. The findings also offer further evidence that cannabinoids can play a role in the alleviation of depression and anxiety, and that cannabis-based medicines may one day offer a safer alternative to conventional anti-depressant pharmaceuticals such as Paxil and Prozac.

(Reference: Cannabinoids promote embryonic and adult hippocampus neurogenesis and produce anxiolytic and depressant-like effects. *The Journal of Clinical Investigation*. 2005)

**CANNABIS & NEUROPROTECTION**

Not only has modern science refuted the notion that marijuana is neurotoxic, recent scientific discoveries have indicated that cannabinoids are, in fact, neuroprotective, particularly against alcohol-induced brain damage. In a recent preclinical study -- the irony of which is obvious to anyone who reads it -- researchers at the US National Institutes of Mental Health (NIMH) reported that the administration of the non-psychoactive cannabinoid cannabidiol (CBD) reduced ethanol-induced cell death in the brain by up to 60 percent. "This study provides the first demonstration of CBD as an *in vivo* neuroprotectant ... in preventing binge ethanol-induced brain injury," the study's authors wrote in the May 2005 issue of the *Journal of Pharmacology and Experimental Therapeutics*. Alcohol poisoning is linked to hundreds of preventable deaths each year in the United States, according to the Centers for Disease Control, while cannabis cannot cause death by overdose.

Of course, many US neurologists have known about cannabis' neuroprotective prowess for years. NIMH scientists in 1998 first touted the ability of natural cannabinoids to stave off the brain-damaging effects of stroke and acute head trauma. Similar findings were then replicated by investigators in the Netherlands and Italy and, most recently, by a Japanese research in 2005. However, attempts to measure the potential neuroprotective effects of synthetic cannabinoid-derived medications in humans have so far been inconclusive.

(References: Comparison of cannabidiol, antioxidants and diuretics in reversing binge ethanol-induced neurotoxicity. *Journal of Pharmacology and Experimental Therapeutics*. 2005 | Cannabidiol prevents cerebral infarction. *Stroke*. 2005 | Post-ischemic treatment with cannabidiol prevents electroencephalographic flattening, hyperlocomotion and neuronal injury in gerbils. *Neuroscience Letters*. 2003 | Neuroprotection by Delta9-tetrahydrocannabinol, the main active compound in marijuana, against ouabain-induced *in vivo* excitotoxicity. *Journal of Neuroscience*. 2001 | Cannabidiol and Delta9-tetrahydrocannabinol are neuroprotective antioxidants. *Proceedings of the National Academy of Sciences*. 1998)

**CANNABINOIDS & GLIOMA**

Of all cancers, few are as aggressive and deadly as glioma. Glioma tumors quickly invade healthy brain tissue and are typically unresponsive to surgery and standard medical treatments. One agent they do respond to is cannabis.

Writing in the August 2005 issue of the *Journal of Neurooncology*, investigators at the California Pacific Medical Center Research Institute reported that the administration of THC on human glioblastoma multiforme cell lines decreased the proliferation of malignant cells and induced apoptosis (programmed cell death) more rapidly than did the administration of the synthetic cannabis receptor agonist, WIN-55,212-2. Researchers also noted that THC selectively targeted malignant cells while ignoring healthy ones in a more profound manner than the synthetic alternative. Patients diagnosed with glioblastoma multiforme typically die within three months without therapy.

Previous research conducted in Italy has also demonstrated the capacity of CBD to inhibit the growth of glioma cells both *in vitro* (e.g., a petri dish) and in animals in a dose dependent manner. As a result, a Spanish research team is currently investigating whether the intracranial administration of cannabinoids can prolong the lives of patients diagnosed with inoperable brain cancer.

Most recently, a scientific analysis in the October issue of the journal *Mini-Reviews in Medicinal Chemistry* noted that, in addition to THC and CBD's brain cancer-fighting ability, studies have also shown cannabinoids to halt the progression of lung carcinoma, leukemia, skin carcinoma, colectoral cancer, prostate cancer and breast cancer.

(References: Cannabinoids selectively inhibit proliferation and induce cell death of cultured human glioblastoma multiforme cells. *Journal of Neurooncology*. 2005 | Cannabinoids and cancer. *Mini-Reviews in Medicinal Chemistry*. 2005 | Anti-tumor effects of cannabidiol, a non-psychotropic cannabinoid, on human glioma cell lines. *Journal of Pharmacology and Experimental Therapeutics*. 2003)

**CANNABINOIDS & NEURODEGENERATION**

Emerging evidence also indicates that cannabinoids may play a role in slowing the progression of certain neurodegenerative diseases, such as Multiple Sclerosis, Parkinson's disease, Alzheimer's, and Amyotrophic Lateral Sclerosis (a.k.a. Lou Gehrig's Disease). Recent animal studies have shown cannabinoids to delay disease progression and inhibit neurodegeneration in mouse models of ALS, Parkinson's, and MS. As a result, the *Journal of Neurological Sciences* recently pronounced, "There is accumulating evidence ... to support the hypothesis that the cannabinoid system can limit the neurodegenerative processes that drive progressive disease," and patient trials investigating whether the use of oral THC and cannabis extracts may slow the progression of MS are now underway in the United Kingdom.

(References: Cannabinoids and neuroprotection in CNS inflammatory disease. *Journal of the Neurological Sciences*. 2005. Amyotrophic lateral sclerosis: delayed disease progression in mice by treatment with a cannabinoid. *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders*. 2004 | Cannabinoids inhibit neurodegeneration in models of multiple sclerosis. *Brain*. 2003)

**CANNABIS & COGNITION**

But what about claims of cannabis' damaging effect of cognition? A review of the scientific literature indicates that rumors regarding the "stoner stupid" stereotype are unfounded. According to clinical trial data published this past spring in the *American Journal of Addictions*, cannabis use -- including heavy, long-term use of the drug -- has, at most, only a negligible impact on cognition and memory. Researchers at Harvard Medical School performed magnetic resonance imaging on the brains of 22 long-term cannabis users (reporting a mean of 20,100 lifetime episodes of smoking) and 26 controls (subjects with no history of cannabis use).

Imaging displayed "no significant differences" between heavy cannabis smokers compared to controls, the study found.

Previous trials tell a similar tale. An October 2004 study published in the journal *Psychological Medicine* examining the potential long-term residual effects of cannabis on cognition in monozygotic male twins reported "an absence of marked long-term residual effects of marijuana use on cognitive abilities." A 2003 meta-analysis published in the *Journal of the International Neuropsychological Society* also "failed to reveal a substantial, systematic effect of long-term, regular cannabis consumption on the neurocognitive functioning of users who were not acutely intoxicated," and a 2002 clinical trial published in the *Canadian Medical Association Journal* determined, "Marijuana does not have a long-term negative impact on global intelligence."

Finally, a 2001 study published in the journal *Archives of General Psychiatry* found that long-term cannabis smokers who abstained from the drug for one week "showed virtually no significant differences from control subjects (those who had smoked marijuana less than 50 times in their lives) on a battery of 10 neuropsychological tests." Investigators further added, "Former heavy users, who had consumed little or no cannabis in the three months before testing, [also] showed no significant differences from control subjects on any of these tests on any of the testing days."

(References: Lack of hippocampal volume change in long-term heavy cannabis users. *American Journal of Addictions*. 2005 | Neuropsychological consequences of regular marijuana use: a twin study. *Psychological Medicine*. 2004 | Non-acute (residual) neurocognitive effects of cannabis use: A meta-analytic study. *Journal of the International Neuropsychological Society*. 2003 | Current and former marijuana use: preliminary findings of a longitudinal study of effects on IQ in young adults. *Canadian Medical Association Journal*. 2002 | Neuropsychological Performance in Long-term Cannabis Users. *Archives of General Psychiatry*. 2001)