

UNDERSTANDING AND TREATING CANNABINOID ADDICTION

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SMOKE WEED**

**BUT, IT HELPS WITH
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DISEASE FROM ALL
THAT BEER I DRANK**

UNDERSTANDING AND TREATING CANNABINOID ADDICTION

- **CANNABIS AND CANNABINOIDS**
- **CANNABINOID EFFECTS AND TOXICITY**
- **MEDICAL CONSEQUENCES**
- **ASSESSMENT AND DSM-5**
- **CRAVING**
- **TREATMENT-PSYCHOPHARMACOLOGY AND PSYCHOTHERAPY**

MARIJUANA PLANT



MAIN COLA



HONEY OIL



HONEY OIL

- Known as “honey oil,” Butane hash oil (BHO) “hash oil,” “dabs,” “earwax,” “butter” or “shatter,” among other names, homemade marijuana concentrates have caught on quickly because of the popularity and availability of e-cigarettes and vaporizer pens, which offer an easy, discreet way to use the drug.

HONEY OIL

- Hash oil is one of the most potent forms of (medical) marijuana. The oil is highly concentrated, with THC levels between 40% and 90%. Hash oil is a resinous matrix of cannabinoids produced by a solvent extraction of marijuana. The oil varies in appearance from a crystal-clear, glossy amber to gold resin, and is usually very thick and viscous. The best quality is transparent and relatively free of impurities.



VAPING AND DABBING

- Now marijuana is smoked through a vaporizer (vape) pen that gives users a faster and stronger high. These new forms of marijuana are available as oils, waxes, and hard crystal wafers called shatter
- *New Forms of Marijuana:*
 - Oil:*

Refined version of marijuana resembling honey. It is created using liquids and gases such as water, butane, alcohol and carbon dioxide.
THC: 60-80%
 - Shatter:*

Created using the same methods as oil repeated multiple times. The extra filtration and purification process increase the potency.
THC: 75-90%
 - Wax:*

Created by a process similar to that of oil. However, the final step of this procedure involves stirring or “whipping” the liquid state to produce the final product.
THC: 60-80%

VAPING AND DABBING

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The new forms of marijuana concentrates are inhaled in two primary ways: *vaping* or *dabbing*:

One way to get the desired effect from the THC is to *vape*, or *vaporize* the drug before breathing it in. The drug is heated by hot air passing over it just prior to breathing it in.

Dabbing requires heating the THC concentrate with an open flame until it turns to smoke. This smoke is collected by the device and is breathed in by the user.

THC oil is the most commonly used form in the vaporizer pens while wax and shatter are typically used as dabbing products.

CANNABIS

- Most commonly used illicit substance
- About 7% of Americans are current users compared to less than 1% for cocaine, heroin and methamphetamine (SAMHSA <http://1.usa.gov/154HYiq>)
- Each year 1.5% of Americans struggle with active addiction (Stinson FS et al, *Psychol Med* 2006;36(10): 1447-1460)

CANNABIS

- Adolescents are 2-4 times more likely to become dependent on the drug within two years after first use compared with adult users.
- Marijuana is the most common substance addiction being treated in adolescents in rehabilitation centers across the country. Like all addictive substances, marijuana is used to lessen uncomfortable feelings like anxiety and depression

Loyola University Health System. "The dangers of teens using marijuana." ScienceDaily. ScienceDaily, 25 September 2014.
<www.sciencedaily.com/releases/2014/09/140925150606.htm>.

CANNABIS

- Approximately 50% of cannabis admissions are for those 25 years of age or younger
- More than 75% of patients resume use within a year of discharge (Sinha R. *Curr Psychiatry Rep* 2011; 13 (5): 398-405)
- 23% of patients with psychosis are current cannabis users (Green B et al. *Br J Psychiatry* 2005; 187(4): 306-313)

CANNABIS

- **CAR ACCIDENTS**

- Marijuana doubles the risk of car accidents when people try to drive soon after using it
- In comparison, driving while legally drunk (0.08% BAL) increases the risk by five times
- Columbia University study found that marijuana contributed to 12% of traffic deaths in 2010
- Marijuana causes more traffic accidents than any other illicit drug

CANNABINOIDS

- **ENDOCANNABINOIDS**
 - Derivative of arachidonic acid
 - Endogenous
- **PHYTOCANNABINOIDS**
 - Include hundreds of naturally occurring compounds
 - Includes THC and cannabidiol
- **SYNTHETIC CANNABINOIDS**
 - Laboratory produced congeners of THC and cannabidiol

CANNABINOIDS

- Two main cannabinoids of interest therapeutically are THC and cannabidiol (CBD)
- THC stimulates appetite and reduces nausea as well as decrease pain and inflammation
- CBD is non-psychoactive cannabinoid that may be useful in reducing pain and inflammation, controlling seizures (Epidiolex) , and possibly treating psychosis and addictions

“SPICE” AND OTHER SYNTHETIC CANNABINOIDS

- **INGREDIENTS**

- **A DIVERSE GROUP OF CANNABINOID
RECEPTOR AGONISTS FALLING INTO
SEVEN MAJOR STRUCTURAL GROUPS**

- **NAPHTOYLINDOLES**
 - **NAPTHYLMETHYLINDOLES**
 - **NAPTHOYLPYRROLES**
 - **NAPTHYLMETHYLINDENES**
 - **PHENYLACETYLINDOLES**
 - **CYCLOHEXYLPHENOLS**
 - **CLASSICAL CANNABINOIDS (DIBENZOPYRAN)**

SYNTHETIC CANNABINOIDS

- **CANNABINOID AGONISTS-RESEARCH CHEMICALS**
 - JWH-015
 - JWH-018
 - JWH-073
 - JWH-081
 - JWH-133
 - JWH-200
 - JWH-250
 - JWH-398
 - CP 47,497
 - CP 55,244
 - HU210
 - WIN 55,212-2

SYNTHETIC CANNABINOIDS- COMMERCIAL

Rimonabant (also known as SR141716; trade names Acomplia, Bethin, Monaslim, Remonabent, Riobant, Slimona, Rimoslim, Zimulti, and Riomont) is an anorectic antiobesity drug. It is an inverse agonist for the cannabinoid receptor CB1. Its main effect is reduction in appetite. Rimonabant blocks the psychoactive and some of the cardiovascular effects of Δ^9 -tetrahydrocannabinol (THC) in humans without affecting the pharmacokinetics.

SYNTHETIC CANNABINOIDS- COMMERCIAL

Dronabinol (Marinol, Delta-9-tetrahydrocannabinol, delta-9-THC) is synthetic THC. It is used to treat nausea and vomiting caused by chemotherapy in people who have already taken other medications to treat this type of nausea and vomiting without good results. Dronabinol is also used to treat loss of appetite and weight loss in people who have acquired immunodeficiency syndrome (AIDS). Dronabinol is in a class of medications called cannabinoids. It works by affecting the area of the brain that controls nausea, vomiting, and appetite.

SYNTHETIC CANNABINOIDS- COMMERCIAL

- Nabilone is a synthetic cannabinoid with therapeutic use as an antiemetic and as an adjunct analgesic for neuropathic pain. It is a synthetic cannabinoid, which mimics the main ingredient of cannabis (THC). Chemically, nabilone is similar to the active ingredient found in naturally occurring *Cannabis sativa* L.
- In Canada, the United States, the United Kingdom and Mexico, nabilone is marketed as Cesamet. It was approved in 1985 by the U.S. Food and Drug Administration (FDA) for treatment of chemotherapy-induced nausea and vomiting that has not responded to conventional antiemetics. Though it was approved by the FDA in 1985, the drug only began marketing in the United States in 2006. It is also approved for use in treatment of anorexia and weight loss in patients with AIDS.
- Although it doesn't have the official indication (except in Mexico), nabilone is widely used as an adjunct therapy for chronic pain management. Numerous trials and case studies have demonstrated various benefits for condition such as fibromyalgia and multiple sclerosis.

SYNTHETIC CANNABINOIDS- COMMERCIAL

- Sativex is an oromucosal (mouth) spray developed by the UK company GW Pharmaceuticals for multiple sclerosis patients, who can use it to alleviate neuropathic pain, spasticity, overactive bladder, and other symptoms. Sativex is also being prescribed to alleviate pain due to cancer and has been researched in various models of peripheral and central neuropathic pain.
- Sativex is distinct from all other pharmaceutically produced cannabinoids currently available because it is derived from botanical material, rather than a solely synthetic process. Sativex is a pharmaceutical product standardized in composition, formulation, and dose. Its principal active cannabinoid components are the cannabinoids: tetrahydrocannabinol (THC) and cannabidiol (CBD). The product is formulated as an oromucosal spray which is administered by spraying into the mouth. Each spray of Sativex delivers a fixed dose of 2.7mg THC and 2.5mg CBD.

SYNTHETIC CANNABINOIDS (SPICE)



SYNTHETIC CANNABINOIDS

{K2 (JWH-018, JWH-073)}



“SPICE” AND OTHER SYNTHETIC CANNABINOIDS

- **PHARMACOLOGY**
 - **CANNABINOID RECEPTOR AGONISTS MIMIC THE EFFECTS OF THC AND ANADAMIDE BY INTERACTING WITH THE CB1 RECEPTOR IN THE BRAIN**
 - **SOME OF THESE SYNTHETICS HAVE A HIGHER AFFINITY FOR THE RECEPTOR THAN CANNABIS THC AND MAY BE PARTICULARLY LONG ACTING**
 - **OFTEN LARGE AMOUNTS OF TOCOPHEROL (VITAMIN E) ADDED TO MASK ANALYSIS**

“SPICE” AND OTHER SYNTHETIC CANNABINOIDS

- **PHARMACOLOGY (CONTINUED)**
 - **SMOKING MIXTURES ARE USUALLY SOLD IN METAL-FOIL SACHETS TYPICALLY CONTAINING THREE GRAMS OF DRIED VEGETABLE MATTER TO WHICH ONE OR MORE OF THE CANNABINOIDS HAVE BEEN ADDED**
- **TRADE NAMES**
 - **“SPICE GOLD”, “SPICE SILVER”, “YUCATAN FIRE”, “CHILL X”, “SENSE” AND MANY OTHERS**

CANNABINOID EFFECTS

- **Appetite, feeding behavior and body weight**
- **Reward and motivation**
- **Mood and anxiety**
- **Pain**
- **Memory**

CANNABINOID EFFECTS

- By observing how the appetite center (a locus of nerve tissue in the ventromedial nucleus of the hypothalamus) of the brain responds to marijuana, we were able to see what drives the hunger brought about by cannabis and how that same mechanism that normally turns off feeding becomes a driver of eating

CANNABINOID EFFECTS

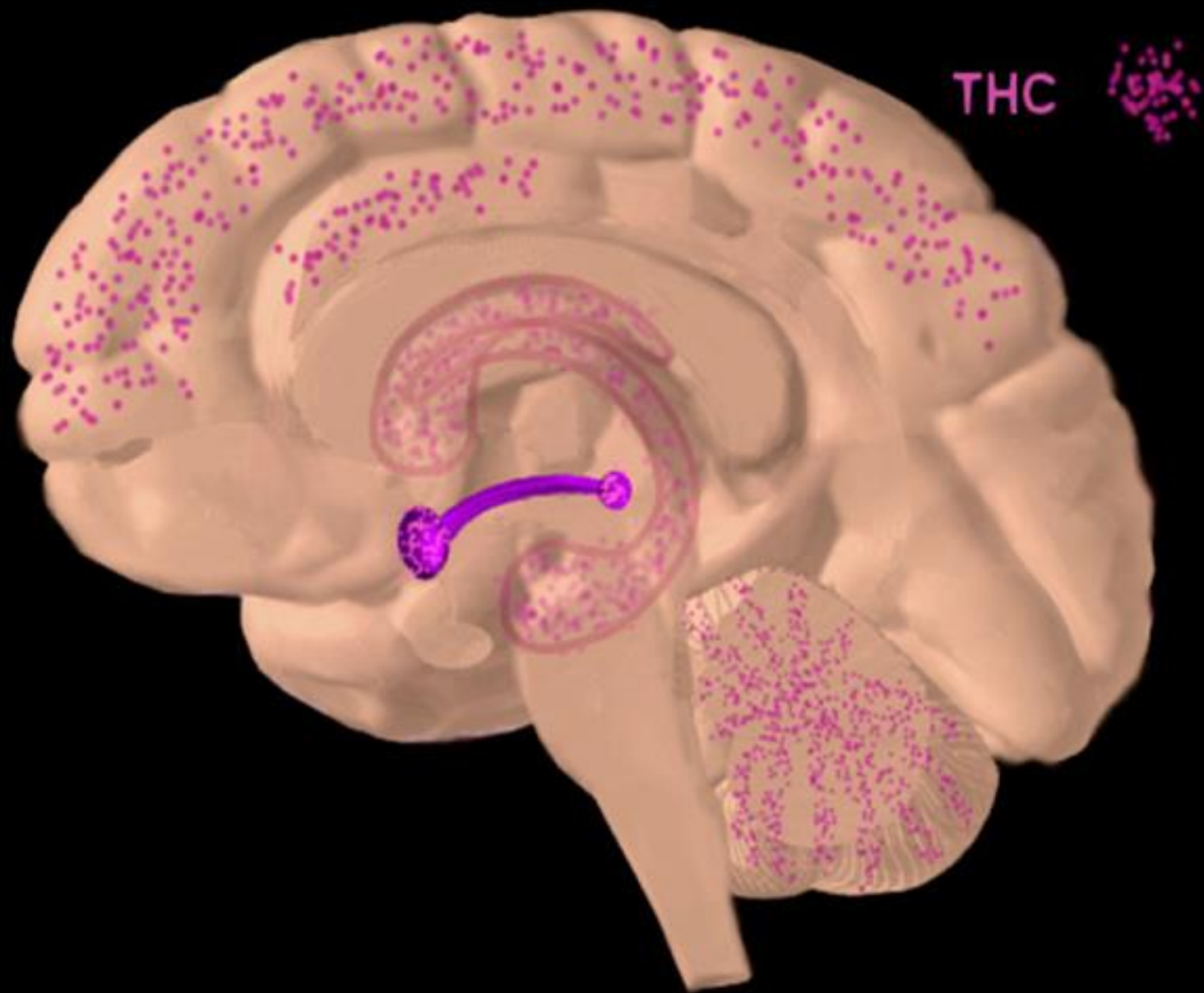
- Tetrahydrocannabinol (THC) has the effect on a brain that not only stimulates their appetite, but also fits into the brain's olfactory bulb. The CB1 receptor there is responsible for the food we smell, and THC significantly increases the person's ability to smell food, which in turn causes salivation and generates a hungrier response.

CANNABINOID EFFECTS

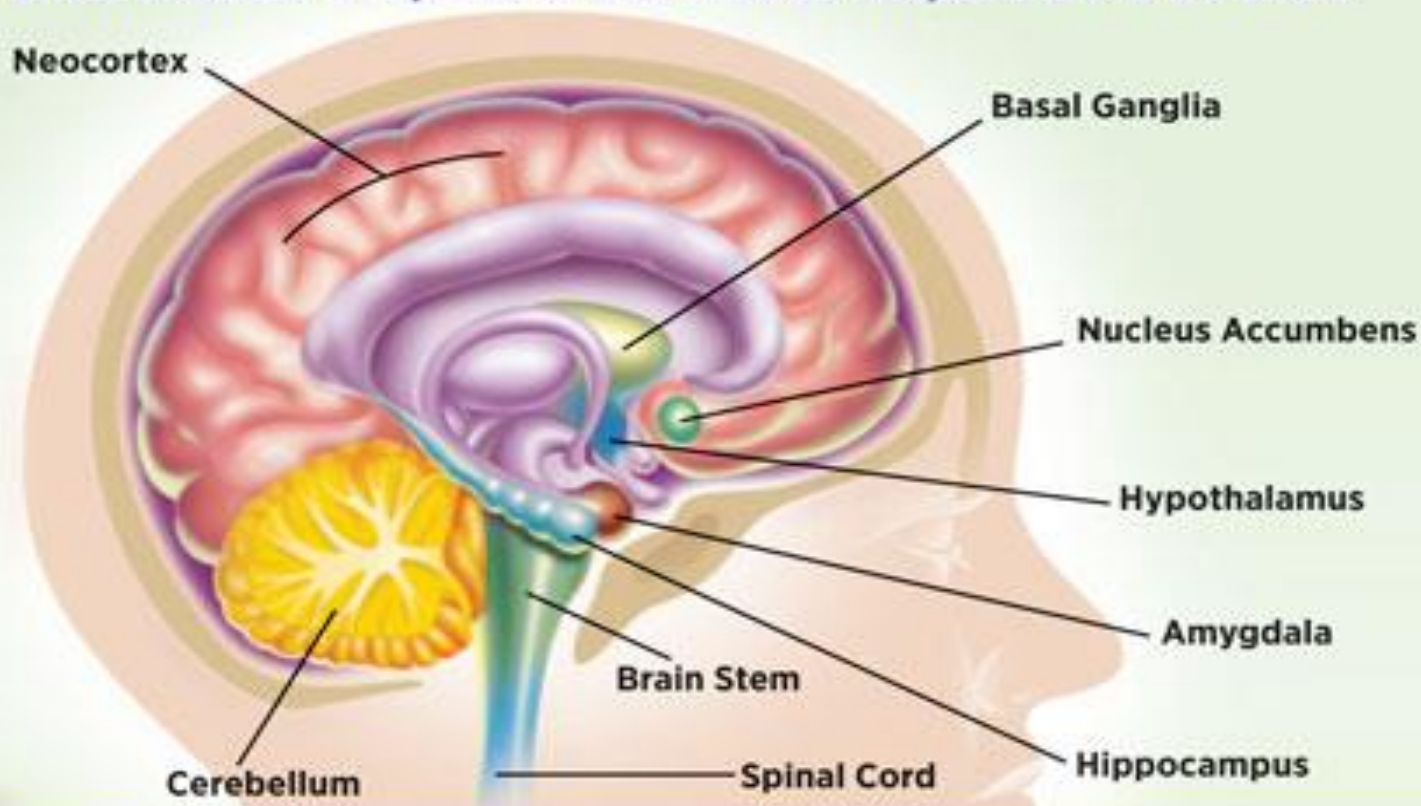
- **ASTROCYTES HAVE A PRINCIPLE ROLE IN WORKING MEMORY**
 - **MARIJUANA IMPAIRS WORKING (SHORT TERM) MEMORY**
 - **EXAMPLE-LOOSE TRAIN OF THOUGHT IN MID-SENTENCE**
 - **DISCOVERED BY REMOVING CB1 RECEPTORS FROM ASTROCYTES LEAVING NO SHORT TERM DEFICIT BUT REMOVING CB1 RECEPTORS FROM NEURONS CREATED FORGETFULNESS IN MICE THE SAME AS WITH RECEPTORS**
 - **“WHAT MARIJUANA REVEALS ABOUT MEMORY” SCAMMIND. JULY/AUGUST, 2012, PG. 10.**

CANNABINOID EFFECTS

- Exogenous cannabis (and its primary psychoactive component, Δ -9-tetrahydrocannabinol [THC]) acts on the endogenous cannabinoid (endocannabinoid) system in the brain and other body tissues by binding to two different types of cannabinoid receptors on cell membranes: *CB1* and *CB2*
- *CB1* receptors are located primarily in pre-synaptic neurons of the CNS and are responsible for the acute psychological and cardiovascular effects of cannabis.



How does THC affect behavior? It depends on where the CB receptors are in the brain.



Brain Structure	Regulates	THC Effect on User
Amygdala	emotions, fear, anxiety	panic/paranoia
Basal Ganglia	planning/starting a movement	slowed reaction time
Brain Stem	information between brain and spinal column	antinausea effects
Cerebellum	motor coordination, balance	impaired coordination
Hippocampus	learning new information	impaired memory
Hypothalamus	eating, sexual behavior	increased appetite
Neocortex	complex thinking, feeling, and movement	altered thinking, judgment, and sensation
Nucleus Accumbens	motivation and reward	euphoria (feeling good)
Spinal Cord	transmission of information between body and brain	altered pain sensitivity

The brain structures illustrated above all contain high numbers of CB receptors

CANNABINOID EFFECTS

- CB2 receptors are located largely in the periphery and modulate immune function and inflammatory response
- Endocannabinoids (endogenous ligands at CB receptors) such as anandamide serve as retrograde neuromodulators of synaptic activity. They are released postsynaptically by a variety of stimuli upon demand, travel across the synaptic cleft, and then activate presynaptic CB receptors. A membrane transporter actively takes anandamide into the cell. Anandamide is then broken down by fatty acid amide hydrolase (FAAH)

Signal direction for neurotransmitters

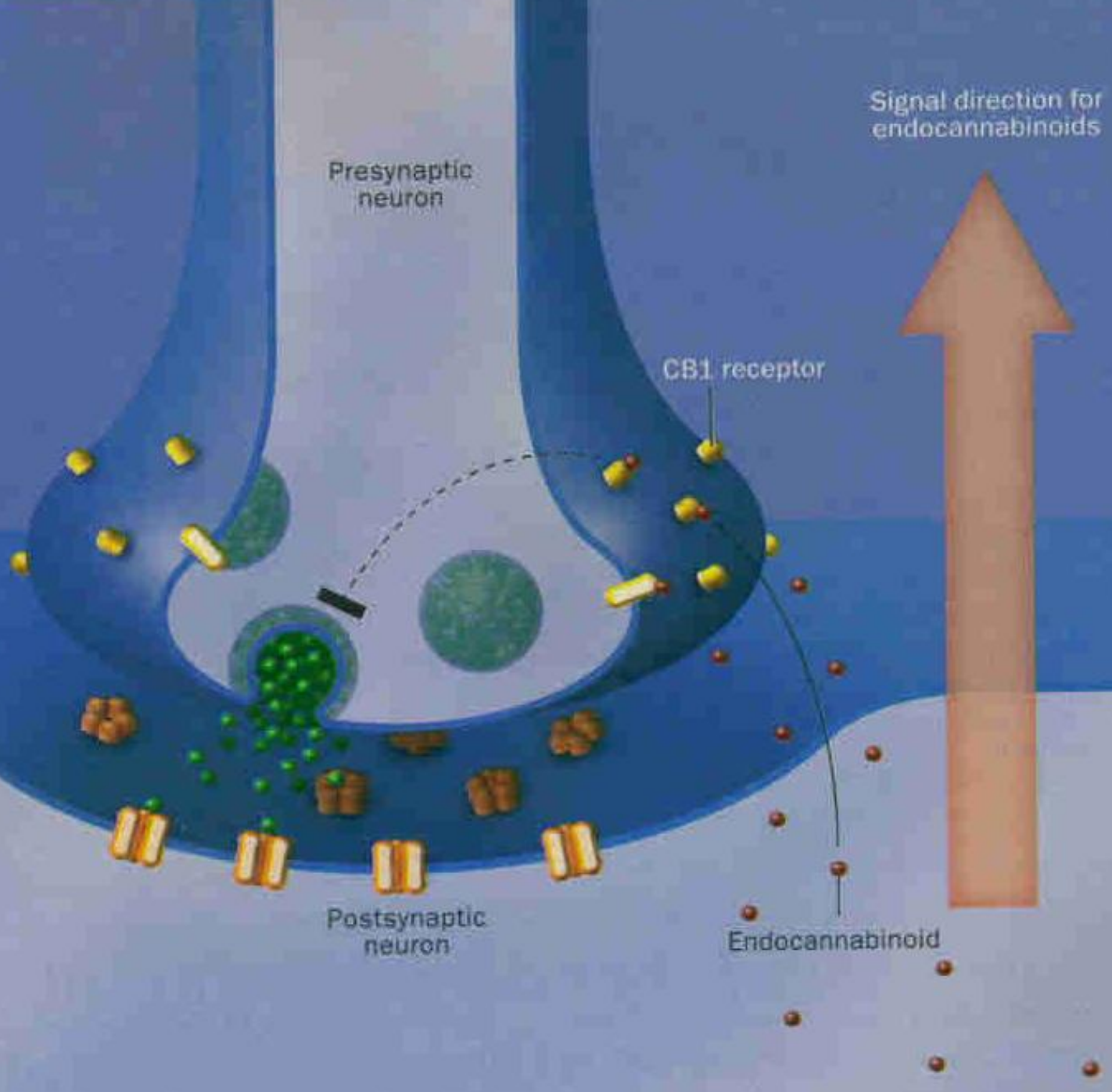
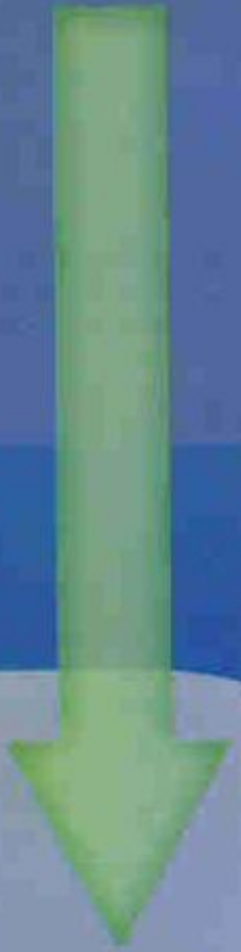
Signal direction for endocannabinoids

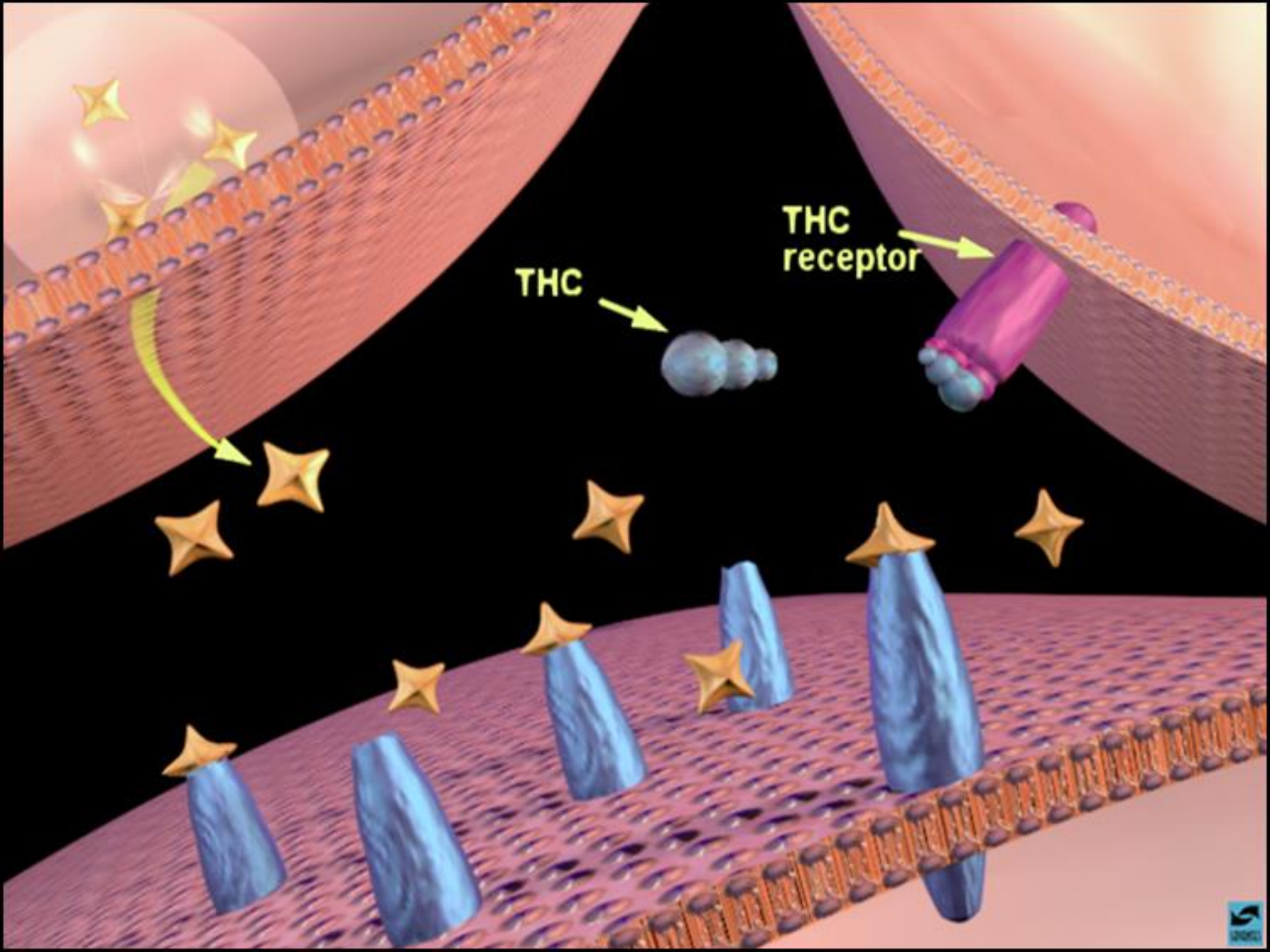
Presynaptic neuron

CB1 receptor

Postsynaptic neuron

Endocannabinoid





CANNABIS

- **GENERAL MEDICAL**

- Cannabis use has been related to a reduction in prosocial goal-directed activity, which some have labeled an *amotivational syndrome*, that manifests itself in poor school performance and employment problems.
- Cannabis smoke contains high levels of carcinogenic compounds that place chronic users at risk for respiratory illnesses similar to those experienced by tobacco smokers.
- Cannabis use can contribute to the onset of an acute psychotic episode, can exacerbate some symptoms, and can adversely affect treatment of a major psychotic illness.

CANNABIS

- **GENERAL MEDICAL**

- Seizures, stroke, abnormal heart rhythms, heart attacks (4.8 times risk within an hour after smoking), psychosis, hallucinations and other serious adverse effects have been associated with smoking synthetic pot.
- Medical journals have also begun to report a growing number of strokes potentially related to the use of natural (non-synthetic) marijuana.

M. J. Freeman, D. Z. Rose, M. A. Myers, C. L. Gooch, A. C. Bozeman, W. S. Burgin. **Ischemic stroke after use of the synthetic marijuana "spice"**. *Neurology*, 2013;

CANNABIS

- **GENERAL MEDICAL**

- linked to a severe form of vomiting syndrome and compulsive bathing behavior. This form of severe vomiting sickness is increasingly recognized with widespread abuse of marijuana. The syndrome usually subsides with strict abstinence from marijuana abuse.
- compulsive hot showering behavior relieves the symptoms of vomiting syndrome

Sontineni et al. Cannabinoid hyperemesis syndrome: Clinical diagnosis of an underrecognised manifestation of chronic cannabis abuse. *World Journal of Gastroenterology*, 2009; 15 (10): 1264

CANNABIS

- **GENERAL MEDICAL**

- The prevalence of non-alcohol drugs detected in fatally injured drivers in the US steadily rose from 1999 to 2010 and especially for drivers who tested positive for marijuana. Researchers found that of 23,591 drivers who were killed within one hour of a crash, 39.7 percent tested positive for alcohol and 24.8 percent for other drugs. The prevalence of non-alcohol drugs rose from 16.6 percent in 1999 to 28.3 percent in 2010; for marijuana, rates rose from 4.2 percent to 12.2 percent.

J. E. Brady, G. Li. Trends in Alcohol and Other Drugs Detected in Fatally Injured Drivers in the United States, 1999-2010. *American Journal of Epidemiology*, 2014

CANNABIS

- **GENERAL MEDICAL**

- Results show that any history of cannabis use was associated with an increased likelihood of reporting difficulty falling asleep, struggling to maintain sleep, experiencing non-restorative sleep, and feeling daytime sleepiness. The strongest association was found in adults who started marijuana use before age 15; they were about twice as likely to have severe problems falling asleep, experiencing non-restorative sleep and feeling overly sleepy during the day.

American Academy of Sleep Medicine. "Marijuana use associated with impaired sleep quality." ScienceDaily. ScienceDaily, 2 June 2014. <www.sciencedaily.com/releases/2014/06/140602102013.htm>.

CANNABIS

- SHORT-TERM HEALTH EFFECTS
 - Cognitive (Intoxication Syndrome)
 - *Euphoria*
 - *Enhanced perception of novelty*
 - *Distractedness*
 - *Decreased processing speed*
 - *Loss of short-term memory*

CANNABIS

- **CONTAMINANTS**

- Aspergillus fungus and bacteria-can lead to pneumonia
- Heavy metals such as aluminum and cadmium
- Organophosphate pesticides
- Glass beads and sand in street cannabis used to increase weight but can damage oral mucosa and lungs

CANNABIS

- **LONG-TERM HEALTH EFFECTS**

- Heavy marijuana use predicts impairments in executive functioning and learning (Gruber SA et al, *Psychol Addict Behav* 2012; 26(3):496-506)
- Persistent users of marijuana particularly those who started in in adolescence had significant decreases in IQ. There was a dose-response relationship (Meier MH et al, *Proc Natl Acad Sci USA* 2012; 109(40):E2657-E2664)
- Loss of 8 IQ points with heavy smoking during teen years
(<http://www.drugabuse.gov/publications/drugfacts/marijuana>)

Why Go To

HIGH SCHOOL

When You
Can Go To

SCHOOL HIGH?



CANNABIS

- **LONG-TERM HEALTH EFFECTS**
- We wanted to answer two questions -- does cannabis use lead to increased occurrence of mania symptoms or manic episodes in individuals with pre-existing bipolar disorder? But also, does cannabis use increase the risk of onset of mania symptoms in those without pre-existing bipolar disorder?"

CANNABIS

- **LONG-TERM HEALTH EFFECTS**

- The observed tendency for cannabis use to precede or coincide with rather than follow mania symptoms, and the more specific association between cannabis use and new onset manic symptoms
- Cannabis use significantly worsened mania symptoms in people who had previously been diagnosed with bipolar disorder.

Melanie Gibbs, Catherine Winsper, Steven Marwaha, Eleanor Gilbert, Matthew Broome, Swaran P. Singh. **Cannabis use and mania symptoms: A systematic review and meta-analysis.** *Journal of Affective Disorders*, 2015; 171: 39
DOI:[10.1016/j.jad.2014.09.016](https://doi.org/10.1016/j.jad.2014.09.016)

CANNABIS

- **LONG-TERM HEALTH EFFECTS**
 - Exposing adolescent rats to THC (tetrahydrocannabinol) —the primary psychoactive ingredient in marijuana—can lead to molecular and behavioral alterations in the next generation of offspring, even though progeny were not directly exposed to the drug
 - Male offspring showed stronger motivation to self-administer heroin during their adulthood and molecular changes in the glutamatergic system, which is the most important excitatory pathway for neurotransmission in the brain.

CANNABIS

- **LONG-TERM HEALTH EFFECTS**
 - **Damage in the glutamate pathway, which regulates synaptic plasticity, has been linked to disturbances in goal-directed behavior and habit formation.**
 - **Future studies are now being explored to determine whether THC effects continue to be transmitted to even the subsequent grandchildren and great-grandchildren generations**

Henrietta Szutorisz, Jennifer A DiNieri, Eric Sweet, Gabor Egervari, Michael Michaelides, Jenna M Carter, Yanhua Ren, Michael L Miller, Robert D Blitzer, Yasmin L Hurd. **Parental THC Exposure Leads to Compulsive Heroin-Seeking and Altered Striatal Synaptic Plasticity in the Subsequent Generation.** *Neuropsychopharmacology*, 2014; DOI: [10.1038/npp.2013.352](https://doi.org/10.1038/npp.2013.352)

CANNABIS

- **LONG-TERM HEALTH EFFECTS**
 - Cannabis use during adolescence and young adulthood increases the risk of psychotic symptoms, while continued cannabis use may increase the risk for psychotic disorder in later life, concludes a new study.
 - However, it is not clear whether the link between cannabis and psychosis is causal, or whether it is because people with psychosis use cannabis to self medicate their symptoms

CANNABIS

- **LONG-TERM HEALTH EFFECTS**

- The researchers excluded anyone who reported cannabis use or pre-existing psychotic symptoms at the start of the study so that they could examine the relation between new (incident) cannabis use and psychotic symptoms.
- The remaining participants were then assessed for cannabis use and psychotic symptoms at three time points over the study period (on average four years apart).
- Incident cannabis use almost doubled the risk of later incident psychotic symptoms, even after accounting for factors such as age, sex, socioeconomic status, use of other drugs, and other psychiatric diagnoses. Furthermore, in those with cannabis use at the start of the study, continued use of cannabis over the study period increased the risk of persistent psychotic symptoms

CANNABIS

- Effects of chronic marijuana use on the brain may depend on age of first use and duration of use
- Chronic marijuana users have smaller brain volume in the orbitofrontal cortex (OFC), a part of the brain commonly associated with addiction, but also increased brain connectivity.

CANNABIS

- Using marijuana in adolescence may do serious long-term damage to the immune system. This damage may result in autoimmune diseases and chronic inflammatory diseases, such as multiple sclerosis, inflammatory bowel disease and rheumatoid arthritis in adulthood.
- The immune system is characterized by an impressive ability to 'remember' previous exposures and changes during the period of immune system development especially early in life can have important long-term consequences

CANNABIS

- These studies not only point to adolescence as a key phase of immune system sensitivity, but also highlight the dramatic and long-lasting negative effects that a common recreational drug abused by teenagers may have on immune function.
- S. Moretti, M. Castelli, S. Franchi, M. A. Raggi, L. Mercolini, M. Protti, L. Somaini, A. E. Panerai, P. Sacerdote. **9-Tetrahydrocannabinol-induced anti-inflammatory responses in adolescent mice switch to proinflammatory in adulthood.** *Journal of Leukocyte Biology*, 2014; 96 (4): 523 DOI:[10.1189/jlb.3HI0713-406RR](https://doi.org/10.1189/jlb.3HI0713-406RR)

CANNABIS

- Alcohol use was more commonly reported to compromise relationships with friends and significant others (e.g., boyfriends), researchers studying its consequences report. It was also reported to lead to more regret, particularly among females. Marijuana use on the other hand was more commonly reported to compromise relationships with teachers or supervisors, result in less energy or interest, and result in lower school or job performance.

Joseph J. Palamar, Michael Fenstermaker, Dimita Kamboukos, Danielle C. Ompad, Charles M. Cleland, Michael Weitzman. **Adverse psychosocial outcomes associated with drug use among US high school seniors: a comparison of alcohol and marijuana.** *The American Journal of Drug and Alcohol Abuse*, 2014; 1 DOI: [10.3109/00952990.2014.943371](https://doi.org/10.3109/00952990.2014.943371)

CANNABIS

- Smoking today's concentrated pot might be risky business for women, according to new research. Thanks to their estrogen levels, female rats are at least 30 percent more sensitive than males to the pain-relieving qualities of THC -- the key active ingredient in cannabis, research shows. Females also develop tolerance to THC more quickly. These sensitivities could increase vulnerability to negative side effects like anxiety, paranoia and addiction.

CANNABIS

- Margaret Haney at the Columbia University Medical Center, has shown that women are more susceptible to cannabis abuse and dependence than men. Haney has documented a cannabis withdrawal syndrome of irritability, sleep disruption and decreased food intake that tends to be more severe in women. Women also have a greater tendency to relapse when trying to stop using the drug

CANNABIS

- We're finding with THC is that you get a very clear spike in drug sensitivity right when the females are ovulating -- right when their estrogen levels have peaked and are coming down

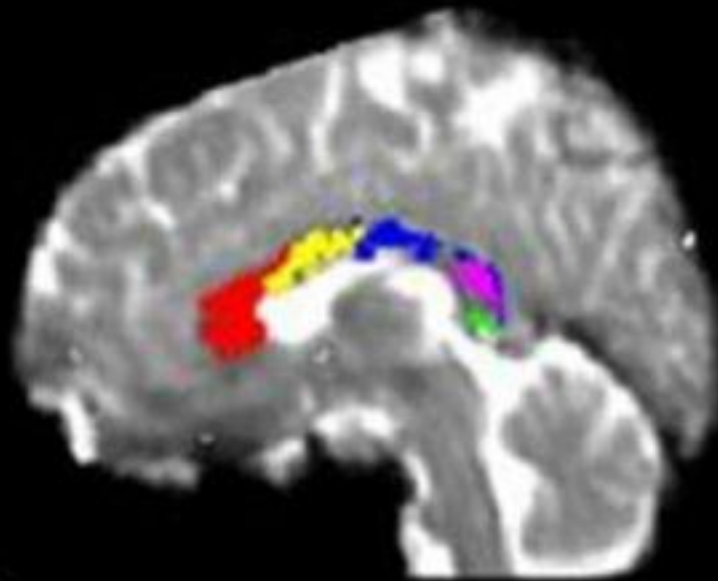
Alexa A. Wakley, Jenny L. Wiley, Rebecca M. Craft. **Sex differences in antinociceptive tolerance to delta-9-tetrahydrocannabinol in the rat.** *Drug and Alcohol Dependence*, 2014;

DOI: [10.1016/j.drugalcdep.2014.07.029](https://doi.org/10.1016/j.drugalcdep.2014.07.029)

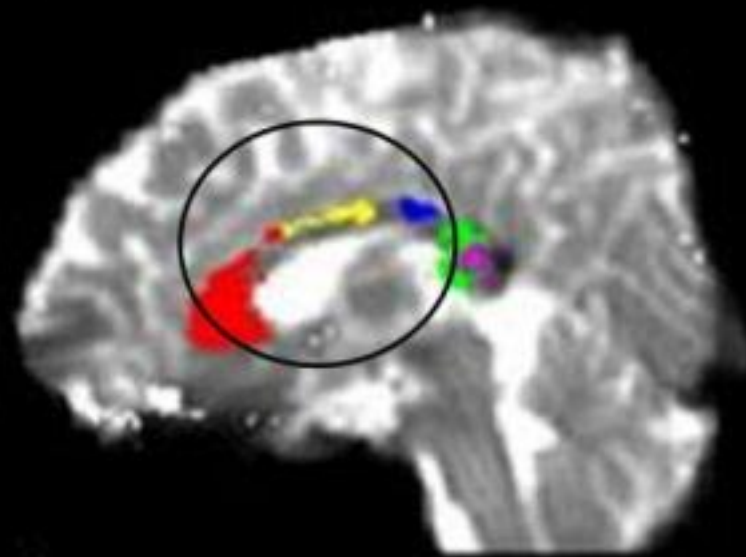
Washington State University. "Estrogen increases cannabis sensitivity, study shows." ScienceDaily. ScienceDaily, 3 September 2014.

<www.sciencedaily.com/releases/2014/09/140903092153.htm>.

White matter structure differences between marijuana users and non-users



Non-user

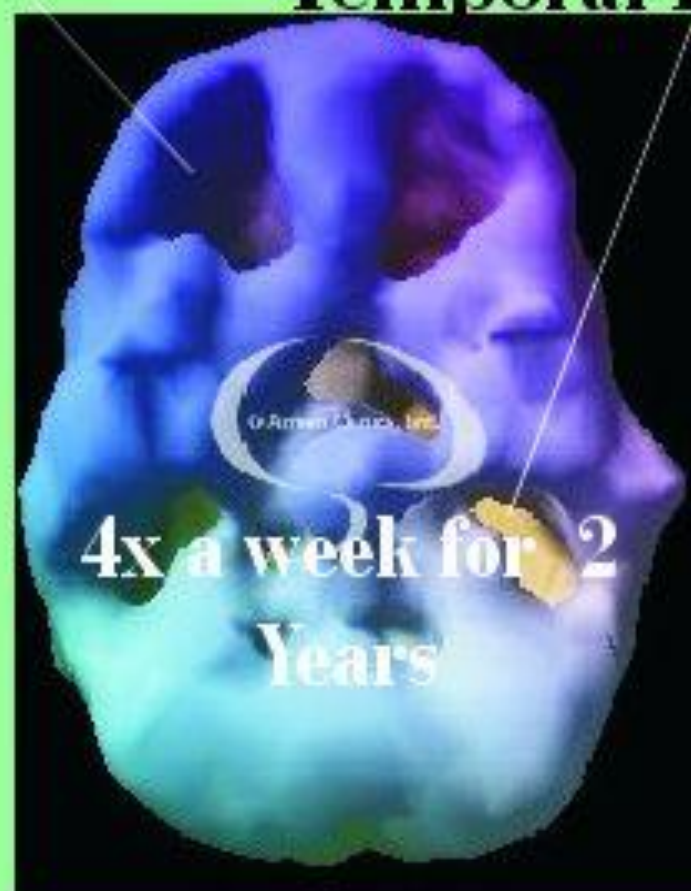
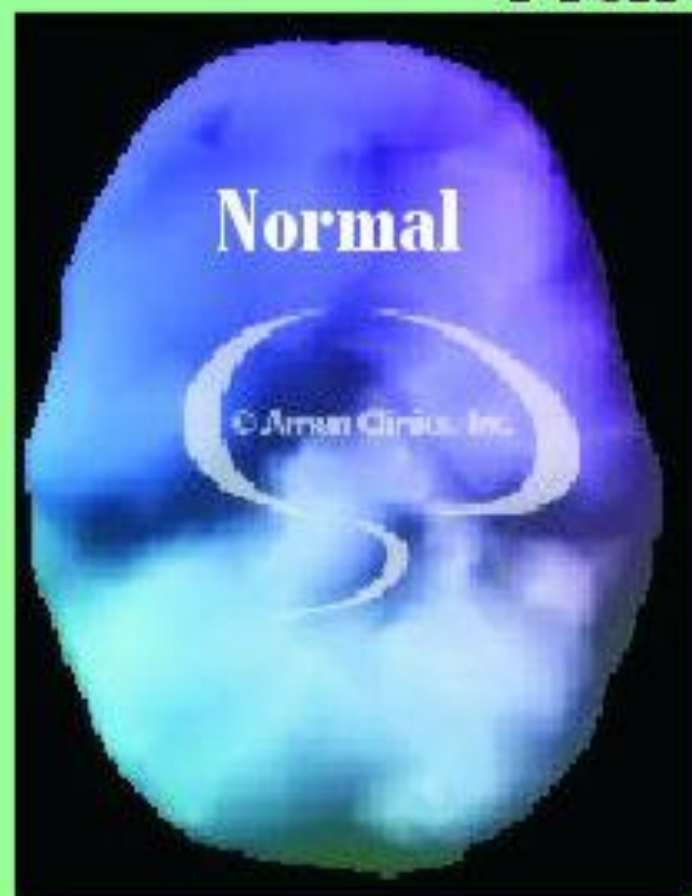


Daily user

Source: Arnone D, Barrick TR, Chengappa S et al. Corpus callosum damage in heavy marijuana use: Preliminary evidence from diffusion tensor tractography and tract-based spatial statistics. *NeuroImage*, 2008; 41:1067-1074

Effects of THC on the Brain

Prefrontal cortex Temporal Lobes



“SPICE” AND OTHER SYNTHETIC CANNABINOIDS

- **The first case of catatonic psychosis caused by a synthetic derivate of Cannabis, Spice, has been described by researchers. The relation between the consumption of this substance, a psychotic break and some locomotor system problems, similar to the ones caused by Parkinson's, have also been described for the first time.**

“SPICE” AND OTHER SYNTHETIC CANNABINOIDS

- **Until now, recent studies had already shown the relation between the spice and different types of psychosis, but this is the first clinical case described on an international scale in which the psychotic break appears with abnormal movements. The movement disorder detected in this case, similar to catatonia, consists in the loss of harmony in the walking process and neck, arms and head stiffness**

“SPICE” AND OTHER SYNTHETIC CANNABINOIDS

- The other relevant aspect is that the motor symptoms and the bent-over posture of "mantis religiosa" persisted even months after stopping the consumption.

Gonzalo Haro, Carmen Ripoll, María Ibáñez, Teresa Orengo, Víctor M. Liaño, Emilio Meneu, Félix Hernández, Francisco Traver. **Could Spice Drugs Induce Psychosis With Abnormal Movements Similar to Catatonia?** *Psychiatry: Interpersonal and Biological Processes*, 2014; 77 (2): 206
DOI:[10.1521/psyc.2014.77.2.206](https://doi.org/10.1521/psyc.2014.77.2.206)

“SPICE” AND OTHER SYNTHETIC CANNABINOIDS



CANNABIS

- Adults seeking treatment have typically been cannabis smokers for over 10 years with repeated attempts to quit. They report...
 - *Relationship problems*
 - *Financial difficulties*
 - *Low self-esteem*
 - *Frustration with their level of productivity*
 - *Sleep and memory problems*
 - *Decreased life satisfaction*

Stephens RS et al. *Addiction* 2002; 97 (Suppl. 1); 109-124.

CANNABIS

- Teens entering treatment do not readily admit life problems but their use puts them at risk for...
 - *Risky sexual behavior*
 - *Sexually transmitted infections*
 - *Unplanned pregnancies*
 - *Low educational achievement*
 - *School drop out*
 - *Legal difficulties*
- Tims FM et al, *Addiction* 2002; 97 (Suppl. 1): 46-57.

ASSESSMENT AND DSM-5

- **Cannabis-Related Disorders**
 - Cannabis Use Disorder
 - Cannabis Intoxication
 - Cannabis Withdrawal
 - Other Cannabis-Induced Disorders
 - Unspecified Cannabis-Related Disorder
- *Cannabis* is the generic and perhaps the most appropriate scientific term for the psychoactive substance(s) derived from the plant, and as such it is *used in this manual to refer to all forms of cannabis-like substances, including synthetic cannabinoid compounds*

ASSESSMENT AND DSM-5

- **Cannabis Use Disorder**
 - A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:
 - Cannabis is often taken in larger amounts or over a longer period than was intended.
 - There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
 - A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.
 - Craving, or a strong desire or urge to use cannabis.

ASSESSMENT AND DSM-5

- **Cannabis Use Disorder (continued)**
 - Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home.
 - Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.
 - Important social, occupational, or recreational activities are given up or reduced because of cannabis use.
 - Recurrent cannabis use in situations in which it is physically hazardous.
 - Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.

ASSESSMENT AND DSM-5

- **Cannabis Use Disorder (continued)**
 - **Tolerance, as defined by either of the following:**
 - A need for markedly increased amounts of cannabis to achieve intoxication or desired effect.
 - Markedly diminished effect with continued use of the same amount of cannabis.
 - **Withdrawal, as manifested by either of the following:**
 - The characteristic withdrawal syndrome for cannabis (refer to Criteria A and B of the criteria set for cannabis withdrawal).
 - Cannabis (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.

ASSESSMENT AND DSM-5

- **Cannabis Use Disorder (continued)**

- *Specifiers*

- **In early remission:** After full criteria for cannabis use disorder were previously met, none of the criteria for cannabis use disorder have been met for at least 3 months but for less than 12 months
 - **In sustained remission:** After full criteria for cannabis use disorder were previously met, none of the criteria for cannabis use disorder have been met at any time during a period of 12 months or longer
 - **In a controlled environment**

ASSESSMENT AND DSM-5

- **Cannabis Use Disorder (continued)**
 - *Severity*
 - **305.20 (F12.10) Mild:** Presence of 2–3 symptoms.
 - **304.30 (F12.20) Moderate:** Presence of 4–5 symptoms.
 - **304.30 (F12.20) Severe:** Presence of 6 or more symptoms.

ASSESSMENT AND DSM-5

Whether or not cannabis is being used for legitimate medical reasons may also affect diagnosis. *When a substance is taken as indicated for a medical condition, symptoms of tolerance and withdrawal will naturally occur and should not be used as the primary criteria for determining a diagnosis of a substance use disorder.* Although medical uses of cannabis remain controversial and equivocal, use for medical circumstances should be considered when a diagnosis is being made.

ASSESSMENT AND DSM-5

Early onset of cannabis use (e.g., prior to age 15 years) is a robust predictor of the development of cannabis use disorder and other types of substance use disorders and mental disorders during young adulthood. Such early onset is likely related to concurrent other externalizing problems, most notably conduct disorder symptoms. However, early onset is also a predictor of internalizing problems and as such probably reflects a general risk factor for the development of mental health disorders.

ASSESSMENT AND DSM-5

- **Cannabis Withdrawal**
 - Three (or more) of the following signs and symptoms develop within approximately 1 week :
 - Irritability, anger, or aggression.
 - Nervousness or anxiety.
 - Sleep difficulty (e.g., insomnia, disturbing dreams).
 - Decreased appetite or weight loss.
 - Restlessness.
 - Depressed mood.
 - At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever

ASSESSMENT AND DSM-5

- **Cannabis Withdrawal**

- *Most symptoms have their onset within the first 24–72 hours of cessation, peak within the first week, and last approximately 1–2 weeks. Sleep difficulties may last more than 30 days. Cannabis withdrawal has been documented among adolescents and adults. Withdrawal tends to be more common and severe among adults, most likely related to the more persistent and greater frequency and quantity of use among adults.*

INCIDENCE AND SEVERITY OF PERCEIVED WITHDRAWAL SYMPTOMS

	none	mild	moderate	severe
1) Shakiness/tremulousness	0	1	2	3
2) Depressed mood	0	1	2	3
3) Decreased appetite	0	1	2	3
4) Nausea	0	1	2	3

INCIDENCE AND SEVERITY OF PERCEIVED WITHDRAWAL SYMPTOMS

5) Irritability	0	1	2	3
6) Sleep difficulty	0	1	2	3
7) Sweating	0	1	2	3
8) Craving to smoke marijuana	0	1	2	3
9) Restlessness	0	1	2	3
10) Nervousness/anxiety	0	1	2	3
11) Increased aggression	0	1	2	3

INCIDENCE AND SEVERITY OF PERCEIVED WITHDRAWAL SYMPTOMS

12) Headaches	0	1	2	3
13) Stomach Pains	0	1	2	3
14) Strange dreams	0	1	2	3
15) Increased anger	0	1	2	3
16) Other (list)				
_____	0	1	2	3

INCIDENCE AND SEVERITY OF PERCEIVED WITHDRAWAL SYMPTOMS

- **SCORING PROCEDURE AND
INTERPRETATION**

- A total score is obtained by summing the severity ratings. Budney et al. (2003) also tested a withdrawal discomfort score (WDS), based on summing the 12 following items: 1-3, 5-7, 9-11, and 13-15. Higher scores indicate more severe symptoms associated with marijuana withdrawal.

Budney, A. J., Novy, P. L., & Hughes, J. R. (1999). Marijuana withdrawal among adults seeking treatment for marijuana dependence. *Addiction*, 94(9), 1311-1322.

CANNABIS WITHDRAWAL- PHARMACOTHERAPY

- **MEDICATION-ASSISTED TREATMENT (MAT) has not been very effective with cannabis**
- **Only one medication has been proven effective although many have been tried including the off-label use of baclofen (Lioresal), bupropion (Wellbutrin), divalproex (Depakote), dronabinol (Marinol), mirtazapine (Remeron), nefazodone (Serzone), and quetiapine (Seroquel) <actually caused increased use>**

Weinstein and Gorelick, *Curr Pharm Des* 2011; 17(14):1351-1358.

CANNABIS WITHDRAWAL- PHARMACOTHERAPY

- In a positive trial using gabapentin, patients received 1200mg per day in divided doses for 12 weeks (Mason BJ et al. *Neuropsychopharmacology* 2012; 37(7): 1689-1698)
- All patients received weekly individual counseling and could use any other support they desired

CANNABIS WITHDRAWAL- PHARMACOTHERAPY

- Symptoms of withdrawal (mood, sleep problems, cravings, etc.) were all improved compared to placebo
- Only 36% of the original 50 patients completed the trial but attrition was equal in both groups
- Gabapentin was well tolerated with only one patient dropping out due to an adverse event (headache)

CANNABIS WITHDRAWAL- PHARMACOTHERAPY

- For further study in regard to the use of pharmacotherapy with cannabis dependence
 - Weinstein and Gorelick. “Pharmacological Treatment of Cannabis Dependence.” *Curr Pharm Des.* 2011;17(14): 1351-1358.
 - Winstock and Lea. Management of Cannabis Withdrawal.” *National cannabis Prevention and Information Centre.* Australian Publication
 - See references to Budney in DSM-5

CANNABIS USE DISORDER- PHARMACOTHERAPY

- **N-Acetylcysteine**
 - 8 week double-blind randomized placebo-controlled trial
 - Age 15-21 years old (N=116)
 - NAC (1200mg) or placebo twice daily along with contingency management
 - Those taking NAC had twice the odds of a negative urine than those taking placebo

Gray et al. “A Double-Blind Randomized Controlled Trial of N-Acetylcysteine in Cannabis-Dependent Adolescents. *Am J Psychiatry* 2012;169:805-812.

CANNABIS USE DISORDER- NATURAL METHODS

- **Drink cranberry juice to help purify and cleanse the body.**
- **Drink plenty of water and clear liquids.**
- **Eliminate fat from the diet until digestion is better.**
- **Exercise not only helps depression and other unpleasant emotions, it helps the body speed up the healing process.**
- **Greatly reduce or eliminate caffeine until the sleep pattern is more normal or restlessness is gone.**

CANNABIS USE DISORDER- NATURAL METHODS

- Hot soaking baths can address emotional and physical symptoms.
- Really excessive sweating can deplete the body of potassium, a necessary mineral. A few foods high in potassium are: melons, bananas, citrus fruits, green leafy vegetables, and tomatoes.
- The old fashioned remedy for insomnia, a glass of warm milk before bedtime, helps some people.
- Address symptoms related to sleep disturbance is to look to increase melatonin during withdrawal.

CRAVING

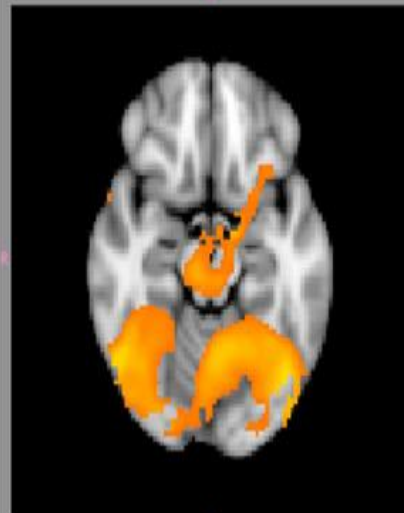
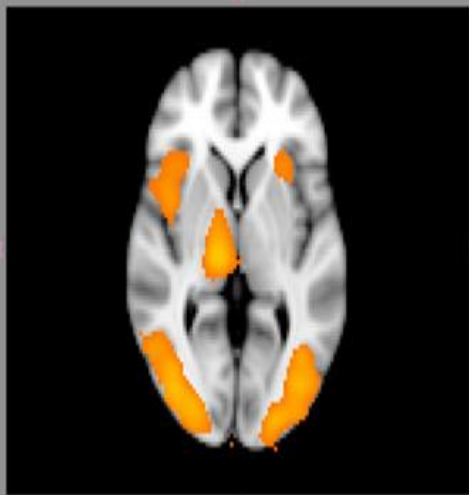
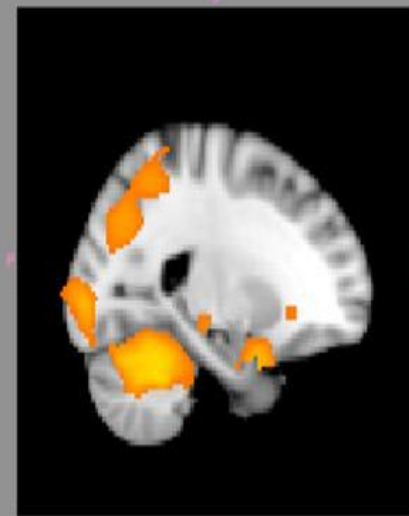
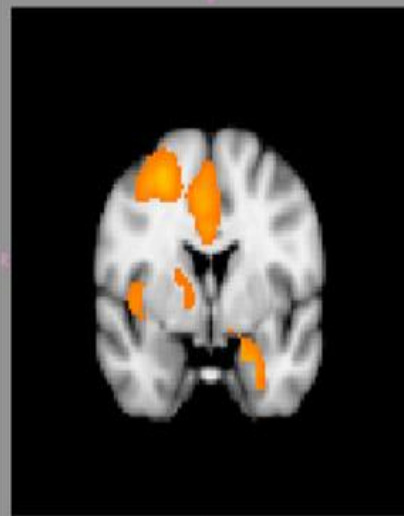
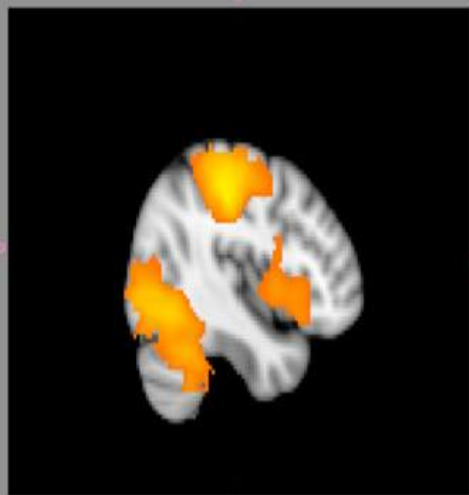
- fMRI used to study cue-elicited craving at 72 hours of abstinence
 - Ventral tegmental area, thalamus, anterior cingulate, insula and amygdala (all parts of the reward pathway) demonstrated greater blood oxygen level dependent (BOLD) activation in response to marijuana cues as compared to neutral one (see fMRI image)
 - These areas underlie motivated behavior, emotional response and the attribution of incentive salience

CRAVING

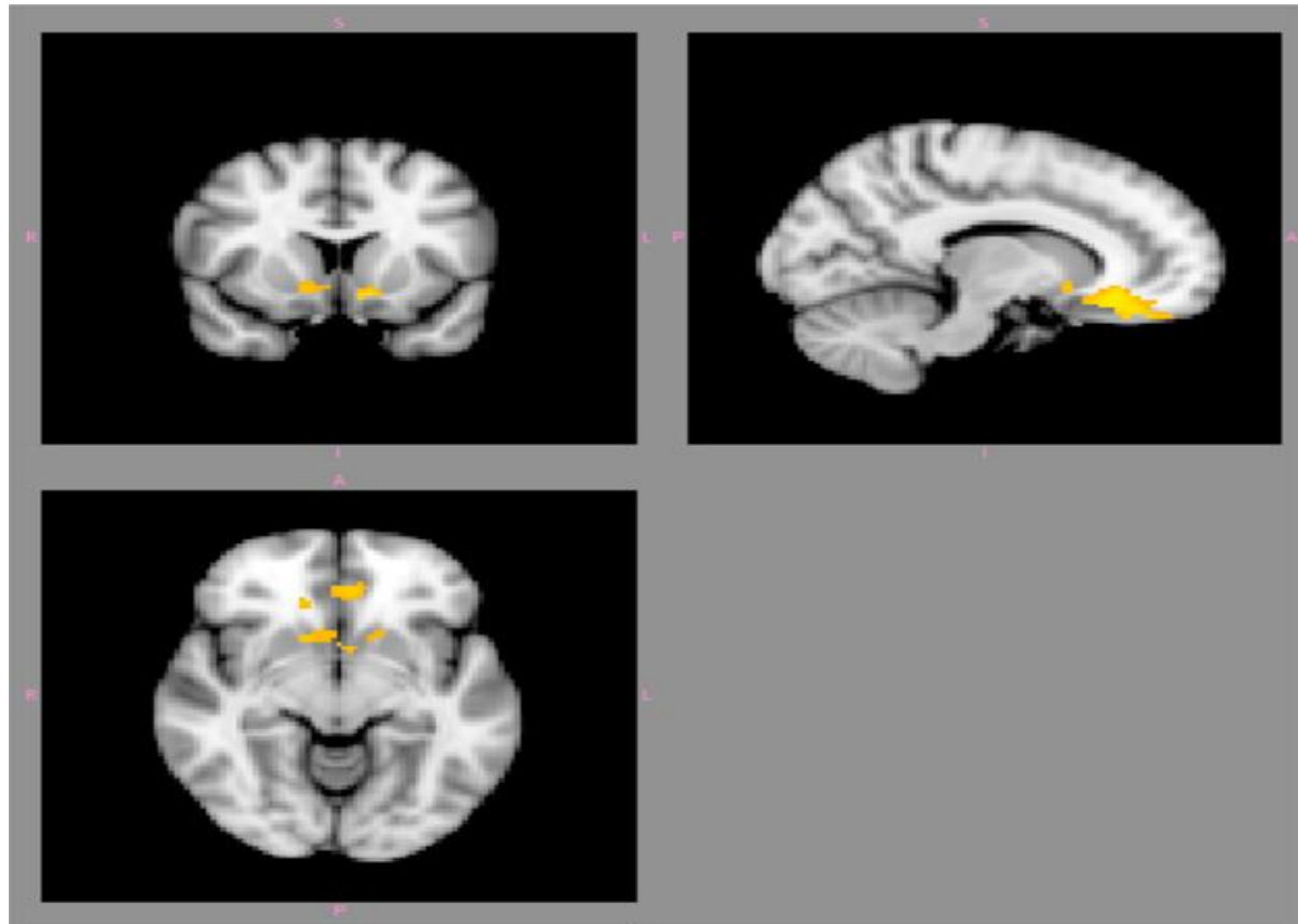
- fMRI used to study cue-elicited craving at 72 hours of abstinence
 - Activation of the orbitofrontal cortex and the nucleus accumbens was also positively correlated with problems related to use
 - The greater the magnitude of activation of these structures the more severe the severity of the cannabis-related problems

Filbey, et al. [www.pnas.org/cgi/doi/10,1073/pnas.0903863106](http://www.pnas.org/cgi/doi/10.1073/pnas.0903863106)

CRAVING-MARIJUANA PIPE



CRAVING-orbitofrontal cortex and nucleus accumbens



CRAVING

▣ *CLASSIFICATION OF CRAVING*

- Situational triggers
 - ▣ Environment (People, Places And Things)
- Emotional triggers
 - ▣ Internal (Hungry, Angry, Lonely, Tired, Reward and Bored)
- Acute Abstinence Syndrome
- Stress
 - CORTISOL

CRAVING:

COMMON CRAVING TRIGGERS

- ▣ In presence of:
 - Alcohol and drugs
 - Alcohol and drug users
 - Places where used to use or purchase
- ▣ Negative feeling states particularly **ANGER** but also:
 - Boredom
 - Loneliness
 - Fear
 - Anxiety

COMMON CRAVING TRIGGERS

- Positive feeling states
- Physical pain
- Use of mood-altering prescription drugs
- Suddenly having a lot of cash
- Complacency
- Insomnia
- Sexual functioning

CRAVING MANAGEMENT

▣ Psychotherapy

▣ Group Approaches

▣ P,P,& T GROUP

■ Behavior Therapy

▣ Structure

▪ Recovery Foundation Program

▣ Changing patterns

▣ Safety Plan

▣ Pharmacotherapy

Behavioral Foundation Program

TASK	MON	TU	WED	THU	FRI	SAT	SUN
SH							
TX							
FUN							
NUT							
PEX							

Behavioral Foundation Program

- **Carter is 24 yo and just getting out of treatment for alcohol and drug addiction**
- **His early A/D history included....**
 - **Started drinking on Friday nights with friends in high school**
 - **Turned-on to and marijuana by friends on weekends**
 - **Started to buy drugs to sell from a distributor on Wed nights**

Using Early Drug History

TASK	MON	TU	WED	THU	FRI	SAT	SUN
SH					X		X
TX			X				
FUN						X	
NUT							
PEX							

Behavioral Safety Plan

- CT: *“Last night I had a dream that I was getting ready to use-it was all on the table in front of me. It was like five minutes before I knew it was a dream.”*
- TH: *“Congratulations on not using, tell the group what you did to deal with the craving.”*
- CT: *“ I went into the kitchen and wrote in my journal everything that happened. Then I said a prayer.”*

Behavioral Safety Plan

- TH: *What else could you have done?*
- CT: *“I know that I can always call my sponsor or my lover. I can also read from a book that I have on recovery or a book of affirmations that I like.”*
- TH: *“That’s great. Now let’s make a safety plan from what you have discovered.”*

Behavioral Safety Plan On 3x5 Index Card

MY PERSONAL SAFETY PLAN

- Remember that craving go away
- I can write in my journal
- I can call my sponsor (299-289-5555)
- I can call my lover (299-426-1776)
- I can read from my favorite recovery book
- I can read affirmations

Behavioral Safety Plan On 3x5 Index Card

- ▣ TH: *“On the back of the index card, come up with a saying or a prayer that gives you comfort and strength.”*
- ▣ CT: *“I have always liked ‘Lord help me to be the best possible person I can be today.’”*

TREATING CANNABIS ADDICTION

- The following three interventions can be utilized singularly or in combination:
 - *MOTIVATIONAL ENHANCEMENT THERAPY (MET)*
 - *COGNITIVE-BEHAVIORAL THERAPY (CBT)*
 - *ABSTINENCE-BASED CONTINGENCY MANAGEMENT (CM)*

TREATING CANNABIS ADDICTION

- In an adult population overall effectiveness of these therapies is difficult to summarize across studies.
- Approximately...
 - *5-10% of patients are abstinent at six month following treatment with MET*
 - *15-25% with CBT or MET/CBT*
 - *25-45% with CBT/MET/CM*

TREATING CANNABIS ADDICTION

- The largest clinical trial for CUD evaluated five manualized, empirically-based outpatient treatments for teens (Dennis M et al, *J Subst Abuse Treat* 2004; 27: 197-213)
 - *MET/CBT5* (two individual and three groups)
 - *MET/CBT12* (two individual and ten groups)
 - *MET/CBT12 plus family support network* (six parent education sessions, four home visits and case management)
 - *Community Reinforcement Approach* (10 individual and four parent sessions)
 - *Multidimensional Family Therapy* (six individual, three parent sessions and six with both patient and family)

TREATING CANNABIS ADDICTION

- Dennis M et al, *J Subst Abuse Treat* 2004; 27: 197-213 (continued)
 - *Significant decreases in cannabis use and symptoms of dependence were observed across treatments*
 - *No between-treatment differences were clearly observed*
 - *Nearly two-thirds of teens continued to report significant problems*

TREATMENT MANUALS

- **ADOLESCENT (Cannabis Youth Treatment Series-CYT, SAMHSA, <http://store.samhsa.gov/list/series?name=Cannabis-Youth-Treatment-Series-CYT>)**
 - Motivational Enhancement Therapy (MET) and Cognitive Behavioral Therapy (CBT)*
 - <http://bit.ly/17KJYwG>
 - Contingency Management (CM)
 - <http://bit.ly/12RPuKp>
 - Brief Strategic Family Therapy*
 - <http://bit.ly/18IiFaP>
 - Multidimensional Family Therapy*
 - <http://bit.ly/13l0tLp>

*=Free

TREATMENT MANUALS

- ADULT
 - Motivational Enhancement Therapy (MET) and Cognitive Behavioral Therapy (CBT)*
 - <http://1.usa.gov/1181MDe>
 - Contingency Management (CM)
 - <http://bit.ly/12RPuKp>

TREATMENT-MET

- In the addictions field, the search for critical conditions that are necessary and sufficient to induce change has led to the identification of six critical elements (Miller & Rollnick, 1991):
 - Feedback regarding personal risk or impairment
 - Emphasis on personal responsibility for change
 - Clear advice to change
 - A menu of alternative change options
 - Therapist empathy
 - Facilitation of client self-efficacy or optimism.

TREATMENT-MET

The MET approach is further grounded in research on processes of change. Prochaska and DiClemente (1984) describe five stages of change that people progress through in modifying problem behaviors (the stages of precontemplation, contemplation, determination, action, and maintenance). The MET approach assists clients in moving through the stages toward action and maintenance.

TREATMENT-CBT

Cognitive behavioral therapy (CBT) is designed to remediate deficits in skills for coping with antecedents to marijuana use. Individuals who rely primarily on marijuana (or other substances) to cope have little choice but to resort to substance use when the need to cope arises. The goal of this intervention is to provide some basic alternative skills to cope with situations that might otherwise lead to substance use. Skill deficits are viewed as central to the relapse process; therefore, the major focus of the CBT groups will be on the development and rehearsal of skills.

TREATMENT-CBT

The focus of CBT treatment is on teaching and practicing overt behaviors, while attempting to keep cognitive demands on clients to a minimum. Repetition is essential to the learning process in order to develop proficiency and to ensure that newly acquired behaviors will be available when needed. Therefore, behavioral rehearsal will be emphasized, using varied, realistic case examples to enhance generalization to real life settings. During the rehearsal periods, clients are asked to identify cues that signal high-risk situations, indicating their recognition of when to employ newly learned coping skills

TREATMENT-CM

Research has demonstrated the effectiveness of treatment approaches using contingency management (CM) principles, which involve giving patients tangible rewards to reinforce positive behaviors such as abstinence. Studies conducted in both methadone programs and psychosocial counseling treatment programs demonstrate that incentive-based interventions are highly effective in increasing treatment retention and promoting abstinence from drugs.

TREATMENT-CM

- **To Reduce Unwanted Behavior**
 - Present something undesirable (additional chores)
 - “Positive Punishment”
 - Keep something desirable (restrict access to video games)
 - “Negative Punishment”
- **To Increase Desired Behavior**
 - Provide something desirable (borrow the car)
 - “Positive Reinforcement”
 - Remove or reduce aversive conditions
 - “Negative Reinforcement”

PARENTAL MONITORING

- Parental monitoring (when the parents know where their children are, who they are with, and what they are doing) has been seen as attenuating a number of negative adolescent behaviors, including gambling, sexual activity, and drug use
- Strong, reliable link between parental monitoring and decreased marijuana usage in adolescents. In addition, the strongest effects were seen in the female-only studies

Association for Psychological Science (2009, November 17). The straight dope: Studies link parental monitoring with decreased teen marijuana usage.

**DO YOU FIND THAT YOUR FRIENDS ARE
DETERMINED BY YOUR MARIJUANA USE?**

DO YOU SMOKE WEED TO AVOID DEALING WITH YOUR FEELINGS?

DO YOU SMOKE WEED TO COPE WITH YOUR FEELINGS?

DOES WEED USE LET YOU LIVE IN A PRIVATELY DEFINED WORLD?

**HAVE YOU EVER FAILED TO KEEP PROMISES YOU HAVE MADE ABOUT
CUTTING DOWN OR CONTROLLING YOUR DOPE SMOKING?**

HAS YOUR USE OF MARIJUANA CAUSED PROBLEMS WITH MEMORY, CONCENTRATION OR MOTIVATION?

**WHEN YOUR STASH IS NEARLY EMPTY, DO YOU EVER FEEL ANXIOUS
OR WORRIED ABOUT HOW ARE YOU GOING TO GET MORE?**

DO YOU PLAN YOUR LIFE AROUND MARIJUANA USE?

**HAVE FRIENDS AND RELATIVES EVER COMPLAINED
TO YOU THAT YOUR MARIJUANA USE IS
DAMAGING YOUR RELATIONSHIP
WITH THEM OR
OTHERS
?**

MEETINGS EVERYDAY
HELPLINE 07940 503438

www.marijuana-anonymous.co.uk



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