Alcoholism and the Endocannabinoid System

By Martin A. Lee

Alcoholism and various mood disorders.

According to several studies, ethanol exposure alters endocannabinoid levels in different regions of the mammalian brain. In a plenary lecture at the 2008 International Cannabinoid Research Society conference, Larry Parsons, Associate Professor at the San Diego-based Scripps Research Institute, discussed the role of endocannabinoids and ethanol in the nucleus accumbens of ethanol-exposed rats. The nucleus accumbens is a section of the brain that mediates the pleasurable effects of drugs of abuse.

In microdialysis studies of the nucleus accumbens in ethanol-exposed rats, the authors observed a corresponding rise in extracellular 2-AG levels. In other words, when a person gets a little tipsy from drinking booze, his or her 2-AG levels rise slightly; when someone gets drunk: a lot of 2-AG levels rise around the brain; and as inebriation fades, 2-AG returns to its normal baseline level. Parsons and a team of researchers also documented that heroin administration triggered a corresponding rise in anandamide (the other key endocannabinoid) that amount of the rat’s nucleus accumbens, but had no effect on 2-AG levels.

Anandamide and 2-AG both activate the all-important CB1 receptor, which is concentrated in the mammalian brain and central nervous system. The CB1 receptor is associated with reward and reactivity when stimulated by THC or synthetic cannabinoid agonists. THC also stimulates CB2 receptor signaling, but this does not relieve the acute inebriative buzz that cannabis is famous for; THC binding to CB1 does the trick.

Parsons’s findings—which were initially reported in the Journal of Neuroscience—raise intriguing questions regarding the causes of alcoholism and drug addiction. Is it possible that the pleasurable effects from alcohol consumption are partly attributable to higher levels of 2-AG and CB1 activity? Why does the endocannabinoid system kick into high gear when a person drinks booze? Do genetic mutations contribute to alcoholic proclivities and skewed endocannabinoid signaling in the brain? Ethanol is metabolized into acetaldehyde, a carcinogen and a mutagen that causes many harmful effects in vital organs. Simply put, alcohol is poison, and science has shown that the basic function of the endocannabinoid system is to defend the brain and, therefore, the cells in the nucleus accumbens during ethanol exposure.

High 2-AG levels are also triggered by stress and other traumatic brain injuries, according to a recent article in Neurotoxicology, which concluded that the endocannabinoid system plays an adverse impact on a plethora of physiological processes that are modulated by the endocannabinoid system.

The struggle between weed and wine continues to unfold in 21st century America, where the alcohol industry funds organizations that seek to mislead marijuana prohibition. Such influence peddling by Booze, Inc. is not only a threat against a recreational competitor; drug war posturing is also involved in the regulation of mood, fear, and impulsive behavior. Alcohol dependence is associated with a reduced ability or inability to adapt to chronic stress, a systemic dysfunction that becomes more pronounced during alcohol withdrawal. Alcohol dependence is linked to the down-regulation of 2-AG and CB1 brain receptors. Prolonged alcohol exposure induces deficits in the brain’s endocannabinoid signaling, which, in turn, contributes to maladaptive stress coping and a renewed desire for booze consumption in a self-destructive attempt to boost CB1 receptor activity. The vicious cycle of addiction feeds on itself.

Given that endocannabinoid signaling is implicated in the behavioral and biochemical processes underlying alcohol addiction, some scientists thought that it might be possible to treat alcoholism by blocking the CB1 receptor in order to interrupt the brain’s drug reward pathway. It was a harebrained theory that never panned out in the lab. Far from being efficacious CB1 blockers, the administration of a CB1 receptor antagonist would block the brain’s crucial neuroprotective response during alcohol poisoning. From a medical perspective, that would be malpractice.

The Buzz on Booze

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As part of the body’s “general protective network, working in conjunction with the immune system and various other physiological systems.” The human brain is a delicate organ, sturdily defended by a thick muscle and a blood-brain barrier primed to keep foreign substances from penetrating. The endocannabinoid system is a crucial component of the brain’s protective apparatus. Parsons put it this way: “Endocannabinoid buffer stress... An increase in endocannabinoid levels is protective in nature: hence the spike in 2-AG and CB1 signaling in the ventral striatum correlates with increased vulnerability to alcohol addiction and suicidal tendencies.” Writing in the Journal of Psychiatric Research, Yarahudri Vinod and colleagues proposed that pharmacological agents which “modulate the endocannabinoid system” might have therapeutic potential in the treatment of alcohol addiction and prevention of suicidal behavior.

Alcohol dependence is linked to down-regulation of 2-AG and CB1 brain receptors. Long-term alcohol abuse depletes endocannabinoid tone, and this, in turn, has an adverse impact on a plethora of physiological processes that are modulated by the endocannabinoid system. The endocannabinoid system interacts with other neurotransmitters (serotonin, dopamine, and endorphins), involved in the regulation of mood, fear, and impulsive behavior. Endocannabinoid deficiency is associated with a reduced ability or inability to adapt to chronic stress, a systemic dysfunction that becomes more pronounced during alcohol withdrawal. Alcohol dependence is linked to the down-regulation of 2-AG and CB1 brain receptors. Prolonged alcohol exposure induces deficits in the brain’s endocannabinoid signaling, which, in turn, contributes to maladaptive stress coping and a renewed desire for booze consumption in a self-destructive attempt to boost CB1 receptor activity. The vicious cycle of addiction feeds on itself.

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ACLCOHOLICS ANONYMOUS defines recovery in terms of abstinence from all illicit substances, including cannabis.

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Enhancing Endocannabinoid Tone

Researchers focusing on alcoholism are currently exploring the possibility of “enhancing endocannabinoid tone” by manipulating the enzymes that control 2-AG and anandamide metabolism. One approach relies on URB-597, an experimental drug that inhibits fatty acid amide hydrolase (FAAH), an enzyme that breaks down endocannabinoids. Forestalling the enzymatic degradation of 2-AG and anandamide raises endogenous cannabinoid levels in the brain. FAAH-inhibitors indirectly bolster CB1 receptor signaling.

Parsons’s rat-brain-microdialysis research suggests that FAAH-inhibitors, by facilitating increased CB1 activity, can reduce anxiety-like behavior associated with alcohol dependence. FAAH inhibitors have also demonstrated therapeutic benefit in animal models of other severe disorders, including neuropathic pain, neural degenerative conditions, epileptic seizures, hypertension, depression, and inflammatory bowel disease, as well as against the proliferation and migration of cancer cells, according to Stephan Petrosino and Vincenzo Di Marzo at the University of Naples.

Additional studies indicate that genetic mutations may contribute to the dysregulation of endocannabinoid signaling. The cannabinoid receptor gene, CB1, is involved in alcoholism and drug use. This same FAAH gene polymorphism, according to German researchers, is often present in patients with obesity and irritable bowel disease.

Of course, there is another way to enhance CB1 signaling and adjust enzymatic processes—one could smoke, vaporize or eat cannabis, a natural, non-toxic herb, and thereby influence gene expression. THC, as noted earlier, activates both the CB1 and CB2 receptors. And CBD, the second most prominent cannabinoid in marijuana, inhibits FAAH! What’s more, THC and CBD work best in tandem, synergistically, so to speak, along with dozens of other phytocannabinoids, terpenes and flavonoids that are found in cannabis.

Endocannabinoid deficiency?

If alcoholism is an endocannabinoid deficiency syndrome, then it makes perfect sense that people might successfully wean themselves from booze by smoking marijuana, which triggers cannabinoid receptor signaling. In 1891, Dr. J.B. Mattison, writing in the St. Louis Medical and Surgical Journal, described cannabis as a “remarkable” treatment for drug and alcohol dependence. Many references in subsequent medical literature support the use of marijuana in the treatment of drug and alcohol addiction.

There is compelling evidence that alcohol consumption diminishes among those who “self-medicate” with cannabis. A National Institute on Drug Abuse-funded investigation in Jamaica in the mid-1970s concluded that ganja smokers drank much less alcohol than non-smokers, lending credence to the notion that widespread marijuana use was the main reason for significantly lower levels of alcoholism in Jamaica than anywhere else in the Caribbean.

Other surveys have shown that a reduction in marijuana use leads to increased alcohol consumption among the stressed-out masses. After medical marijuana was legalized in California in 1996, Dr. Tod Mikuriya and several like-minded physicians successfully treated hundreds of alcoholic patients who got their lives back after switching to pot.

Parsons’ brain research implicitly validates cannabis substitution as a harm reduction strategy for treating alcoholism. But the idea of substituting marijuana for alcohol and other addictive substances is still strictly taboo in NIDA- contracted scientific laboratories, where synthetic enzyme-tweakers are favored over the “kind bud.”

FAAH-inhibitors are still years away from FDA approval. For those who are unable or disinclined to stop using psychoactive substances completely, marijuana may provide a safe and effective alternative to Alcoholics Anonymous, which emphasizes complete abstinence.

To assess the extent to which medical marijuana patients are using the herb as a replacement for alcohol and/or prescription pharmaceuticals, Amanda Reiman, a lecturer at the University of California’s School of Social Welfare in Berkeley, surveyed 350 members of the Berkeley Patients Group (BPG), a city-licensed medical marijuana dispensary. Reiman, BPG’s research director, presented her findings at the 2009 ICRS conference which was attended by a BPG activist contingent. Forty percent of respondents said they used marijuana as a substitute for alcohol.

“Smoking a thousand joints, but never open up the bottle. No one ever won the war against John Barleycorn.” —Lord Buckley

“Many references in the medical literature support the use of marijuana in the treatment of drug and alcohol addiction.” —A. Reiman

References

1. Cocaine had no measurable effect on endocannabinoid levels in the nucleus accumbens.

Fellowship of 12-Step Programs is useful to addicts and alcoholics in recovery. But those who use cannabis to reduce the craving for alcohol and/or hard drugs must practice less than rigorous honesty if they attend meetings. Some cannabis dispensaries now sponsor recovery-oriented support groups.


5. Journal of Pharmacology and Experimental Therapeutics cited in “Pot Compound Protects Against Alcohol-Induced Brain Damage,” NORML News, May 26, 2005


10. Vera Rubin and Lambros Comitas, Ganja in Jamaica, pp. 149, 155