

Marijuana Use Disorder and Addiction

Dr. Joseph E. Graas, Scientific Director
Dr. Edward Moore, Medical Director
Dr. Renee Kilmer, Medical Director

The plant called *Cannabis indica* and *Cannabis Sativa* have been known and used for at least 6000 years, however the pharmacological properties and studies have been added to our knowledge base only in the late nineteenth century. The active components of the two subspecies are generally referred to as cannabis or cannabinoids and are comprised of 60 compounds, some of them having opposing biological effects. Cannabis is the most widely used illicit drug in the world and has been associated with various mental health problems, however not everyone is affected adversely. The large number of active compounds, when separated and purified, are reduced to two compounds of interest for recreational and medicinal effects: tetrahydrocannabinol (THC) and cannabidiol (CBD). These two compounds were identified and chemically characterized in the early 1960s. In 1988, two human receptors in the cannabinoid receptor system were identified and labeled as CBR1 and CBR2. THC binds primarily to CBR1 and CBD binds to CBR2. There is some cross over in the binding and activity at the different receptors and neither one of them binds selectively.

When evaluating receptor responses to exogenous (external) or xenobiotic (foreign) compounds, there are usually endogenous (internal) compounds that have the same response at the site. As an example, the opioid compounds have activity at the mu, kappa, and delta receptors while endogenous compounds that serve the same function are the endorphins and enkephalins. Shortly after the discovery of the CBR2 receptor, two molecules were found to have agonist activity at the two cannabinoid receptors. The first anandamide (also known as arachidonylethanolamide or AEA) and the second, discovered a short time later, arachidonoylglycer-

ol (2-AG). These two neurotransmitters, and the system that produces them, is called the endocannabinoid system. They function the same way as THC and CBD, however with less efficacy. Research is ongoing to understand the endocannabinoid compounds and how these natural compounds function in the normal and abnormal human conditions.

The legal status of THC and CBD remains one of geography and authority. Many states have legalized marijuana for medicinal use and some states have legalized its use for recreational purposes. In nine states it is still illegal to possess, sell, grow, and use any part of the plant. The Federal Government Drug Enforcement Agency (DEA) has marijuana classified as a Schedule 1 drug in their classification system, which is defined as marijuana having:

1. High potential for abuse.
2. No currently accepted medical use.
3. Lack of accepted safety for use under medical supervision.

In 2018 CBD was removed from schedule 1 and placed in Schedule 5. There are two medications approved by the Food and Drug Administration (FDA) as safe and effective that are based on marijuana plant derived CBD products. THC, however, remains as a DEA Schedule 1 drug. This creates problems with the criminal justice system, commerce and individual transport across state lines and jurisdictions.

Marijuana's level of THC content has been steadily rising according to a publication by the National Institute on Drug Abuse (NIDA). "In the early 1990s, the average THC content in confiscated marijuana samples was roughly 3.8%. In 2014, it was 12.2%. The average marijuana extract contains more than 50% THC, with some samples exceeding 80%. These trends raise concerns that the consequences of marijuana use could be worse than in the past,

particularly among those who are new to marijuana use or in young people, whose brains are still developing." Smoking marijuana cigarettes delivers much more THC than in the past and with "vaping" the content is clearly an option of the person putting the concentrated material in the device to achieve a higher dose. The growers are continuing to breed plants for their active content, and the chemistry of extraction and isolation yields higher purity products. These trends clearly portend problems now and in the future for recreational users.

The medical community has classified heavy marijuana users into 2 categories, Marijuana use disorder and marijuana dependency. Marijuana use disorder is defined as a person having habitual use of marijuana and cannot seem to stop. If the user attempts to stop they become irritable, have difficulties sleeping, have a decreased appetite, and experience cravings and restlessness. These symptoms tend to peak within the first week after quitting and may last up to 2 weeks. Marijuana dependency (addiction) is defined as a person who uses marijuana routinely and continually increase their use or potency for the desired effects. The danger in dependency is the brain adapts to the continuous, frequent, and elevated levels such that the endocannabinoid neurotransmitters have been reduced and/or there is a loss in sensitivity to the marijuana. The literature states that the number of marijuana users that have use disorder is an unknown number and very difficult to assess. It is only when they seek help can the severity of the marijuana use be assessed. The NIDA publication referred to studies that suggest that 9% of the marijuana using population will become dependent or addicted to the drug.

References:

1. Hall, W. and Dragenhardt, L. (2007), *Curr Opin Psychiatry* 20: 393-397.
2. NIDA. (2018, June 25). Marijuana. Retrieved from <https://www.drugabuse.gov/publications/research-reports/marijuana> on 2019, June 19
3. Atakan, Z., (2012), *Ther Adv Psychopharmacol*, 2(6) 241-254