

Marijuana and its effects in Brain

Abstract: *Cannabis sativa* (hemp) plant is the source of cannabis-based products which comes from any part of the plant such as seeds, stems and flowering tops. The products of this plant are used for recreational purpose. It can also be used to sooth the pain and other medical conditions. Not all products of this plant is mind altering but some of them posses the psychotic effect. The active ingredient of the plant is called as cannabinoids. Almost 120 active chemicals are present in cannabis. According to the scientific reports these cannabis can be used to chronic pain in adults, nausea and vomiting resulting from chemotherapy treatment, some symptoms of multiple sclerosis (MS).These cannabis can be ingested in various forms such as smoking, taking it as supplements, topical treatment, eating either raw or with candies, can be added in tea as a brew. This chapter will address the effect of these cannabis in human brain and its mechanisms of action.

Keywords: cannabinoids, Cannabenoid receptors, dopaminergic neuron, endocannabinoids, Δ 9-tetrahydrocannabinol (THC)

INTRODUCTION

From the plant *Cannabis sativa*, Marijuana is synthesized, especially from a shredded, green-brown mix of dried flowers, stems, and leaves. It is the most addictive drug apart from alcohol and tobacco. Marijuana is used as hand rolled cigarettes or in pipes or water pipes. Marijuana use is higher in younger people. More than 11.8 million young adults have abused marijuana in 2018. Delta-9-tetrahydrocannabinol (THC) is a cannabinoid molecule in marijuana from *Cannabis sativa* (hemp) plant. In rats exposed to THC from gestational day 15 to postnatal day 9, with THC at a daily dose (5 *per os*) has caused subtle neurofunctional deficits (Campolongo et al., 2007). THC, can also affect the rodent ontogeny process, especially on dopaminergic neuron development and enkephalinergic neuron. Cannabinoid receptors (CB1) are seen during prenatal development and there are higher chances of these receptors to be transferred from mother to the offspring through placenta in both human and rodents (Dalterio, 1986). Young pregnant women tend to abuse this drug, in western culture. In 2014, approximately 183 million people used marijuana and in 2016, 22 million people abused cannabis (United Nations Office on Drugs and Crime. World drug report.2015.; The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016).

Animal studies

During active brain development, cannabinoid receptors are expressed in high level in areas such as hippocampus, amygdala, and prefrontal cortex (PFC). The age of exposure to cannabis affects the prenatal, perinatal and adolescent periods of life (Hurd *et al.*, 2019). In rats, THC pretreated animals has shown worse performance with a defect in spatial working memory when tested in radial arm maze (Rubino *et al.*, 2009). This clearly indicates that in

experimental models, adolescent chronic exposure in rats to THC has serious impact on learning and memory. In adolescent rats exposed to THC, it caused defects in synaptic plasticity in hippocampus (Le et al., 2022). Endocannabinoid system is a neuromodulatory network in brain plays a major role in cognitive and physiological process. Heavy marijuana use alters the brain tissue analysed by Voxel-based morphometry (Matochik et al., 2005).

Δ^9 -tetrahydrocannabinol is the primary chemical binds with cannabinoid receptors. Anandamide (N-arachidonylethanolamine) and 2-arachidonoyl glycerol (2-AG) in animals are the main endocannabinoids. CB1 and CB2 receptors, mediate the binding of phyto as well as endocannabinoids. Inside the brain those areas with higher cognitive functions, motor control regions, hindbrain regions express high level of CB1 receptors (Glass et al., 1997).

Cannabis use and cognitive functions

Regular cannabis usage affects various functions of the brain such as working memory, attention, and cognitive control processing (Kim et al., 2019). Functional MRI has shown there is an interaction between recreational cannabis use and cognitive function (Sagar et al., 2018). Adult chronic cannabis users have reduced attention, cognitive control, poor memory, improper decision-making, motor performance and affective processing (Chang et al., 2006; Jager et al., 2006; Kanayama et al., 2004; Bechara et al., 2000; Nestor et al., 2009; Vaidya et al., 2012; Wesley et al., 2010; King et al., 2011; Gruber et al., 2009). A metaanalysis on CANN+ patients with CANN- has revealed several cognitive dysfunctions when tested in premorbid IQ, current IQ, verbal learning, verbal working memory, motor inhibition (Bogaty et al., 2018). CBD induces alterations in brain activity in both the healthy volunteers and people with psychiatric disorder (Batalla *et al.*, 2021).

Schizophrenia-like psychosis

The *CNRI*, *AKTI*, *DBH* and *5-HTT/SLC6A4* genes may also be involved in modulating the neurological effects of cannabis use. All these genes are also known to be linked with schizophrenia (Cosker *et al.*, 2018). ‘psychotomimetic’ effects of Δ^9 -tetrahydrocannabinol (THC)- haloperidol and their combination was investigated in a double-blind, placebo-controlled, partial three-way crossover ascending dose study in 35 healthy, male mild cannabis users. THC significantly decreased many ‘psychotomimetic’ effects of CNS (Liem-Moolenaar *et al.*, 2010). Schizophrenia-like psychosis is reported from heavy use of cannabis as per the recent findings. In a study conducted in twenty two adult males it was found that THC can induce acute psychotic reaction in psychiatrically well individuals (Morrison *et al.*, 2019). Executive function and inhibitory motor control are also affected by high potency marijuana (Ramaekers *et al.*, 2006). And MRI study has revealed that orbitofrontal gyri volume was significantly lower in marijuana users followed by orbitofrontal cortex and forceps minor innervations was higher (Filbey *et al.*, 2014)..

Alternations in neural connectivity

Apart from natural source from cannabis plant this also is produced synthetically in names such as spice, K2 or Kronic being widely misused . Although cannabis is used in various treatments still its danger can not be overlooked. Consuming delta-9-tetrahydrocannabinol (THC) has lot of effects on synaptic plasticity as a short term change and neuronal structural alternations as the long term change and it affects the endocannabinoid system Exposure to THC at the early life leads to the alternations in neural connectivity in areas such as cognition and behaviour. Marijuana use not only affects the brain but it also effects the sympathetic nervous system, that controls blood pressure, platelet activation, and electrophysiological effects. During periods of aactive neuronal development, cannabinoid receptors are highly

expressed in areas that control cognitive and behaviour. Animal studies have shown that exocannabinoids can damage the processes that control cognition and behaviour (Testai et al., 2022).

Route of entry

Marijuana is smoked and enters blood stream through lungs , if taken orally through digestive system it enters the blood. Through blood it reaches brain where it binds with cannabinoid receptors causing alterations. From childhood if it is taken then through midlife it causes neuropsychological decline (Meier et al., 2012). In adolescent period if marijuana is used it leads to long term effects on the how the neural connections are made within the brain (NIH, 2019). These changes in the neural network can impact attention, memory, and learning. THC cause “high” feeling in people. Cannabinoid hyperemesis syndrome are characterised by vomiting. Nausea and dehydration (Gali et al., 2012). The other names of cannabis are pot, weed and ganja that is the most widely used recreational drug globally. USA and Canada has legalised this drug that increasing the usage in teen population (Thomas et al., 2014; Wolff and Jouanjus, 2017).

Stroke and marijuana use

Ischemic stroke can occur in individuals who chronically use marijuana (Thanvi and Treadwell 2009). Cerebral infarct is another effects of cannabinoids noted through inhalation and combustion (Garret et al., 1977; Wolff and Jouanjus, 2017). CB-1 receptor agonist WIN 55,212-2 is a synthetic cannabis upon injection in Adult male Sprague–Dawley rats for 22 days it caused significant hippocampal morphological alternations (Lawston et al., 2000). Early cannabis exposure causes psychotic like experience in adolescents (Dennisoff et al., 2022). THC alters the inhibitory interneurons in cerebellum (Ma et al., 2009). Marijuana smoking can increase stroke , a case study who used marijuana regular end up with having

the stroke in occipital lobe , the subject is also positive for heterozygous for factor V Leiden associated with thrombosis (Marinella et al., 2001; Mateo et al., 2006). THC can impact prenatal life which is a time for normal signalling pathways and also it affects the adolescence time by altering the brain maturation. In USA marijuana use is higher and approximately 3 in 10 patients express marijunana use disorder (Hasin et al., 2015)..

Conclusion

Though marijuana is said to be harmless our understanding on its effects in brain has revealed the presence of exiting evidence on abnormal changes in brain and behaviour, so this drug must carefully be used by pregnant mothers and adolescents. Genetic variations also impact the use of cannabis , in subjects wit h Val COMT allele there was a reduced functions of working memory, verbal and visual memory . Adult chronic cannabis users have reduced attention, cognitive control, poor memory, improper decision-making, motor performance and affective processing. Cortical gene expression and neurotransmission are also affected in rats due to delta-9-tetrahydrocannabinol. Visual-attention network and cerebellar hypoactivation is also noted in marijuana users.

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