

The Harm of Cannabis in Adolescents

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<http://dx.doi.org/10.13005/bpj/1667>

(Published date: 15 June 2019)

Cannabis from the plant *Cannabis sativa* is the most widely used psychoactive substance worldwide¹. The term cannabis refers to the two commonly used preparations from the female plant *Cannabis sativa*, namely, marijuana or the dried leaves and flowering tops and the compressed cannabis resin or hashish². The United Nations Office on Drugs and Crime (UNODC) estimated that 183 million people have used the drug in 2014³. The use of cannabis is widespread among adolescents and it is estimated that 5.6% of students globally have used cannabis in the last year¹. In United States and Western countries, cannabis is the most used substance during adolescence, and in conjunction with other illicit substances and precedes their use¹. National surveys conducted in 2008 in Canada on students grades 7-9, reported 17% being trying cannabis⁴. Figures from the United States in 2013 showed that 7.5% (19.8 million) of the population over the age of 12 years have reported using the drug in the preceding month. Moreover, there has been an increase in cannabis usage since 2002 among those aged 18 years or more⁵. Data from National surveys from the European Union members, Norway and Turkey

conducted between 2012-2015 indicated that ~ 25% of those aged 15-24 years are life-time users and ~15% have used cannabis in the past year¹. Cannabis abuse is also a problem among school and University students in other countries as well such as Ireland⁶, and Egypt⁷. Gender difference exists where the use of cannabis is more prevalent among adolescent males compared with females⁸.

But what makes cannabis so popular among adolescents ? The use of cannabis by adolescents seems to be driven by a number of factors that includes (i) a decrease in the awareness of the adolescent and parents of potential health consequences and other risks from the drug; (ii) the ease of obtaining cannabis for personal use especially in some countries where there has been legalization of marijuana for medical or recreational use^{6,9}; (iii) to increase sociability and experience the euphoric and intoxicating effects¹⁰; (iv) curiosity about drug effects; (v) to cope with psychological or physical stress during work or study⁷.

Cannabis is known for its recreational uses and is usually smoked in cigarettes, mixing with tobacco, the so called “joint” and also in a

water pipe. Users report mild euphoria or feeling “high”, relaxation, and anxiety. There are also distortion of time perception and intensification of sensory experiences. These effects are caused by delta-9-tetrahydrocannabinol (D⁹-THC)² which is the major psychotropic agent in the plant¹¹ and were demonstrated in healthy humans following its intravenous administration¹². Over 120 terpenophenolic compounds similar to D⁹-THC and known as cannabinoids have been identified in *Cannabis sativa*. Most are not psychoactive and are present in very low concentrations. Examples are cannabinal and cannabidiol¹³. Cannabis also contains hundreds of other chemical constituents and the effects of smoked cannabis is thus the sum of the effect of several cannabinoids and other ingredients in herbal cannabis¹⁴ (Russo and McPartland 2003). Some cannabinoids exert synergistic effects whilst others are even antagonistic to the D⁹-THC effects [15]. The effect of the whole plant is thus likely to differ from that of only D⁹-THC. It has been shown that D⁹-THC (and other cannabinoids) exerts its effects by acting on two types of G-protein-coupled cannabinoid (CB) receptors, with CB1 receptors being expressed mainly in brain, and spinal cord and CB2 receptors present mainly on immune cells. In the brain, CB1 receptors are found in high density on neuronal terminals in areas associated with cognition, emotions, cognition, memory, appetite, and movement such as the cortex, limbic system, hippocampus, cerebellum, and basal ganglia¹⁶.

But is cannabis is an innocent drug?. Scientific evidence indicates that this is not the case, especially during adolescence where the brain is still in the maturation process. Results from animal experiments showed that heavy cannabis consumption during adolescence appear to induce subtle changes in brain circuits with the result of altered emotional behavior, and sensitivity towards rewarding stimuli with an increase in the likelihood for the use of more serious illicit and addictive substances¹⁷. Brain imaging studies suggested that heavy usage of cannabis is associated with structural brain changes such as thinning of cortices in temporal and frontal regions¹⁸ and reduced volumes of orbitofrontal gyri¹⁹. The impact of adolescence use of cannabis is maintained into later life. Older adults with a history of early life use of

cannabis showed reduced hippocampus thickness²⁰. Studies in healthy volunteers showed that oral D⁹-THC impairs both episodic memory and learning with the effect being a dose-dependent one²¹. Users of cannabis exhibit memory problems eg., altered neuronal functioning during visuospatial working memory²². In those who started using cannabis at an early age and continued into later adulthood, there were evidence of neurophysiological decline and cognitive problems with these effects being dependent on cannabis dosage²³. The most disastrous consequence of cannabis in adolescence is undoubtedly the risk of developing psychotic events later in life. There is an increasingly accumulating evidence which suggests a link between the use of cannabis and schizophrenia²⁴. Using cannabis was also associated with an earlier age at the first psychotic event²⁵. This psychotic potential of cannabis has been shown in healthy subjects with no prior history of exposure to cannabis. These individuals developed transient schizophrenic-like symptoms when intravenously dosed with D⁹-THC (12. Transient psychotic symptoms eg., depersonalization, and paranoid feelings could also be induced in healthy subjects following oral ingestion of synthetic D⁹-THC or THC decoction²⁶.

Results from animal studies have shown that cannabis or D⁹-THC is toxic to neurons²⁷. Cannabis is thus a major health problem, especially among adolescents, a period which is marked by rapid increase of the mental and physical capabilities of the individual and where the brain is vulnerable to the cannabis effects. This is because: (i) adolescence represents a critical period for brain development (neuronal maturation, myelination, synaptic pruning, dendritic plasticity, volumetric growth etc...) ²⁸; (ii) there is an increase in social behavior and also “reckless” behavior and in risk and sensation seeking and consequently drug abuse^{29,30}. The use of cannabis in adolescents is associated with poor physical health status³¹, poor performance at school, decreased academic achievement and an increase in the likelihood for dropout³². Moreover, cannabis is a likely “gateway” for other addictive substances³³.

Measures should therefore be taken to discourage the use of cannabis during adolescence. There is a need for educating both the adolescent and the family better understanding of the potential risks of cannabis. Smoking cigarettes including the

e-cigarettes has been identified as a confounding factor in cannabis usage³³, thereby, necessitating taking measures to reduce smoking in schools. More oriented research into the field of cannabis will help delineate the biological targets, and effects of herbal cannabis on brain structure and functioning and the pathways by which cannabis affect the maturing brain.

REFERENCES

- World Drug Report 2018 (United Nations publication, Sales No. E.18.XI.9).
- Huestis MA. Cannabis (Marijuana)—effects on human behavior and performance. *Forensic Sci Rev*; **14**:15 (2002).
- Market analysis of plant-based drugs—Opiates, cocaine, cannabis. United Nations Office on Drugs and Crime, World Drug Report. United Nations publication, Sales No. E.17.XI.9, Vienna, Austria, p. 37-45 (2017).
- Hammond D, Ahmed R, Yang WS, Brukhalter R, Leatherdale S. Illicit substance use among Canadian youth: trends between 2002 and 2008. *Can J Public Health.*; **102**(1):7-12 (2011).
- Azofeifa A, Mattson ME, Schauer G, McAfee T, Grant A, Lyerla R. National Estimates of Marijuana Use and Related Indicators - National Survey on Drug Use and Health, United States, 2002-2014. *MMWR Surveill Summ.*; **65**(11):1-28 (2016).
- Hope A, Dring C, Dring J. College lifestyle and attitudinal national (CLAN) survey. Dublin: Health Promotion Unit, (2005).
- Abdel-Salam OME, Galal AF, Elshebiny SA, Gaafar AEDM. International Aspects of Cannabis Use and Misuse: Egypt. In: Handbook of Cannabis and Related Pathologies: Biology, Pharmacology, Diagnosis, and Treatment, 1st Edition. Editors: Victor Preedy. Academic Press, Elsevier Science Publishing Co Inc..pp. 505-516 (2017).
- Ter Bogt TF, de Looze M, Molcho M, Godeau E, Hublet A, Kokkevi A, Kuntsche E, Nic Gabhainn S, Frelenc IP, Simons-Morton B, Sznitman S, Vieno A, Vollebergh W, Pickett W. Do societal wealth, family affluence and gender account for trends in adolescent cannabis use? A 30 country cross-national study. *Addiction*; **109**(2):273-83 (2014).
- Wadsworth E, Hammond D. International differences in patterns of cannabis use among youth: Prevalence, perceptions of harm, and driving under the influence in Canada, England & United States. *Addict Behav*; **90**:171-175 (2019).
- Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. *Lancet*; **374**: 1383–91 (2009).
- Mechoulam R, Gaoni Y. The absolute configuration of delta-1-tetrahydrocannabinol, the major active constituent of hashish. *Tetrahedron Lett*; **12**:1109-11 (19670).
- D'Souza DC, Perry E, MacDougall L, Ammerman Y, Cooper T, Wu YT, Braley G, Gueorguieva R, Krystal JH. The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis. *Neuropsychopharmacology*; **29**(8):1558-72 (2004).
- ElShohly MA. Chemical constituents of cannabis. In: Grotenhermen F, Russo E, editors. Cannabis and cannabinoids. Pharmacology, toxicology and therapeutic potential. New York: Haworth Press Inc; 2002, p. 27-36.
- Russo EB, McPartland JM. Cannabis is more than simply D9-tetrahydrocannabinol. *Psycho pharmacology*; **165**: 431–432 (2003)
- Pertwee RG. The diverse CB1 and CB2 receptor pharmacology of three plant cannabinoids: delta9-tetrahydrocannabinol, cannabidiol and delta9-tetrahydrocannabivarin. *Br J Pharmacol*; **153**(2): 199-215 (2008).
- Svíženská I, Dubový P, Šulcová A. Cannabinoid receptors 1 and 2 (CB1 and CB2), their distribution, ligands and functional involvement in nervous system structures —A short review. *Pharmacol Biochem Behav*; **90**(4):501-11 (2008).
- Rubino T, Vigano' D, Realini N, Guidali C, Braida D, Capurro V, Castiglioni C, Cherubino F, Romualdi P, Candeletti S, Sala M, Parolaro D. Chronic D9-tetrahydrocannabinol during adolescence provokes sex-dependent changes in the emotional profile in adult rats: behavioral and biochemical correlates. *Neuropsychopharmacology*; **33**: 2760–2771 (2008).
- Jacobus J, Squeglia LM, Sorg SF, Nguyen-Louie TT, Tapert SF. Cortical thickness and neurocognition in adolescent marijuana and alcohol users following 28 days of monitored abstinence. *J Stud Alcohol Drugs*; **75**(5): 729-43 (2014).
- Filbeya FM, Aslana S, Calhoun VD, Spence JS, Damarajuc E, Caprihanc A, Segallc J. Long-term effects of marijuana use on the brain. *Proc Natl Acad Sci U S A.*, **111**(47): 16913–16918 (2014).
- Burggren AC, Siddarth P, Mahmood Z, London ED, Harrison TM, Merrill DA, Small GW, Bookheimer SY. Subregional hippocampal thickness abnormalities in older adults with a history of heavy cannabis use. *Cannabis and*

- Cannabinoid Research* **208**; 3.1: (2018).
21. Curran HV, Brignell C, Fletcher S, Middleton P, Henry J. Cognitive and subjective dose-response effects of acute oral D9-tetrahydrocannabinol (THC) in infrequent cannabis users. *Psychopharmacology*; **164**: 61–70 (2002).
 22. Smith AM, Longo CA, Fried PA, Hogan MJ, Cameron I. Effects of marijuana on visuospatial working memory: an fMRI study in young adults. *Psychopharmacology*; **210**:429–438 (2010).
 23. Meier MH, Caspi A, Ambler A, Harrington H, Houts R, Keefe RSE, McDonald K, Ward A, Poulton R, Moffitt TE. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci U S A.*, **109**(40): E2657-E2664 (2012).
 24. Mulè A, Sideli L, Colli G, Ferraro L, La Cascia C, Sartorio C, Seminerio F, Tripoli G, Di Forti M, La Barbera D, Murray R. Cannabis consumption and the risk of psychosis. *Evidence-based Psychiatric Care*; **3**:25-31 (2017).
 25. Barnes TR, Mutsatsa SH, Hutton SB, Watt HC, Joyce EM. Comorbid substance use and age at onset of schizophrenia. *Br J Psychiatry*.; **188**:237-42 (2006).
 26. Favrat B, Ménétrey A, Augsburger M, Rothuizen LE, Appenzeller M, Buclin T, Pin M, Mangin P, Giroud C. Two cases of “cannabis acute psychosis” following the administration of oral cannabis. *BMC Psychiatry*, **5**:17 (2005).
 27. Abdel-Salam OME, Youness ER, Shaffee N. Biochemical, immunological, DNA and histopathological changes caused by Cannabis Sativa in the rat. *J Neurol Epidemiol*; **2**: 6-16 (2014).
 28. Malone DT, Hill MN, Rubino T. Adolescent cannabis use and psychosis: epidemiology and neurodevelopmental models. *Br J Pharmacol*; **160**(3): 511–522 (2010).
 29. Spear LP. The adolescent brain and age-related behavioral manifestations. *Neuroscience and Biobehavioral Reviews*; **24**: 417–463 (2000).
 30. Dahl RE. Adolescent brain development: a period of vulnerabilities and opportunities. Keynote address. *Ann N Y Acad Sci*; **1021**: 1–22 (2004).
 31. Herbeck DM, Brecht ML, Lovinger K, Raihan A, Christou D, Sheaff P. Poly-drug and marijuana use among adults who primarily used methamphetamine. *J Psychoactive Drugs*. **45**(2):132-40 (2013).
 32. Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. *N Engl J Med*; **370**:2219–27 (2014).
 33. De Luca MA, Di Chiara G, Cadoni C, Lecca D, Orsolini L, Papanti D, Corkery J, Schifano F. Cannabis; epidemiological, neurobiological and psychopathological issues: an update. *CNS Neurol Disord Drug Targets.*; **16**(5):598-609 (2017).
 34. Martínez C, Baena A, Castellano Y, Fu M, Margalef M, Tigova O, Feliu A, Laroussy K, Galimany J, Puig M, Bueno A, López A, Fernández E. Prevalence and determinants of tobacco, e-cigarettes, and cannabis use among nursing students: A multicenter cross-sectional study. *Nurse Educ Today.*; **74**:61-68 (2019).