
Conference Paper

Controversies on the Repercussions of Cannabis Use on Mental Health: Critical Clarifications

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Abstract: Background. It is scientifically undeniable that there is a relationship between cannabis use, psychoses of different types and other mental disorders. Frequent use of cannabis as well as high potency synthetic cannabis has special clinical significance for public health. Method. A review of the best and most current specialized literature published in order to clarify possible controversies that still persist. The aim is to resolve certain doubts so that scientifically supported criteria on the risks and dangers of cannabis use for mental health can be issued without any prejudices. Result. Cannabis is the most used illegal drug in the US and worldwide over the past year. Some authors hypothesize about interaction bias and confounding that could annul the internal validity of many studies reporting on the dangers of cannabis for mental health. They also emphasize that cannabis use should not be criminalized. This is, however, a merely speculative or unrealistic hope that disregards the wealth of scientific data that reject the authors' aspiration according to the available evidence consulted. Conclusion. The most qualified scientific journals, in line with the main professional institutions, have been rigorously and accurately informing their readers -and must continue doing it- of the dangers and harm caused by substance use, including cannabis. In short, the issue is to try to decrease the incidence of the related mental disorders which are sufficiently acknowledged. Mental health professionals cannot and must not be neutral or ambiguous regarding cannabis use, its collective spreading and the health risks that it entails.

Keywords: Cannabis, Psychiatry, Clinical Psychology, Mental Disorder, Legalization

1. Current State of the Matter

The relationship or link between the use of cannabis, different types of psychoses and other mental disorders is undeniable. High potency cannabis has a particular clinical significance for public health [1], as is generally the case with synthetically produced cannabinoids [2], as well as with their daily use [3]. Many of those cannabinoids are included in the New Psychoactive Substances (NPS). The same authors from the previous citation conjectured that one in every five cases of psychosis may be related to daily use of cannabis. Likewise, it has been estimated that the first psychotic episodes in cannabis users occurred approximately six years from when the use of cannabis became regular [4]. Even though the causal link cannabis-psychosis has not been firmly established,

this is the direction that all relevant investigations are headed [5, 6]. This direction was established, in a very convincing way, after the study of 26 systematic revisions and meta-analysis published until 2016 [7]. On the other hand, clinical reports on the pharmacological interactions related to cannabis, its kinetics and the adverse events are becoming increasingly frequent [8].

Additionally, there is the hypothesis, endorsed by a very recent study by Manza et al. (2019) [9], that there may be a deterioration of the separation between cognitive and emotional processes in cannabis-dependency, which may contribute to a deficient cognitive control in conditions of high emotional demand. As was already known and has been recently confirmed, regular use of cannabis produces volumetric structural changes in gray and white matter of the brain, particularly in the hippocampus and the amygdala [10,

11]. Therefore, all evidence available to this date fully justifies the implementation of preventive and damage reduction strategies. Aside from the link cannabis-psychosis, there likely is also a relation between cannabis and mood disorders, also known as affective disorders [12].

2. Effects of Cannabis Use

The favorable effects of cannabis for epilepsy, multiple sclerosis and chronic pain has been relatively backed up by evidence [13, 14]. The so-called medical cannabis may be pharmacologically helpful for pain treated with opioids, according to the Canadian Medical Cannabis –Opioid Reduction Program–MCORP– [15], although these conclusions must be properly corroborated. But the supposed –and desired by many– benefits of cannabis use for mental or physical health in general are still, after many decades, object of a continuous and apparently never-ending worldwide discussion due to conflicting opinions [13, 16]. That is a trend that arises, in a way, due to the desire to medicate ordinary human conditions. See regarding this: Alvarez-Roldán et al. (2018) [17], and Fernández-Artamendi (2018) [18], to mention some of the work by Spanish authors, as well as Borodovsky and Budney (2018) [19], among many other authors.

It should be noted, as an exception, the favorable effects of cannabidiol –CBD– on patients suffering from early psychosis and cannabis use [9, 20], assuming that cannabis use is particularly frequent among those patients. CBD, not to be confused with cannabiol –CBN–, is a phytocannabinoid found in cannabis at low concentrations in the most modern strains, and antagonizes the psychotomimetic effects produced by delta-9-tetrahydrocannabinol –THC– [21]. Even though THC is the main active ingredient in marijuana –a genetic line of hemp, also called Indian hemp, or better yet, *cannabis sativa*–, CBD is also obtained from hemp. There are also products considered as dietary supplements containing cannabidiol on the market. In all likelihood, the amount of CBD in those products does not appear correctly on their labels. CBD is responsible for the incredible increase of people using products with cannabis in the UK. Something similar occurs with cannabichromene –CBC– [22], which may contribute to the potential therapeutic efficiency of certain cannabis preparations. However, regarding most psychiatric disorders, the results of the investigations on the cannabinoid system present in all mammals is not at all conclusive, despite the vast amount of international scientific publications on this subject. More quality studies, especially follow-up studies, are needed.

It should be reminded that Bolla et al. already noted in 2002 that among cognitive abnormalities caused by severe cannabis abuse, there was a general and persistent abnormality that affected executive functions as well as memory [23]. In addition to its negative effects as a drug that is illegal in many countries, the long-term therapeutic use of cannabinoid-based medicines has a negative effect on memory [11, 24]. Similarly, it is inevitable to keep in mind the important and current scandal faced by the US regarding the damage caused by the

prescription of the opioid oxycodone hydrochloride, and in general, by the “opioid epidemic” in the US. The use of cannabis is emerging too frequently and to a too large extent as one of the several factors that interact and can negatively affect brain development and mental function [25]. In most studies, findings suggest that the start age and the frequency of cannabis use are key variables to predict a lower neuronal health [26].

3. Factors Contributing to Cannabis Use

It is unnecessary to illustrate the enormous financial interests that are unquestionably contributing to the persistent debate on the benefits and harms regarding the link cannabis-psychosis, its relation to other similar disorders, as well as the normalized use of cannabis and its derivatives. This normalization occurs regardless of whether the use of cannabis is excessive or exaggerated, industrial, recreational, medical or paramedical. The paramedical use of cannabis is common under the pretext of the mistakenly called complementary and alternative medicines, but they are not a real alternative to medicine. Likewise, social cannabis clubs are becoming fashionable and there are even Standard THC Units to guide users and promote safer use patterns [27]. In this regard and particularly for the case of minors, please refer to Piñero-Pérez et al. (2019) [28].

Regarding the above mentioned financial interests related to cannabis use, it is hardly surprising the supporting and not at all innocent nor impartial proselytism by certain organizations, such as the International Association for Cannabinoid Medicines (IACM) or the American Academy of Cannabinoid Medicine (AACM), among other organizations from different American countries. In Europe, the European Monitoring Centre for Drugs and Drug Addictions (EMCDDA) simply describes but does not analyze the cannabis use characteristics, and the European Observatory on Cannabis Use and Cultivation (OECCC in Spanish) as well as the Spanish Observatory of Medicinal Cannabis (OEDCM in Spanish), among others, advocate for legalization. So, all the observatories in favor of cannabis use are behind the publication of certain articles and the organization of conferences that are inevitably biased by opposing conflicting interests. Those observatories, in the most part, are supposed to be non-profit associations that advocate for the regulation of cannabis use –sometimes found under the names “cannabis light” or “ultralight” and the NPS concept discussed earlier–, as well as its self-cultivation and the creation of commercialization companies. In any case, none of the European Union countries that allow the medical use of cannabis products recommend smoking them.

As a matter of fact, regarding the enormous and singular dissemination of the use of cannabis, according to the estimations of the United Nations Office on Drugs and Crime –UNODC– in 2019, cannabis is the most used drug all over the world and it is estimated that 188 million of people consumed it in 2017. Particularly in Spain, cannabis is also the illegal drug which has been most often consumed recently

—9.5%; 2.1% daily—, according to the data of the Survey on Alcohol and Drugs in Spain (EDADES in Spanish) 2015-2016. Precisely, Spain is one of the countries in the world where cannabis is more consumed and an important European distributor of the drug coming mainly from Morocco. On the contrary, in some other countries such as France, cannabis production, possession, sale or purchase are forbidden even for medicinal use. In the United Kingdom, cannabis possession is penalized from 100 grams and, as is the case for the other class B drugs, the corresponding penalties are damage category 4—using their own terminology—, although an extenuating circumstance could be applied if it is amassed due to medical prescription.

4. Quality of Researches and Normative Regulations

Certain matters are sometimes considered as doubtful although they already are scientifically quite well elucidated. Currently, most of the quality scientific studies disseminated show no proof or evidence of confusion due to variables—confusion bias— or effect modification—interaction— regarding cannabis. As a matter of fact, many of those studies appear in important publications, as the relative quality indexes show such as the Journal Citation Reports—JCR— or the Scimago Journal Rank—SJR—, and others. There is no evidence that most part of the researchers did not control the aforementioned supposed confusion or did not eliminate those variables since in the event that one or both occur, the internal validity of the studies would be damaged. There is no evidence that noticeable problems between correlation and causality occur in the important published researches. So, as of today, there is no discussion about the documented harmful influence of cannabis in the emergence and clinical expression of psychosis and in the potential deterioration of other mental disorders.

On the other hand, it is commonly recognized that the sought after need of a “more suitable” normative regulation for cannabis use will undoubtedly entail psychopathological risks which are unacceptable for the specialized scientific community. This is so regardless of how much overtolerance is being exerted in certain number of countries, including the US [29], where the named laws of medicinal marijuana [30] have been proposed to be supported as a last resort, and no matter how many favorable opinions and indulgent tendencies there are in many other countries [31]. According to the National Survey on Drug Use and Health (2008-2016) conducted in the United States among 505,796 respondent participants, the risk of diseases due to marijuana use among the respondents of 12 to 17 years of age and the increase of the frequent use and of the same diseases among adults of 26 years of age or older, reveals a potential public health problem [32]. Moreover, the perceived parental condescension is especially important for cannabis use by children and adolescents [33], being childhood and adolescence more vulnerable periods to cannabis effects [10], as are pregnancy and prenatal periods [34]. In relation with this, the fact that the

hyperactivity of the serotonin receptor 2A has been identified at a molecular level for the first time signifies an important scientific milestone. This hyperactivity of the serotonin receptor 2A could be a key issue in order to explain the relationship between cannabis use in adolescence and the increase in risk for the onset of schizophrenia [35].

Regarding the best information currently available on this matter from reliable institutions which are internationally very prestigious, it is essential to refer to all that has been published about the diagnostic group for disorders related to cannabis—use, intoxication, abstinence, other disorders and no specified disorder— in DSM-5 [36] of 2013. In a general way, it recognizes the negative repercussion of cannabis use in mental health. The same occurs for ICD-10: Diagnostic Research Criteria, 1993 [37]. In Spain, the National Strategy on Addictions of the Social Welfare, Consumption and Health Ministry suggests achieving a healthier and better informed society by means of reducing drug demand and general addiction prevalence in order to reach a safer society. Mental health prevention, particularly regarding drug addiction prevention, is not aiming at criminalizing anybody in any country, in opposition to what some people seem to insinuate. On the contrary, it is an objective to inform in a disinterested, precise and objective way about the true dangers and harm of certain substance uses in order to reduce the incidence of mental disorders related to them.

5. Conclusions

In order to conclude this study, it is completely reasonable to consider that doctors, especially psychiatrists, and also psychologists, particularly those specialized in clinical psychology, cannot and must not be neutral or ambiguous regarding cannabis use, its collective spreading and, particularly, the health risks that it entails. That is so because both doctors and psychologists are scientists trained to conduct independent research and are socially very well valued. In an up-to-date epidemiological study carried out in the Spanish city of Granada, Cervilla et al. (2018) [38] recently brought to light that the mental disorders found in their research correlated with cannabis use among other factors. So, the proposals quite often made about liberalizing cannabis use with few or no restrictions are in fact speculative or chimerical suggestions that disregard and underestimate the host of scientific data that reject them.

Conflict of Interest

The author reported no conflicts of interest.

References

- [1] Freeman TP, van der Pol P, Kuijpers W, Wisselink J, Das RK, Rigtter S, et al. Changes in cannabis potency and first-time admissions to drug treatment: a 16-year study in the Netherlands. *Psychological Medicine* 2018; 48 (14): 2346–52. doi: 10.1017/S0033291717003877.

- [2] Cohen K, Weinstein AM. Synthetic and non-synthetic cannabinoid drugs and their adverse effects - a review from public health prospective. *Frontiers in Public Health* 2018; 6: 162. doi: 10.3389/fpubh.2018.00162.
- [3] Di Forti M, Quattrone D, Freeman T, Tripoli G, Gayer-Anderson C, Quigley H, et al. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): A multicentre case-control study. *The Lancet Psychiatry* 2019; 6 (5): 427–36. doi: 10.1016/S2215-0366 (19) 30048-3.
- [4] Myles H, Myles N, Large M. Cannabis use in first episode psychosis: Meta-analysis of prevalence, and the time course of initiation and continued use. *Australian and New Zealand Journal of Psychiatry* 2016; 50 (3): 208–19. doi: 10.1177/0004867415599846.
- [5] Gage SH, Hickman M, Zammit S. Association between cannabis and psychosis: Epidemiologic evidence. *Biological Psychiatry* 2016; 79 (7): 549–56. doi: 10.1016/j.biopsych.2015.08.001.
- [6] Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E. Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophrenia Bulletin* 2016; 42 (5): 1262–9. doi: 10.1093/schbul/sbw003.
- [7] Hasan A, von Keller R, Friemel CM, Hall W, Schneider M, Koethe D, et al. Cannabis use and psychosis: A review of reviews. *European Archives of Psychiatry and Clinical Neuroscience* 2019. [Epub ahead of print] doi: 10.1007/s00406-019-01068-z.
- [8] Foster BC, Abramovici H, Harris CS. Cannabis and cannabinoids: Kinetics and interactions. *The American Journal of Medicine* 2019; 132 (11): 1266–70. doi: 10.1016/j.amjmed.2019.05.017.
- [9] Manza P, Shokri-Kojori E, Volkow ND. Reduced segregation between cognitive and emotional processes in cannabis dependence. *Cerebral Cortex* 2019. [Epub ahead of print] doi: 10.1093/cercor/bhz113.
- [10] Weinstein A, Livny A, Weizman A. Brain imaging studies on the cognitive, pharmacological and neurobiological effects of cannabis in humans: Evidence from studies of adult users. *Current Pharmaceutical Design* 2016; 22 (42): 6366–79. doi: 10.2174/1381612822666160822151323.
- [11] Blest-Hopley G, O'Neill A, Wilson R, Giampietro V, Lythgoe D, Egerton A, et al. Adolescent-onset heavy cannabis use associated with significantly reduced glial but not neuronal markers and glutamate levels in the hippocampus. *Addiction Biology* 2019; e12827. doi: 10.1111/adb.12827.
- [12] Bertolín-Guillén JM, López-Arquero FJ, Martínez-Franco L. Cannabis-induced mania? *Journal of Substance Use* 2008; 13 (2): 139–41. doi: 10.1080/14659890701374661.
- [13] National Academies of Sciences, Engineering, and Medicine. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research. Washington (DC): National Academies Press, 2017. Available in <https://www.doi.org/10.17226/24625>.
- [14] Sánchez-Nácher N. Cannabis y dolor. ¿Podremos ver el bosque tras los árboles? [Cannabis and pain. Will we be able to see the wood for the trees?] *Revista Española de Drogodependencias* 2019; 44 (3): 5–12. Available in https://www.aesed.com/upload/files/Editorial_Noemi.pdf.
- [15] Rod K. A pilot study of a medical cannabis - opioid reduction program. *American Journal of Psychiatry and Neuroscience* 2019; 7 (3): 74–7. doi: 10.11648/j.ajpn.20190703.14.
- [16] Pacula RL, Smart R. Medical marijuana and marijuana legalization. *Annual Review of Clinical Psychology* 2017; 13: 397–419. doi: 10.1146/annurev-clinpsy-032816-045128.
- [17] Alvarez-Roldán A, Gamella JF, Parra I. La legalización del cannabis: un experimento americano de consecuencias globales. [The legalization of cannabis: An American experiment with global consequences.] *Revista Española de Drogodependencias* 2018; 43 (4): 22–38. Available in <https://www.aesed.com/upload/files/v43n4-1-cannabis-r.pdf>.
- [18] Fernández-Artamendi S. Deshojando la marihuana: cannabis, cannabinoides y salud mental. [Deciphering marijuana: Cannabis, cannabinoids and mental health.] *Revista Española de Drogodependencias* 2018; 43 (3): 5–12. Available in <https://www.aesed.com/upload/files/v43n3-editorial.pdf>.
- [19] Borodovsky JT, Budney AJ. Cannabis regulatory science: Risk-benefit considerations for mental disorders. *International Review of Psychiatry* 2018; 30 (3): 183–202. doi: 10.1080/09540261.2018.1454406.
- [20] Hahn B. The potential of cannabidiol treatment for cannabis users with recent-onset psychosis. *Schizophrenia Bulletin* 2018; 44 (1): 46–53. doi: 10.1093/schbul/sbx105.
- [21] Elsaid S, Kloiber S, Le Foll B. Effects of cannabidiol (CBD) in neuropsychiatric disorders: A review of pre-clinical and clinical findings. *Progress in Molecular Biology and Translational Science* 2019; 167: 25–75. doi: 10.1016/bs.pmbts.2019.06.005.
- [22] Udoh M, Santiago M, Devenish S, McGregor IS, Connor M. Cannabichromene is a cannabinoid CB2 receptor agonist. *British Journal of Pharmacology* 2019. doi: 10.1111/bph.14815 - Available in <https://www.biorxiv.org/content/biorxiv/early/2018/11/27/435057.full.pdf>.
- [23] Bolla KI, Brown K, Eldreth D, Tate K, Cadet JL. Dose-related neurocognitive effects of marijuana use. *Neurology* 2002; 59 (9): 1337–43. doi: 10.1212/01.wnl.0000031422.66442.49.
- [24] Mouro FM, Ribeiro JA, Sebastião AM, Dawson N. Chronic, intermittent treatment with a cannabinoid receptor agonist impairs recognition memory and brain network functional connectivity. *Journal of Neurochemistry* 2018; 147 (1): 71–83. doi: 10.1111/jnc.14549.
- [25] Volkow ND, Swanson JM, Evins AE, DeLisi LE, Meier MH, Gonzalez R, et al. Effects of cannabis use on human behavior, including cognition, motivation, and psychosis: A review. *JAMA Psychiatry* 2016; 73 (3): 292–7. doi: 10.1001/jamapsychiatry.2015.3278.
- [26] Jacobus J, Courtney KE, Hodgdon EA, Baca R. Cannabis and the developing brain: What does the evidence say? *Birth Defects Research* 2019; 111 (17): 1302-7. doi: 10.1002/bdr2.1572.
- [27] Freeman TP, Lorenzetti V. 'Standard THC Units': Proposal to standardise dose across all cannabis products and methods of administration. *Addiction* 2019. [Epub ahead of print] doi: 10.1111/add.14842.

- [28] Piñeiro-Pérez R, Núñez-Cuadros E, Rodríguez-Marrodan B, García-Cabrera L, Manzano-Blanco S, Escrig-Fernández R, et al. Posicionamiento del Comité de Medicamentos de la Asociación Española de Pediatría en relación con el uso de medicinas alternativas y pseudociencias en niños. [Position statement from the Spanish Association of Paediatrics Medicines Committee concerning the use of alternative medicine and pseudo-science in children.] *Anales de Pediatría (Barcelona)* 2019; 91 (4): 272.e1–272.e5. doi: 10.1016/j.anpedi.2019.04.013.
- [29] Hall W, Lynskey M. Evaluating the public health impacts of legalizing recreational cannabis use in the United States. *Addiction* 2016; 111 (10): 1764–73. doi: 10.1111/add.13428.
- [30] Flexon JL, Stolzenberg L, D'Alessio SJ. The effect of cannabis laws on opioid use. *International Journal of Drug Policy* 2019; 74: 152–9. doi: 10.1016/j.drugpo.2019.09.013.
- [31] Crépault JF. Cannabis legalization in Canada: Reflections on public health and the governance of legal psychoactive substances. *Frontiers in Public Health* 2018; 6: 220. doi: 10.3389/fpubh.2018.00220.
- [32] Cerdá M, Mauro C, Hamilton A, Levy NS, Santaella-Tenorio J, Hasin D, et al. Association between recreational marijuana legalization in the United States and changes in marijuana use and cannabis use disorder from 2008 to 2016. *JAMA Psychiatry* 2019. [Epub ahead of print] doi: 10.1001/jamapsychiatry.2019.3254.
- [33] Becoña E, Martínez U, Calafat A, Fernández-Hermida JR, Juan M, Sumnall H, et al. Parental permissiveness, control, and affect and drug use among adolescents. *Psicothema* 2013; 25 (3): 292–8. doi: 10.7334/psicothema2012.294.
- [34] Hurd YL, Manzoni OJ, Pletnikov MV, Lee FS, Bhattacharyya S, Melis M. Cannabis and the developing brain: Insights into its long-lasting effects. *The Journal of Neuroscience* 2019; 39 (42): 8250–8. doi: 10.1523/JNEUROSCI.1165-19.2019.
- [35] Ibarra-Lecue I, Mollinedo-Gajate I, Meana JJ, Callado LF, Díez-Alarcia R, Urigüen L. Chronic cannabis promotes pro-hallucinogenic signaling of 5-HT_{2A} receptors through Akt/mTOR pathway. *Neuropsychopharmacology* 2018; 43 (10): 2028–35. doi: 10.1038/s41386-018-0076.
- [36] American Psychiatric Association. *Diagnostic and statistical manual of mental disorders: DSM-5*. Washington, DC (USA): American Psychiatric Association, 2013.
- [37] World Health Organization. *The ICD-10 classification of mental and behavioural disorders: Diagnostic criteria for research*. Geneva (Switzerland): World Health Organization, 1993.
- [38] Cervilla JA, Gutiérrez B, Rodríguez-Barranco M, Ibanez-Casas I, Pérez-García M, Valmisa E, et al. A cross-sectional study on the prevalence and risk correlates of mental disorders. The GRANADEP Study. *The Journal of Nervous and Mental Disease* 2018; 206 (9): 716–25. doi: 10.1097/NMD.0000000000000873.