

EDITORIAL

Emerging synthetic cannabinoids and the risk of psychosis: a growing concern for public health

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New psychoactive substances have emerged as a global public health concern since the mid-2000s. These substances, comprised of various chemical groups intended for abuse, aim to produce effects similar to established drugs, such as natural cannabis, cocaine, heroin, lysergic acid diethylamide (LSD), 3,4-methylenedioxy-methamphetamine (MDMA), and methamphetamine. Synthetic cannabinoid receptor agonists (SCRAs) have been identified as the most significant category of all new psychoactive substances since 2008.¹ SCRA designer drugs share chemical similarities with delta-9-tetrahydrocannabinol (Δ 9-THC), the main psychoactive phytocannabinoid in the *Cannabis* plant.

There are several hundred different SCRAs and an unknown number of products using these chemical compounds, marketed under various names, such as K2, K4, K9, or Spice. They are commonly found in “herbal” mixtures, made by soaking or spraying SCRA-based solutions onto inert plant carrier materials to be smoked. These substances can also be mixed into a liquid and vaped in electronic nicotine delivery devices (such as e-cigarettes) or presented in tablet form as a white crystalline solid or a powder intended for oral consumption or nasal insufflation. The contents of substances marketed as synthetic cannabinoids remain unknown, with varying concentrations and compositions. As a result, the use of these substances can be highly unpredictable and potentially harmful.²

The primary public health concerns linked to synthetic cannabinoid receptor agonists have to do with their potency, since their binding affinity to CB1 and CB2 receptors is considerably higher than Δ 9-THC. Indeed, SCRAs can exhibit potency several hundred-fold greater than Δ 9-THC. This heightened potency is associated with an increased risk of toxicity and potential fatalities. SCRA users are 30 times more likely to need emergency medical treatment than “natural” cannabis users.³ Synthetic cannabinoids significantly impact physiological and psychological functions, negatively affecting various physiological processes, such as the neurological,

cardiovascular, gastrointestinal, and urinary systems. Additionally, SCRAs can broadly affect an individual’s psychological state, including mood, and may contribute to suicidal thoughts and psychosis. As a result of a more substantial effect on the CB1 receptor, SCRAs lead to a more potent inhibition of GABA-mediated neurotransmission than Δ 9-THC.⁴ This overactivation of dopaminergic activity in the prefrontal cortex is thought to result in psychotic symptoms.⁵ Furthermore, the long-term use of SCRAs is associated with abnormal white matter integrity, which may be a mechanism of vulnerability to psychosis.⁶

Synthetic cannabinoid use has been documented in Brazil since 2015. Although they are used by a relatively small proportion of the population, their use has recently increased significantly, particularly in the city of São Paulo. Despite different socioeconomic and age profiles, users are primarily young men, individuals in socially vulnerable situations, and prisoners.

Substantial evidence links the use of natural cannabis to psychosis. According to a recent large-scale Danish study, heavy use of marijuana may contribute to up to 30% of psychosis diagnoses in young men.⁷ The widespread recreational use of synthetic cannabinoids in Brazil poses a significant risk for early-onset psychosis, both transient and persistent psychotic episodes, as well as the recurrence and exacerbation of preexisting psychotic disorders.

The current situation poses an imminent threat that could lead to significant national public health and security crises. Therefore, it is crucial to implement a set of measures to control both supply and demand, along with evidence-based primary and secondary health prevention strategies. Actions aimed at reducing drug availability play an essential role, since they can disrupt the production chain by identifying and controlling the commercialization of synthesis precursors. Furthermore, reducing barriers to health and social care among socially vulnerable populations is also a priority. Providing evidence-based treatment approaches for individuals who have developed psychosis or dependence on synthetic cannabinoids is

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critical to achieving positive outcomes among those who reach out to public health services. This could include a range of interventions, such as a multidisciplinary approach, medication management, and support services.

In recent years, international legislation on cannabis use has experienced a notable relaxation, resulting in a prevailing perception of low risk associated with this substance. However, this perception must not be extrapolated to synthetic cannabinoids, since they entail considerably greater risks and potential severity than natural cannabis. Hence, there is a pressing need for public awareness of the inherent risks of SCARs.

In conclusion, the escalating use of synthetic cannabinoids in Brazil is a notable public health concern, and it must be addressed with prompt and decisive measures. As scientists and healthcare providers, it is imperative for us to heighten awareness about this issue and advocate for evidence-based solutions.

Disclosure

The authors report no conflicts of interest.

References

- 1 Hobbs M, Kalk NJ, Morrison PD, Stone JM. Spicing it up - synthetic cannabinoid receptor agonists and psychosis - a systematic review. *Eur Neuropsychopharmacol.* 2018;28:1289-304.
- 2 Deng H, Verrico CD, Kosten TR, Nielsen DA. Psychosis and synthetic cannabinoids. *Psychiatry Res.* 2018;268:400-12.
- 3 Winstock A, Lynskey M, Borschmann R, Waldron J. Risk of emergency medical treatment following consumption of cannabis or synthetic cannabinoids in a large global sample. *J Psychopharmacol.* 2015;29:698-703.
- 4 Van Amsterdam J, Brunt T, van den Brink W. The adverse health effects of synthetic cannabinoids with emphasis on psychosis-like effects. *J Psychopharmacol.* 2015;29:254-63.
- 5 Bossong MG, Niesink RJ. Adolescent brain maturation, the endogenous cannabinoid system and the neurobiology of cannabis-induced schizophrenia. *Prog Neurobiol.* 2010;92:370-85.
- 6 Zorlu N, Di Biase MA, Kalaycı ÇÇ, Zalesky A, Bağcı B, Oğuz N, et al. Abnormal white matter integrity in synthetic cannabinoid users. *Eur Neuropsychopharmacol.* 2016;26:1818-25.
- 7 Hjørthøj C, Compton W, Starzer M, Nordholm D, Einstein E, Erlangsen A, et al. Association between cannabis use disorder and schizophrenia stronger in young males than in females. *Psychol Med.* 2023;1-7.