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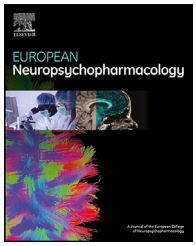

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INSIGHTS

Cannabis use and psychosis susceptibility: A call to action

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Psychosis is understood as an heterogeneous spectrum of symptoms, ranging from transient, subclinical psychotic experiences to severe and disabling phenotypes. Within this frame, the diathesis-stress model states that sub-threshold psychotic experiences can persist and become clinically relevant depending on individual environmental aspects and genetic liability. Several factors have been identified that may trigger the onset and progression of psychotic symptoms, such as childhood trauma, urban environment and substance use. Here, we focus on the latter, particularly on cannabis use disorder (CUD), as this is a highly prevalent comorbid condition, noted as an important modifiable environmental factor to be targeted in both clinical- as well as public health care.

Clinical health care: Globally, the prevalence of cannabis users, high-potency products [i.e. tetrahydrocannabinol (THC)-rich] and CUD treatment demand continue to rise, while risk perception among young people decreases (United Nations Office on Drugs and Crime, 2021). This is worrisome, as frequent cannabis use and high-potency products are associated with increased risk of psychosis and earlier age of onset, and those with psychosis susceptibility often report cannabis use (Hjorthoj et al., 2021; Lahteenvuo et al., 2021). Importantly, persistent cannabis use is known to negatively affect the course of psychosis while discontinued use has been associated with higher functioning (Schoeler et al., 2016).

Because of the high prevalence of substance use disorders (SUD) in people with psychosis susceptibility, assessment of substance use or systematic screening should be set as a standard in clinical care. Regarding cannabis assessment, and while awaiting consensus about the much-needed standardization of use, good clinical practice would include, as a minimum, assessment of the quantity, frequency and mode of administration. From all the available screening options, The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) stands out. This is a valid, comprehensive and short tool that allows simultaneous screening of tobacco, alcohol and other substance misuse. In addition, it has the great advantage to also serve as a brief intervention.

Substance-induced psychotic disorders are defined as brief psychotic syndromes, persisting for days to weeks after intoxication has resolved. Despite the wide-spread idea that this concerns a limiting condition, one-third of those initially classified as 'substance-induced' will later be diagnosed with more severe phenotypes (e.g. schizophrenia or bipolar disorder) (Murrie et al., 2020). Of note, increased liability for severe or persistent psychotic phenotypes is reported in those using cannabis, with a positive family history of psychosis and persistent psychotic symptoms after intoxication is resolved (Murrie et al., 2020).

Although the best evidence to date suggests that integrated treatment leads to the best outcomes, treatment of

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SUD is often not integrated with other mental health services.

Cognitive behavioral therapy, motivational enhancement therapy and contingency management are currently the most effective strategies for treating CUD (Connor et al., 2021). Several research-based recommendations for targeting cannabis use among young adults with psychosis susceptibility are available. First, because subjects with psychosis may be more sensitive to the positive effects of cannabis, understanding users' motivations and expectations, considering gender perspective, is important to establish a person-centered treatment approach (Arranz et al., 2020; Marino et al., 2021). Second, combining psychoeducation and psychosocial interventions, such as involvement of the family and using peers and peer support, may enhance outcomes (Connor et al., 2021; Marino et al., 2021). Third, cannabis is frequently used together with tobacco, therefore interventions addressing tobacco and cannabis simultaneously are needed in order to reduce relapse rates. Lastly, exciting innovative digital health interventions are being tested to extend the reach and improve the efficacy of current treatments (Hides et al., 2020).

To date there are no pharmacotherapies available for CUD. A new emerging avenue in this respect is targeting the endocannabinoid system, which seems to be involved in both addiction and psychosis (Batalla et al., 2020). The non-intoxicating compound cannabidiol (CBD) has shown potential for the treatment of CUD and antipsychotic properties in short-term trials, making this compound particularly suitable for those cannabis users with psychosis susceptibility. However, trials assessing the long-term effects in CUD and psychosis are still lacking, and it is unclear whether a CBD dose exists that is able to offset the harmful effects of THC. Hence, research on this topic is of uttermost importance, and will help to prevent frequent misconceptions among cannabis users. The fallacy that over-the-counter products (mostly containing low CBD doses, with low bioavailability) or any cannabis product containing CBD, regardless of THC use, might be protective or used as treatment for addiction or psychosis is particularly harmful for those with psychosis susceptibility. In this sense, experimental studies may prove useful to clarify whether there exists a 'safe' (or safer) THC/CBD ratio. This knowledge could be used for developing harm-reduction programs (e.g. medicinal cannabis) in those presenting with resistant CUD and severe or persistent psychosis phenotypes.

Public health care: Young adults consume the highest quantity of cannabis compared to other age groups and are the least likely to seek treatment for cannabis-related problems. Therefore, primary prevention and targeted interventions aimed at delaying or avoiding the onset of cannabis use are a pressing need (Maldonado and Torrens, 2020; Marino et al., 2021). Because school and work play an important role in the decision to reduce or stop using cannabis, creating employment and housing opportunities together with identity-development and resilience trainings may contribute to the cessation of drug use, as persistent use becomes incompatible with healthy life goals. In addition, targeted school-based programs offer diverse possibilities for prevention and reduction of substance use (Onrust et al., 2016). For instance, universal intervention programs could focus on enhancing self-regulating behavior for children and psychoeducation and parenting support training for their elders (Onrust et al., 2016). This education is now pressingly important because of global changes in cannabis policies, which may lead to the unjust public perception of safety.

In summary, cannabis use is a modifiable factor comprised in a complex constellation of individual genetic and environmental liability for psychosis. Discontinuation may contribute to attenuate or even prevent severe or persistent psychotic phenotypes. Therefore, detection and treatment of SUD should be set as standard procedure in those with psychosis susceptibility, with accessible and integrated psychosocial interventions as first-line treatment. In a context of rapid global changes on cannabis policies, efforts on primary prevention are a pressing need to stop the decreasing perception of risk among youth.

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