Psychotic-like experiences and cannabis use in adolescents from the general population

Experiencias psicóticas atenuadas y consumo de cannabis en adolescentes de la población general

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Abstract

The purpose of this study was to analyze the relationship between psychotic-like experiences and cannabis use in a representative sample of adolescents from the general population. A total of 1,588 students (*M*=16.13 years, *SD* = 1.36), 739 men (46.5%), selected by stratified random sampling by conglomerates from 98 classes in 34 schools participated in the survey. The instruments used were the Prodromal Questionnaire-Brief, the Strengths and Difficulties Questionnaire, the Modified Substance Use Questionnaire, the Penn Matrix Reasoning Test, the Family Affluence Scale-II, and the Oviedo Infrequency Scale. Results showed that a percentage of adolescents reported psychotic-like experiences and/or cannabis use. Prior to controlling for multiple confounders (gender, age, socio-economic level, smoking, alcohol use, emotional and behavioral problems, and IQ), cannabis use was associated with psychotic-like experiences. After adjustment for confounders, psychotic-like experiences were not seen to be associated with cannabis use. Mediational analyses showed that emotional and behavioral problems mediate the relationship between cannabis use and risk of psychosis. It seems that once the effect of multiple confounding variables is controlled for, the use of cannabis increases the risk of comorbid psychopathology and this, in turn, increases the risk of psychosis. These results suggest that the relationships established between psychotic-like experiences and cannabis are complex and mediated by relevant variables. Further studies should examine this relationship in follow-up studies and gene-environmental designs.
Keywords: Risk of psychosis; Adolescence; Cannabis; Drugs use; Psychotic-like experiences.

Resumen

El propósito de este estudio fue analizar la relación entre las experiencias psicóticas atenuadas y el consumo de cannabis en una muestra representativa de adolescentes de la población general. Un total de 1,588 estudiantes (*M*=16,13 años; *DT* = 1,36), 739 eran hombres (46,5%), pertenecientes a 34 escuelas y 98 aulas, seleccionados mediante muestreo aleatorio estratificado por conglomerados, fueron encuestados. Los instrumentos administrados fueron el Cuestionario de Pródromos de Psicosis-Breve, el Cuestionario de Capacidades y Dificultades, el Cuestionario de Consumo de Sustancias Modificado, el *Penn Matrix Reasoning Test* (PMRT), la *Family Affluence Scale*-II y la Escala Oviedo de Infrecuencia de Respuesta. Los resultados mostraron que un porcentaje de adolescentes informaron de experiencias psicóticas atenuadas y/o consumo de cannabis. Antes de controlar el efecto de múltiples covariables (género, edad, nivel socio-económico, consumo de tabaco y alcohol, problemas emocionales y CI), los jóvenes consumidores de cannabis informaron de un mayor riesgo teórico de psicosis. Cuando se controló el efecto de las covariables, las experiencias psicóticas no se asociaron con el consumo de cannabis. El análisis mediacional indicó que los problemas en el ajuste emocional y comportamental mediaban en la relación entre consumo de cannabis y experiencias psicotiformes. Parece ser que, una vez controlado el efecto de las múltiples variables de confundido, el uso de cannabis aumenta el riesgo de psicopatología comórbida y esta a su vez el riesgo de psicosis (mayor frecuencia de experiencias psicóticas). Estos resultados sugieren que la relación que se establece entre las experiencias psicóticas y el cannabis es compleja y se encuentra mediada por variables relevantes. Futuros estudios deberán examinar las interacciones Gen x Ambiente en estudios longitudinales.
Palabras clave: Riesgo de psicosis; Adolescencia; Cannabis; Consumo de drogas; Experiencias psicóticas atenuadas.

Psychotic-like experiences during adolescence can be considered a risk marker for suffering from psychotic spectrum disorders (Debbané et al., 2015; Kaymaz et al., 2012; Zammit et al., 2013) or mental health (e.g. depression) in later adult life (Fisher et al., 2013). Previous studies have also shown that such experiences are associated with the same genetic, sociodemographic, and environmental risk factors found in patients with psychosis, such as affective symptoms, trauma experiences, cannabis and alcohol use, or family history of mental disorder (Dolphin, Dooley & Fitzgerald, 2015; Fonseca-Pedrero et al., 2018; Fonseca-Pedrero & Debbané, 2017; Linscott & van Os, 2013; Strauss, Raugh, Mittal, Gibb & Coles, 2018).

Having such subclinical experiences during adolescence is a predictor with low specificity and prognostic capacity of developing mental related problems in later stages (Wallace & Linscott, 2018). Therefore, they cannot be considered a necessary or sufficient condition for the subsequent development of a psychotic disorder (or other mental disorder). Nevertheless, previous studies indicate that their persistence, associated with substance consumption, affective symptomatology or trauma, increases the subsequent risk of psychosis (Bak et al., 2005; Fonseca-Pedrero, 2018; Fusar-Poli et al., 2017; Kelleher et al., 2013; Linscott & van Os, 2013). It is therefore necessary to analyze their relationship and interaction with other factors and variables from multiple levels of analysis (e.g., genetic, brain, cognitive, behavioral) in order to improve prevention strategies and/or understand the possible etiological mechanisms underlying psychotic spectrum disorders.

One of the most widely analyzed risk factors in the field of psychosis is cannabis use. Prior studies appear to show that early cannabis use increases the risk of developing later psychosis spectrum disorders, with a dose-response relationship between level of use and the risk of psychosis (Giordano, Ohlsson, Sundquist, Sundquist & Kendler, 2015; Henquet et al., 2005; Large, Sharma, Compton, Slade & Nielssen, 2011; Marconi, Di Forti, Lewis, Murray & Vassos, 2016; Moore et al., 2007; Verdoux, Sorbara, Gindre, Swendsen & van Os, 2002). Cannabis use has been specifically associated with different expressions of the psychosis phenotype (Linscott & van Os, 2013), such as schizotypal traits (Esterberg, Goulding, McClure-Tone & Compton, 2009; Szoke et al., 2014), psychotic-like experiences (Dolphin et al., 2015; Fonseca-Pedrero, Ortuño-Sierra, Paino & Muñiz, 2016; Hides et al., 2009; MacKie, Castellanos-Ryan & Conrod, 2011), high-risk mental states (Carney, Yung, et al., 2017; Carney, Cotter, Firth, Bradshaw & Yung, 2017; Kraan et al., 2016; Valmaggia et al., 2014), schizotypal personality disorder (Davis, Compton, Wang, Levin & Blanco, 2013), and clinical psychosis (Davis et al., 2013; Stanley Zammit & Lewis, 2004).

Within the dimensional models, it is hypothesized that the relationship between cannabis use and psychosis will become apparent at both clinical and subclinical levels. More specifically, cannabis use is linked to earlier onset of the first psychotic experiences (Large et al., 2011), predicts later psychotic experiences (Jones et al., 2018), and is associated with their greater persistence (Mackie et al., 2013). In adittion, cannabis use moderately increases the risk of psychotic symptoms but has a much stronger effect in those with evidence of predisposition for psychosis or those reporting a family history of psychosis (Henquet et al., 2005; Stowkowy & Addington, 2013). Furthermore, the possible effect of substance use in individuals at risk of psychosis (e.g., those reporting psychotic experiences or subclinical symptoms) is modulated by different factors such as the age of onset, the pattern and frequency of substance use (particularly tobacco), preexisting vulnerability, gender, educational level or emotional symptomatology (Mackie et al., 2013; Mackie et al., 2011). The cannabis-psychosis links across the psychosis phenotype are, thus, complex and bidirectional, so that many people with substance abuse develop psychotic symptoms, or people with psychotic symptoms develop substance use and abuse (Degenhardt et al., 2018). Similarly, gene-environment interactions and those between different environmental risk factors (e.g., cannabis-trauma) should not be overlooked (Henquet, Di Forti, Morrison, Kuepper & Murray, 2008; Morgan et al., 2014; Nesvåg et al., 2016; Shakoor et al., 2015; Van Winkel, 2015).

The relationship between psychotic-like experiences, the risk of psychosis and the use and abuse of cannabis seems to be clear enough; nevertheless, causality between the two has not yet been definitively established and some studies still present certain methodological limitations. Indeed, previous studies have not examined the joint influence of multiple relevant variables such as age, gender, educational level, socioeconomic status, smoking or comorbid psychopathology (e.g., emotional and behavioral problems) on the relationship between cannabis use and risk of psychosis. There is ongoing debate about the possible factors that may be modifying the complex interactions taking place between the risk of psychosis and cannabis use. Applying more complex models and adequate methodology is necessary to investigate the multiple interactions that occur between variables more realistically and to draw appropriate conclusions (Fonseca-Pedrero, 2017). In Spain, such relationships have scarcely been analyzed in representative samples of young people from the general population.

Given that polydrug use is a public health problem at both national and international levels (Bousoño et al., 2017; Hernández Serrano, Font-Mayolas & Gras Pérez, 2015), and that cannabis is the most widely used illicit drug in Spain (Díaz Geada, Busto Miramontes & Caamaño Isorna, 2018; Ministerio de Sanidad Servicios Sociales e Igual-

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dad, 2016) (e.g., in 2014, 29.1% of the participants had used cannabis *at some time in their lives*), while also being associated with a low perception of risk and yet seemingly linked to an increased risk of suffering a serious mental disorder such as psychosis, it appears logical that a more detailed analysis between the extended psychosis phenotype and the use of cannabis is justified.

Within this research framework, the main objective of our study was to explore the relationship between psychotic-like experiences and cannabis use in a representative sample of Spanish adolescents. To this end, the effect of gender, age, socioeconomic level, smoking, alcohol use, and IQ was controlled for. Similarly, the possible mediating factor of comorbid psychopathology in the relationship between cannabis use and risk of psychosis was examined. In accordance with the literature, we expect to find a relationship between psychotic-like experiences and cannabis use.

Method

Participants

We applied stratified random sampling by conglomerates at the school classroom level in a population of approximately 15,000 students selected from the Autonomous Community of La Rioja and attending different schools (public and state-funded private) and vocational training centers (basic, middle and higher levels). The strata were created according to school (public/private) and the school level (lower and higher secondary school, and vocational training), where the probability that a particular class at a given school was selected was based on the number of students.

Of the initial sample of 1,881 students, those with a high score on the Oviedo Response Frequency Scale (more than 3 points) ($n = 104$) were eliminated, as were those aged over 19 ($n = 170$) and those who did not complete the test ($n = 76$). This left a total of 1,588 students, with 739 men (46.5%) and 849 (53.5%) women, from 98 classes in 34 schools participating in the study. Average age was 16.13 years ($SD = 1.36$), ranging from 14 to 19 years (14 years: $n = 213$, 15: $n = 337$, 16: $n = 400$, 17: $n = 382$, 18: $n = 180$, 19: $n = 76$).

Nationalities were distributed as follows: 89.9% Spanish, 3.7% Latin American (from Bolivia, Argentina, Colombia and Ecuador), 0.7% Portuguese, 2.4% Romanian, 1% Moroccan, 0.7% Pakistani, and 2% other nationalities.

Instruments

Prodromal Questionnaire-Brief Version (PQ-B) (Loewy, Pearson, Vinogradov, Bearden & Cannon, 2011). The PQ-B is a self-report questionnaire with 21 items assessing prodromal symptoms of positive dimension of psychosis. The item format is true/false dichotomous response. An affirmative response to an item requires the participant to

indicate the degree of concern or discomfort that it causes on a five-option Likert scale (1 = totally disagree, 5 = totally agree). In the general population, this instrument can also be used as a screening tool for the risk of psychosis (Savill, D'Ambrosio, Cannon & Loewy, 2017) or as a measure in the assessment of psychotic-like experiences. The PQ-B has demonstrated its usefulness in the assessment of attenuated psychotic symptoms in young people (Kline & Schiffman, 2014).

The PQ-B possesses adequate psychometric properties in terms of reliability (Internal consistency = 0.93), as well as an essentially one-dimensional structure in samples of Spanish adolescents (Fonseca-Pedrero, Gooding, Ortuño-Sierra & Paino, 2016).

Modified Substance Use Questionnaire. The substance use questionnaire employed in our study is an abbreviated modification of the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST v3.0) (WHO ASSIST Working Group, 2002). ASSIST is an interview used as a screening tool in the detection of drug users developed by the WHO. It consists of different items for the assessment of, among other aspects, the frequency of use of different substances (alcohol, tobacco, cannabis, cocaine, etc.) in the three months prior to the completion of the questionnaire. ASSIST has been translated into Spanish and validated (Soto-Brandt et al., 2014).

Our study used two of the ASSIST questions applied in self-report format. Item 1 asked: "In your life, which of the following substances have you ever used?" Participants respond in a dichotomous format, Yes/No, for the following substances: a) Tobacco (cigarettes, cigars, chewing tobacco, pipe, etc.); b) Alcoholic beverages (beer, wine, liqueurs, spirits, etc.); c) Cannabis (marijuana, pot, grass, hashish, etc.); and d) Other (e.g., cocaine, amphetamines, inhalants, hallucinogens, opiates, etc.). An affirmative answer to any substances in item 1 then led to item 2, which asked about the frequency of use in the previous three months.

Strengths and Difficulties Questionnaire, self-report version, (SDQ) (Goodman, 1997). This measurement instrument is used for the detection of behavioral and emotional difficulties and has also been used as a tool for screening and epidemiological analysis of mental health status in children and adolescents (Ortuño-Sierra, Fonseca-Pedrero, Paino, Sastre i Riba & Muñiz, 2015; Ortuño-Sierra, Fonseca-Pedrero, Inchausti & Sastre i Riba, 2016). The SDQ comprises 25 items in a Likert-type response format with three options (0 = No, never, 1 = Sometimes, 2 = Yes, always). Items are grouped into five dimensions (with five items each): emotional symptoms, behavior problems, hyperactivity, peer problems, and prosocial behavior. The first four subscales make up a Total Difficulties score. The higher the score, the greater the level of emotional and behavioral difficulty, except for the subscale of Prosocial Behavior, where a lower score means worse adjustment.

The psychometric properties of the SDQ have been analyzed in previous studies at international and national level (Ortuño-Sierra, Fonseca-Pedrero, Aritio-Solana, et al., 2015; Ortuño-Sierra, Fonseca-Pedrero, Paino, Sastre i Riba & Muñiz, 2015).

Penn Matrix Reasoning Test (PMRT) (Gur et al., 2012; Moore, Reise, Gur, Hakonarson & Gur, 2015). This is a task from the Penn-Computerized Neurocognitive Battery, developed to measure nonverbal reasoning (using matrix reasoning problems as in the Raven Progressive Matrices Test), within the domain of complex cognition. This 20-item task can be seen as an estimate of IQ. The battery includes different neurobehavioral indicators, with different tasks adapted to guarantee psychometric properties and their connection with brain systems among children.

The Family Affluence Scale-II (FAS-II) (Boyce, Torsheim, Currie & Zambon, 2006). Socioeconomic status was calculated using a measure of family wealth involving four items appropriate to children with score ranging from 0 to 9. Previous international studies have shown adequate psychometric properties (Boyce et al., 2006).

Oviedo Infrequency Scale (INF-OV) (Fonseca-Pedrero, Paino-Piñeiro, Lemos-Giráldez, Villazón-García & Muñiz, 2009). The INF-OV was developed to detect random, pseudo-random or untruthful responses to the measurement instruments administered. The INF-OV is a 12-item Likert-type self-report instrument with five responses reflecting degrees of agreement (1 = Strongly disagree, 2 = Disagree, 3 = Neither disagree nor agree; = Agree, and 5 = Strongly agree). After dichotomizing the items, students scoring more than two items of the INF-OV incorrectly are eliminated from the study.

Procedure

The research was approved by the General Directorate of Education of the Government of La Rioja and the Clinical Research Ethics Committee of La Rioja (CEICLAR). Schools were contacted by phone, email or by mail. Initial contact with schools was via the director, the Head of Studies, or the orientation department.

To standardize the administration process, all researchers were provided with a protocol and guidelines to be adhered to before, during and after administration of measurement instruments. The questionnaires were administered by computer and collectively in groups of between 10 and 30 participants.

Participants were informed at all times regarding the confidentiality of their responses and the voluntary nature of their participation. Participation was not remunerated. Whenever necessary, authorization was sought to allow minors to participate. This study forms part of a broader project on the early detection of mental health problems.

Data analysis

First, the percentage of participants with psychotic-like experiences and substance use was analyzed.

Second, to examine the relationship between psychotic-like experiences and cannabis use, several analyses were carried out as follows:

A) Multivariate analysis of variance (MANOVA) was use to examine the relationship between total PQ-B scores for frequency of cannabis use and discomfort without the role of possible covariates.

B) In order to examine the relationship between theoretical risk or non-risk of psychosis and cannabis, two groups of participants were created according to the PQ-B total frequency score (values higher than 8 points). To analyze if there were statistically significant differences, a χ^2 test was performed.

C) Given that gender, age, socioeconomic level, smoking, alcohol use, IQ, and emotional-behavioral problems may affect the expression of the relationship between psychotic-like experiences and cannabis use, these were considered covariables and multivariate analysis of covariance (MANCOVA) was performed. Partial eta squared (partial η^2) was used to calculate effect size.

Third, in order to examine the possible mediating role of difficulties in emotional and behavioral adjustment in the relationship between cannabis use and risk of psychosis, a mediation analysis was performed using the PROCESS macro (Hayes, 2013). Gender, age, socioeconomic level, smoking, alcohol use, and IQ were included in the analysis as covariates. To estimate the significance of the indirect effect, a bootstrapping (1000 re-samples) with a confidence interval of 95% was applied. The effect is significant if the associated confidence interval does not contain zero. The Sobel test was also carried out to verify the significance of the possible indirect effect.

The analyses were carried out using the statistical package SPSS v22 (IBM Corp Released, 2013) and the PROCESS macro (Hayes, 2013).

Results

Descriptive statistics: prevalence

The lifetime prevalence of substance use was 40.4% ($n = 641$) for tobacco and 23.7% ($n = 377$) for cannabis. Using cannabis once or twice in their life was reported by 15.1% ($n = 239$) of the sample, monthly cannabis use by 2.9% ($n = 46$), weekly use by 1.8% ($n = 29$), and daily use by 1.8% ($n = 29$), while 65.9% ($n = 1047$) indicated that they had never used cannabis. The question regarding cannabis use in the previous 3 months was left unanswered by 12.5% ($n = 198$) of the sample.

The results showed that 27.3% ($n = 434$) of the adolescents obtained scores of 8 or higher on the PQ-B were con-

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sidered as a risk group. While 8.6% ($n = 136$) of the sample did not report any psychotic-like experiences (score 0 in the PQ-B), this type of experience did not cause any kind of discomfort for 13.9% ($n = 220$).

Relationship between psychotic-like experiences and cannabis use

Regarding, exclusively, the relationship between PQ-B score dimensions (frequency and distress) and cannabis use, the MANOVA revealed the existence of statistically significant differences ($\lambda = 0.994$; $F_{(2,1585)} = 5.049$, $p = 0.007$). Compared to non-users, the frequency and distress associated with psychotic-like experiences among adolescent cannabis users increased. The results are shown in Table 1.

Similar results were found when comparing psychosis risk groups (risk vs. no risk) with cannabis use ($\chi^2_{(1)} = 8.450$, $p = 0.004$). The results are shown in Table 2.

A MANCOVA was then carried out with PQ-B scores as dependent variables, cannabis consumption as fixed factor (lifetime prevalence) and controlling for covariates gender, age, smoking, alcohol use, IQ, socioeconomic level and emotional and behavioral problems. In this case, results yielded an absence of statistically significant differences between groups ($\lambda = 0.999$, $F_{(1.1580)} = 0.523$, $p = 0.593$). More specifically, the largest effect size was observed for the total score of SDQ ($\lambda = 0.695$, $F_{(2.1580)} = 347.71$, $p < 0.001$, partial $\eta^2 = 0.306$). Given these results, and bearing in mind previous studies, the possible mediating role of emotional and behavioral problems between cannabis and psychotic-like experiences was investigated.

Psychotic-like experiences and cannabis: the mediating role of emotional and behavioral difficulties

Mediation analysis revealed that the total effect of cannabis use on psychotic-like experiences was positive and statistically significant ($B = 0.687$, $p < 0.05$, 95% CI: 0.06 – 1.32). However, the direct effect was not statistically significant ($B = 0.084$, $p = 0.76$, 95% CI: -0.45 – 0.62). The indirect effect was also positive and significant ($B = 0.603$, 95% CI: 0.25-0.94), indicating that the SDQ scores fully mediated the relationship between cannabis use and the risk of psychosis. Similarly, the Sobel test also revealed the significance of the indirect effect ($z = 3.56$, $p < 0.001$). These results show that difficulties in emotional and behavioral adjustment fully mediate the relationship between cannabis use and risk of psychosis. In the mediation analysis, the variables gender, age, socioeconomic level, smoking, alcohol use and IQ were controlled for.
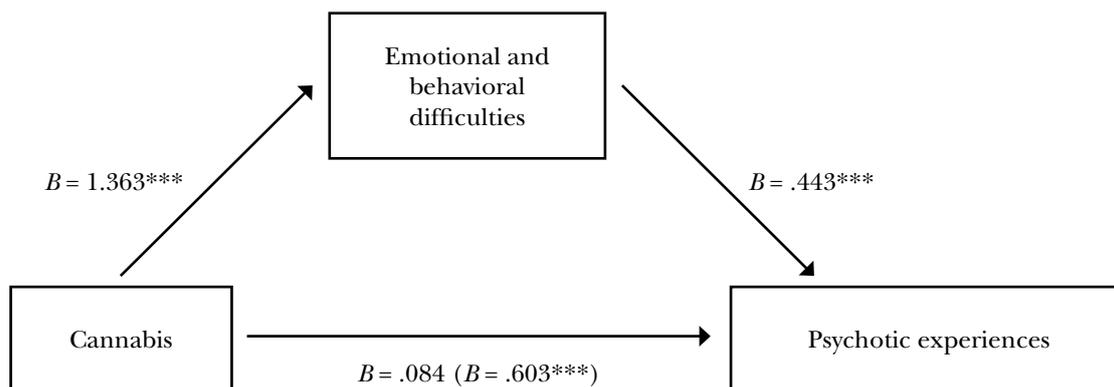
Discussion

Our main goal was to analyze the relationship between psychotic-like experiences and cannabis use in a representative sample of Spanish adolescents. The results derived from this study show that: a) young cannabis users reported higher levels of psychotic-like experiences, both in terms of frequency and associated distress compared to non-users; b) the link between cannabis use and psychotic experiences disappeared when the effect of multiple covariates was taken into account; and c) mediational analysis

Table 1. *Means' comparisons between users and non-users of cannabis and psychotic-like experiences (frequency and distress)*

	Non-users		Users		F	p	partial n²
	M	SD	M	ST			
PQ-B distress	10.64	11.12	12.59	12.45	8.341	0.004	0.005
PQ-B frequency	5.83	4.37	6.64	4.41	9.883	0.002	0.006

Table 2. *Relationship between risk of psychosis and cannabis prevalence*

			Risk of psychosis		
			No	Yes	Total
Cannabis prevalence	No	n	902	309	1211
		% cannabis prevalence	74.50%	25.50%	100.00%
		% risk of psychosis	78.20%	71.20%	76.30%
	Yes	n	252	125	377
		% cannabis prevalence	66.80%	33.20%	100.00%
		% risk of psychosis	21.80%	28.80%	23.70%
Total		N	1154	434	1588
		% cannabis prevalence	72.70%	27.30%	100.00%
		% risk of psychosis	100.00%	100.00%	100.00%

Note. *** p < .001

Figure 1. Direct and indirect effects of cannabis use and emotional and behavioral difficulties on psychotic experiences. The indirect effect of cannabis use on the risk of psychosis through emotional and behavioral difficulties is in parentheses. Non-standardized coefficients.

indicated that emotional and behavioral problems mediated the relationship between cannabis use and the risk of psychosis, after controlling for the effect of multiple confounding variables.

Previous studies appear to show, on the one hand, that cannabis use increases the risk of developing psychosis spectrum disorders, with a dose-response relationship (Davis, Compton, Wang, Levin & Blanco, 2013; Degenhardt et al., 2018; Henquet et al., 2008; Kuepper et al., 2011), and on the other hand, that the association between cannabis and psychosis is found throughout the continuum of the psychosis phenotype (attenuated psychotic experiences, schizotypal traits, subclinical psychotic symptoms, psychotic symptoms) (Dolphin et al., 2015; Esterberg et al., 2009; Fonseca-Pedrero et al., 2016; Hides et al., 2009; Linscott & van Os, 2013; Mackie et al., 2011); nevertheless, there is ongoing debate as to possible moderating, mediating or confounding factors, as well as cause-effect relationships that may be modifying the complex interactions between genetic and environmental influences and between the psychosis phenotype and substance use, specifically cannabis.

In this study, it was found that after controlling for the effect of the multiple relevant covariables, the use of cannabis was not related to the frequency and distress associated with psychotic experiences reported by adolescents. Previous studies with adolescents and young adults have met with similar results when analyzing the psychotic phenotype at subclinical or population level (Dolphin et al., 2015; Fusar-Poli et al., 2017; Mackie et al., 2011); others, however, did find such a link (Hides et al., 2009; Jones et al., 2018). For example, in a representative sample of adolescents, Dolphin et al. (2015) revealed that all relationships were significant in the univariate analysis between substance abuse and psychotic experiences, although the only significant relationship in the multivariate analysis was between auditory hallucinations and cannabis use in the past 30 days, which points to a confounding with other

predictor variables. A recent meta-analysis conducted by Fusar-Poli et al. (2017) found no relationship between cannabis use and the ultra-high risk of psychosis.

The mediational analysis indicated that reported comorbid psychopathology mediated the relationship between cannabis use and the frequency of psychotic experiences, after adjustment for multiple confounding variables. More specifically, the use of cannabis increased the risk of comorbid psychopathology and this, in turn, the frequency of psychotic experiences. Previous studies of young people in the general population reach similar conclusions (Bourque, Afzali, O'Leary-Barrett & Conrod, 2017). For example, a longitudinal study with adolescents by Bourque et al. (2017) found that symptoms of depression partially mediated the longitudinal link between cannabis use and psychotic experiences. Analogous results are found in adults, where the mediating role of anxiety between cannabis use and psychotic experiences is observed (Reeves et al., 2014). More complex studies involving gene-environment interaction have found that the link between symptoms of substance use disorder and psychotic-like experiences is explained by shared genetic and environmental factors and by the direct effects between substance use and the risk of psychotic experiences (Nesvåg et al., 2016). Nevertheless, it seems that cannabis use accounts for 2-5% of the variance in psychotic-like experiences of a positive, cognitive, and negative type (Shakoor et al., 2015). Overall, these results highlight the importance of the study of environmental and psychological variables such as comorbid psychopathology, attachment, smoking or trauma, and victimization experiences in developmental stages at special risk of suffering mental disorders and before the transition to a clinical phase and the need for treatment.

As risk markers for psychosis spectrum disorders, psychotic-like experiences should be used in combination with other risk markers (proximal or distal) and variables such as substance use or abuse, trauma experiences, family

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history of obstetric disorders or complications (Linscott & van Os, 2013; Van Os & Linscott, 2012). Possible underlying etiological mechanisms can, thus, be analyzed, and strategies and programs for early detection and prevention can be improved. At the same time, the most current etiological hypotheses in this field, such as the propensity-persistence-disability model (Cougnard et al., 2007; Linscott & van Os, 2013) or neurodevelopmental models (Fonseca-Pedrero, 2018; Fusar-Poli et al., 2017; Millan et al., 2016), believe that certain environmental impacts (environmental or adverse risk) occur during the course of development, both in the pre/perinatal (first wave) and in adolescent (second wave) stages, which, in combination with genetic and/or personal factors, can lead to such psychotic experiences (as a phenotypic expression of existing vulnerability) becoming abnormally persistent, triggering a first psychotic episode, disability, and a need for treatment.

This study allows us to tentatively draw some relevant clinical and prevention implications. As regards prevention, the mediating role of emotional and behavioral problems in young people with psychotic-like experiences and cannabis use highlights the need for early intervention programs in psychosis to be aimed not only at preventing the use of cannabis, but also, and in particular, at preventing and intervening in emotional and behavioral difficulties. It, therefore, seems sensible to design emotional well-being programs to promote social-emotional competence in school contexts. For example by providing young people with tools to better manage their emotions and build an appropriate image of themselves with positive personal motivations and values, and encouraging the implementation of adaptive strategies to cope with their problems. Furthering the positive development of adolescents and the strengthening of school students (Oliva, 2015) is crucial. Prevention will always be the most thorough response when it comes to reducing mental health problems and risk factors and while also promoting protective factors and the development of socio-emotional strategies.

The present study is not without limitations, some of which are discussed below. First, mental health indicators were assessed using self-report instruments, with the corresponding limitations of these types of tools. Second, the sample is from a Spanish autonomous community, which, despite stratified random sampling by conglomerates, partially limits the generalization of the results to the whole country. Third, a cross-sectional study, such as this, does not permit causal relationships to be established. Fourth, it would have been interesting to collect data on other levels of analysis (e.g., genetic, cerebral, physiological, etc.), which are aspects that could modulate the results. Finally, this paper only analyzed the role of psychotic experiences of the positive dimension (e.g., delusional ideation or hallucinatory experiences), so future studies should investi-

gate the relationship between the negative (e.g., flattened affect or anhedonia) or disorganized dimensions of the psychotic phenotype (Fonseca-Pedrero et al., 2018).

Despite its limitations, the present study yields new results in the study of the relationship between cannabis use and psychotic experiences at the population level. Future studies should continue to analyze the complex interactions that are established between the use of substances such as cannabis, and the risk of psychosis in longitudinal studies, taking into account the complexity of gene-environment interactions and people's real-life settings (ecological validity). This, will provide knowledge of the underlying and etiological mechanisms that can inform the design of mental health promotion programs as well as the setting of new therapeutic targets.

Acknowledgements

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