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86	Abstract		**Purpose of Review:** This systematic review aimed to investigate the relation between cannabis use and dissociation. **Recent Findings:** Four analytical and 14 descriptive cross-sectional studies were included. There is no variation in the rates of cannabis use among individuals with dissociative experiences compared with the general population. In addition, the prevalence of dissociative disorders in subjects using cannabis is not different from those not using cannabis. The majority of the studies employed inadequate sampling procedures and a concurrent or retrospective assessment of the two variables, which might have increased the risk of bias, and only a few of them controlled for potential confounders. **Summary:** The limited number of eligible studies, combined with the heterogeneity of study design and methodological limitations, do not support the association between cannabis and dissociative experiences and prevent from any inference about the direction of causality.
87	Keywords separated by ' - '		Cannabis - Marijuana - Dissociation - Depersonalization - Out-of-body experiences - Dissociative experience scale

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DISSOCIATION AND ADDICTIVE BEHAVIORS (J BILLIEUX AND A SCHIMMENTI, SECTION EDITORS)

The Relationship Between Dissociative Experiences and Cannabis Use: a Systematic Review

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Abstract

Purpose of Review This systematic review aimed to investigate the relation between cannabis use and dissociation.

Recent Findings Four analytical and 14 descriptive cross-sectional studies were included. There is no variation in the rates of cannabis use among individuals with dissociative experiences compared with the general population. In addition, the prevalence of dissociative disorders in subjects using cannabis is not different from those not using cannabis. The majority of the studies employed inadequate sampling procedures and a concurrent or retrospective assessment of the two variables, which might have increased the risk of bias, and only a few of them controlled for potential confounders.

Summary The limited number of eligible studies, combined with the heterogeneity of study design and methodological limitations, do not support the association between cannabis and dissociative experiences and prevent from any inference about the direction of causality.

Keywords Cannabis · Marijuana · Dissociation · Depersonalization · Out-of-body experiences · Dissociative experience scale

Introduction

Cannabis is the most widely consumed illicit drug in Europe and over the world [1]: recent estimates indicate that 26.3% of European adults aged 15–64 years have used cannabis at least once in their life and 7% in the previous year [2]. Furthermore, a higher prevalence of lifetime cannabis use (30.7%) was found in young adults (15–34 years) [3]. Research suggests that dependence occurs in about 11% of lifetime cannabis users, with a higher risk for early cannabis users and daily users [4].

Cannabis use is associated with several psychopathological outcomes. There is compelling evidence that cannabis use increases the risk of both psychotic symptoms and schizophrenia-like psychosis [5, 6], with the highest risk among those using high-potency varieties and synthetic cannabinoids [7••, 8–10]. According to meta-analyses and epidemiological studies, early cannabis use increases the odds of later psychosis [11] with a dose–response relation [12, 13••]. Moreover, daily use, especially of high-potency cannabis, may lead to an earlier onset of psychosis [7••, 14].

There is less consistent evidence of the association between cannabis use and non-psychotic mental disorders. According to systematic reviews and longitudinal studies, cannabis use had a modest effect on the onset of depressive disorders, with stronger evidence for heavy cannabis use (defined either as being affected with DSM-IV cannabis use disorder or using cannabis at least weekly) compared with light use and non-use [15, 16, 17•, 18]. There is a high prevalence of anxiety disorders among cannabis users, and patients with anxiety disorders have relatively high rates of cannabis use and cannabis

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use disorders [19, 20]; furthermore, people affected with panic disorder are thought to be more prone to use cannabis as a self-medication [21•]. Finally, there is a high prevalence of attention-deficit/hyperactivity disorder (ADHD) in adults seeking treatment for cannabis use disorders [22]. However, the nature of this relationship is not well-established [23–25].

According to the self-medication hypothesis, cannabis use may be a way to cope with traumatic experiences and post-traumatic stress disorder (PTSD) [26]. Kevorkian and colleagues [27••] found that lifetime trauma was related with high odds of lifetime cannabis use, and PTSD was associated with increased odds of cannabis use disorder, and similar findings were also reported by Kilpatrick and colleagues [28]. In a large representative US cohort, Cougle and colleagues [29] reported that PTSD was associated with lifetime cannabis use, as well as past daily cannabis use. The direction of this relationship is uncertain: some studies suggest that traumatic experiences and subsequent PTSD increase the risk of drug abuse, although the possibility of a shared vulnerability to PTSD and drug use disorders cannot be excluded [30]. For example, Vlahov et al. [31] found that those who reported an increase in the use of cannabis in Manhattan after September 11th, 2001 had a higher prevalence of PTSD, compared with those who did not experienced such increase.

Little is known about the relationship between cannabis use and dissociation. Previous reviews suggested an association between cannabis use and depersonalization symptoms that are also a clinical feature of cannabis-induced psychosis [32, 33], and a recent study pointed out the similarity between subjective reports of cannabis consumers and dream narratives [34]. Cannabis intoxication may induce acute and transient states of depersonalization/derealization (DP/DR), which may also be associated to alterations of "salience attribution" and psychotic symptoms, often during an experience of "bad trip". DP/DR complex is characterised by a feeling of detachment from one's surrounding (DR), and one's emotions, sensory perception, and sense of self (DP). Other symptoms that may occur include temporal disintegration, perceptual anomalies, sensation of living in a dream and outside of reality, emotional blunting and marked emotional numbing, desomatization, alterations in bodily self-integration, out-of-body experiences such as a feeling of separation from one's own body, and experiences of autoscopy [35–37].

This systematic review aimed to investigate the relation between cannabis and dissociation in the general and clinical populations.

Materials and Methods

A systematic search was carried out in January 2017 and re-run in July 2018 on PsychInfo, Embase classic and Embase, and Ovid MEDLINE(R), using the following keywords combined with the Boolean operator "AND": (1) cannabis-related terms (cannabi* OR marijuana OR hash OR THC) and (2) dissociation-related terms (dissociat* OR depersonalization OR depersonalisation OR derealization OR derealisation). To be included in this review, publications had to (1) be original articles, (2) be written in English, (3) include an abstract, (4) report human epidemiological studies (either cross-sectional, or case–control, or cohort), and (5) assess the relation between cannabis use and dissociative symptoms/traits. Publications were excluded if (1) they were not original articles (e.g., opinion paper, review, case series or case report, dissertation, conference paper, or proceeding), and (2) they reported experimental findings (e.g., trials). When multiple articles were available for the same study, only one was included in this review. In addition to the systematic search, further records were identified throughout the hand search.

Results

Following abstract and full-text screening (see Fig. 1), a total of 18 studies were selected: four analytical studies (one prospective and three case–control studies) and fourteen descriptive cross-sectional studies. Tables 1 and 2 present a summary of the main findings.

Findings from Analytical Studies

In the only prospective study included in this review, Goldstein and colleagues [38] assessed 253 adolescents aged 15–20 years under welfare care, to investigate the relationship between childhood trauma at baseline, PTSD-related dissociative symptoms at 6 months follow-up, and frequency of cannabis use at a 1-year follow-up. Dissociative symptoms did not correlate with frequency of cannabis use. By contrast, cannabis consumption correlated with and was predicted by PTSD-related depressive symptoms at 6 months ($\beta = -0.287$, $p < 0.05$) and by child maltreatment at baseline ($\beta = 0.175$, $p < 0.01$), controlling for age, gender, and welfare status. The maltreatment and adolescent pathways (MAP) by Goldstein and colleagues [38] was the only selected study to adopt a random selection sampling from a caseload of children under welfare care, although the high attrition rate (42.6%, by the 1-year follow-up) suggests that teenagers at higher risk of substance use and mental disorders might have dropped out from the study, thus biasing the findings and reducing generalizability. Furthermore, dissociative symptoms were assessed using a broad instrument such as the Trauma Symptom Checklist for Children (TSCC) [54] that includes only ten items on dissociation.

According to a case–control study on Romanian samples of substance users, dissociative experiences were not related to

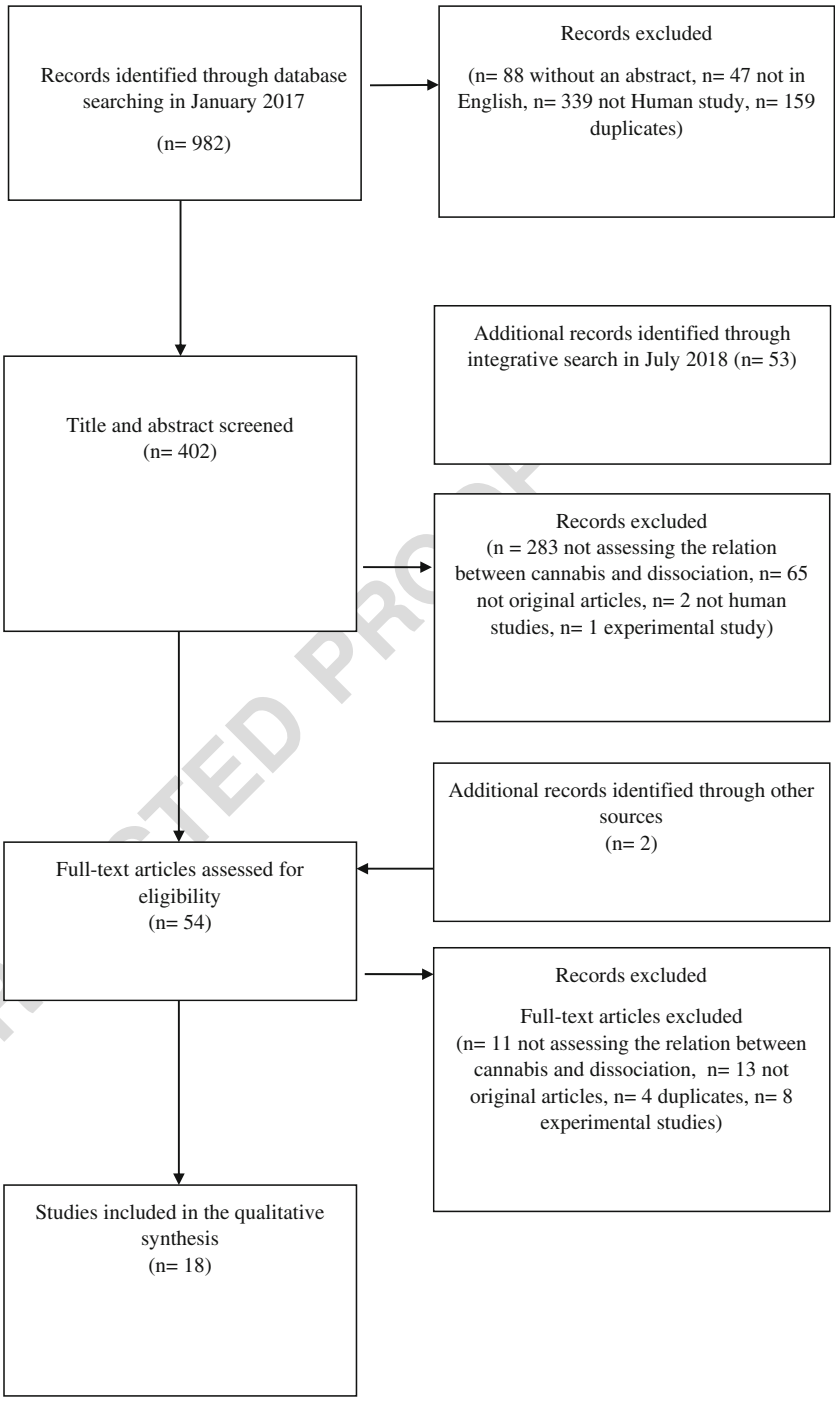

Fig. 1 Flow chart of the selection process, from database search to selected studies

cannabis use more than any legal substance; Bulai and Enea [39] found no difference in the Dissociative Experience Scale-II (DES-II) [55] scores between patients with clinically defined recurrent cannabis abuse and patients with frequent alcohol abuse, tobacco abuse, and healthy controls. One limitation of the study is the lack of information about social and clinical characteristics of the groups that might have confounded the association between substance abuse and dissociation. Additionally, the alcohol abuse group showed significantly higher scores of alexithymia ($F = 8.61$, $p < 0.001$) compared to the other clinical groups and healthy controls, and few correlations were found between the Toronto Alexithymia Scale [56] and the DES-II [55] total score and subscales across all four groups but especially in the control group. Specifically, among cannabis abusers, only the DES-II total score was significantly correlated with the "Difficulty in describing feelings" factor of the Toronto Alexithymia Scale [56] (correlation coefficient = 0.43,

t1.1 **Table 1** Findings of the selected analytical studies

t1.2	Authors, year, study name, country	Sample and study design	Definition of cannabis use	Measure of cannabis use	Definition of dissociation	Measure of dissociation	Main findings
t1.3	Goldstein et al. [38], maltreatment and adolescent pathways (MAP), Canada	$N = 253$ adolescents; prospective study (1 year)	Past year frequency of marijuana use (never used, 1–5, 6–19, or 20+ times in the past year)	Ontario Student Drug Use Survey (OSDUS)	Dissociative symptoms of post-traumatic stress disorder, (mean 47.98, sd 11.01)	Trauma Symptom Checklist for Children (TSCC)	The frequency of cannabis use at 1 year did not correlate and was not predicted by dissociative PTSD symptoms at 6 months (correlation coefficient = 0.10, $p > 0.05$)
t1.4	Bulai and Enea, [39], Romania	$N = 22$ cannabis abusers, $N = 32$ alcohol abusers, $N = 31$ tobacco abusers, and $N = 46$ controls; case–control	Lifetime cannabis use	Not specified	Dissociative experiences (cannabis abusers mean 37.0 (sd 28.0); alcohol abusers mean 42.5 (sd 34.7); tobacco abusers mean 50.1 (sd 26.6); healthy controls mean 47.2 (sd 37.1))	Dissociative Experiences Scale-II (DES-II).	Authors did not find differences between groups in dissociative experiences ($F = 0.89$, $p > 0.44$).
t1.5	Núñez and Gurpegui [40], Spain	$N = 26$ cases with cannabis-induced psychosis and $N = 35$ controls with acute schizophrenia, case–control	Current cannabis use	Urine screen	Presence of derealization and depersonalization symptoms scored 1 (cannabis-induced psychosis 30.8% vs acute schizophrenia 35.7%) or 2 (cannabis-induced psychosis 42.3% vs acute schizophrenia 15.7%) at the PSE-9	Present State Examination, ninth edition, (PSE-9)	Derealization and depersonalization were more frequent in the cannabis-induced psychosis group than in the acute schizophrenia group (Mann–Whitney U test, $p < 0.001$)
t1.6	Rottanburg et al. [41], South Africa	$N = 20$ patients with psychosis and current cannabis use and $N = 20$ controls with psychosis without current cannabis use; case–control	Current cannabis use	Urine screen	Presence of depersonalization symptoms in the month before the admission (cannabis users n 4 vs non-users n 3) and 7 days later (cannabis users n 0 vs non-users n 2)	Present State Examination, ninth edition, (PSE-9)	There were no differences between groups in prevalence of the derealization and depersonalization both in the month before psychiatric admission and in the subsequent 7 days (Fisher's exact test's, $p > 0.05$)

t2.1 **Table 2** Findings of the selected observational studies on clinical and non-clinical populations

t2.2 Authors, year, study name, country	Sample and study design	Definition of cannabis use	Measure of cannabis use	Definition of dissociation	Measure of dissociation	Main findings
t2.3 Studies on clinical populations						
t2.4 Ahmed et al. [42], India	$N = 150$ patients with substance use disorders for at least 1 year, cross-sectional	Past year cannabis use	Self-reported cannabis use	Dissociative disorders according to ICD-10 diagnostic criteria	Present State Examination (PSE)	Among patients who reported cannabis mono-use ($N = 72$), there were no comorbidities for dissociative disorders. No dissociative comorbidities were found in alcohol and heroine mono-use but 7.69% of benzodiazepine users.
t2.5 Medford, et al. [35], United Kingdom	$N = 164$ individuals with chronic depersonalization, cross-sectional	Lifetime cannabis use	Ad hoc questionnaire	Dissociative experiences, depersonalization Trait	Dissociative Experiences Scale (DES), Cambridge Depersonalization Traits Scale (CTDS)	Among the 40 individuals who reported drug-induced depersonalization, 20 attributed its onset to cannabis use. The only difference between non-drug users and patients with cannabis-induced disorder was in the mean score on item 28 of the CTDS that was higher in non-drug users ($t = -2.17$, $p = 0.034$) and in the prevalence of seeing flashes of light, which was higher in the cannabis group ($\chi^2 = 13.9$, $p < 0.001$).
t2.6 Najavits and Walsh [43], USA	$N = 77$ women with current post-traumatic stress disorder and substance use disorder, cross-sectional	Cannabis use in the previous month; years of cannabis use	Addiction Severity Index (ASI)	Dissociative experience (high-dissociation group: $N = 16$, 20.8%)	Dissociative Experiences Scale (DES)	No differences were found between the high- and low-dissociation group regarding the number of days of cannabis use in the previous month and number of years of cannabis use
t2.7 Simeon et al. [44], USA	$N = 117$ patients with depersonalization disorder, cross-sectional	Lifetime cannabis dependence ($N = 10$, 8.5%); lifetime cannabis abuse ($N = 5$, 4.3%)	Structured Clinical Interview for DSM III-R or DSM IV Disorders-Patient Version (SCID-I), unpublished semistructured interview inquiring about onset and course of depersonalization disorder	Dissociative disorders, dissociative experiences (total score mean = 24.9, sd = 14.7; depersonalization score mean = 47.5, sd = 20.6)	Structured Clinical Inteview for Dissociative Disorders (SCID-D), Dissociative Experiences Scale (DES)	Marijuana ingestion ($N = 15$, 13%) was the second most common precipitants of depersonalization disorder after severe stress ($N = 29$, 25%). However, when the five most common triggers were included in a linear regression model, none of them predicted depersonalization severity ($F = 1.94$, $p = 0.09$)
t2.8 Simeon et al. [37], USA	$N = 394$ individuals with self-reported depersonalization disorder (33.2% received a diagnosis by a professional), cross-sectional		Unpublished online survey inquiring about onset and course of depersonalization disorder	Depersonalization and derealization, symptoms (mean = 120.0, sd = 54.4)	Cambridge Depersonalization Scale (CDS)	89 individuals (45.4%) attributed the onset of their depersonalization disorder to cannabis mono-use
t2.9 Wenzel et al., [45], USA	$N = 138$ veterans affected with alcohol or drug dependence, cross-sectional	Days of cannabis use in the past month (alcohol dependence group mean 13.3 (sd 14.1), drug dependence mean 7.4 (sd 10.7); years of lifetime cannabis use (alcohol dependence group mean 8.5 (sd 9.2), drug dependence mean 10.2 (sd 7.6)	Addiction Severity Index (ASI)	Dissociative experiences (alcohol dependence group mean 26.2 (sd 18.2), drug dependence mean 18.0 (sd 12.5)	Dissociative Experiences Scale (DES).	Only in the drug dependence group, years of cannabis use correlated with the absorption subscale of the DES ($r = 0.28$, $p < 0.05$), but the correlation became non-significant after controlling for alcohol use (partial $r = 0.23$, $p > 0.10$)

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t2.10 **Table 2** (continued)

	Authors, year, study name, country	Sample and study design	Definition of cannabis use	Measure of cannabis use	Definition of dissociation	Measure of dissociation	Main findings
t2.11	Studies on non-clinical populations						
t2.12	Ames et al. [46], USA	$N = 467$ high schools students, cross-sectional	Frequency of lifetime (mean = 6.9, sd = 3.9) and past 6 months cannabis use (mean = 4.7, sd = 3.3); personal consequences (mean = 2.8, sd = 5.5), dependence (mean = 15.5, sd = 6.8), and abuse (mean = 6.4 sd = 2.9) of cannabis use	Ad hoc questionnaires	Dissociative experiences	Modified version of the Dissociative Experiences Scale (DES) (derealization mean = 4.0, sd = 1.6; amnesia mean = 3.6, sd = 1.5; absorption mean = 12.9, sd = 3.3)	Two cumulative factors were calculated for the frequency and consequences of cannabis use. Dissociative experiences correlated with consequences of cannabis use (correlation coefficient = 0.380, $p < 0.001$) but not with the frequency of its use.
t2.13	Barratt et al. [47], Australia	$N = 316$ lifetime users of synthetic cannabinoids, cross-sectional	Synthetic cannabinoids use during the past 12 months	Ad hoc online questionnaire	Dissociative symptoms	Ad hoc online questionnaire about side effects of synthetic cannabinoids	68% of the sample reported at least one side effect, and 22% of this group referred dissociation.
Q1 t2.14	Halikas et al. [48], USA	$N = 100$ regular cannabis users, cross-sectional	Smoking 50 times or more in the previous 6 months	Ad hoc interview	Depersonalization and derealization experiences	Ad hoc checklist about side effects of marijuana	Dissociative side effects were reported during intoxication but not after. Separation from the self and detachment from reality were respectively experienced by 12% and 10% "usually" by 49% and 55% "occasionally," and by 39% and 35% "once or never."
t2.15	Luke and Kittenis [49], USA	$N = 139$, cross-sectional	Frequency of lifetime cannabis use	Ad hoc online questionnaire	Out-of-body experiences	Ad hoc online questionnaire	Among substance users ($n = 110$), 77.7% smoked cannabis lifetime, most of whom were poly-consumers. A bivariate correlation was found between the frequency of cannabis use and out-of-body experiences ($r = 0.17$, $p = 0.048$).
t2.16	Michal et al. [50], Germany	$N = 3809$ secondary and vocational students, cross-sectional	Any cannabis use in the previous 12 months (none vs 1–9 times vs 10–39 times vs more than 40 times)	Ad hoc, two-item questionnaire	Depersonalization symptoms ($N = 452$, 11.9%)	2-item version of the Cambridge Depersonalization Scale (CDS-2)	Depersonalization was associated with cannabis use in the previous 12 months (χ^2 $p = 0.003$), and severity of depersonalization was related with the frequency of cannabis abuse (Jonckheere–Terpstra trend test, $p < 0.001$).
Q2 t2.17	Pekala et al. [51], USA	$N = 413$ university students, cross-sectional	Lifetime cannabis use	Cannabis subscale of the Anomalous Experiences Inventory (AEI)	Level of dissociative experiences (low $N = 51$; low–medium, $N = 158$; high–medium, $N = 51$; and high, $N = 59$)	Dissociative Experiences Scale (DES)	Lifetime cannabis use was not associated with dissociation score ($\chi^2 = 4.78$, $p = 0.19$).
t2.18	Tolmunen et al. [52], Finland	$N = 4019$ students, cross-sectional	Lifetime cannabis use (8% in the high-dissociation group, 3.1% in the	Ad hoc questionnaire	High dissociation defined as being in the highest decile of the A-DES score distribution ($N = 401$)	Adolescent Dissociative Experiences Scale (A-DES)	Lifetime cannabis use predicted high dissociation (OR = 1.82, 95% CI 1.14–2.89, $p = 0.012$) after controlling for social confounders and substance misuse.

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t2.19 **Table 2** (continued)

Authors, year, study name, country	Sample and study design	Definition of cannabis use	Measure of cannabis use	Definition of dissociation	Measure of dissociation	Main findings
		low dissociation group)				
t2.19 Wilkins et al. [53], Canada	$N = 192$, cross-sectional	Self-reported past and current recreational cannabis use	Online questionnaire based on Curran and Morgan's questionnaire	Dissociative states: out-of-body feeling (OBF), out-of-body autoscopy (OBA), illusory movements, elevator sensations, andvestibular-motion sensations	Online questionnaire partially derived by the Waterloo Unusual Sleep Experiences Scale (WUSES)	The majority of the sample consisted of poly-drug users, with cannabis being used by 99%. Significant correlations were found between being under the effect of cannabis at the time of the unusual body experience and OBF ($r = 0.24$), elevator ($r = 0.26$), illusory movement ($r = 0.33$), and vestibular motions ($r = 0.27$), as well as between lifetime cannabis use and illusory movement ($r = 0.22$). Furthermore, after controlling for other substances use, cannabis ($\beta = 0.28$; $p < 0.05$) and ketamine ($\beta = 0.52$; $p < 0.05$) significantly predicted illusory movement ($R^2 = 0.37$; $p < 0.001$).

CI confidence interval, *OR* odds ratio, *sd* standard deviation

$p < 0.05$). However, caution is needed in the interpreting the finding given the vast number of correlations that were not controlled for multiple testing.

The other case–control studies focused on psychosis and cannabis-related psychosis, yielding to contradictory findings. Rottanburg and colleagues [41] did not observe any difference in DP and DR severity between two groups of patients affected with psychosis International Classification of Disease, ninth edition (ICD-9) [57], with or without current cannabis use, who were matched for age and clinical diagnosis and were diagnosed according to the same criteria. By contrast, Núñez and Gurpegui [40] found more severe dissociative symptoms in patients with diagnosis of cannabis-induced psychosis according to the Diagnostic and Statistical Manual for Mental Disorders, third edition, revised (DSM-III-R) [58] criteria for cannabis delusional disorder, compared to patients with diagnosis of acute schizophrenia according to the Research Diagnostic Criteria [59]. However, both studies were limited by the small sample size.

Findings from Descriptive Studies on Clinical and Non-clinical Populations

In an American sample of patients with a clinical diagnosis of DP disorder, according to DSM-III-R [58] and DSM-IV [60] criteria, Simeon and colleagues [44] found a prevalence of 4.3% lifetime cannabis abuse and 8.5% lifetime cannabis dependence [61, 62]; 13% of this sample attributed the onset of the disease to cannabis use. However, when the five most common precipitants identified by the patients (severe stress, marijuana ingestion, panic attacks, depression, and hallucinogen ingestion) were included in the same model, none of them predicted the DES [63] depersonalization score and the statistical model was not significant ($F = 1.94$, $p = 0.09$). Since the interview allowed participants to indicate more than one factor, it cannot be excluded that the lack of an effect might be due to additional precipitant factors, which were not included in the model. In an online survey carried out by the same research group [37], cannabis mono-use was claimed as the precipitant factor of self-reported DP disorder by 45.4% of the sample. Of these, 28.1% smoked cannabis 100–500 times, 9% 51–100 times, 27% 11–50 times, and 22.5% 2–10 times. The majority of them (66.3%) reported DP shortly after cannabis consumption, and most of the group (70.8%) never used it again. The observation was consistently replicated in a UK clinical caseload: Medford and colleagues [35] found that 50% of a sample with self-reported drug-induced DP attributed the onset of their symptoms to cannabis use alone. Nevertheless, this study found no differences between patients with self-reported cannabis-induced DP and non-drug user patients (matched for age and gender) in the total DES [63] and the total Cambridge Depersonalization Trait Scale (CDTS) [64] score. The only exceptions were the mean score

on CDTS item 28 ("I seem to have lost some bodily sensations, such as thirst or hunger") that was higher in non-drug users and the experience of seeing flashes of light that was more common in the cannabis-induced group.

In the only study assessing the prevalence of International Classification of Disease, tenth edition (ICD-10) [65] dissociative disorders in a convenience sample of patients with substance use disorders, the authors found no comorbidities with cannabis, alcohol, and heroine mono-use, in contrast with the 7.69% found with benzodiazepine mono-use [42]. Another study by Najavits and Walsh [43] found no difference in the past month and past year frequency of cannabis use between two groups of women with high or low levels of dissociative experiences (DES scores ≥ 30) in the context of PTSD. However, findings are difficult to interpret since the authors did not report any statistics supporting this information. Also, generalization is limited by the recruitment of only female participants and, given the lack of knowledge about social and clinical characteristics of the two groups, the role of potential confounders is not clear [43]. Weak evidence of association between cannabis use and dissociation comes from a study [45] of US veterans self-referring for DSM-III-R [58] alcohol or drug (cocaine or heroin) dependence: authors found in the drug dependence group only a correlation between years of cannabis use and the absorption subscale of the DES, but it became non-significant after controlling for years of alcohol use.

A few descriptive studies assessed the prevalence of cannabis use in non-clinical populations. A survey of a large sample of Finnish teenagers employing the A-DES [66] found that 8% of students with high dissociation had smoked cannabis lifetime, compared with 3.1% of students with low dissociation [52]. Lifetime cannabis use increased by nearly twice the odds of presenting high dissociation scores, accounting for the effect of age, daily cigarette smoking, frequent alcohol use, abuse of legal drugs, social isolation, and poor school performance in mathematics. However, the cross-sectional design prevents any causational inference.

According to one of the first surveys on regular cannabis smokers (defined as individuals who smoked at least 50 times in the previous 6 months), separation from the self and detachment from reality were experienced "occasionally" by 49–55% of the sample and "usually" by 10–12% of the sample [48]. In the only study about synthetic cannabinoids users, recruited through an online survey, 68% of the sample reported at least one side effect, and 22% of this group found dissociation [47].

Several studies assessed the correlation between dissociative experiences and frequency of cannabis use. In a sample of American students attending a continuation high school for teenagers at high risk of not completing their education, Ames and colleagues [46] found that the total score of a modified version of the DES scale correlated with consequences of cannabis use but not with lifetime and past 6-month frequency of cannabis use. The authors used a modified version of the DES, including only 12 of the less severe dissociative experiences; therefore, it cannot be excluded that authors underestimated the correlation with frequency of cannabis use.

Out-of-body experiences (OBE) represent a particular type of dissociative experiences including out of body feelings (perceived separation by own physical body), autoscopy (seeing her/his own body from an external point of view), or a combination of the two. In a sample of Canadian individuals referring recreational substance use, Wilkins and colleagues [53] found medium-size correlations between being under the effect of cannabis at the time of the experience and frequency of out-of-body feelings, feeling of elevator, illusory movements, and vestibular motions, as well as between lifetime cannabis use and illusory movements. When they included different substances in the same regression model, the only drug showing a more than average effect on all out of body experiences was ketamine, while cannabis predicted only illusory movements. However, the findings are difficult to interpret due to the authors not reporting summary statistics. Another study on OBE found a mild correlation between frequency of lifetime cannabis use and out-of-body experiences, both assessed using ad hoc non-validated online questionnaire; additionally, since the authors stated that most of cannabis users were poly-consumers, it would have been useful adjusting the analysis for other substance use [49].

Other cross-sectional studies assessed the association between dissociation and cannabis use either comparing proportions or means with mixed findings. In a US university sample, no relation was found between lifetime cannabis use and levels of dissociative experiences assessed with the DES [51]. By contrast, the frequency of past year cannabis use correlated with severity of DP in a large sample of German secondary school students [50]. However, measures of cannabis and dissociation here consisted of only two-item questionnaires.

Discussion

Comorbidity Between Cannabis Use and Dissociation

This systematic review found that epidemiological evidence about the comorbidity between cannabis use and dissociative disorders was scarce, perhaps due to the low prevalence of dissociative disorders in the general population and the exclusion of dissociative disorders from the major epidemiological surveys on cannabis. In a small Indian study, no dissociative disorders were diagnosed in cannabis users [42], while studies on individuals with dissociative disorders [37] and traits [52] found 8% of cannabis use, 4.3% of comorbid cannabis abuse, and 8.5% of cannabis dependence. These percentages do not exceed those described in the general population, by European reports (34% cannabis use among young adults [2]) and large

epidemiological surveys, such as the US National Longitudinal Study of Adolescent Health study (3.9% and 8.3% cannabis abuse and dependence, [67]).

Psychopathological Pathways Linking Early Trauma, Dissociative Experiences, and Cannabis Use

The only study assessing the effect of trauma and dissociative experience on cannabis use using a longitudinal design was the MAP study on Canadian teenagers at higher risk of mental disorders [38]. The study did not find any effect of PTSD-related dissociative symptoms on cannabis use which, however, was influenced by child maltreatment and PTSD-related depressive symptoms. Moreover, another publication from the same study [68], which was not included in this review as duplicate, found that dissociation, although not directly related with cannabis use (direct effect $B = 0.012$, SE = 0.08, $p = 0.089$), mediated the effect of witnessing interpersonal violence on frequency of marijuana use (indirect effect $B = 0.041$, SE = 0.03, 95% CI 0.001–0.123). This evidence suggests a potential role for dissociation in the psychopathological pathway between trauma and cannabis use, which deserves further investigation.

Accumulating evidence supports an association between early trauma and later cannabis use in the general population [69•, 70•], and it was hypothesised that individuals exposed to developmental trauma might resort to alcohol and drugs to regulate negative emotions [71–74]. In this view, dissociative mechanisms, aimed to disengage the individual from painful mental states, are strongly related with alexithymia, meaning the difficulty in recognising and regulating unpleasant emotions, often arising from childhood trauma [75, 76]. In line with this model, a case–control study [39] compared dissociative experiences and alexithymia of cannabis, alcohol, and tobacco users, and healthy controls, finding a few correlations between dissociation and alexithymia across groups. Caution is needed in interpreting these findings, given the retrospective study design, the small sample size, and the lack of adjustment for confounders.

The Role of Cannabis Use in the Onset of Dissociative Disorders and Dissociative Symptoms

Following the early interest in the dissociative effect of cannabis use, showed by initial case reports [36, 77] and trials [78–80], a few studies investigated the role of cannabis use in the onset of dissociative disorders. According to a study on individuals with a clinical diagnosis of DP disorder and an online survey of individuals acknowledging themselves the symptoms of the disorder, cannabis use was claimed as precipitant factor in about 50% of the cases [35, 37], although the former found only minimal differences between patients with and without cannabis-induced DP [35]. In a further investigation, only 13% of the sample attributed the onset of DP disorder to cannabis use [44] but, adjusting for the other triggers, the effect of cannabis use on DP score was not significant.

The most robust finding in these cross-sectional studies was reported in a large sample of teenagers [52], among whom those with lifetime cannabis use had twice the dissociation score of those not using cannabis, even adjusting the analysis for several confounders. Furthermore, in a sample of poly-drug users, current cannabis use was related to a specific type of OBE, i.e., illusory movements [53]. However, the cross-sectional study design does not allow to make any inference on the nature of the association.

Other Evidence of a Relationship

Some studies assessed the relation between cannabis and dissociation using simple association or correlation analyses, with mixed findings. Among the studies on clinical populations, one study reported an association between cannabis-related psychosis and current DR/ DP symptoms [40]; however, this association was not confirmed in another study [41]. Besides, no relation between frequency of cannabis use and level of dissociative experiences was found in two studies of patients with substance-related disorders, the second of whom also controlled for alcohol abuse [43, 45].

Similarly, in two studies on the general population, dissociative experiences related to the frequency of cannabis use [49, 50], while in two other studies, it was not the case [46, 51]. As noted by Najavitz and Walsh [43], these contradictory results might be explained by speculating that in substance users who were exposed to trauma, the "chemical dissociation" induced by substance use may substitute any form of endogenous dissociative experiences [81, 82], providing them with an effective "psychic retreats" from trauma-related painful mental states [83, 84]. The chemical dissociation, hence, would make substance users showing lower dissociation score than non-users in those questionnaires, such as the DES and the DES-II, which, by definition, exclude every dissociative experience occurring under the effect of alcohol and other substances.

Methodological Appraisal

With few exceptions, the majority of the researches had a good sample size, ranging from 100 up to 4000 of participants. Among the analytical studies, only the prospective one employed a random selection strategy [38], while the remaining adopted non-random or not specified sampling strategies [39–41]. Furthermore, most of the descriptive studies employed convenience sampling or consecutively recruitment [35, 37, 42, 44, 45, 47, 49, 53]. Such recruitment methods are prone to selection bias, and they may limit the

representativeness of the sample and the generalizability of the findings.

A number of studies [35, 39, 43, 45, 46, 51] defined dissociation in terms of dissociative experiences and assessed it using the DES [63] and the DES-II [55], although these scales rely on self-report information and, therefore, may be prone to recall bias, they are regarded as reliable and valid instruments to assess dissociative experiences [55, 63]. In addition, two studies on youth samples [38, 52] used the more specific A-DES [66] and the dissociative subscale of the TSCC [54]; three studies [35, 37, 50] were focused only on DP symptoms, mostly assessed using the Cambridge Depersonalization Scale (CDS) [64, 85]. Notably, few studies [40–42, 44] used psychiatric interviews such as the Present State Examination (PSE) [86] or the Structured Clinical Inteview (SCI) for Dissociative Disorders (SCID-D) [87]. The remaining studies investigated dissociative OBE [49, 53] or dissociative side effects [47, 48] using ad hoc non-validated self-report questionnaire.

Regarding cannabis use, all but one study were focused on natural cannabis, without information about type or content of THC (the main psychoactive ingredient in marijuana), with only one research on synthetic cannabinoids [47]. Seven studies [38, 43–46, 49, 53] assessed the frequency of cannabis use, while the remaining assessed lifetime or current cannabis use as a categorical variable. Only two studies [40, 41] ascertained current cannabis use by urine screening, one study [44] assessed cannabis-related disorders using the SCID [61, 62], others [43, 45] investigated frequency of cannabis use with the Addiction Severity Index [88], but the majority used ad hoc non-validated questionnaires or interviews. While on the one hand, the use of self-report questionnaires may encourage self-disclosure of substance-related information, on the other hand, they may also be prone to recall bias, especially when referred to lifetime consumption habits. Above all, the heterogeneity of definitions of dissociation and cannabis consumption, the variety of psychometric instruments, and the inconsistent levels of measure (somewhere categorical, elsewhere continuous) employed by the studies significantly reduce the comparability and do not allow a quantitative synthesis.

The study design of the selected researches prevents from drawing any firm conclusion about the effect of dissociation on cannabis use and vice versa. In fact, only one study [38] employed a prospective study design (though limited to a 6-month and a 12-month follow-up) and only a half of the included studies accounted for the effect of potential confounder, either statistically controlling for them [44, 45, 52, 53], or using specific sampling strategies, such as restriction [43] or matching [35, 41].

Conclusion

Taken together, the findings of this systematic review suggest that there is no variation in the rates of cannabis use among individuals with dissociative experiences compared with the general population. In addition, the prevalence of dissociative disorders in subjects using cannabis is not different from those not using cannabis. Moreover, despite a few results about the association between dissociation and cannabis, only one study reported an effect of cannabis use on dissociative experiences. Also, weak evidence supports a mediating role of dissociation in the psychopathological pathway between trauma and cannabis use. The limited number of eligible studies, with only four analytical studies, combined with the heterogeneity of the definition of the variables and statistical analyses prevent from any quantitative synthesis as well as clear inference about the direction of the association. Therefore, further methodologically robust studies are warranted to clarify the relationship between dissociation and cannabis use disorder.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES.

Q1. The citation “Halikas et al., 1971” has been changed to “Halikas et al., 1972” to match the author name/date in the reference list. Please check if the change is fine in this occurrence and modify the subsequent occurrences, if necessary.
Q2. The citation “Pekala, 1995” has been changed to “Pekala et al., 1995” to match the author name/date in the reference list. Please check if the change is fine in this occurrence and modify the subsequent occurrences, if necessary.
Q3. The first occurrence of the abbreviation “SCID” was changed to “SCI”. Please check if the captured definition for the said abbreviation is correct. Thank you.
Q4. Please provide complete bibliographic details of these references: 1-4 and 22