



Contextual factors associated with subjective effects of cannabis: A systematic review and meta-analysis

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ABSTRACT

Background: Cannabis is consumed in various social and environmental settings, and such contexts may be important predictors of subjective effects. The aim of this systematic review and meta-analysis was to examine the relationship between contextual factors and subjective effects of cannabis.

Methods: A PRISMA-guided search of MEDLINE, Embase, PsycINFO, Global Health, and Google Scholar yielded 29 studies.

Results: Study type (Ecological Momentary Assessment or Experimental) was a significant predictor of intoxication effects, and experimental studies had a greater pooled effect size ($z = .296, 95\% \text{ CI } [.132, .478]$, $p = .004$) than Ecological Momentary Assessment (EMA) studies ($z = .071, 95\% \text{ CI } [.011, .130]$, $p = .02$). Contextual conditions (environment, social group, expectancy, time of day, day of week) were not significant predictors of cannabis effects.

Conclusion: Findings did not point to a significant association between contextual conditions and subjective effects. However, as current literature is methodologically weak, it may be premature to conclude that subjective effects are not shaped by contextual factors. In view of policy and therapeutic implications, replications and study refinements are recommended.

1. Introduction

1.1. Overview

The non-therapeutic use of cannabis is increasing, with an estimated 4.3 % of the global adult population reporting use in 2021 (United Nations Publications, 2023). Policy changes have introduced legally regulated cannabis markets in some jurisdictions, whilst many other countries have adopted non-punitive responses to possession offences (Bae and Kerr, 2020; Hall et al., 2023; Hughes, 2015; Manthey et al., 2021). Cannabis consumption produces a wide range of subjective effects (Zeiger et al., 2012), and people who use the drug report contradictory or even paradoxical effects, including positive and negative outcomes (Burt et al., 2021; Green et al., 2003). Common subjective effects include altered time perception among people who use cannabis infrequently (Sewell et al., 2013; Tinklenberg et al., 1976), euphoria, improved sleep, elevated appetite, and increased concentration, as well as varied and, at times, contrary effects such as relaxation, anxiety, stimulation, and sedation (Fergusson et al., 2003; Green et al., 2003;

Hunault et al., 2014; Sexton et al., 2019). Minor acute adverse effects include paranoia, experience of dry mouth, and light-headedness (LaFrance et al., 2020). However, high and/or frequent doses of THC increase the risk of cannabinoid hyperemesis syndrome (i.e., cycles of nausea, vomiting, and abdominal pain) (Allen et al., 2004) or acute psychiatric symptoms including psychosis (Monte et al., 2019).

The context in which substance use occurs has also been suggested to affect subjective experiences in humans. Zinberg's (1986) influential "drug, set and setting" account theorizes that responses to drugs are not shaped solely by pharmacological factors, but are also influenced by expectations and their social and environmental contexts (Hartogsohn, 2016). With renewed interest in the therapeutic uses of psychedelics, researchers have begun to revisit this framework and suggest that features in the micro-environment of drug consumption – such as potential for social interaction or positive subjectivity in interpreting intoxication (Engel et al., 2021; Thal et al., 2022) – may play a significant role in shaping the quality of a drug experience (Carhart-Harris et al., 2018). Indeed, previous literature has found that context contributes to broader aspects of cannabis use. For example, people are likely to increase their

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cannabis consumption in social settings where peers are also using cannabis (Buckner et al., 2012; Hughes et al., 2014), while social isolation and loneliness may also lead to higher levels of cannabis use (Bartel et al., 2020). Furthermore, exposure to cues which are unique to a person's substance use experience can increase craving and subsequent use likelihood (Fatseas et al., 2015), highlighting how individual social environments reinforce the salience of drug-related cues (Berridge and Robinson, 2016). Any efforts to consolidate the evidence base regarding subjective experiences of cannabis use should therefore try to account for the possible influence of wider contextual influences.

1.2. Contextual factors

Despite the purported importance of environmental settings, systematic consideration of contextual factors which may influence the experience of cannabis intoxication is lacking (Asbridge et al., 2014). Furthermore, as Becker (1953) notes in a seminal contribution, the peer group is potentially important in managing unpleasant symptoms in novice users, thereby helping redefine their experience. In other words, a person may be presented with an alternative, socially shaped interpretation of events which can be used to label the experience of cannabis intoxication as enjoyable. This is supported by interview data (Hallstone, 2002) and, more recently, by Ecological Momentary Assessment (EMA) work which documented heightened paranoia and negative affect (respectively) during solitary use compared to social use (Denson et al., 2023). Consequently, it is important to understand how social and physical contexts may modulate the experience of cannabis intoxication.

There has been an increase in the use of EMA methodologies to assess variations in cannabis intoxication (Shiffman, 2009). For example, one EMA study found that 83 % percent of variance in participants' ratings of "how high" they were, as well as over half of the variance in reports of sedation and stimulation, was associated with specific to momentary factors, although which factors were not specified (Treloar Padovano and Miranda, 2018). However, few studies have examined the association between intoxication and context in greater detail, and these have yielded mixed results. For example, Jackson et al. (2021) found that social context, but not physical context, was associated with greater subjective intoxication, while Cloutier et al. (2021) did not find any association between physical or social context and intoxication. One reason for this discrepancy could be due to differences in variable samples and power of individual studies, which could be overcome by meta-analytically combining relevant contributions. Consequently, as the unique methodology of EMA studies captures variability in cannabis dosage and intoxication over a period of days as opposed to the typical single-administration sessions of experimental studies, the impact of study design on the relationship between context and intoxication should also be examined meta-analytically (Shiffman, 2009; Spindle et al., 2018).

1.3. Psychological factors

Research is also beginning to indicate that at high doses, the subjective effects of cannabis can mirror those of psychedelics. For example, THC can imitate psychedelic substances at high doses to induce feelings of spirituality (Kuc et al., 2021). Although this does not appear to occur to the same magnitude as serotonergic psychedelics such as psilocybin (Earleywine et al., 2021), people nevertheless report using cannabis to expand perceptual awareness (Johnstad, 2020). This work brings into focus the possibility that at high doses, cannabis effects may be mediated by the motivations and expectations users bring to the behavior as is suggested for psychedelics. When using placebo doses in lab studies, participants who expected to ingest cannabis but received a placebo instead still reported overall increases in acute, cannabis-like subjective effects and affect (Kirk et al., 1998; Loflin et al., 2017). Tension reduction expectancies, in particular, appear related to an increased likelihood of reporting euphoria or positive affect (Barkus et al., 2015; Metrik

et al., 2011). Therefore, a relationship between expectancies and subjective effects may help explain counterintuitive evidence of feeling stimulated or sedated when using cannabis and should be explored as a potential moderator for acute cannabis intoxication (Burt et al., 2021).

As such, while attracting little explicit research attention to date, micro-environmental factors may help explain why contradictory subjective effects are found (e.g., sedating versus stimulating) even when controlling for mode of use and dosage of THC (Block et al., 1998). Although one reason for such discrepancies could relate to individual differences such as tolerance to cannabis (Colizzi and Bhattacharyya, 2018), it is possible that the variation in subjective effects between people who use cannabis may not be explained solely by pharmacological properties of cannabis. For example, some evidence suggests that the endocannabinoid system is impacted by exposure to acute stressors in the environment (Albrechet-Souza et al., 2021; Morena et al., 2016), pointing to a possible interaction between pharmacological and contextual influences in shaping varied subjective effects. Similarly, it has been found that people who use cannabis for conformity motives appear more likely to report acute adverse and distressing reactions to cannabis intoxication than participants using for social motives (LaFrance et al., 2020), indicating that acute stress in the environment may play a role in mediating cannabis effects. Consequently, the psychological expectancies with which cannabis is approached may affect the experience of intoxication (Carhart-Harris et al., 2018).

1.4. Aims and objectives

Overall, there is body of work highlighting that, in addition to settings in which the substance is used, subjective effects of cannabis may also be shaped by the psychopharmacological effects and psychological drivers for use. However, three issues should be addressed. First, little is known about how environmental setting shapes cannabis effects. Second, the extent to which psychological factors (i.e., expectancies) influence the experience of cannabis intoxication is unknown. Finally, with the development of methodologies which allow real-time measurements of cannabis intoxication, study design may emerge as a moderating factor. As such, a systematic review and meta-analysis of this body of knowledge is needed to determine their relative importance to the experience of cannabis intoxication, and consolidating the existing literature will help map out an agenda for future research and theory development.

This review investigated which contextual factors moderate the acute subjective effects of cannabis. The specific objectives were to (1) examine which contextual factors are associated with acute subjective effects of cannabis, (2) consider which psychological factors are associated with acute subjective effects of cannabis and (3) compare how experimental (laboratory) and naturalistic setting administration may moderate acute subjective effects of cannabis.

2. Methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Page et al., 2021), and the review protocol was registered on OSF (<https://osf.io/cnxvw>) on 4th May, 2022. The authors declare no competing interests. This study was funded by Edge Hill University.

2.1. Search strategy

The databases Medline, Embase, PsycINFO, Global Health, CENTRAL, and the top 400 results of Google Scholar were electronically searched within a timeframe of the database inception date to 5th May, 2022. Results from the database searches were imported into Endnote X7, and references of relevant studies were examined on 15th July, 2023.

Title and abstract were searched with the following keyword

strategy: (Cannabis OR Marijuana OR THC) AND (dose* or randomi* or laboratory or placebo or Ecological or Smartphone or Mobile or Daily or Interactive Voice Response or Experience sampling method or intensive longitudinal) AND (high or intoxicat* or subjective or acute). Due to character limits, the term “high” was not included in the Google Scholar search.

2.2. Eligibility criteria

Studies were included if they examined acute cannabis subjective effects or intoxication as an outcome of any contextual variable, were peer-reviewed papers, grey literature, or unpublished data, and were reported in English. Exclusion criteria were clinical studies examining the efficacy or effectiveness of interventions aiming to alter cannabis consumption patterns or treat withdrawal symptoms, clinical trials examining the tolerability or side-effect profile of cannabis as a medication (antiemetic, analgesic, or anesthetic), reviews, books, posters, abstracts, editorials, and animal studies. Additionally, EMA Studies which used non-electronic diaries were excluded due to potential methodological issues from “car park compliance”, which refers to completion of reports just prior to their submission (Smyth and Stone, 2003).

The population included adults who used cannabis (infrequent, moderate, heavy, or clinical level of administration), and the context was the laboratory or the participants’ environment. For experimental studies, the comparator was a within- or between-cohort comparison of different contextual variables (e.g. music versus no-music condition). In EMA studies, contextual measures (e.g., physical location or peer group) were considered as the main exposure variables. Main outcome variables included any reported measurement of subjective effects due to cannabis use. Commonly used scales included the Self-Assessment Manikin (SAM), ARCI-Marijuana Scale (ARCI-M), Profile of Mood States (POMS), Cannabis Experiences Questionnaire (CEQ), Drug Experiences Questionnaire (DEQ), Modified Lyons Battery for Subjective Effects (MLBSE), or Visual Analog Scales (VAS) for specific effects such as anxiety or paranoia (Bradley and Lang, 1994; Haertzen and Hickey, 1987; Lyons et al., 1997; McNair et al., 1971; Morean et al., 2013; Quinn et al., 2017). No secondary outcomes were considered.

2.3. Data extraction and quality assessment

One independent reviewer determined if studies met the eligibility requirement by first examining the title and abstract of studies returned from the database search. Following this, the full text of studies which passed the title and abstract screening were further examined. In the event of uncertainty regarding inclusion (157 cases), studies were discussed with a second reviewer and the reason for inclusion or exclusion was agreed upon (see Appendix C). A summary of the extracted variables is presented in Table 1.

Finally, since the review included observational and experimental studies, the risk of bias tool developed by Kmet and colleagues (2004) was used to assess primary research papers.

2.4. Meta-analytic strategy

A multivariate meta-analysis was conducted with study type (EMA or Experimental) and contextual conditions which emerged during the literature search (environment, social group, expectancy, time of day, day of week) as predictors of the effect size. Additionally, pooled effect sizes of EMA and experimental studies were compared. Data were first transformed to Cohen’s *d* (assuming equal sizes in each group) and reviewed for normal distribution before conducting the meta-analysis. Effect sizes not reported by a study were calculated and the effect size of the relationship between each exposure variable and the outcome variable was reported as Pearson’s *r*. Heterogeneity of studies was assessed using I^2 statistics. Finally, publication bias was assessed using a

funnel plot of cannabis intoxication scores and Egger’s test. Statistics were run in R v4.2.3 using the packages *effectsize* ver.0.8.5, *DescTools* ver.0.99.49, and *metafor* ver.4.2–0.

3. Results

The literature search yielded a total of 11,979 results, of which 5860 were duplicates. After further screening and reference searches, a total of 29 studies were identified as meeting the inclusion criteria (Fig. 1). The characteristics of these studies are listed in Tables 2–3. The top three reasons for exclusion were that the study did not measure context as a study condition, the study was a review or only the abstract was available, and that acute THC intoxication was not measured. Other potentially relevant studies were not included as they were published past the search timeline of May 2022 (i.e., Denson et al., 2023).

3.1. Study characteristics

Overall, 27 studies were conducted in North America, one was conducted in Spain, and one was conducted in New Zealand. One included study was a dissertation publication that was not a peer-reviewed journal article (Rudy, 2020). Contextual variables included environment relaxedness, social group, expectancy, time of day, and day of week. Intoxication was evaluated using a variety of outcome measures, including self-rated intoxication scales, the ARCI, Waskow’s Subjective Drug Effects Questionnaire, the Clyde Mood Scale, POMS, and PANAS (Fisher et al., 1969; Haertzen and Hickey, 1987; McNair et al., 1971; Watson et al., 1988). The Risk of Bias evaluation tool identified one experimental study as “high risk”, whereas all ten EMA studies and one experimental study were classified as “low risk”, and the remaining 17 experimental studies were assessed as “medium risk”.

3.1.1. Experimental studies

Nineteen studies utilized an experimental design, of which eighteen studies were placebo-controlled. Sample sizes ranged from 9 to 114 participants, were predominantly male, and drawn from a non-clinical population. Furthermore, 63 % of studies reported a sample of 100 % male participants; no study had a majority female sample, and prior history of a psychiatric or substance use disorder was an exclusion criterion for thirteen studies. One study was conducted in a treatment center for criminal offenders. Finally, the mean age of the study samples ranged from 20.1 years (SD = 1.1) to 27.2 years (SD = 5.6).

There was variability in the experimental design and procedures. Where THC dosage was reported as a percentage, the range was between 0.9 % and 11.5 % THC. Where THC dosage was reported in mg, the available range was between 3 mg to 42 mg. However, due to variation in the smoking administration procedure between studies, several studies could not clearly report how much THC was ingested by each participant when they were not required to consume the entire cigarette. Among the seventeen studies where cannabis was smoked, the first measurement of subjective intoxication was taken anywhere between 0 minutes (just after administration) to 120 minutes. Finally, two studies administered cannabis orally. In the first study, intoxication was measured at 90 and 210 minutes. In the second study, measurements of intoxication were taken at 30-minute intervals up to 300 minutes, starting at ingestion (0 minutes).

3.1.2. EMA studies

Ten EMA studies met the inclusion criteria. All ten studies used signal-contingent methodology, with a range of one to six signals sent per day and daily compliance rates between 58.4 % and 95 %. The study periods were between 10 and 70 days, and several studies sent signals in multiple 14-day bursts. With the exception of gender, sample characteristics in the EMA study were similar to the samples recruited in the experimental studies. 60 % of studies reported a majority female sample, and only one study recruited young adults from a medical clinic. The

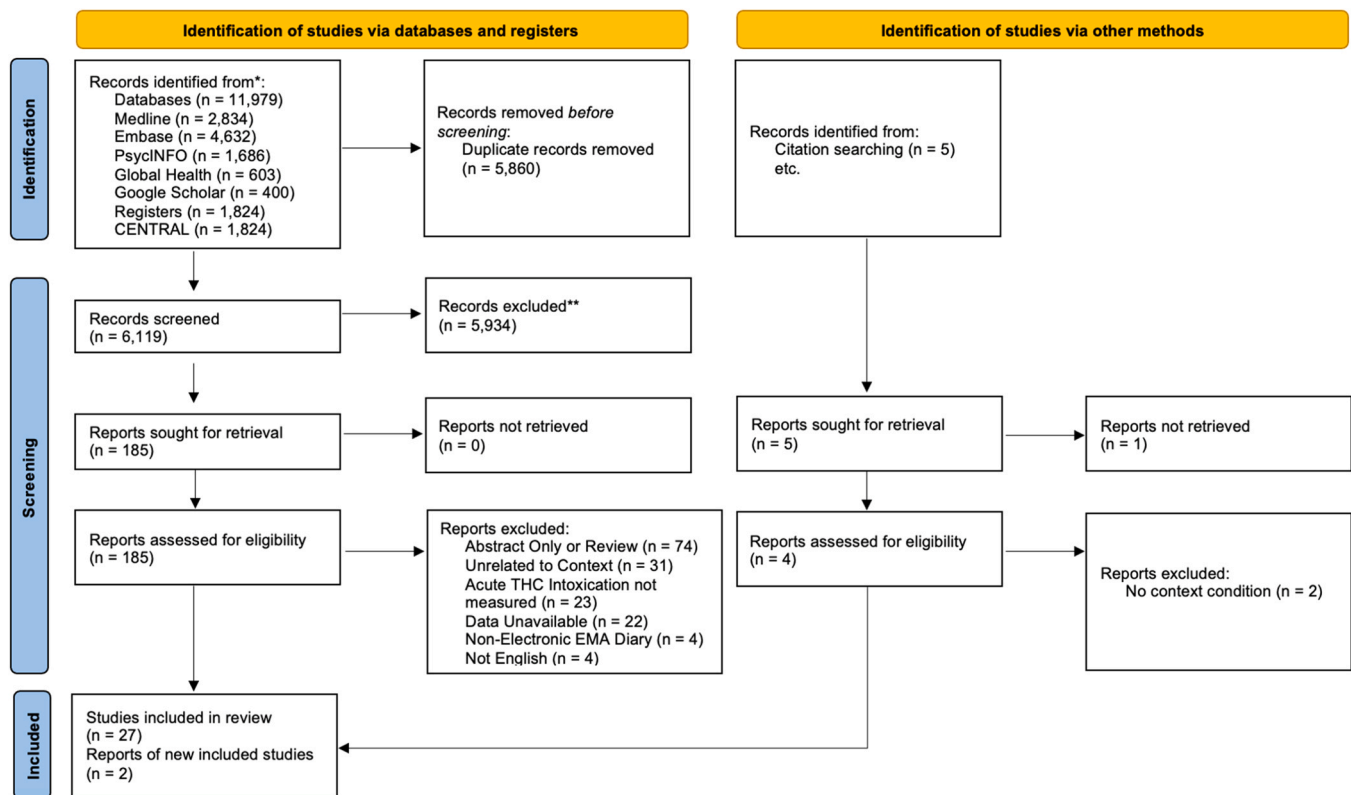


Fig. 1. PRISMA Flowchart of study search and selection process. Note. The PRISMA flowchart illustrates the number of records identified from databases (n=11,979) and citation searching (n=5), the number of duplicates removed (n=5860), total records screened (n=6119), studies assessed for eligibility (n=185), number of studies excluded with reasons, and the total number of studies included in the review (n=29).

mean age of the participants ranged from 18.7 years (SD = 2.1) to 24.3 years (SD = 7.4). Overall, the sample sizes used in the studies ranged between 27 and 341 participants. 80 % of EMA studies assessed the quantity of cannabis used by participants; four studies counted the number of hits (Shrier et al., 2013; Linden-Carmichael et al., 2020; Rudy, 2020; Cloutier et al., 2021), three studies reported the number of grams (Bravo et al., 2017; Fairlie et al., 2021; Patrick et al., 2020), and one study calculated potency (Trull et al., 2022). Of the studies examining quantity of cannabis used by grams, only one differentiated between personal and shared consumption (Patrick et al., 2020). Finally, all EMA studies assessed contextual variables at a within-person level. Four studies included mode of cannabis use as a pharmacological covariate (Cloutier et al., 2021; Shrier et al., 2013; Sokolovsky et al., 2020; Trull et al., 2022), and two studies controlled for quantity of use (Cloutier et al., 2021; Trull et al., 2022).

3.2. Contextual variables

3.2.1. Expectancies

Experimental studies examining expectancies were methodologically heterogeneous, including in use of outcome measures. One study examined aversive, non-cannabis odor as an expectancy (Pihl et al., 1978a), while four studies examined an instructional set (telling participants they will receive THC or placebo) (Camí et al., 1991; Kirk et al., 1998; Metrik et al., 2011, 2009). The study which examined self-rated intoxication based on an aversive odor or no-odor condition found no significant effect, and did not report any directional effect sizes or p-values (Pihl et al., 1978a).

When comparing subjective effects for the conditions “informed” (received THC when expecting THC) or “non-informed” (received THC when not expecting THC), Kirk et al. (1998) found that the informed group reported greater intoxication than the non-informed group on the

ARCI-M (Euphoria scale) (p-value not reported). However, no significant effect was found for self-reported VAS responses to “stimulated” or “anxious”. Other studies which compared these conditions did not report any effects for the ARCI-M or self-rated intoxication scales (Camí et al., 1991; Metrik et al., 2009). On the POMS, a significant effect for expectancies was observed for the Vigor-Activity subscales ($p < .05$), but not the Tension-Anxiety subscales (p-value not reported) (Metrik et al., 2011). Finally, in one study which compared the conditions “Received, Not Expected” to “Not Received, Expected”, a time-course graph showed that overall high of both conditions reached a similar peak; however, neither the effect size nor significance of this comparison was reported (Camí et al., 1991). Further emphasizing the heterogeneity in methodology and outcome is Kirk et al. (1998)’s study, which administered oral cannabis in contrast to other studies which examined expectancy of smoked cannabis. It is possible that the delay in intoxication from oral consumption contributed to a stronger expectancy effect, which was consequently large enough to be captured on the ARCI-M measurement tool. However, since oral consumption of cannabis and the ARCI-M were not utilized in other expectancy studies (i.e., Camí et al., 1991), it is difficult to narratively compare results across literature in order to establish this conclusion. As such, while the range of subjective effects measured in expectancy studies highlights the multidimensional nature of cannabis intoxication, further studies are required to understand the extent to which momentary expectancies influence cannabis intoxication.

Overall, momentary expectancies may be more important for oral cannabis consumption than for smoked consumption due to a delayed onset of high, whereas expectancies about consuming THC when consuming placebo appears less relevant to cannabis intoxication in a real-world setting. However, due to methodological heterogeneity amongst studies and the lack of studies examining oral cannabis expectancies, it is difficult to draw any conclusions on the relationship

Table 2
Study Characteristics for Experimental Studies.

Authors, Year, Location	Condition(s)	Sample Characteristics	Dosage and Mode of Cannabis Use	Design and Analysis	Risk of Bias	Outcome Measurement	Measurement timepoint(s)	Main Findings
[1] Carlin et al., (1972) (Study 1); USA	Social setting through accomplice modeling	40 participants, 100 % male, aged 21 – 32 years, Mean age (SD) = 24 years (NR)	1.5 % THC, total of 15 mg THC; Smoked cigarette	[D] Placebo-controlled, double-blind [A] 2 × 2 ANOVA, Between-person	0.54	Self-rated Intoxication Scale	60 minutes	Ratings of intoxication were a function of whether one received drug or placebo only and not significantly by social setting; p-values not reported.
[2] Carlin et al., (1972) (Study 2); USA	Social Setting through accomplice modeling	80 participants, 100 % male, aged 21 – 34 years, Mean age (SD) = 23.7 years (NR)	7.5 mg (low dose group) and 15 mg THC (high dose group); Smoked cigarette	[D] Placebo-controlled, double-blind [A] 2 × 2 ANOVA, Between-person	0.54	Self-rated Intoxication Scale	60 minutes	Social facilitation and dosage had no effect on the ratings; p-values not reported.
[3] Carlin et al., (1974) ; USA	Social Setting through accomplice modeling	40 participants, 100 % male, aged 21 – 34 years, Mean age = 24.2 years (NR)	1.5 % THC, total of 15 mg THC; Smoked cigarette	[D] Placebo-controlled [A] ANOVA, Between-person	0.54	Self-rated Intoxication Scale; Linten and Lang	30 minutes	Social modeling variable had no effect on ratings of intoxication or number of items endorsed on Linten and Lang checklist; p-values not reported.
[4] Hollister et al., (1975) ; USA	Social setting through favorable versus austere environment	12 participants, 100 % male, age not reported	19 mg THC; Smoked cigarette	[D] Placebo-controlled [A] Euphoria: ANOVA (subjects x conditions x drugs x time periods); ARCI: fully crossed, four-way repeated ANOVA (subjects x drugs x conditions x time periods), Within-person	0.46	Self-rated Euphoria Scale (“Sadness – Happiness”); ARCI	Euphoria scale: 30, 60, 120, and 180 minutes; ARCI: 60 and 120 minutes	Significant effects of condition were not seen for Euphoria nor ARCI-M; p-values not reported.
[5] Stillman et al., (1976) ; USA	Stress condition	9 participants, 100 % male, age not reported	10 mg THC; Smoked cigarette	[D] Placebo-controlled [A] 2 × 2 ANOVA, Between-person	0.43	Self-rated intoxication scale; Waskow Subjective Drug Effects	15 minutes, 30 minutes, 60 minutes, 2 hours, 4 hours, 8 hours, 24 hours	A significant stress effect was present for self-rated intoxication ($p < .01$) and the following subjective effects on the Waskow Subjective Drug Effects: “Head lighter” ($p < .01$), “See images” ($p < .05$), “Felt Sleepier” ($p < .05$), “Felt more nervous” ($p < .01$), “Felt more calm and steady” ($p < .01$), “On top of the world” ($p < .01$); Exact p-values not reported.
[6] Pihl et al., (1977) ; Canada	Social setting through aversive stimuli	96 participants, 100 % male, aged 18 – 35 years, Mean age (SD) = 23 years (NR)	4 cigarettes of 5 mg THC & 4 cigarettes of 3 mg THC (low dose), 4 cigarettes of 6 mg THC & 4 cigarettes of 4.5 mg THC (high dose); Smoked cigarette shared among participants	[D] Placebo-controlled, single-blind [A] ANOVA (environment x drug x times), Between-person	0.54	Clyde Mood Scale; Self-rated intoxication scale (graph); Self-rated ‘How Relaxed’ scale (“relaxed” – “tense”)	0, 20, 30, 40, 60, 70, and 80 minutes	Analysis yielded a significant environment effect for the self-rated intoxication scale ($p < .05$) and “relaxed” scale ($p < .05$); no significant findings in The Clyde Mood Scale for drug or environment effect (p-value not reported); Exact p-values not reported.
[7] Pihl et al., 1978a (Study	Social setting through aversive and	48 participants, 100 % male, aged 19 – 25 years, Mean age = 23 years (NR)	4 cigarettes of 5 mg THC & 4 cigarettes of 3 mg THC (low	[D] Placebo-controlled, double-blind; Counterbalanced	0.57	- Self-rated intoxication scale (graph); Self-rated ‘How	0, 20, 30, 40, 60, 70, and 80 minutes	Significant interaction between dosage and the order of stimulus presentation (music vs.

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Table 2 (continued)

Authors ₂ , Year, Location	Condition(s)	Sample Characteristics	Dosage and Mode of Cannabis Use	Design and Analysis	Risk of Bias	Outcome Measurement	Measurement timepoint(s)	Main Findings
1); Canada	favorable stimuli		dose), 4 cigarettes of 6 mg THC & 4 cigarettes of 4.5 mg THC (high dose); Smoked cigarette	[A] Four Factor ANOVA (drug x time x environmental condition x order of presentation), Within- person		Relaxed' scale ("relaxed" – "tense")		odor) ($p < .001$); the 'How Relaxed' Scale yielded only a significant drug effect ($p < .002$); Exact p- values not reported.
[8] Pihl et al., 1978a (Study 2); Canada	Negative Expectancy	24 participants, gender and age not reported	4 cigarettes of 5 mg THC & 4 cigarettes of 3 mg THC (low dose), 4 cigarettes of 6 mg THC & 4 cigarettes of 4.5 mg THC (high dose); Smoked cigarette	[D] Not placebo- controlled [A] Analysis method not stated, Between- person	0.21	Self-rated intoxication scale (graph)	0, 20, 30, 40, 60, 70, and 80 minutes	When the expectancy group of aversive odor was compared with the no odor group, no significant condition effects occurred; p- values not reported.
[9] Pihl et al., 1978b; Canada	Stress Condition	60 participants, 100 % male, aged 18 – 31 years, Mean age (SD) = 21.6 (NR)	1 % THC, total of 6 mg THC; Smoked cigarette	[D] Placebo-controlled [A] Three-way ANOVA (Drug x Environment x Time), Between-person	0.36	Self-rated intoxication scale; Self-rated 'How Relaxed' scale ("neutral" – "relaxed")	0, 10, 20, and 30 minutes	There was a significant difference in the ratings of cannabis intoxication ($p < .05$) and relaxation ($p < .001$) between the threat and no-threat group; Exact p-values not reported.
[10] Stark- Adamec et al., (1981); Canada	Social group	24 participants, 100 % male, aged 21 – 31 years, Mean age = 24 years (NR)	1.5 % THC, total of 3–5 mg THC; Smoked cigarette	[D] Placebo-controlled [A] Three-way MANOVA (Drug x Social condition x Order), Between- person	0.36	High Questionnaire	120 minutes	The only significant main effect was for drug effects ($p < .208$).
[11] Marks and Pow, (1989); New Zealand	Social group	24 participants, 50 % male, aged 19 – 24 years, Mean age & SD not reported	2.4 % THC, combined with placebo to create different dosages (0, 3.5, 7.0, 10.5 or 14.0 mg THC) at the same weight; Smoked pipe	[D] Placebo- controlled, double- blind; Counterbalanced [A] $2 \times 2 \times 2 \times 5$ ANOVA (Main Effects: sex of subjects, acquaintanceship, subjects, time, and cannabis), Between- person	0.43	Self-rated intoxication scale; Self-rated highness scale	0 and 120 minutes	Significant interaction between cannabis highness ($p < .001$) or intoxication level ($p < .01$) and acquaintanceship interactions; Exact p- values not reported.
[12] Cami et al., 1991; Spain	Told THC/ Placebo Expectancy	96 participants, 100 % male, aged 21 – 31 years, Mean age & SD not reported	11.5 % THC, total of 23 mg THC combined with tobacco; Smoked cigarettes	[D] Placebo- controlled, double- blind; Counterbalanced [A] Mann-Whitney Test, Between-person	0.54	Self-rated intoxication scale	0, 50, 100, 150, 200, 250, and 300 minutes.	Statistically significant differences were not found for high between subjects who received the drug with Told THC or Told Placebo; p-values not reported.
[13] Kirk et al., (1998); USA	Told THC/ Placebo Expectancy	35 participants, 54 % male, Mean age (SD) = 23.5 years (4.3)	7.5 mg (low dose group) and 15 mg THC (high dose group); Oral THC	[D] Placebo- controlled, double- blind, randomized [A] Mixed-factor three- way ANOVA (dose x hour x group), Between-person	0.54	VAS "stimulated", "anxious", "sedated"; ARCI	0, 30, 60, 90, 120, 150, 180, 210, 240, 270, 300 minutes	The "told THC" group reported higher ratings on ARCI's euphoria scale than the "told placebo" group following placebo or either dose of THC; drug, but not group, increased VAS ratings; exact p-values not reported.

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Table 2 (continued)

Authors ₂ Year, Location	Condition(s)	Sample Characteristics	Dosage and Mode of Cannabis Use	Design and Analysis	Risk of Bias	Outcome Measurement	Measurement timepoint(s)	Main Findings
[14] Metrik et al., (2009); USA	Told THC/ Placebo Expectancy	20 participants, 75 % male, Mean age (SD) = 20.1 years (1.1)	2.8 % THC; Smoked cigarette	[D] Placebo- controlled, double- blind, randomized [A] Between-subjects factors ANOVA (instructions x drugs); Regression Analysis (pre-smoking ratings, pharmacologic effect, expectancy effect)	0.57	Self Assessment Manikin Scale; ARCI-M	0 and 45 minutes	The main and interaction effects of expectancy were not significant for ARCI-M ratings; stimulus expectancy non- significantly decreased self-reported levels of arousal on the SAM at the end of the smoking, with a large size effect; p-values not reported.
[15] Metrik et al., (2011); USA	Told THC/ Placebo Expectancy	114 participants, 66 % male, Mean age (SD) = 21.5 years (3.3 years)	2.8 % THC; Smoked cigarette	[D] Placebo- controlled, double- blind, randomized [A] 2x2x2 Repeated Measures ANOVA (Timepoint x Drug x Expectancy); Multiple regression analyses, Between-person	0.75	Self Assessment Manikin Scale; ARCI-M; POMS	0 and 16 minutes	On the ARCI-M, the main and interaction effects of stimulus expectancy were not significant; significant main effects for stimulus expectancy were observed for POMS vigor-activity ($p < .05$) but not the POMS Tension- Anxiety; exact p-values not reported.
[16] Keith et al., (2017); USA	Time of Day	10 participants, 70 % male, Mean age (SD) = 27.2 years (5.6)	1.9 % or 3.56 % THC; Smoked cigarette	[D] Placebo-controlled [A] 3-factor Repeated Measures ANOVA (drug x shift condition x day within condition), Within- person	0.43	Self-rated intoxication scale; VAS: Mood, Drug Effect; DEQ: Good Drug Effect and Bad Drug Effect	Self-rated intoxication scale & VAS (mood, drug effect): 45 minutes; DEQ: 15 minutes	Ratings of “stimulated” were increased by low and high THC dosage on the day shift; ratings of “stimulated” were increased only by high THC dose on the night shift ($p < .05$); exact p- values not reported.
[17] Waskow et al., (1970); USA	Social setting through favorable versus austere environment	32 participants, 100 % male, age not reported	20 mg THC; Oral THC	[D] Placebo- controlled, double- blind, randomized [A] Mann-Whitney Test, Between-person	0.50	SDEQ; Clyde Mood Scale (Friendly, Sleepy, Unhappy, Dizzy)	90 and 210 minutes	There were no significant effects of music condition on the Clyde Mood Scale or the SDEQ; p-values not reported
[18] Adamec and Pihl, (1978); Canada	Social group	16 participants, 50 % male, females aged 22 – 30 years, Mean age (SD) = 24.8 years (NR), males aged 21 – 30 years, Mean age (SD) = 22 years (NR)	1.5 % THC (Maximum 8 mg THC); Smoked Cigarette	[D] Placebo-controlled [A] MANOVA, Within- person	0.36	Self-rated intoxication scale; Mood Scale (Smith and Beecher, 1959)	30, 59, 90, 125, 190 and 210 minutes	Friends rated themselves more stoned than strangers on four placebo trials and five cannabis timepoints ($p < .05$); there were no statistically significant drug effects or drug interaction effects on mood; exact p-values not reported
[19] Jones, (1971); USA	Social group	100 participants, 100 % male, aged 21 – 30 years, Mean age & SD not reported	0.9 % THC (9 mg THC); Smoked Cigarette	[D] Placebo-controlled [A] Not specified, Within-person	0.36	Self-rated intoxication scale; SDEQ	Self-rated intoxication scale: 30 minutes; SDEQ: 45 minutes	A statistically significant difference was found between the group setting and the solitary setting for euphoria ($p < .01$) and perceptual change ($p < .05$); exact p- values not reported

Note: "SD" denotes standard deviation, "NR" denotes data not reported, "ARCI" stands for the Addiction Research Center Inventory, "VAS" stands for Visual Analog Scale, "ARCI" stands for Addiction Research Center Inventory, "POMS" stands for Profile of Mood States, and "SDEQ" stands for Subjective Drug Effects Questionnaire. Study design is denoted by [D], and the study's analysis methods are denoted by [A]. Regarding Risk of Bias, scores exceeding 0.66 indicate a low risk of bias, scores between 0.33 and 0.66 indicate a medium risk of bias, and scores equal to or less than 0.33 indicate a high risk of bias. Exact p-values are provided where available, else it is noted that “exact p-values not reported” (in cases where only a range is given) or “p-values not reported” (in cases where the p-value was not given).

Table 3
Study Characteristics for EMA Studies.

Authors, Year, Location	Sample Characteristics	Design and Analysis	Compliance Rate	Risk of Bias	Variables Measured	Outcome Measurement	Main Findings
[20] Shrier et al., (2013); USA	44 participants, 42 % male, aged 15 – 24, Mean age (SD) = 18.7 years (2.1)	[D] Signal-contingent sampling: Total 4–6 signals per day & Event-contingent sampling: Just after using; Length of Study: 10–14 days [A] Multivariate model, Within-person	Mean Rate of Response (SD) = 71 % (21 %)	1.00	Contextual: Companionship (home, friend's house, school, work, other), Physical Setting (Friend's house; school, work, other; home), Time of Day, Day of Week (Weekend: Fri 3 pm - Sun 11:59 pm); Pharmacological: Mode of Use (joint, blunt, pipe, bong, ate it, vaporizer, other)	Subjective Intoxication "How High"; Quantity: Number of hits	Location (p=0.58), time of day (p=0.38), and day of week (p=.99) not significant predictors for high; Referent to friends, participants less likely to be high when parents or significant other are present, or when alone (p=0.23).
[21] Linden-Carmichael et al., (2020); USA	154 participants, 42.2 % male, Mean age (SD) = 20.24 years (1.45)	[D] Signal-contingent sample: Total 1 signal per day; Length of Study: 14 days [A] Multilevel Modeling (Level 1 – day level, Group mean centered), Within-person	Mean Daily Surveys Completed per person (SD) = 13.13 (1.95); Participants who completed all 14 daily surveys: 58.4 %	0.91	Contextual: Day of Week (Weekend: Thu – Sat)	Subjective Intoxication "How High"; Quantity: Number of hits	Weekends significantly predicted greater levels of subjective cannabis intoxication (p<.05); exact p-value not reported.
[22] Patrick et al., (2020); USA	281 participants, 50 % male, Mean age (SD) = 21.8 years (2.16)	[D] Signal-contingent sample: Total 2 signals per day; Length of Study: 28 days (Two 14-day bursts) [A] Multilevel Modeling, Within-person	Completed morning surveys in Burst 1: 88 % (M= 12.38, SD=2.21); Completed morning surveys in Burst 2 = 80 % (M=11.19, SD=3.89)	1.00	Contextual: Day of Week (Weekend: Thu – Sat)	Subjective intoxication "How High"; Quantity: Number of grams	Weekend predictor of 'how high' was not significant; exact p-value not reported.
[23] Sokolovsky et al., 2020	341 participants, 48.7 % male, Mean age (SD) = 19.8 years (1.32)	[D] Signal-contingent sample: Total 5 signals per day; Length of Study: 56 days (Two 28-day bursts) [A] Linear mixed effects model with Random Effects (Level 1 – day level), Within-person	All available prompts completed = 61.3 %; Daily coverage = 75.4 %	0.95	Contextual: Day of Week (Fri or Sat); Pharmacological: Mode of use (dry leaf, concentrate, edible)	Subjective Intoxication; Quantity: Not reported	Weekends significantly predicted greater levels of subjective cannabis intoxication (p<.001); exact p-value not reported.
[24] Cloutier et al., (2021); USA	105 participants, 49 % male, Mean age (SD) = 20.28 years (1.49)	[D] Signal-contingent sample: Total 1 signal per day; Length of Study: 14 days [A] Multilevel Modeling (level 1 – day level), Within-person	Participants who completed at least one daily survey: 95 %; Mean Daily Surveys Completed (SD) = 13.13 (1.95)	1.00	Contextual: Companionship (alone vs. 1+ people), Physical Setting (Home; Not Home); Pharmacological: Mode of Use (joint, blunt, bong, pipe, vaped, edible)	Subjective Intoxication "How High"; Quantity: Number of hits	Social use and home use were not significant predictors of intoxication; p-value not reported.

(continued on next page)

Table 3 (continued)

Authors, Year, Location	Sample Characteristics	Design and Analysis	Compliance Rate	Risk of Bias	Variables Measured	Outcome Measurement	Main Findings
[25] Fairlie et al., (2021); USA	321 participants, 49.1 % male, Mean age (SD) = 21.61 years (2.17)	[D] Signal contingent sample: Total 2 signals per day; Length of Study: 70 days (Five 14-day bursts) [A] Multilevel Model (level 1), Within-person	Morning surveys completed = 79.64 %; Afternoon surveys completed = 80.07 %	1.00	Contextual: Day of Week (Weekend: Thu – Sat)	Subjective intoxication “How High”; Quantity: Number of grams	Relative to weekdays, weekend days were significantly associated with greater subjective high on SAM days ($p < .001$); exact p-value not reported.
[26] Jackson et al., (2021); USA	341 participants, 38.6 % male, Mean age (SD) = 19.8 years (1.3)	[D] Signal contingent sample: Total 5 signals per day; Length of Study: 56 days (Two 28-day bursts) [A] - Multilevel Modeling (level 1 – survey, day mean centered & level 2 – day, person mean centered), Within-person	Not reported	0.95	Contextual: Companionship (Alone, Significant Other, Roommate, Friend, Family, Strangers, Acquaintance, Someone Else), Physical Setting (home; friend’s place)	Subjective Intoxication; Quantity: Not reported	Using with friends ($p < .01$) and at a friend’s place ($p < .01$) were significantly associated with greater odds of intoxication; exact p-values not reported.
[27] Rudy, (2020); USA	27 participants, 51.9 % male, Mean age (SD) = 19.8 Years (1.2)	[D] Signal contingent sample: Total 3 signals per day; Length of Study: 14 days [A] Linear Mixed Model, Fixed Factors, Within-person	Total completed daily surveys administered to all participants: 91.9 %	1.00	Contextual: Time of Day, Day of Week (Weekend: Not defined);	Subjective intoxication; Quantity: Number of hits	Intoxication symptom scores were significantly higher in afternoon compared to mornings ($p < .001$); evening intoxication scores were significantly higher compared to afternoons ($p < .001$); There was insufficient evidence to suggest that intoxication symptoms varied significantly by day of week; exact p-values not reported.
[28] Trull et al., (2022); USA	50 participants, 52 % male, aged 18 – 50 years, Mean age (SD) = 24.32 years (7.36)	[D] Signal contingent sample: Total 5 signals per day & Event Contingent sample: Self-initiated report after using cannabis; Length of Study: 14 days [A] Multilevel Modeling using momentary-, day-level predictors, Within-person	Total random prompts completed: 73 %; Total morning prompts completed: 91 %	0.95	Contextual: Companionship (Alone or with others); Pharmacological: Mode of Use (smoke, vape, edible)	Subjective intoxication “Feeling High”, ARCI-M; Quantity: Number of grams	Being with others significantly predicted scores of, subjective intoxication ($p = .009$) but not ARCI-M + high ($p = .12$)

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Table 3 (continued)

Authors, Year, Location	Sample Characteristics	Design and Analysis	Compliance Rate	Risk of Bias	Variables Measured	Outcome Measurement	Main Findings
[29] Bravo et al., (2017); USA	59 participants, 30.5 % male, Mean age (SD) = 23.24 years (8.21)	[D] Signal contingent sample: Total 1 signal per day; Length of Study: 12 days [A] One-way repeated-measure ANOVA, Within-person	Total surveys completed: 73.1 %	0.82	Contextual: 4/20 Event, Day of Week (Weekend: Thu – Sat)	Subjective Intoxication “How High”; Quantity: - Number of grams	There was no significant relationship between day of week or 4/20 event and subjective intoxication (p= .213).

Note. "SD" denotes standard deviation, "ARCI" stands for Addiction Research Center Inventory. Study design is denoted by [D], and the study's analysis methods are denoted by [A]. Regarding Risk of Bias, scores exceeding 0.66 indicate a low risk of bias, scores between 0.34 and 0.66 indicate a medium risk of bias, and scores equal to or less than 0.33 indicate a high risk of bias. Exact p-values are provided where available, else it is noted that "exact p-values not reported" (in cases where only a range is given) or "p-values not reported" (in cases where the p-value was not given).

between momentary expectancies and cannabis intoxication.

3.2.2. Social group

Findings were inconclusive in experimental studies which examined the impact of social group on cannabis intoxication. In a series of studies where an accomplice modeled intoxicated behaviors to participants, no significant effects were found for the relationship between social modeling behavior and self-rated intoxication (p-values not reported) (Carlin et al., 1972; Carlin et al., 1974). Additionally, no significant effect was found for the relationship between intoxication and using cannabis with friends, strangers, or when alone, as measured by the High Questionnaire and a mood scale by Smith and Beecher (1959) (p-values not reported) (Adamec and Pihl, 1978; Stark-Adamec et al., 1981). However, contrary to non-significant results using the mood scale, Adamec and Pihl (1978) found that friends rated themselves significantly more stoned than strangers at varying timepoints ($p < .05$). Potentially, this indicates that the outcome measurement tool may play a role in the mixed results (Adamec and Pihl, 1978). Marks and Pow (1989) also found a significant relationship between THC dose, acquaintanceship, and self-rated intoxication ($p < .001$), wherein strangers reported greater intoxication than friends at low doses. However, overall, strangers reported being less 'high' than friends, which continues to highlight a potential distinction in results depending on whether participants were asked about being 'intoxicated' or being 'high'. Finally, Jones (1971) found that ratings of euphoria ($p < .01$) and perceptual change ($p < .05$) on the SDEQ were significantly greater in a group setting compared to a solitary setting. Therefore, although there is some experimental indication that presence of a social group impacts cannabis intoxication, this evidence appears dependent on the outcome measurement scale utilized.

Four EMA studies tentatively suggested that relative to being alone, being with company was associated with increased subjective cannabis intoxication (Cloutier et al., 2021; Jackson et al., 2021; Shrier et al., 2013; Trull et al., 2022). Both Shrier et al. (2013) and Jackson et al. (2021) reported that using with friends specifically was associated with greater intoxication, although this association was significant only in Jackson et al. (2021) ($p < .01$). Additionally, while Cloutier et al. (2021) and Trull et al. (2022) did not examine a specific breakdown of social group, using cannabis with at least one other person present was associated with greater intoxication than using cannabis alone. Interestingly, however, this association was significant in Trull et al. (2022) when using an outcome measure of subjective highness ($p = .009$) instead of the ARCI-M.

Overall, experimental and EMA studies found that relative to using alone or with strangers, consuming cannabis with friends was associated with greater intoxication. Tentatively, results from experimental studies on social modeling suggest that seeing other people intoxicated is not a major driver of intoxication in social groups. The importance of social

group is further supported by EMA studies which found that using cannabis at alone was associated with less peak intoxication than using cannabis with friends. Finally, there is some evidence to suggest that unfavorable or stressful stimuli can reduce intoxication levels. However, the risk of bias for experimental studies examining social group and experimental setting was rated medium to high, and the variation in significance implies that some results may be attributable to chance rather than a true statistical difference. Of the studies which were significant, this could potentially be attributed to the higher dosage of THC administered (Marks and Pow, 1989) or a greater sample to detect differences (Jackson et al., 2021; Jones, 1971). Therefore, although evidence suggests that the presence of a social group influences cannabis intoxication, support is limited for this conclusion due to methodological limitations and insufficient evidence.

3.2.3. Environmental characteristics

3.2.3.1. Experimental setting. There is minimal support from experimental studies that a relationship exists between environmental characteristics and cannabis intoxication. Two studies found no significant effects of pleasant sensory stimuli on measures of the ARCI-M, SDEQ, or the Clyde Mood Scale (p-values not reported) (Hollister et al., 1975; Waskow et al., 1970). Furthermore, in Pihl et al. (1977), there were no differences between a music condition and noise condition when using the Clyde Mood Scale. However, this same study found a significant environmental effect when using a self-rated intoxication ($p < .05$) instead of the Clyde Mood Scale, with participants reporting a greater high in the music condition versus noise condition.

Further studies provide evidence that environmental setting alters self-rated intoxication. Pihl et al. (1978a) found that aversive stimuli (noise) led to a greater high in lower doses of cannabis, whereas pleasant stimuli (music) was associated with a greater self-reported high in larger doses of cannabis ($p < .001$). Finally, there was a significantly faster decline in self-rated intoxication in a stress condition compared to a no-stress condition (p-value not reported) (Stillman et al., 1976), and participants reported significantly greater overall high in the neutral condition compared to a stress condition ($p < .05$) (Pihl et al., 1978b). When considered cumulatively, experimental studies therefore suggest that self-rated intoxication is altered by the presence of unfavorable (but not favorable) sensory stimuli.

3.2.3.2. Physical location. A total of three EMA studies examined the physical location of cannabis use as a predictor of subjective intoxication (Cloutier et al., 2021; Jackson et al., 2021; Shrier et al., 2013). Findings from all three studies suggest that using cannabis at home tends to be associated with less self-reported intoxication than using cannabis outside of the home, and specifically, two studies found that using cannabis at a friend's place predicts greater peak intoxication (Jackson et al., 2021; Shrier et al., 2013). This association was significant in only one study, however, potentially due to a greater sample size ($p < .01$) (Jackson et al., 2021). Furthermore, the relationship between contextual and pharmacological factors was confounded, as cannabis and alcohol intoxication were combined into a single outcome scale. Therefore, the collective evidence is weak regarding the association between physical location and subjective intoxication.

3.2.4. Temporal measures

3.2.4.1. Time of day. One experimental study and two EMA studies examined the time of day as a predictor of cannabis intoxication (Keith et al., 2017; Rudy, 2020; Shrier et al., 2013). The experimental study by Keith et al. (2017) found that ratings of being "stimulated" were increased by low and high THC dosages during the day, whereas ratings of stimulation at night were increased only by the high THC dose ($p < .05$). This suggests that low doses are more likely to cause self-reported

Table 4
Multivariate meta-analysis model with contextual factors as predictors.

Model Results	Estimate (fisher z)	Standard error	95 % CI (Lower)	95 % CI (Upper)	p-value
Intercept	0.0718	0.0557	-0.0424	0.1860	0.208
Environment	-0.0698	0.0813	-0.2364	0.0968	0.398
Expectancy	-0.2760	0.1637	-0.6113	0.0593	0.103
Social Group	0.0326	0.0698	-0.1104	0.1756	0.644
Time of Day	-0.0126	0.1120	-0.2420	0.2169	0.912
Experimental*	0.3422	0.0919	0.1541	0.5304	0.001

Note. The results represent estimates (fisher z), standard errors, 95 % confidence intervals (CI), and p-values from a multivariate meta-analytic random-effects model examining the effects of context and type of study (Environment, Expectancy, Social Group, Time of Day, Experimental) on the outcome variable (Intoxication). The model was fitted using the restricted maximum likelihood (REML) method with random effects specified for study-level variables. Significant results ($p < 0.05$) are indicated with an asterisk (*).

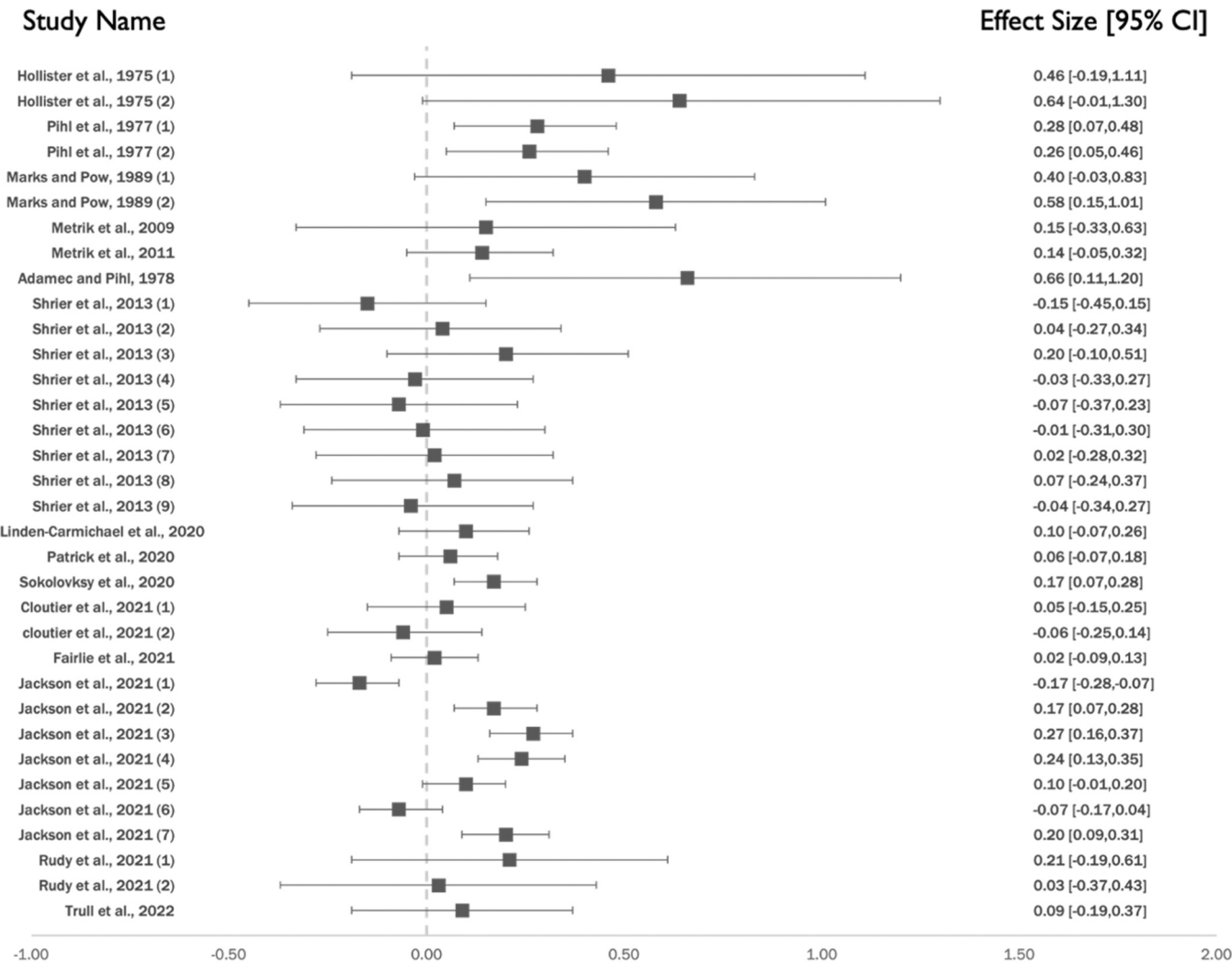


Fig. 2. Forest plot of studies examining relationship between context and magnitude of cannabis intoxication. Note. This forest plot shows the fisher-z effect size of each study included in the multivariate meta-analysis examining the association between contextual factors and the magnitude of cannabis intoxication.

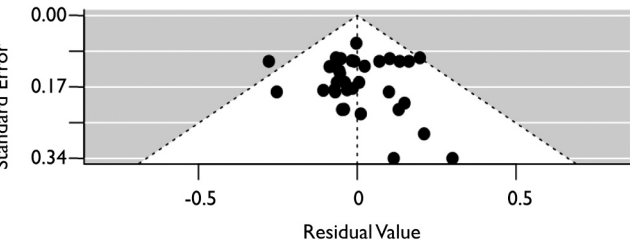


Fig. 3. Funnel plot of cannabis intoxication scores. Note. The funnel plot assesses the distribution of cannabis intoxication scores across studies included in the multivariate meta-analysis. Study precision (SE) is plotted against the effect size (fisher's z) ($\rho = 0.8$).

stimulation only during the day, although further studies are needed to verify this result. The two EMA studies suggest that self-rated intoxication scores are higher in the evening or night relative to the afternoon or morning (Rudy, 2020; Shrier et al., 2013). However, this relationship was significant in only one study ($p < .001$) (Rudy, 2020); considering that the sample size was larger in Shrier et al. (2013) compared to the other two studies (Keith et al., 2017; Rudy, 2020), it is unlikely that the reason for non-significance was due to insufficient power. Therefore, overall evidence is weak on the relationship between the time of day and cannabis intoxication.

3.2.4.2. Day of week. Seven EMA studies reported on the association between the day of week and self-rated cannabis intoxication. Six studies reported that the weekend was associated with a greater level of being high than non-weekend days. Contrary to this, one study found that referent to weekday, weekends are associated with slightly less intoxication (Shrier et al., 2013); However, this association was non-significant ($p = 0.99$). This is possibly due to the definition of weekend used in Shrier et al. (2013) which included Sunday, whereas other studies did not code Sunday as part of the weekend. Regardless, results on whether the weekend is associated with greater cannabis intoxication are inconclusive, as half the studies reported that this association was non-significant (p -values not reported) (Bravo et al., 2017; Patrick et al., 2020; Rudy, 2020). Finally, Bravo et al. (2017) found that the “cannabis holiday” date of 20th April (4/20) was not significantly associated with a greater high ($p = .213$), offering further evidence that temporal factors are not strong predictors of cannabis intoxication

3.3. Overall review of evidence

3.3.1. Measurement of intoxication

Three studies found significant results using a self-rated intoxication scale, but not for mood scales nor the ARCI-M (Adamec and Pihl, 1978; Pihl et al., 1977; Trull et al., 2022). Certain subjective effects may not positively correlate with overall intoxication levels, as seen in Keith

et al. (2017)'s study which found that 'stimulation' was greater in the day while overall high was greater in the evening. Finally, Marks and Pow (1989) found that ratings of 'highness' was greater overall among friends than strangers, but ratings of 'intoxication' were greater among strangers at low doses. In other words, participants in this study attributed different meanings to being 'high' and being 'intoxicated'.

3.3.2. Dose-dependent relationship

A low dose of THC significantly increased ratings of stimulation only during the day, whereas a high dose of THC increased ratings of stimulation during both day and night (Keith et al., 2017). Furthermore, there was a dose interaction effect with acquaintanceship; Intoxication was rated higher among friends than strangers in high doses, but rated higher among strangers than friends in low doses (Marks and Pow, 1989).

3.3.3. Summary

Overall, although the narrative review revealed several patterns between the association of context and intoxication, studies are few and varied in significance. Contextual factors with the least discernible pattern include time of day and expectancies. Other contextual factors with clearer patterns include social group, experimental setting, day of week, and physical location. However, the strength of the evidence was not enough to establish whether these patterns reflected a true relationship between these factors and self-reported cannabis intoxication.

3.4. Meta-analysis

3.4.1. Multivariate meta-analysis with predictors

34 effect sizes from 15 studies were run in a multivariate meta-analysis, where contextual conditions and study type were entered as predictors in the multivariate model. Results showed that study type (EMA or Experimental) was a significant predictor of intoxication. On the other hand, contextual conditions (environment, social group, expectancy, time of day, day of week) were not significant predictors (Table 4). A forest plot of the results is shown in Fig. 2.

3.4.2. Comparison of experimental and EMA studies

A total of 9 effect sizes were pooled across 6 experimental studies, and 25 effect sizes were pooled across 9 EMA studies. A comparison showed that experimental studies had a greater pooled effect size ($z = .296$, 95 % CI [.132,.478], $p = .004$) than EMA studies ($z = .071$, 95 % CI [.011,.130], $p = .02$). Additionally, there was greater statistical heterogeneity in EMA studies ($I^2 = 63$ %) compared to experimental studies ($I^2 = 31$ %).

3.4.3. Publication bias

An Egger's regression test of all 34 effect sizes included in the meta-analysis indicated no publication bias ($t = 1.509$, $p = .138$). This result was supported by visually examining a funnel plot of cannabis intoxication scores (Fig. 3). Although several studies did not report effect sizes for non-significant results, Egger's test nevertheless showed no publication bias in the analysis conducted, suggesting that evidence in this field is not over-represented by significant results.

4. Discussion

4.1. Overview

This work is the first to systematically examine the extent to which cannabis intoxication is associated with the context in which cannabis use takes place. Overall, findings fail to support the argument that social and environmental contexts shape the ways in which people subjectively experience the effects of cannabis. Upon examining specific contextual variables, no evidence was found that expectancies, social group, physical location, environmental setting, or temporal variables

moderate the subjective effects of cannabis. However, both the narrative and meta-analytical components of this review indicate that the methodological approaches used in the literature need substantive refinement before concluding that social ecological effects are not important to the experience of subjective intoxication. We first consider the state of the current body of knowledge and highlight possible directions for future research, before finally considering broader theoretical implications.

4.2. Review of the evidence

The earliest studies uncovered in this review published in the 1970s and 1980s are characterized by small sample sizes and a high risk of bias. Further, over half the experimental studies included in this review used a concentration of THC that is weaker than cannabis products currently and that is available in both legal and illicit markets (Chandra et al., 2019). In light of research which shows THC concentration is increasing in cannabis products (Freeman et al., 2021), these studies should be replicated with doses reflecting current consumption patterns. Although it is possible that the magnitude of contextual influences is weakened under the influence of a higher THC dosage, several studies have indicated a potential dose-dependent relationship between contextual influences and cannabis intoxication (Keith et al., 2017; Marks and Pow, 1989). Therefore, this interaction should be examined systematically in future experimental studies.

The meta-analysis provides additional evidence that the methodological approach has a significant impact on our ability to detect effects. As such, EMA and experimental designs were a significant predictor of intoxication. This association was explored by comparing pooled effect sizes between EMA and experimental studies, revealing that experimental studies reported greater magnitude of effect than EMA studies. A potential reason for this result is that the influence of contextual factors is stronger in a controlled setting compared to a real-world context, where there may be multiple confounding factors such as tolerance level or THC dosage (Colizzi and Bhattacharyya, 2018; Zuurman et al., 2009). For example, only two studies controlled for the quantity of cannabis used (Cloutier et al., 2021; Trull et al., 2022), and only one acknowledged that people might share cannabis in social settings (Patrick et al., 2020). However, as reflected in the narrative review, the dosage of THC used is difficult to determine due to the lack of a consistent methodological approach when measuring cannabis intake and intoxication using EMA methodology. This variability is also apparent when examining which studies controlled for further pharmacological variables such as mode of use, as this difference might also contribute to heterogeneity shown by EMA studies. Finally, another explanation for this apparent difference between experimental and EMA studies may lie in the analysis method utilized by each study type. Whereas EMA studies examined within-person differences in intoxication, experimental studies interrogated differences predominantly between-persons. As such, while studies suggest that the magnitude of effect is smaller in EMA studies, it may be possible that this variation was driven by which person-level analysis method was applied (Rush and Hofer, 2014). Future meta-analysis studies could therefore benefit from the inclusion of both within- and between-person analysis as a predictor.

To summarize, although it is possible that the association between contextual effects and cannabis intoxication is weak due to an overriding influence of purely pharmacological effects, it is difficult to conclude this for certain based on the evidence of the EMA studies included in this review. Therefore, without controlling for pharmacological factors such as tolerance, dosage, or mode of use, future EMA studies may struggle to determine the magnitude of the relationship between cannabis intoxication and contextual factors. This is especially relevant for THC dose, as previous studies have already highlighted the inaccuracy of using self-report measures to quantify cannabis use (see: Parnes et al., 2018; Prince et al., 2018; Wycoff et al., 2018). This limitation was reflected in the heterogeneous methodologies used by EMA studies included in this

review, which quantified cannabis by asking participants to estimate the number of hits or number of grams. Further, even if the amount of cannabis used was estimated correctly in self-reports, it can be difficult to ascertain the dose consumed when the THC concentration is unknown. As such, while researchers have proposed a standard dose of THC in legal jurisdictions to facilitate an estimate of consumption (Freeman and Lorenzetti, 2020; Zeisser et al., 2012), alternative methods for measuring cannabis potency are recommended in jurisdictions where no standard dose of THC has been implemented. For example, the enhanced cannabis timeline follow-back (EC-TLFB) developed by Petrilli et al. (2024) provides pictorial aids of categories of cannabis products as proxies for their typical potencies to assist estimates. Alternatively, researchers may use a portable device that measures THC concentration (Trull et al., 2022) or use the ‘number of hours high’ as a proxy measurement if sensitivity to tolerance is not a consideration (Calhoun et al., 2022). Thus far, however, it is highly likely that the dose of THC is a residual confounder when modeling the association between contextual factors and cannabis intoxication in non-experimental settings.

While the EMA studies included in this review acknowledged the impact of contextual factors such as social group, environmental characteristics, and temporal measures, other factors remain underexplored. Social cognitive theory proposes that situational factors influence expectations regarding the outcome of drug use, thus highlighting the fluctuating nature of expectancies depending on context (Niaura, 2000). However, no EMA studies included in this review measured cannabis expectancies as a momentary factor, nor as a potential mediator of the link between context and pharmacological outcomes. It is possible that different contextual situations drive positive expectancies and lead to elevated consumption, or to an increased likelihood that a person who uses cannabis will focus on and self-report positive subjective effects such as euphoria. Importantly, the relationship between momentary expectancies and drug-related outcomes has been studied with other substances, highlighting a gap in cannabis literature. Potter et al. (2022), for example, found that positive outcome expectancies regarding affect predicted a higher likelihood of smoking relapse, and that such expectancies are dynamic. Similarly, alcohol consumption was found to mediate the likelihood of smoking relapse by increasing positive smoking outcome expectancies (Lam et al., 2014). Such studies are consistent with social cognitive theory and point towards the impact of shifting contexts on cognitive mechanisms which drive drug-related outcomes. Despite this link, however, the relationship between momentary expectancies and subjective effects has yet to be explored in cannabis EMA studies.

The impact of expectancies should also be explored systematically in experimental studies. Although experimental studies included in this review examined the impact of tension-reduction expectancies and a THC/no THC stimulus expectancy set on subjective effects, no studies were found which compared receiving a high dose of THC when expecting a low dose or vice versa, despite potential real-world implications of such a low dose/high dose expectancy. For example, due to a delayed onset of intoxication when consuming cannabis orally, edible cannabis users have reported difficulty in accurately titrating their dose (Barrus et al., 2016), thus leading to a variable and unpredictable intoxication experience from THC edibles (Giombi et al., 2018). Considering the risk of hospitalization involved from overdosing on edible THC (Monte et al., 2019), it might therefore be important to examine how expectancies may moderate the relationship between and oral THC consumption and subjective effects such as anxiety.

Finally, larger social ecological factors may also be important when examining the relationship between cannabis intoxication and micro-contextual factors such as expectancies. Studies conducted with participants living in North America should consider the impact of cannabis’ legal status as an additional layer of context, as there is emerging evidence that legalizing cannabis may predict changes in social attitudes towards cannabis by increasing acceptability and decreasing

stigmatization (Amroussia et al., 2020; Kilwein et al., 2020). This change in attitudes and the decreased risk perception of cannabis may drive a change in expectancies, potentially changing the experience of intoxication in areas where cannabis is legal. Thus, to truly understand the impact of contextual factors on cannabis intoxication, the link between social factors and expectancies should be studied in greater detail.

4.3. Methodological considerations

There are three overarching considerations based on both the EMA and experimental studies included in this review. First, although 37.9 % of the included studies were rated with a low risk of bias, the meta-analysis shows a large range of possible effect sizes in both significant and non-significant results (Fig. 2). Therefore, studies included in this review – particularly earlier studies examining contextual variables in an experimental setting – should be replicated to understand where the true value of the effect lies.

Second, this review reaffirmed that various measurement tools are available to measure acute cannabis intoxication across both experimental and EMA studies. Importantly, the choice of measurement appeared to impact the significance of results in several studies, demonstrating that the nature and validity of tools for measuring cannabis intoxication appear worthy of careful consideration. Other studies have shown the importance of updating the language of intoxication measurements to reflect current usage. In a sliding scale measuring cannabis intoxication from 0 to 100, the top anchor (100) was modified to say “stoned/baked” rather than “very high”, which in turn led to a greater variance of intoxication in the revised item (Cloutier et al., 2022; Linden-Carmichael et al., 2020). Thus, a wider range of subjective effects were captured in the modified scale which used contemporary language, raising the issue of a ceiling effect when measuring extreme intoxication using the term “high/very high”. Further evidence exists of the discrepancies in terminology used between researchers and experienced cannabis users when referring to high-THC cannabis products and various strains (indica/sativa) potentially responsible for different subjective effects (Lau et al., 2015; Mason et al., 2021). It is important to note that no gold-standard field test exists to measure cannabis intoxication objectively, as current pharmacokinetic measurements such as blood THC concentration do not accurately correlate with the level of acute intoxication (Huestis, 2015; Huestis and Smith, 2018). This is especially the case in people who use cannabis regularly (Karschner et al., 2009). It is crucial, therefore, that subjective self-report scales of cannabis intoxication can more accurately capture the nuances of the cannabis intoxication experience. Overall, more understanding is needed for how people who use cannabis interpret intoxication measurement scales, and how these scales relate to their experience of intoxication.

Third and lastly, the participants recruited for contextual studies examining cannabis use should be more diverse. The sample characteristics of the studies included in the review were predominantly male, non-clinical, young adults from universities, and North American, therefore limiting generalizability of the results. This is a crucial oversight, as cannabis is the most widely used drug worldwide and the number of lifetime users has increased by 23 % over the past decade across the globe (United Nations Publications, 2023). Regulatory policies of cannabis also vary widely depending on the country (Ransing et al., 2022), thus potentially impacting cannabis use norms and behaviors across locations. Therefore, it is important to consider contextual differences in cannabis use behaviors across gender, age, and country of residence, as the overall lack of diverse participants in psychological research is a continuing issue which limits our understanding of cannabis intoxication.

4.4. Theoretical considerations

Due to the disparate state of the current literature, a definitive

conclusion cannot be drawn on the relationship between contextual factors and cannabis intoxication. Simultaneously, this lack of unity highlights the need to evaluate potential theoretical underpinnings of contextual research examining drug effects. In addition to the resurgent “Drug, Set and Setting” notion proposed by Zinberg (1986), theories applicable to understanding the role of context have been evaluated in adjacent areas such as health behavior, harm reduction, craving, and even child development (Bronfenbrenner, 1977; Burke et al., 2009; Niaura, 2000; Rhodes, 2002), thus yielding guidance on avenues for future research. For example, the cognitive social learning theory (CLST) model (Niaura, 2000) proposed a relationship between outcome expectancies and craving. Building upon this, it was found that heavy cannabis users experience cravings in response to cannabis cues (Slavin et al., 2018). A recent EMA study also demonstrated that cannabis expectancies positively predict greater momentary craving (Enkema et al., 2020). Furthermore, context has been identified as relevant for additional factors such as problematic cannabis use (Asbridge, 2014). As such, although context does not appear to be a strong predictor of cannabis intoxication based on the current study, it may still be important to elucidating the broader spectrum of cannabis use predictors. An updated framework would constructively guide future research towards a more holistic understanding of the relationship between context and drug effects.

Indeed, an approach which explores more broadly the impact of context on cannabis could yield important insights into treatments such as psychedelic-assisted therapy or the use of medical cannabis for anxiety or depression (Brunt et al., 2014; Hartogsohn, 2016, 2017). In combination with Becker’s (1953) earlier framework for understanding how someone initiates and sustains cannabis use, an interaction is proposed between contextual factors and cognitive mechanisms potentially underpinning the interpretation of cannabis intoxication. For example, it is possible that the impact of context on cannabis intoxication is relevant in unique situations where expectancies are still being developed, and it may be worth exploring whether the impact of context is stronger in specific conditions such as the initiation period of cannabis use.

However, there are several limitations when applying these theories to current cannabis research examining context. First, due to increases in cannabis potency and legalization, people currently use cannabis in markedly divergent contexts than people during Becker and Zinberg’s time (Chandra et al., 2019; Hammond et al., 2020). Thus, researchers have acknowledged the importance of updating theory to reflect current cannabis use practices (Hallstone, 2002). Furthermore, the impact of macro-contextual factors such as cannabis markets on micro-contextual variables is largely undiscussed, as Zinberg’s work is mostly limited to understanding the influence of peer group norms. Therefore, in light of changing norms and social attitudes towards cannabis use due to legalization, this approach may benefit from being updated to acknowledge more explicitly the impact of macro-contextual variables on the experience of cannabis intoxication.

Such frameworks exist, and Rhodes (2002) acknowledges that physical, social, economic, and policy environments are important for understanding harms from drug use. Furthermore, it is argued that macro-contexts such as policy enforcement and economic environments can impact micro-contexts such as drug use norms and the physical location where drugs are used. Alternatively, Bronfenbrenner (1977) defines context to include individual, family, community, and societal factors. Regardless of how context is operationalized, it is clear that several levels of contextual factors exist and act upon each other (Bronfenbrenner, 1977; Rhodes, 2002). Thus, building on Burke’s (2009) assertion that contexts are dynamic, future research in the area of cannabis intoxication should also be guided by an acknowledgement of rapidly changing macro-contexts such as the presence of legal markets, an increased variety of cannabis products, and an extended range of cannabis potency (Chandra et al., 2019; Hammond et al., 2020; Schauer et al., 2020). Additionally, no framework exists to examine drug effects

resulting from the interaction between macro-contexts (i.e., policy changes), micro-contexts (such as physical setting or social interaction), and cognitive mechanisms (such as expectancies). Thus, these various aspects of context have not been unified in a broader theoretical model.

To summarize, several key threads of contextual theories stand out: The dynamic nature of context, acknowledgement of various levels of context such as macro- versus micro- environments, and the impact of contextual variables upon each other and upon cognitive mechanisms. Additionally, when examining these factors in relation to drug effects, the impact of pharmacological variables should not be ignored (Englund et al., 2022; Zuurman et al., 2009). This is further highlighted by the potential dose-dependent relationship between context and cannabis intoxication, as shown in this review. Therefore, an updated theory is required that combines a social-ecological model of drug effects while acknowledging the importance of pharmacology. Although developing such a theory is outside the scope of this systematic review, a unified framework acknowledging these various elements may help the field of contextual cannabis research to develop in a more cohesive manner.

4.5. Limitations

This review has several limitations which should be taken into consideration. Although PRISMA guidelines were followed, the title and abstract screening and full-text screening were not conducted by a second independent reviewer. A second review was used in cases where inclusion or exclusion criteria were ambiguous (i.e., the study participants’ age range), to ensure applicable studies were included; nevertheless, there is some risk that relevant studies were missed during screening (Gartlehner et al., 2020). However, this issue was potentially mitigated by reviewing the references of relevant studies, providing a supplemental search of the literature.

Kmet et al. (2004)’s assessment tool, “standard quality assessment criteria for evaluating primary research papers from a variety of fields” was used in place of Cochrane’s tool (RoB 2) to evaluate the risk of bias of studies (Higgins et al., 2011). This decision was made as the RoB 2 is designed primarily for randomized control trials and cannot be used to evaluate EMA methodology. Although researchers have used the tool developed by Kmet et al. (2004) to compare bias across experimental and EMA methodologies (Tovmasyan et al., 2022), the tool itself has not been as extensively evaluated or standardized in the literature as the RoB 2. The RoB 2 has additional criteria sections that are not included in Kmet et al. (2004)’s tool, thereby providing more stringent criteria with which to evaluate randomized control trials. However, since the majority of experimental studies were already rated as medium to high risk of bias, it is unlikely that the use of the RoB 2 would alter the conclusion that experimental evidence in this review is weak and requires replication.

Finally, there were limitations specific to the meta-analysis. Cohen’s *d* was calculated with the assumption of equal sizes in each group, as information on group sizes could not be obtained due to missing data and the publication age of experimental studies. In general, data included in the narrative review were missing from the meta-analysis, since studies which did not report effect sizes of non-significant results had to be excluded. Nevertheless, this likely had a minimal impact on the overall results: no publication bias was found, and the results in general did not suggest a significant relationship between contextual factors and cannabis intoxication.

4.6. Conclusions

Overall, this review found no conclusive evidence that contextual factors impact the experience of cannabis intoxication. However, it identified key issues related to methodology and theory, which should be addressed when researching this area. First, sensitivity of research designs towards pharmacological factors such as THC content and quantity of cannabis ingested is required for EMA studies. Second, there

is a need for earlier studies included in this review to be replicated, while future work should use a standardized measurement tool for cannabis intoxication and recruit a more diverse sample. Finally, an updated and cohesive theoretical framework which acknowledges the dynamic nature and various levels of context would help to unify the field of contextual cannabis research.

Data Availability

I have additional data I am happy to share that have not been attached to the manuscript - please see appendix for list of data further available.

Appendix A. Figures and tables

Table 1
Variables Extracted from Studies

All Studies	Experimental Studies	EMA Studies
Author, Year	Comparator Group	Cannabis Dose Measurement
Region	Quantity of Cannabis	Length of Study
Sample Size	Timepoints of Intoxication Measurement	Signal Type
Participant Characteristics		Compliance Rate of Signal
Mode of Use		
Exposure: Contextual Variables		
Outcome: Intoxication Measurement		
Main Findings		
Effect Size		

Note: Variables listed in column “all studies” were extracted for both experimental and EMA studies, whereas variables underneath the columns “experimental studies” and “EMA studies” are unique to the respective study type.

Appendix B. PRISMA checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	pg.1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	pg.2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	pg.6–7
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	pg.7
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	pg.8–9
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	pg.8
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	pg.8–9
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	pg.8–9
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	pg.9
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	pg.9
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	pg.8–9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	pg.9
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	pg.9–10
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	pg.9–10

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Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	pg.10
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	pg.10
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	pg.10
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	pg.10
	13 f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	pg.10
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	pg.10
Study characteristics	17	Cite each included study and present its characteristics.	Tables 2–3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Tables 2–3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 2–3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	pg.10–12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Fig. 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	pg.13–14,21
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Fig. 2
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	pg.21–22
	23b	Discuss any limitations of the evidence included in the review.	pg.22–23,25–28
	23c	Discuss any limitations of the review processes used.	pg.31
	23d	Discuss implications of the results for practice, policy, and future research.	pg.28–31
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	pg.7–8
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	pg.7–8
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Appendix C
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Pg.8
Competing interests	26	Declare any competing interests of review authors.	pg.8
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	A: Template Data Collection, Data Extracted and used for Meta-analysis can all be made available through supplemental data B: Analytic Code – made available through appendix

Appendix C. . Review protocol

Research Question

Which factors moderate the acute subjective effects of cannabis?

Objectives

- Compare how experimental (laboratory) and contextual (real-world) settings may moderate acute subjective effects of cannabis and pharmacological, environmental, and participant-level factors.

Protocol Step	Changes with Reason	Additional Comments
I will search Medline, Embase, PsycINFO, Global Health, CENTRAL, Google Scholar (Top 400 Search Results) and references of relevant studies.	No changes.	
Authors of relevant studies will be contacted to ask for any relevant unpublished data.	Due to time restraints, authors were not contacted	
Search Strategy Published studies (title and abstract) will be searched using the following terms: (Cannabis OR Marijuana OR THC) AND (dose* or randomi* or laboratory or placebo or Ecological or Smartphone or Mobile or Daily or Interactive Voice Response or Experience sampling method or intensive longitudinal) AND (high or intoxicat* or subjective or acute)	06/05/22: • Google Scholar: The term “high” was not included in the search, due to automatic truncation by Google because of character limits.	
Timeframe: From timeframe covered by database to current date of review (2022, TBD)	No changes.	
Grey literature (including conference publications) will be considered.	Due to volume of eligible studies, conference publications (abstract only publications) were excluded.	
Inclusion Criteria • Studies that examine a [primary] outcome of acute subjective effects or acute intoxication of cannabis using experimental or EMA methodologies • Studies conducted with young adults or adults (16–64yo) • Studies published in English • Studies on humans (clinical or non-clinical) • Peer-reviewed papers, grey literature, or unpublished data	17/08/22: • Age criteria for “studies conducted with young adults or adults” was removed in order to consider all ages falling under “young adult or adults” as defined by studies. This is because studies were identified during the title/abstract screening which included participant age criteria that overlapped with specified age bracket. <i>Exclusion criteria: Studies examining only adolescents.</i> • After the first round of title/abstract screening, approximately 1004 studies were identified for full-text screening. These studies were re-reviewed with stricter criteria (see Additional Comments, Updated Criteria).	17/08/22: Updated Criteria Clinical trials were excluded which examined cannabis/delta–9-THC/synthetic cannabinoids as a medication (for example, an anti-emetic, analgesic, or anesthetic), or measured subjective/adverse effects to determine tolerability or side-effect profile. Studies were excluded which co-administered delta–9-THC with another drug to determine CB1 receptor antagonism. Studies were excluded which examined acute delta–9-THC administration but did not mention outcomes of intoxication or subjective effects in the abstract.
Exclusion Criteria • Studies that examine the efficacy or effectiveness of interventions aiming to alter cannabis consumption patterns. After reviewing the studies, additional exclusion criteria were added (See Additional Comments, Updated Criteria) • EMA Studies that use paper/pen or other non-electronic/non-mobile diaries (where response time stamps cannot be captured) will be excluded, due to potential methodological issues from “car park compliance” (Smyth and Stone, 2003) -where participants provide their responses retrospectively rather than at the time requested/prompted. • Reviews, books, posters, [case studies], and editorials • Animal studies	17/08/22: Updated Criteria • Studies treating cannabis withdrawal were added to the exclusion criteria. 26/04/2023: Updated criteria • inclusion criteria were updated: Main aim of study should systematically measure intoxication or subjective effects of cannabis • To answer question of “factors of intoxication”, i.e., examine relationship between set/setting and intoxication, experimental studies must compare intoxication between conditions (i.e., not just placebo vs. Single dosage of cannabis, not within-participants)	01/06/2023: Updated Criteria • Only including studies examining variables related to context & expectancies. • Not including CBD:THC Ratio, THC dose, time curve (i.e., pharmacokinetics/dynamics), due to prior research/SR in these areas.
Participants: Cannabis users with any level of use (infrequent, moderate, heavy, or clinical). Adults.	No changes	
Context: The context will be the laboratory or the participants' environment.	No changes	
Main Exposure Variable(s) Exposure (covariate) variables will include, but are not limited to:	Focused only on contextual variables.	
• Pharmacological measures such as dosage, THC:CBD ratios, mode of use, simultaneous use of other drugs (e.g., alcohol, nicotine, MDMA), and quantity of cannabis used. • Contextual measures such as environmental factors (e.g., location or peer group), and legal status of recreational cannabis use. • Participant measures such as demographic data (gender, location of participants), CUDIT-R scores, frequency of use.		
Main Outcome Variable(s) • Any reported measurement of subjective effects due to cannabis use. Commonly used scales might comprise of the Self-Assessment Manikin (SAM), ARCI-Marijuana Scale (ARCI-M), Profile of Mood States (POMS), Cannabis Experiences Questionnaire (CEQ), Drug Experiences Questionnaire (DEQ), Modified Lyons Battery for	17/08/22 • Include psychotomimetic measures.	

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Protocol Step	Changes with Reason	Additional Comments
<p>Subjective Effects (MLBSE), or Visual Analog Scales (VAS) for specific effects such as anxiety or paranoia (Bradley and Lang, 1994; Haertzen and Hickey, 1987; Lyons et al., 1997; McNair et al., 1971; Morean et al., 2013; Quinn et al., 2017).</p> <ul style="list-style-type: none"> Any measurement of cannabis intoxication. Commonly, this might be a scale that asks the participant to rate “how high” they are on a scaled anchored between 0 and 100. <p>No secondary outcome variables will be considered.</p> <p>Data Extraction: Two independent reviewers will determine if studies meet the eligibility requirement by first examining the title/abstract of studies that were returned from the database search, and then examining the full text of studies which passed the title/abstract screening. In the event there is a disagreement on study eligibility, a third reviewer will be involved and reason for inclusion or exclusion clearly documented.</p>	<ul style="list-style-type: none"> Records reviewed by team. 	
<p>Quality Assessment: Since the review will include observational studies not evaluating any intervention, traditional risk of bias assessment tools (such as Cochrane’s Risk of Bias Tool or Cochrane’s Risk Of Bias In Non-Randomized Studies - of Interventions) may not be suited. We will instead use the tool, “Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields”</p>	No changes	
<p>Data Synthesis Strategy: A random effects meta-analysis will be conducted, with the effect size of the relationship between each exposure variable and the outcome variable reported as Pearson’s r. Data will be reviewed (1) for normal distribution and (2) to account for the category of the reported outcome variables (i.e., categorical vs. continuous) before conducting a meta-analysis. Heterogeneity of studies will be assessed using I^2 and τ^2 statistics. If effect sizes are not reported by the study, they will be calculated. Authors will be contacted if the information necessary to calculate effect sizes are not available.</p>	No changes	<p>Conversion of Effect Sizes for Analysis Step 1: Effect sizes calculated using R (package: effectsize ver.0.8.5) F to cohen’s d or to cohen’s d Step 2: Effect sizes calculated using formula B to d; $d = (B/SD)$, $SD = \sqrt{r(n+1)}$ Step 3: Convert all cohen’s d to r using R (package: effectsize ver.0.8.5) Assumes equal sizes in each group Step 4: Calculate fisher’s z from r (package: DescTools ver.0.99.49) fisher’s z variance = $1/(N-3)$ fisher’s z SE = $\sqrt{\text{variance}}$ Multivariate Meta-analysis (without predictors, nopredictor.model; EMA studies only, EMA.model; EXP studies only, EXP.model) Step 1: rma.mv function(package: metafor ver.4.2-0); t-test, REML method Step 2: Convert effect size z to r (package: esc ver.0.5.1), function convertz_r HeterogeneityBetween-study heterogeneity variance τ^2 (from rma.mv model results) Cochrane’s Q (from rma.mv model results) I^2 (package: dmetar)</p>
<p>Publication Bias: Publication bias will be assessed using Egger’s test, and results will be adjusted if a bias is found. Additionally, a p-curve analysis will be conducted if publication bias is suspected.</p>	No changes	
<p>Sensitivity Analysis: If studies are excluded from the meta-analysis due to poor quality, or if effect sizes cannot be determined, then a sensitivity analysis will be conducted to account for these factors.</p>	Sensitivity analysis not required	
<p>Meta-Regression/Subgroup Analysis: Meta-Regression (moderator) variables will include the following categorical predictors: (1) Study Type/Study Context (Laboratory/Experimental vs. EMA/Contextual studies), (2) Clinical vs. Community population sample, and (3) Geographic Location of Study.</p>	No changes	<p>Multivariate Meta-analysis (with predictors, predictor.model) Step 1: rma.mv function(package: metafor ver.4.2-0); t-test, REML method</p> <ul style="list-style-type: none"> Predictors: Type.of.Study (EMA or EXP), Condition (Environment, Social Group, Expectancy, Time of Day, Day of Week)

Appendix D. . Meta-analysis code

```

##Cannabis Intoxication and Context Model with predictors
library(metafor)
library(effectsize)
library(DescTools)

predictor.model <- rma.mv(yi = fisherz,
  V = variance,
  mods = ~ Type.of.Study + Exposure.Conditions,
  slab = Author.Year,
  data = MetaAnalysisDataset,
  random = ~ 1 | Author.Year/study.id,
  test = "t",
  method = "REML")

summary(predictor.model)

##Separate data into EMA studies and EXP studies and analyze separately

EMA <- subset(MetaAnalysisDataset,Type.of.Study=="EMA",c(1:16))
EXP <- subset(MetaAnalysisDataset,Type.of.Study=="EXP",c(1:16))

EMA.model <- rma.mv(yi = fisherz,
  V = variance,
  slab = Author.Year,
  data = EMA,
  random = ~ 1 | Author.Year/study.id,
  test = "t",
  method = "REML")

summary(EMA.model)

EXP.model <- rma.mv(yi = fisherz,
  V = variance,
  slab = Author.Year,
  data = EXP,
  random = ~ 1 | Author.Year/study.id,
  test = "t",
  method = "REML")

summary(EXP.model)

##calculate pooled effect size, convert from z to r
library(esc)

##nopredictor.model
convert_z2r #(0.1148)

##EMA.model
convert_z2r #(0.0705)

##EXP.model
convert_z2r #(0.3050)

##Funnel Plot
funnel.rma(predictor.model)

##Egger's Test
library(robumeta)

Egger <- robu(fisherz ~ SE,
  data = MetaAnalysisDataset,
  studynum = study.id,
  var.eff.size = variance,
  rho = .8,
  small = TRUE
)

##forestplot
forest.rma(predictor.model)
forest.rma(EMA.model)
forest.rma(EXP.model)

```

Image 1

References

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