Cannabis
2022, Volume 5 (1)

researchmj.org
DOI: 10.26828/cannabis/2022.01.005

Momentary Patterns of Alcohol and Cannabis Co-use in College Students: Assessing the Temporal Association with Anxiety

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ABSTRACT

Using ecological momentary assessment (EMA), we assessed momentary patterns of alcohol and cannabis co-use in college students and whether state-level and baseline reports of anxiety varied based on type of substance(s) consumed. Students (N=109) reporting regular cannabis use completed a baseline assessment and two-week signal-contingent EMA, with three random prompts/day. At each EMA instance, we categorized instances of substance "usage" as: 1) no use, 2) cannabis-only, 3) alcohol-only, or 4) co-use of alcohol and cannabis (i.e., reports of alcohol and cannabis use within the same prompt). Using temporal sequenced data, we explored how state-level anxiety varied before and after usage type using multiple multilevel structural equation models (MSEMs) and whether baseline factors (general anxiety, social anxiety, and sex) influenced the relation between usage type and state-level anxiety. Participants were 63.3% White, 58.7% female, used cannabis near-daily, and commonly reported co-use. Models examining whether usage type predicted subsequent state-level anxiety were predominantly significant, with the majority of relationships being more pronounced for participants with higher baseline general anxiety. In examining whether momentary state-level anxiety predicted usage type, in instances when participants reported higher levels of momentary anxiety, they were more likely to report no use compared to co-use and cannabis-only, with sex moderating some of the relationships. Social anxiety did not moderate any of the within-person associations between state-level anxiety and usage type. This study provides preliminary evidence that report of momentary anxiety varies based on substance type. Future research is needed to establish co-use related synergistic effects and correlates.

Key words: cannabis; alcohol; co-use; anxiety; ecological momentary assessment

Alcohol and cannabis are commonly used both singularly and together among college students (Yurasek et al., 2017). Varying terms have been used to describe the combined use of alcohol and cannabis, including "co-use or concurrent alcohol and cannabis use," often used to describe asynchronous, independent use of both alcohol and cannabis within the past 30 days or some other timeframe and "simultaneous use," defined as use of both substances at the same time with overlapping effects (Jackson et al., 2020). Approximately one-fourth of full-time college

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students report any cannabis use in the past month, with 5.9% reporting daily use (Schulenberg et al., 2020). Higher rates of past month cannabis use have been reported among students living in states with legal recreational cannabis use (38%) compared to students living in states without such laws (24%; Pearson et al., 2017). Although recent data shows that male and female students have similar rates of past month cannabis use, males are more likely (7.2%) to use daily compared to females (5%; Schulenberg et al., 2020). In comparison, about 60% of college students report use of alcohol in the past 30 days, with 33% reporting heavy episodic drinking in the past 2 weeks (aka, binge drinking; 4-5+ drinks in one occasion), again with higher rates for males (Schulenberg et al., 2020).

A recent longitudinal study found a prevalence rate of 23% for simultaneous alcohol and cannabis use within the past year among emerging adults, with greater odds of simultaneous use for males (Patrick et al., 2019). Daily cannabis use in college students is associated with greater alcohol consumption and estimated blood alcohol concentration (Gunn et al., 2018) and young adults have been shown to consume more alcohol on simultaneous days compared to days with singular alcohol use (Lee et al., 2020). Patterns of co-use may vary based on cannabis legality, with recent work finding that rates of cannabis use in college students increased from pre- to post-cannabis legalization in Oregon, although only among those who used alcohol heavily (Kerr et al., 2017).

Accumulating evidence suggests that co-use of alcohol and cannabis leads to more negative consequences than use of either substance alone (Cummings et al., 2019; Davis et al., 2019; Egan et al., 2019; Jackson et al., 2020; Lee et al., 2020; Linden-Carmichael et al., 2020). It is possible that simultaneous alcohol and cannabis use (aka "cross-fading") may produce synergistic effects and hence greater feelings of intoxication (Lee et al., 2017; Patrick & Lee, 2018). Lab studies have shown that simultaneous use can alter the absorption and concentration of each substance, contributing to more significant impairment (Hartman et al., 2015; Lukas et al., 1992; Lukas & Orozco, 2001). Those who engage in simultaneous use report greater negative cognitive and physiological subjective effects during simultaneous use compared to using alcohol or cannabis alone (Lee et al., 2017). The interaction of the two substances is poorly understood and challenging to study due to a combination of regulatory barriers related to cannabis research and the numerous forms, potencies, and methods of cannabis ingestion that can impact findings (National Academies of Sciences & Medicine, 2017; Singh, 2019).

Past research has not examined whether simultaneous or co-use of cannabis and alcohol is associated with affective symptoms. As a means of understanding negative outcomes associated with co-use, the affective-motivational model of drug addiction suggests that substance use may serve as a means of negative reinforcement to self-treat affective symptoms (Baker et al., 2004). Though many persons using substances initiate substance use to experience positive effects (i.e., positive reinforcement), as individuals progress towards addiction, using to reduce negative affect, stress, and withdrawal become more prominent (Robinson & Berridge, 2003; Wycoff et al., 2018). Interoceptive or internal cues of anxiety may contribute to a momentary desire to use substances for symptom relief; alleviation of anxiety symptoms post-use subsequently increases the likelihood of future substance use (Baker et al., 2004; Dunn et al., 2010). It is possible that co-use of cannabis and alcohol may lead to specific anxiolytic effects, even above and beyond those of each substance alone.

Evidence supporting the affective-motivational model comes from a range of epidemiological and intensive longitudinal design (ILD) studies. At the diagnostic level, epidemiological studies have shown relationships between specific anxiety disorders and Cannabis Use Disorder (CUD) or Alcohol Use Disorder (AUD; Grant et al., 2015; Hasin et al., 2016). Of studies examining co-occurring anxiety disorders, evidence suggests co-morbidity between AUD or CUD and select disorders, such as Generalized Anxiety Disorder (GAD) and Social Anxiety Disorder (Social Phobia; Grant et al., 2015; Hasin et al., 2016; Schneier et al., 2010). Meta-analytic work has shown that social anxiety is negatively associated with alcohol use, but positively associated with alcohol-related problems (Schry & White, 2013), prompting work to examine possible moderators (Adams et al., 2019). Vulnerability for the development of anxiety disorders, CUD, and AUD is greater during young adulthood (Substance Abuse and Mental Health Service Administration [SAMHSA], 2019) and recent work with a psychiatric sample of emerging adults with predominantly anxiety and depressive disorders found that those engaging in frequent co-

use were more likely to have higher rates of cannabis- and alcohol-related problems compared to groups who used or co-used less frequently (Blevins et al., 2019). Most of the past work examining these relations has focused on singular cannabis or alcohol use; more research is needed to better understand the complex relationship between underlying anxiety disorders and co-use of cannabis and alcohol or CUD/AUD.

At the symptom level, individuals with underlying anxiety may use cannabis or alcohol to cope with their symptomatic distress (Bakhshaie et al., 2020; Blevins et al., 2019; Villarosa et al., 2019). However, research has yet to explore whether decisions to co-use are prompted by momentary anxiety or nervousness. Affect variables, such as anxiety, fluctuate considerably and have been related to use of individual substances when examined in the momentary context (Dvorak et al., 2018; Treloar Padovano & Miranda, 2018). ILD studies, such as ecological momentary assessment (EMA), are well-suited to study affect and co-use, can capture participants' experiences around the time of the prompt, and can be useful to disentangle state-level versus (v.) underlying anxiety influences (Bolger & Laurenceau, 2013; Shiffman, 2009).

Findings from studies assessing the relation between cannabis and state-level anxiety have been mixed, with most of the evidence looking at negative affect as an aggregate (e.g., combining anxiety, sadness, anger, etc.) rather than anxiety alone (Wycoff et al., 2018). A recent systematic review (Wycoff et al., 2018) of ILD studies indicated that the association between cannabis use and negative affect in community samples is variable. However, in clinical samples, they found more consistent evidence that negative affect is higher before cannabis use and decreases following use. Select studies have shown that anxiety is elevated prior to cannabis use (Buckner et al., 2012) and reduced post-cannabis use (Gruber et al., 2012), but other work has found no relation between cannabis use and state-level anxiety (Swendsen et al., 2011; Trull et al., 2016). Cuttler et al. (2018) analyzed archival data from medical cannabis users who were tracking their use of cannabis in real-time to treat symptoms of anxiety, stress, and other symptoms. Findings suggested reduced anxiety from pre- to post-cannabis use, with greater decreases for women.

Limited ILD studies have examined associations between state-level anxiety or negative affect and alcohol use in young adults. In undergraduate students, Tournier et al. (2003) found an association between lower state-level anxiety during periods of alcohol use compared to no alcohol use. Dvorak and colleagues (2018) found that state-level anxiety was lower following alcohol use compared to anxiety level prior to drinking in college students. In a young adult sample, Gorka et al. (2017) found that participants with greater anxiety symptoms reported reduced negative affect while drinking compared to not drinking, as compared to those with lower anxiety. Contradictory to these studies, O'Donnell and colleagues (2019) found no relation between negative affect and subsequent drinking in Australian young adults.

To our knowledge, no past EMA studies have examined momentary anxiety in relation to alcohol-cannabis co-use. The current paper was a secondary analysis of a larger EMA study on cannabis with data collected in a state with legal recreational cannabis use (Colorado). We examined two-week signal-contingent EMA data collected from college students who reported regular cannabis use. The goal of the current paper was to explore the temporal association of momentary anxiety with alcohol and cannabis use, particularly co-use instances, while also examining the moderating effect of baseline general anxiety, social anxiety, and sex. Specifically, we examined the following questions: 1) Does momentary anxiety predict a next use instance of alcohol, cannabis, or co-use? and 2) Does type of use (i.e., no use, alcohol-only use, cannabis-only use, co-use) predict momentary anxiety following a use episode? In addition, we sought to determine whether between-person levels of general anxiety, social anxiety, and sex might moderate state-level relationships between use and anxiety. Due to mixed past literature on the association between momentary anxiety and singular cannabis or alcohol use, and the absence of data related to momentary anxiety and co-use, our analyses were primarily exploratory. However, in line with the affective-motivational model of addiction, we hypothesized that alcohol-only, cannabis-only, and co-use would predict lower momentary anxiety, as compared to no use. Additionally, we expected male status and greater baseline general and social anxiety to moderate

these comparisons due to prior literature which has shown that males and those with anxiety disorders either use alcohol or cannabis more frequently or are more prone to developing AUD or CUD.

METHODS

Participants and Procedures

Participants (N= 109) were recruited from 2016-2019 from a western four-year university for a study focused on cannabis use through flyers, class announcements, and emails. Potential participants were screened by phone or in-person. Flyers listed the study phone number and in-person screening session dates that potential participants could attend. To participate, students met these eligibility criteria: 1) enrollment at the university for at least one prior semester, 2) age over 18 years, 3) own a smartphone, 4) report using cannabis at least two days per week (with recent use within the last week), and 5) positive THC urine screen (single panel cannabis urine dip test; .50 ng/mL cutoff; Redwood Toxicology Laboratory). Over the course of the study, 210 students were screened for eligibility and 113 were eligible, consented, and completed the study. Four participants had technical issues and were excluded from analyses, leaving 109 with usable data. Eligible participants were scheduled for an in-person baseline appointment that took approximately two hours and included completion of the urine screen (which could serve as a rule-out), informed consent, cognitive testing (part of a different study aim), interview, and completion of self-report questionnaires through Qualtrics.

Towards the end of the baseline appointment, participants downloaded the smartphone application (app; ©LifeData, RealLife EXP app; www.lifedatacorp.com/) and were trained on the two-week signal-contingent EMA. Participants were sent a series of practice questions prior to the end of the appointment to address questions about the app or how to respond. Prior to leaving the lab, participants were reminded to respond promptly to the EMA messages and were informed that compensation was based on their response rate. Participants were compensated with either a $40 (under 80% response rate) or $50 (above 80% response rate) gift card at the end of the study period.

EMA questions (below) were sent to participants from the app beginning the day following the baseline appointment. Based on past feasibility work (Phillips et al., 2014), participants were given one hour to respond to prompts. A randomized prompt schedule was developed for each participant within three time blocks (morning, afternoon, and evening) over a two-week period, for a total of 42 prompts. Responses were logged in the app, time stamped, and downloaded from the app server by the researchers. Response rate over the two-week period was 79.7% and ranged from 70.6% to 88.7% per day across the 14-day period, and from 75.1% (Sunday) to 84.5% (Tuesday) per day across days of the week. The response rate was consistent and slightly higher than EMA compliance rates reported in a recent meta-analysis (75%; Jones et al., 2019). Following the random prompt, participants completed the signal-contingent assessments on average 46.76 (SD = 91.85, Mdn = 11 minutes) minutes after the signal occurred. All procedures were approved by the institutional review board at the University of Northern Colorado and a National Institutes of Health certificate of confidentiality was obtained.

Baseline Measures

As part of the larger study, participants completed a wide range of assessment measures. The current analysis focused on the following baseline assessments.

Background characteristics. Participant sex, age, race/ethnicity, and year at the university were collected.

Alcohol use. To characterize the sample, we included single-item questions on participant alcohol use. Participants who endorsed any alcohol use in the past month were asked to report the average number of standard alcohol drinks consumed on a typical drinking day and the number of heavy episodic drinking episodes (number of times participant consumed four+ [women] or five+ [men] drinks on one drinking occasion in a two-hour period) within the past month.

Cannabis use. To better characterize the sample, we used select items from the psychometrically validated Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory (DFAQ-CU; Cuttler & Spradlin, 2017). Specifically, we report on cannabis frequency (number of days cannabis was consumed in the past month), primary form (flower/bud, concentrates,

edibles, and other), and primary method of ingestion (smoke, vape, oral, dab) currently used.

Beck Anxiety Inventory (BAI). The BAI is a psychometrically-validated (Beck et al., 1988) 21-item measure that assesses various dimensions of anxiety, such as feeling nervous, dizzy, or having difficulty breathing, over the last month (α = .94 for scores in the current sample). Items are rated from 0-3 and total score was used. Scoring ranges for the BAI are as follows: 0-7 = minimal anxiety, 8-15 = mild anxiety, 16-25 = moderate anxiety, and 26-63 = severe anxiety (Beck & Steer, 1993).

Social Interaction Anxiety Scale, Short Form (SIAS-SF). Social anxiety/phobia was measured with the SIAS-SF (Mattick & Clarke, 1998), which is a six-item scale with items rated from 0-4 (not at all to extremely). The measure has strong internal consistency (α = .88 for scores in the current sample) and test-retest reliability in a college population (Fergus et al., 2012). A suggested cutoff score of 9 has been shown to discriminate high v. low social anxiety (Fergus et al., 2012).

EMA Data Sources

The EMA protocol consisted of 11 questions that were sent via the Life Data app and included items related to cannabis use, alcohol use, social context, anxiety, mood, cannabis craving, exercise, and academics. Due to skip logic that included follow-up questions, some participants may have received only 8 questions. The same questions were assessed at each of the 42 prompts. Three particular EMA questions were used for this study as described below.

Types of substance use. For each EMA time block, we assessed whether cannabis or alcohol were used (yes/no) since the last prompt and then categorized each response into the following groups: no substance use, alcohol-only, cannabis-only, or co-use. "Co-use" was defined as any report of both cannabis and alcohol during the same time block, but did not include information regarding the timing (when each substance was used) or ordering (which substance was used first) of use. Therefore, we were unable to determine whether co-use was actual simultaneous use, i.e., if the effects of alcohol and cannabis overlapped.

State-level anxiety. We modified a single question from Buckner et al. (2012) to assess anxiety state. At each prompt, participants were asked: "Please rate your current anxiety on a scale of 0-10, with 0 being "totally relaxed" and 10 being "extremely intense anxiety."

Data Analyses

Missing data were handled using full information maximum likelihood, commonly used for two-level data (Schminkey et al., 2016). Co-use was analyzed using a combination of descriptive statistics and multilevel structural equation models (MSEMs; cf. Curran, 2003; Mehta & Neale, 2005). To account for the repeated measures aspect of the ILD data and to allow for simultaneous tests of effects, two sets of MSEMs were conducted using Mplus 8 (Muthén & Muthén, 1998–2017) to test the temporal association between anxiety and various categories of use.

The first set of models were used to investigate the research question of whether momentary state-level anxiety prior to use predicted the likelihood of different usage types (i.e., no use, alcohol-only, cannabis-only, or co-use) at the next timepoint. To examine these relations, the dataset was re-organized to address the time-lagged data. The second set of models examined whether usage type predicted state-level anxiety after use instances. In these models, the substance use EMA variables were naturally time-lagged due to the usage type questions examining any use since the last timepoint, while anxiety was assessed as a rating in the current moment. It is important to note that because "usage type" is a categorical variable with four categories, dummy coded variables were created and the models were re-run redundantly to get different dummy effect estimates (i.e., pairwise comparisons). For example, Table 2 is a combination of three models, with redundant information removed. Model 1 used co-use as the referent group and compared each of the other usage types (i.e., no use, alcohol-only, cannabis-only) to co-use. Then, in Model 2, alcohol use was the referent group and there were two new comparisons (alcohol-only v. no use; alcohol-only v. cannabis-only) and one redundant comparison (alcohol-only v. co-use) that was not repeated in the table. In Model 3, cannabis-only was the referent group with one new comparison (cannabis-only v. no use) and two redundant comparisons (cannabis-only v. alcohol-only; cannabis-only v. co-use) that were not shown. This procedure was repeated in Table 3 presenting

three models in one table and excluding redundant information.

MSEMs were utilized for both research questions to test all pairwise comparisons based on the use of dummy codes for the categorical variable of usage type. The key difference between the MSEMs was the within-level random slopes. In Table 2 the random slopes represent momentary anxiety modeling categorical usage type (with reference groups indicating the pairwise comparisons). In Table 3 the random slopes represent dummy coded usage types modeling momentary anxiety. Due to running multiple models for each research question, the absolute magnitudes of the parameter estimate values in Tables 2 and 3 are difficult to compare across the models. However, because all pairwise comparisons are accounted for at each iteration, it is possible to draw conclusions about the relative ordering of the four usage types.

These random slopes were then predicted by baseline time-invariant variables, including baseline anxiety (BAI), baseline social anxiety (SIAS-SF), and sex (male as referent) to test the moderation hypotheses. This approach is a 2 X (1–1) moderation MSEM (Preacher et al., 2010; Preacher et al., 2016) because the predictor (state-level anxiety for question 1; usage type for question 2) and the outcome variables (usage type for question 1; state-level anxiety for question 2) were measured on the momentary level, and the moderators (i.e., baseline general anxiety, social anxiety, and sex) were measured once at baseline; this is called the random coefficient prediction method. Dummy coding was utilized for usage type that allowed for all pairwise comparisons through multiple iterations of the models with varying reference groups.

RESULTS

Sample Characteristics

Participants' age ranged from 18 to 46 (M = 20.21; SD = 3.48). The sample included 64 females (58.7%) and 45 males (41.3%), 69 (63.3%) who were White, and 40 (36.7%) who were underrepresented minorities, which included 21 (19.3%) Latinx, 12 (11%) multiracial, and 7 (6.4%) African American individuals. Participants included 47 (43.1%) first-year, 31 (28.4%) second-year, 20 (18.3%) third-year, and 11 (10.1%) fourth-year students.

Descriptive statistics for baseline and EMA substance-related and other model variables can be found in Table 1. At the baseline appointment, participants self-reported near-daily cannabis use, on average. The majority of participants reported that flower was the primary form of cannabis used. Smoking, via a bong/water pipe, hand pipe, or joint/blunt, was the primary method of ingestion. Most participants reported alcohol use within the past 30 days at baseline, consuming a mean number of 4.3 (SD = 4.6) standard alcohol drinks on a typical drinking day in the past month. Mean number of heavy episodic drinking occasions (consuming four/five+ drinks per drinking occasion for women/men in a two-hour period) in the past 30 days was 2.27 (SD = 3.58) times for females and 2.59 (SD = 3.56) times for males. Mean levels of anxiety on the BAI and SIAS-SF were above respective measure cut-off scores, indicating possible clinically significant anxiety. More specifically, 40.4% of participants scored higher than 16 on the BAI and 79.8% had scores above 9 on the SIAS-SF.

Overall, 85 participants (78%) reported any co-use within the 14-day EMA period. Out of all EMA instances, 928 were missing from the total 4578 prompts. Of those remaining, the majority were coded as no substance use (n = 1698, 46.5%), followed by cannabis-only (n = 1449, 39.7%), co-use (n = 298, 8.2%), and alcohol-only (n = 205, 5.6%). EMA state-level anxiety ranged from 0 – 6, with an average of 2.49 (SD = 1.53).

Does Momentary Anxiety Predict Alcohol, Cannabis, or Co-use?

State-level anxiety predicted the likelihood of subsequent substance use in two pairwise comparisons. In instances when participants reported higher levels of momentary anxiety, they were more likely to report no use compared to co-use (see Table 2, S1, state-level) and cannabis-only (see Table 2, S6, state-level). When examining baseline moderators (BAI, SIAS-SF, and sex) of the random slope between momentary state-level anxiety and usage type, several random slopes were moderated by sex (see Table 2, baseline level). Specifically, we found a stronger relationship for women compared to men for momentary state-level anxiety predicting a higher likelihood no use episodes when compared to co-use (S1), alcohol-only (S4), and cannabis-only (S6).

Table 1. *Descriptive statistics for alcohol, cannabis, and other model variables (N = 109)*

Variable	n (%)	Range	Median	Mean	Standard Deviation
Primary method of cannabis ingestion[a]					
Smoke					
Bong/water pipe	36 (33%)				
Hand pipe	31 (28.4%)				
Joint/blunt	10 (9.2%)				
Vape	13 (11.9%)				
Oral (edibles)	8 (7.3%)				
Dab rig	10 (9.17%)				
Other	1 (<1%)				
Primary form of cannabis used[a]					
Flower	74 (67.9%)				
Concentrates/dabs	27 (24.8%)				
Edibles	7 (6.4%)				
Other	1 (<1%)				
Any alcohol use, past month[a]	93 (85.3%)				
Standard alcohol drinks consumed on a typical drinking day, last month[ac]		1 – 20	3	4.3	4.6
Days used cannabis, last month[a]		3 – 30	25	22.6	7.5
Beck Anxiety Inventory (BAI)[a]		0 – 48	10	14.1	12.6
Social Interaction Anxiety Scale, Short Form (SIAS-SF)[a]		6 – 30	12	12.8	5.2
State-level anxiety (per subject)[b]		0 – 6	2.5	2.49	1.53
Substance use instances[bd]					
No substance use	1698 (46.5%)				
Cannabis-only use	1449 (39.7%)				
Co-use	298 (8.2%)				
Alcohol-only use	205 (5.6%)				

Note. If frequency or percentage < 109 or 100%, due to missing data. [a] = baseline variable, [b] = EMA variable, [c] = Out of those who reported drinking (n = 93), [d] = Out of 3650 available EMA responses. Cutoff scores: BAI, mild to severe anxiety = 7 or higher (Beck & Steer, 1993); SIAS-SF, high social anxiety = 9 or higher (Fergus et al., 2012).

Table 2. *Summary of results from Multilevel Structural Equation Models examining the predictive nature of momentary anxiety on usage type.*

State-Level					
Random Slope (S) *anxiety predicting*:			**estimates**	**SE**	***t***	***p***
No use v. co-use (S1)			.318	.137	2.316	**.021**
Cannabis-only v. co-use (S2)			.153	.132	1.158	.247
Alcohol-only v. co-use (S3)			-.108	.201	-.534	.593
No use v. alcohol-only (S4)			.176	.136	1.289	.197
Cannabis-only v. alcohol-only (S5)			-.273	.189	-1.444	.149
No use v. cannabis-only (S6)			.415	.117	3.559	**<.001**
Baseline Level						
Outcome		**Predictor**	**estimates**	**SE**	***t***	***p***
S1	On	BAI	.002	.004	.420	.675
		SIAS-SF	-.014	.010	-1.447	.148
		SEX (male)	-.293	.102	-2.875	**.004**
S2	On	BAI	.006	.004	1.455	.146
		SIAS-SF	-.011	.009	-1.185	.236
		SEX (male)	-.028	.082	-.339	.735
S3	On	BAI	.004	.005	.884	.377
		SIAS-SF	-.015	.011	-1.413	.158
		SEX (male)	-.014	.128	-.106	.915
S4	On	BAI	.000	.004	-.097	.923
		SIAS-SF	.003	.008	.424	.672
		SEX (male)	-1.82	.084	-2.159	**.031**
S5	On	BAI	.006	.006	1.106	.269
		SIAS-SF	.013	.011	1.190	.234
		SEX (male)	.068	.121	.559	.576
S6	On	BAI	-.006	.004	-1.484	.138
		SIAS-SF	-.009	.009	-1.068	.286
		SEX (male)	-.241	.087	-2.785	**.005**

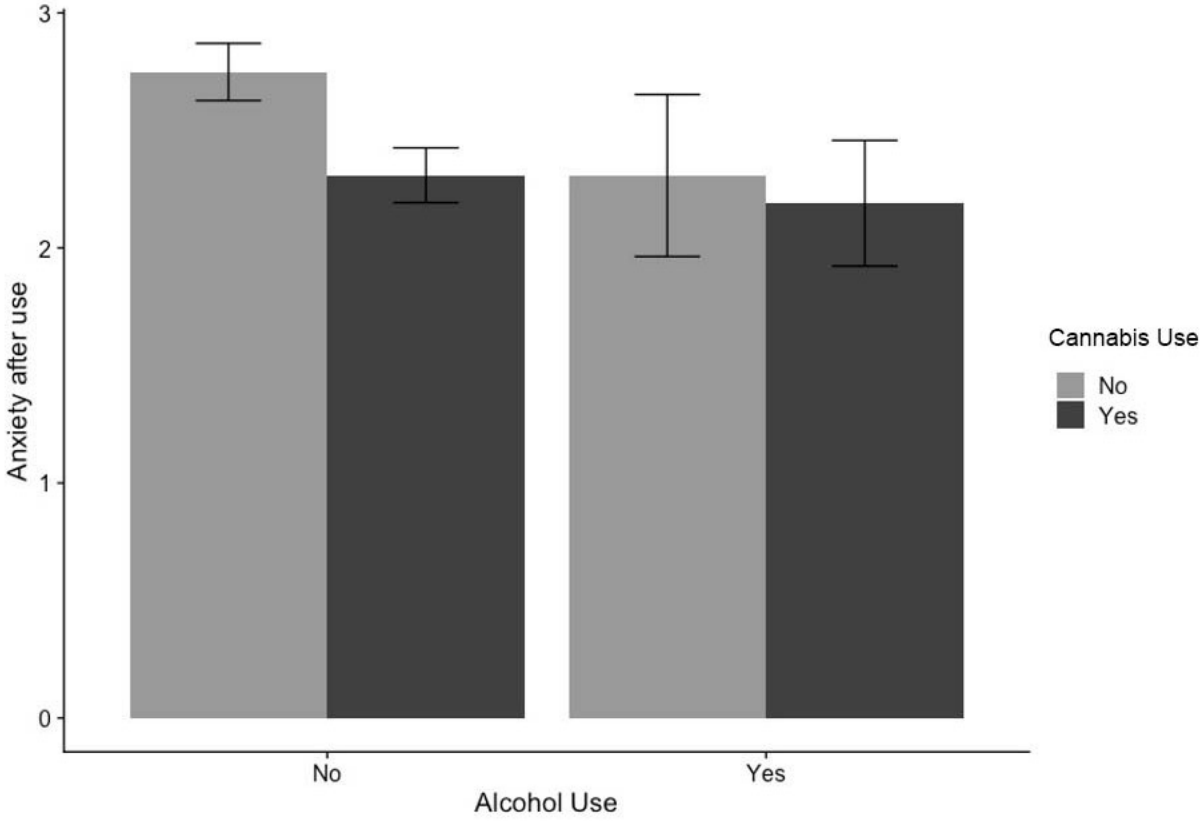
Note. This table represents 3 models with redundant information removed (see analysis plan for a full description). For comparisons by sex, male = 1, female = 0. S1 compared co-use to no use and no use was the more likely outcome, S4 compared alcohol-only to no use and no use was the more likely outcome. S2, S3, S5, and S6 usage types were statistically equivalently likely. The sign of the estimates is relative to the referent group coding in Mplus. BAI = Beck Anxiety Inventory; SIAS-SF = Social Interaction Anxiety Scale, Short Form; estimates = unstandardized regression coefficients; SE = Standard Error. $p<.05$ bolded.

Table 3. *Summary of results from Multilevel Structural Equation Models examining predictive nature type of usage type (i.e., no use, alcohol-only use, cannabis-only use, co-use) on momentary anxiety.*

State-Level					
Random Slope (S) ***predicting anxiety***			**estimates**	**SE**	**t**	**p**
No use v. co-use (S1)			-1.523	.479	-3.180	**.001**
No use v. alcohol-only (S2)			-1.773	.591	-2.999	**.003**
No use v. cannabis-only (S3)			-1.859	.366	-5.078	**.000**
Alcohol-only v. co-use (S4)			-1.005	.536	-1.874	.061
Alcohol-only v. cannabis-only (S5)			-1.346	.449	-2.998	**.003**
Cannabis-only v. co-use (S6)			-1.090	.496	-2.199	**.028**
Baseline Level						
Outcome (raw)		**Predictor (raw)**	**estimates**	**SE**	**t**	**p**
S1	On	BAI	.058	.018	3.266	**.001**
		SIAS-SF	.006	.039	.151	.880
		SEX (male)	.008	.367	.022	.983
S2	On	BAI	.062	.020	3.104	**.002**
		SIAS-SF	.043	.045	.946	.344
		SEX (male)	-.287	.447	-.643	.520
S3	On	BAI	.055	.011	4.908	**.000**
		SIAS-SF	.043	.026	1.625	.104
		SEX (male)	-.024	.259	-.093	.926
S4	On	BAI	.058	.018	3.246	**.001**
		SIAS-SF	.006	.039	.143	.886
		SEX (male)	.005	.370	.014	.989
S5	On	BAI	.054	.011	4.901	**.000**
		SIAS-SF	.043	.026	1.646	.100
		SEX (male)	-.027	.259	-.106	.916
S6	On	BAI	.058	.018	3.262	**.001**
		SIAS-SF	.006	.039	.151	.880
		SEX (male)	.007	.368	.018	.985

Note. This table represents 3 models with redundant information removed (see analysis plan for a full description). In the state-level comparisons, the first usage type listed is the referent. For comparisons by sex, male = 1, female = 0. BAI = Beck Anxiety Inventory; SIAS-SF = Social Interaction Anxiety Scale, Short Form; estimates = unstandardized regression coefficients; SE = Standard Error. $p<.05$ bolded.

Figure 1. *Pattern of usage types predicting momentary state-level anxiety*



Note. This figure illustrates average state-level anxiety for each substance usage type across the two-week EMA period. Anxiety is the highest during episodes of no use, followed by cannabis-only and alcohol-only, followed by co-use, which had the lowest state-level anxiety levels. Error bars represent the standard error around the means.

Does Type of Use (i.e., No Use, Alcohol-only, Cannabis-only, Co-use) Predict Momentary Anxiety Following a Use Episode?

There was a consistent pattern of usage types predicting momentary state-level anxiety, with all comparisons except one (alcohol-only v. co-use) demonstrating statistically significant differences. As noted in Table 3 (state-levels), based on the pairwise comparisons, there was a progression from higher to lower average state-level anxiety for no use, cannabis-only and alcohol-only (which had similar state-anxiety levels), followed by co-use, which had the lowest state-level anxiety levels. Though the magnitude of differences were not compared statistically, Figure 1 demonstrates this progression.

Examination of baseline moderators (BAI, SIAS-SF, and sex) revealed that BAI score impacted the usage type relation to state-level anxiety for all six comparisons (see Table 3, baseline level). SIAS-SF and sex did not moderate any of the relationships. As demonstrated with negative slopes at the state-level (Table 3, S1-S6, state-level), higher baseline anxiety (BAI) contributed to a stronger relative effect of usage type predicting anxiety for all six comparisons.

DISCUSSION

The current analysis focused on examining the temporal association between state-level anxiety and different substance usage categories among a sample of college students who use cannabis regularly and live in a state with legal recreational cannabis. Participants engaged in regular co-use of cannabis and alcohol, with a majority (78%) reporting at least one instance of co-use during the 2-week EMA period. Overall, findings provide partial support for the affective-motivational model of drug addiction. In our first set of models

examining whether momentary anxiety predicted usage type, participants who reported higher levels of anxiety were more likely to report no substance use when compared to co-use or cannabis-only episodes. In our second set of models examining whether usage type predicted state-level anxiety, usage types largely predicted momentary state-level anxiety, with all comparisons except one (alcohol-only v. co-use) demonstrating statistically significant differences.

We found insufficient evidence that prior state-level anxiety predicted usage type, with two exceptions. When anxiety level was high, participants were more likely to report no use compared to co-use and no use compared to cannabis-only. When examining baseline moderators, we found stronger associations for women compared to men for several of the pairwise comparisons (i.e., momentary anxiety and higher likelihood of no use compared to all three substance usage types). This finding suggests that women may be less likely than men to engage in substance use despite feelings of anxiety. Past research has shown that women use substances less often than men; however, women have higher rates of anxiety disorders (McLean et al., 2011; Schulenberg et al., 2020). One potential explanation for our finding is that women may be utilizing other coping strategies (e.g., reappraisal, distraction, problem-focused coping) to manage symptoms of anxiety and thus are less likely to use substances to cope (Nolen-Hoeksema et al., 2012). This finding needs to be further explored in future work. We also found that baseline social anxiety did not moderate any of the pairwise comparisons. This finding is contrary with other work (Buckner et al., 2008) that suggests that persons with social anxiety may drink or use cannabis to decrease discomfort associated with social interaction. In a review of the literature, Morris and colleagues (2005) found that studies examining the co-morbidity between social anxiety disorder (SAD) and alcohol use disorder (AUD) have been inconsistent and that mixed findings may be explained by unexamined moderating factors (e.g., alcohol expectancies, social context, sex).

Our findings are consistent with our hypothesis that alcohol-only, cannabis-only, and co-use would lead to lower state-level anxiety when compared to no use. This finding is also consistent with select EMA studies that have shown that use of cannabis or alcohol independently are associated with lower levels of negative affect or anxiety following use (Buckner et al., 2015; Dvorak et al., 2018). Co-use generally had the lowest levels of anxiety post-use across the different usage types, as shown in Figure 1. One explanation for this finding is that co-use produces decreased anxiety due to direct, pharmacological effects. To our knowledge, no prior studies have examined the impact of co-use on anxiety. Past research has shown that simultaneous cannabis and alcohol use may lead to increased intoxication effects, with more pronounced feelings of confusion, dizziness, clumsiness, and difficulty concentrating (Hartman et al., 2015; Lee et al., 2017; Lukas et al., 1992; Lukas & Orozco, 2001). It is possible that enhanced feelings of intoxication, in-the-moment, may override sensations of anxiety, making it less noticeable. Controlled lab-based studies would best address the impact of co-use on anxiety.

In our data, relationships between usage types and lower anxiety were moderated by higher baseline general anxiety across all six comparisons. Past work has found high rates of co-morbidity between anxiety and substance use disorders (Blevins et al., 2019; Buckner et al., 2017). However, the relationship between anxiety and substance use in-the-moment among those with anxiety disorders is not well understood. It is possible that cannabis and/or alcohol use may differentially affect the momentary expression of anxiety in those with higher levels of baseline anxiety. Specific anxiety symptoms may prompt coping-related substance use. We utilized the Beck Anxiety Inventory to assess general anxiety symptoms, which focuses extensively on physiological/somatic (e.g., "heart pounding") and cognitive (e.g., "fear of losing control") aspects of anxiety. Future research should explore how particular anxiety symptoms and coping motives relate to alcohol, cannabis, and co-use in-the-moment for persons with higher levels of anxiety to drive future real-time interventions. Furthermore, assessing outcome expectancies related to alcohol, cannabis, and co-use is warranted, as such beliefs may drive anxiety management and can be addressed as part of intervention.

The relation between momentary anxiety and alcohol, cannabis, or co-use may also be a function of product type, dose used, specific substance use patterns, and tolerance. Classic research has

shown that a wide range of factors (e.g., dose, particular conditions) likely determine whether alcohol has any impact on anxiety (Wilson, 1988). Alcohol is known to have biphasic stimulatory and sedating effects, which may function differently in light and heavy drinkers (King et al., 2002). Research on the anxiolytic effects of cannabis (including THC and cannabidiol) is ongoing, but thus far inconsistent (Van Ameringen et al., 2020). Recent experimental work (Childs et al., 2017) demonstrated that low-dose oral THC (7.5 mg) decreased anxiety associated with an experimental stress task, while high-dose oral THC (12.5 mg) increased anxiety. It is currently unclear how variations in cannabis form (e.g., edibles, concentrates), dose, potency level, and route of ingestion (e.g., vaping, dabbing) may influence the experience of anxiety. Due to the complex and possibly synergistic effects of cannabis and alcohol, there is a need for additional research on the effects of these substances on anxiety in a laboratory setting.

Limitations and Future Directions

There has been increased attention to alcohol and cannabis co-use due to the increased risk for negative consequences resulting from using both substances compared to using either substance alone (Yurasek et al., 2017). The majority of co-use studies have been cross-sectional, suggesting a need for ILD studies (e.g., daily or EMA designs; Yurasek et al., 2017). Future ILD studies should be designed to gather data specifically on episode-level simultaneous use to better understand predictors and sequalae of simultaneous use. We did not assess negative consequences associated with co-use in-the-moment, which could be associated with coping-related alcohol or cannabis use and should be explored in future work. In addition, we did not assess other potentially important variables that might contribute to co-use behavior, such as trait impulsivity. The current study was a secondary analysis of data from a larger study focused on a cohort of college students using cannabis near-daily. Findings may not generalize to those who use cannabis at low to moderate levels. Though most participants also drank alcohol, examination of alcohol variables and measures were not an original study goal. We also did not assess the quantity/potency of cannabis or alcohol use in-the-moment, other substance use (e.g., prescription stimulants), or other potentially influential momentary factors, such as positive affect or motives for use (Slavish et al., 2019), which may relate to co-use. It is unclear if participants used the same dose of alcohol and/or cannabis when using together v. during singular use; as such any differences across usage groups may reflect dose effects and not potentiation. In addition, we did not control for pre-level of anxiety in our analyses due to the time span between prompts. Due to power concerns, we also did not control for other potentially important variables, such as time/day of study, baseline substance use, and the social context of one's use (e.g., with others or alone). The majority (96%) of our participants were under age 24, but four were over age 28, which should be noted when considering generalizability. Finally, this study should be replicated in a general population sample. While college students are an important and high-risk group in need of study, it is important for the purposes of generalizability to understand if correlates of co-use identified generalize to a general population sample.

Conclusions

The present study provided an initial examination of the association between co-use and state-level/baseline anxiety. Though our findings did not suggest that anxiety (conscious or not) broadly drives various types of substance use in-the-moment, we did find that participants largely experienced lower anxiety after cannabis-only, alcohol-only, or co-use as compared to no use, with general anxiety moderating these relationships. Future research is needed to better understand co-use, how it functions in different contexts, and whether it's related to a wide range of affect variables, including positive affect. Moving forward, it is important to recognize potential benefits that participants may experience as a result of substance use, as such factors could interfere with successful treatment completion. Consequently, clinicians should consider assessing for underlying anxiety and potential motives for use in those seeking substance-related treatment services. Future research, particularly lab-based studies, should explore the combined effects of cannabis and alcohol on participant outcomes, as well as factors that may moderate these relations.

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Funding and Acknowledgements: This study was funded by the National Institutes of Health (R15DA041656; Phillips, K.; Phillips, M.)