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From mood to use: Using ecological momentary assessments to examine how anhedonia and depressed mood impact cannabis use in a depressed sample

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ABSTRACT

Anhedonia and depressed mood are two cardinal symptoms of major depressive disorder (MDD). Prior work has demonstrated that cannabis consumers often endorse anhedonia and depressed mood, which may contribute to greater cannabis use (CU) over time. However, it is unclear (1) how the unique influence of anhedonia and depressed mood affect CU and (2) how these symptoms predict CU over more proximal periods of time, including the next day or week (rather than proceeding weeks or months). The current study used data collected from ecological momentary assessment (EMA) in a sample with MDD ($N = 55$) and employed mixed effects models to detect and predict weekly and daily CU from anhedonia and depressed mood over 90 days. Results indicated that anhedonia and depressed mood were significantly associated with CU, yet varied at daily and weekly scales. Moreover, these associations varied in both strength and directionality. In weekly models, less anhedonia and greater depressed mood were associated with greater CU, and directionality of associations were reversed in the models looking at any CU (compared to none). Findings provide evidence that anhedonia and depressed mood demonstrate complex associations with CU and emphasize leveraging EMA-based studies to understand these associations with more fine-grained detail.

1. Introduction

Major depressive disorder (MDD) is a debilitating disorder, impacting 17 % of adults in the United States (U.S. Department of Health and Human Services, 2022). MDD is defined by symptoms occurring most of the day and nearly every day for at least two weeks, including the cardinal symptoms of depressed mood and anhedonia (American Psychiatric Association, 2013). MDD is highly comorbid with other disorders, including substance use disorders (SUDs): 25 % of individuals with MDD also meet criteria for a SUD (Davis et al., 2023; Hunt et al., 2020). Anhedonia—the loss of interest or pleasure—may be an important transdiagnostic characteristic (Destoop et al., 2019) spanning across disorders, and may be especially common among those with SUDs and other disorders involving diminished positive moods, such as MDD (Stull et al., 2022).

Across the SUD literature, anhedonia has been shown to be positively related to relapse of nicotine use and alcohol use (Nguyen et al., 2020), opioid cravings (Petrie et al., 2022), and treatment outcomes for cocaine dependence (Crits-Christoph et al., 2018). Prior work has also indicated that anhedonia and depressed mood are independently related to

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substance use behaviors and treatment outcomes, including cocaine use disorder (Crits-Christoph et al., 2018) and smoking cessation (Leventhal et al., 2014). When compared to overall levels of MDD, anhedonia severity predicted poorer smoking cessation outcomes (Crits-Christoph et al., 2018). Lifetime anhedonia is also a stronger predictor of smoking cessation than depressed mood or MDD (Leventhal et al., 2014), indicating that a MDD diagnosis may obscure the role of more predictive symptomatology. Existing research on the temporal relationship between comorbid depressive symptomatology and SUDs primarily focuses on nicotine use (Garfield et al., 2014), thus a more explicit attempt to distinguish the relative predictive power of anhedonia and depressed mood on CU is warranted.

1.1. The role of anhedonia in cannabis use

Greater anhedonia is associated with increased cannabis cravings, potentially reflecting underlying neurochemical changes that are associated with the negative reinforcement aspect of addiction (Blum et al., 2021; Bovasso, 2001; Destoop et al., 2019; Hatzigiakoumis et al., 2011; Kuhns et al., 2022). However, few studies have examined the impact of anhedonia on CU. One study found that anhedonia positively predicts the rate of increase in CU frequency in adolescents across time (Leventhal et al., 2017). No studies to the authors' knowledge have explored the effects of anhedonia on subsequent CU over shorter timeframes (e.g., daily, weekly). Research has shown that MDD symptomatology (including anhedonia) can both fluctuate over short periods of time (Nemesure et al., 2024), which could impact the frequency or amount that one uses cannabis to cope with these changes. Thus, it is important to investigate associations between depressed mood and anhedonia with CU, with sensitivity to their presentation at multiple levels of temporal resolution.

1.2. The role of negative affect and depressed mood in cannabis use

Unlike anhedonia, research has focused more on how negative affect or depressed mood are associated with CU. For example, cannabis consumers often report using cannabis to cope with negative emotions and psychological distress, which may increase risk for cannabis-related problems (Moitra et al., 2015). Nevertheless, findings regarding momentary associations between specific types of negative affect and CU are somewhat inconclusive within community and clinical populations (Wycoff et al., 2018). When examining the momentary associations between negative affect and CU in community samples, some studies have reported elevated negative affect immediately prior to CU (i.e., Buckner et al., 2013, 2015; Shrier et al., 2014), suggesting that individuals may use cannabis as a coping mechanism for temporary mood alleviation. Conversely, others have found that depressed mood was negatively associated with subsequent CU (Chakroun et al., 2010; Swendsen et al., 2011), indicating that those with more persistent depressed mood might use cannabis less frequently. In clinical samples, momentary negative affect is elevated before CU and diminished after use (Wycoff et al., 2018). This pattern is consistent with the negative reinforcement theory of CU: individuals with affective-related mental health disorders are particularly likely to use cannabis to alleviate situational MDD symptoms or negative affect (Walukevich-Dienst et al., 2023; Wycoff et al., 2018). Thus, it appears that negative mood states predict CU, potentially as a way for individuals to manage their symptoms; however, a further investigation into these relationships in a depressed population is warranted.

1.3. Temporal relationships between CU and depression

Longitudinal studies have provided evidence that depressive symptoms, including anhedonia, predict later cannabis behaviors (Leventhal et al., 2017; Lydiard et al., 2023). However, the distal timeframes utilized for these designs may have precluded an ability to detect any potential impact of transient depressive symptoms on cannabis behaviors. Toward finer temporal contextualization, ecological momentary assessment (EMA) offers an innovative alternative to explore dynamic associations between depressive symptoms and subsequent cannabis behaviors. EMA typically involves data collection at multiple timepoints throughout the day, allowing researchers to capture fluctuating symptoms and explore associations over time (e.g., momentary, daily, weekly, etc.).

No EMA studies have directly examined the role of anhedonia on subsequent CU. Such research could complement existing EMA data focused on the second cardinal symptom of MDD: depressed mood. These designs have largely emphasized shorter time scales (i.e., momentary or daily) across samples (Wycoff et al., 2018). Within these works, findings have demonstrated variability in the associations between depressed mood states and subsequent CU across proximal (momentary) and distal (24 h) timepoints (Shrier et al., 2014). Where brief collection periods such as these are important for answering questions about transient and variable mood states, longer units of time (i.e., weekly) hold promise to explore the potential impacts of persistent depressed mood states. Taken together, the literature indicates that (a) it is essential to examine anhedonia and depressed mood separately from one another and (b) the associations with CU likely vary as a function of time, warranting a further investigation into how these associations emerge over daily and weekly timeframes.

1.4. Rationale

Our study aimed to investigate the independent associations between CU and the two cardinal symptoms of MDD—depressed mood and anhedonia—based on 90-day EMA data collected as part of a larger, ongoing study of a cohort of individuals with MDD (Nemesure et al., 2024). Given that depression is a heterogeneous disorder, it is plausible that individuals with a primarily more anhedonic presentation may be at greater risk for substance use than individuals with a primarily depressed mood presentation. Indeed, individuals with maladaptive substance use may experience difficulties with positive affect and reward processing, specifically in response to *non-drug* rewards. This may result from the habituated positive affect drug response, as evidenced by neuroimaging studies showing reduced reward sensitivity and motivation for non-drug reward (Myerson et al., 2024; Spanagel, 2020).

The current study aimed to fill three gaps in the literature. First, prior research examining associations between MDD and CU has focused on sum score/holistic presentation of MDD (rather than on individual symptoms); thus, we independently investigated the two cardinal symptoms of MDD, depressed mood and anhedonia (Cook et al., 2010; Nguyen et al., 2020). Second, the impact of depressed mood and anhedonia on CU is emphasized far less than the reverse association, so we investigated how depressed mood and anhedonia predict CU. Third, to provide further insight into the temporal nature of these relationships, we examined both daily and weekly associations (i.e., anhedonia and/or depressed mood predicting CU). Based on prior work, we hypothesized that depressed mood and anhedonia would both be independently, positively associated with same- and next-day CU and same- and next-week CU in a sample with MDD. We also hypothesized that anhedonia, in comparison to depressed mood, would demonstrate a stronger association with subsequent CU, similar to what has been reported with other substances (Crits-Christoph et al., 2018; Leventhal et al., 2017).

2. Methods

2.1. Participants

The study received approval from the Committee for the Protection of Human Subjects at Dartmouth College (STUDY00032081), and participants provided written and verbal consent prior to starting the

study's procedures. Adult participants across the United States were recruited online via Google and Meta Ads to participate in the current study. Participants viewed a targeted ad regarding a study on depression on either Google, Facebook, or Instagram, and clicking on the ad brought participants to the landing page with more information about the study and the screener. After providing consent on the screener, participants completed initial questions, including the Patient Health Questionnaire-9 (PHQ-9) and demographics. Participants who (1) endorsed moderate MDD symptoms (i.e., PHQ-9 $\geq$ 10), (2) were at least age 18 or older, and (3) used an Android as their primary device due to compatibility requirements with the application used for EMAs, MLife, were invited to complete a more detailed set of screeners. Specifically, participants were administered the Structured Clinical Interview for DSM-5 (SCID-5) via Zoom with a board-certified psychiatrist or clinical psychology fellow. Participants who met criteria for current MDD (i.e., over the past 30 days) and did not meet criteria or endorse (1) a history of mania symptoms, (2) active suicidal thoughts or behaviors, and/or (3) active psychoses, as determined by the SCID-5 and/or study team, were invited to enroll in the main study (see Fig. 1 for the recruitment process). At the time of the analyses, 235 participants met criteria for current MDD and completed the 90-day study. Of these 235 participants, only participants who endorsed CU at any time during the study were included in the analyses, resulting in a sample size of 55 for the current manuscript (Table 1).

2.2. Measures

2.2.1. Ecological momentary assessment

The EMA included a mobile-friendly version of the Patient Health Questionnaire-9 (Kroenke and Spitzer, 2002; Torous et al., 2015) to assess for momentary MDD symptoms. Participants responded regarding their symptoms over the past four hours using a sliding scale from 0 ("not at all") to 100 ("constantly") for each question. Participants were instructed to report their symptoms with reference to the best ("0″) or worst ("100″) they have ever been in their lifetime. The PHQ-9 items of anhedonia (i.e., "I have had little interest or pleasure in doing things") and depressed mood (i.e., "I have felt down, depressed, or hopeless") were included in analyses.

2.2.2. Weekly assessment

The Timeline FollowBack (TLFB) was administered weekly to assess CU (Robinson et al., 2014). Of importance to note, the TLFB was not administered within the EMAs but rather as a single, weekly survey. Participants received this prompt on Monday morning and were asked to indicate CU over the past seven days (e.g., if the prompt was answered on Monday, they were asked to report their CU from Monday-Sunday of the prior week). Participants were given the instructions: "Select all the days in which you consumed marijuana over the past seven days." Participants who endorsed CU on a given day were also asked "Relative to your usual use, how much marijuana did you use?" on a 3-point scale where -1 = "less than usual", 0 = "the same as usual", and 1 = "more than usual".

2.3. Procedure

Participants completed EMAs three times a day for 90 days, which included the mobile-friendly PHQ-9. Participants received the first EMA prompt of the day four hours after their self-reported wake-up time and received the two other prompts at four-hour intervals thereafter. Participants completed the weekly assessment once a week, which was available on Monday morning. Participants were paid $1 for each EMA they completed, including the weekly assessment.

2.4. Data analytic plan

All analyses were run in R (version 4.2.2), and formula specifications for each of the models can be found in the Supplemental Materials. Importantly, we investigated how depressed mood and anhedonia detected and predicted CU in the different models. In the detection models, we examined how the severity of anhedonia and depressed mood in a given day or week were associated with CU in the same day or week. In the prediction models, we examined how the severity of anhedonia and depressed mood in a given day or week were associated with CU in the next day or week to further investigate the temporal relationships of MDD and CU.

2.4.1. Weekly data preprocessing

Participants' PHQ-9 EMAs from a given week (i.e., a maximum of 21 EMAs) were averaged across the week for the anhedonia and depressed mood items, resulting in two individual MDD symptom scores for each participant for each week. The TLFB responses for CU were preprocessed in two ways. First, a count variable was created for each participant, reflecting the number of days in a given week that participant endorsed CU (i.e., ranging from 0 to 7). Second, we averaged the degree to which participants used less, the same, or more cannabis on a given day. We recoded this use data to interval data, ranging from 0 to 3, to indicate whether a participant used no cannabis ("0″), less than usual ("1″), the same as usual ("2″), or more than usual ("3″). Then, we averaged this score across an entire week. Thus, each participant had an average amount of use for each week (i.e., ranging from 0 to 3).

2.4.1.1. Weekly data analysis. To investigate how weekly averaged anhedonia and depressed mood were associated with CU, we implemented four zero-inflated (ZI) mixed effects models using the *glmmTMB* package in R (v4.2.2) to detect and predict the same- and next-week CU. ZI models were necessary given the number of instances where participants indicated no CU on a given day (i.e., "0″). For all models, time ("week") was operationalized in absolute time and treated as both a nested within participant ("uid") random effect and as a fixed effect. The ZI component of the models included self-report weekly-averaged anhedonia, depressed mood, time, and participant (where convergence permitted, see below). The detection models leveraged PHQ-9 and TLFB data from the same week (*t*), whereas the prediction models incorporated lagged PHQ-9 data by one week (*t-1*) to establish a temporal precedent (e.g., anhedonia and depressed mood from week 1 were used to predict CU from week 2). In the first two models using TLFB count data, we implemented a ZI negative binomial model to detect and predict both the number of days of CU (non-ZI component) as well as *any* CU (ZI component) across a given week.[1] In the second set of models which leveraged TFLB interval data, a ZI Gaussian model was used to detect and predict the average weekly CU across a given week.

2.4.2. Daily data preprocessing

To investigate CU on the daily level, we only operationalized this as a single outcome. Similar to the weekly models, CU data was re-coded to interval data, ranging from 0 to 3, to indicate whether a participant used no cannabis ("0″), less than usual ("1″), the same usual ("2″), or more than usual ("3″). This resulted in a single score for each day.

2.4.2.2. Daily data analysis. Given the lack of any CU for a large proportion of days (Fig. 2), we used two ZI models to detect and predict same- and next-day CU, respectively.

The fixed and random effects structure, as well as the ZI component specification, was consistent with previous models. Time ("day") was modeled as a continuous variable in absolute time. PHQ-9 data was lagged by one day relative to the TLFB data in the prediction models to establish temporal precedence. As daily data only involved interval data,

[1] In these models, the participant variable ("uid") could not be included within the ZI component due to an inability for the model to converge after trying all available optimizers within *glmmTMB*

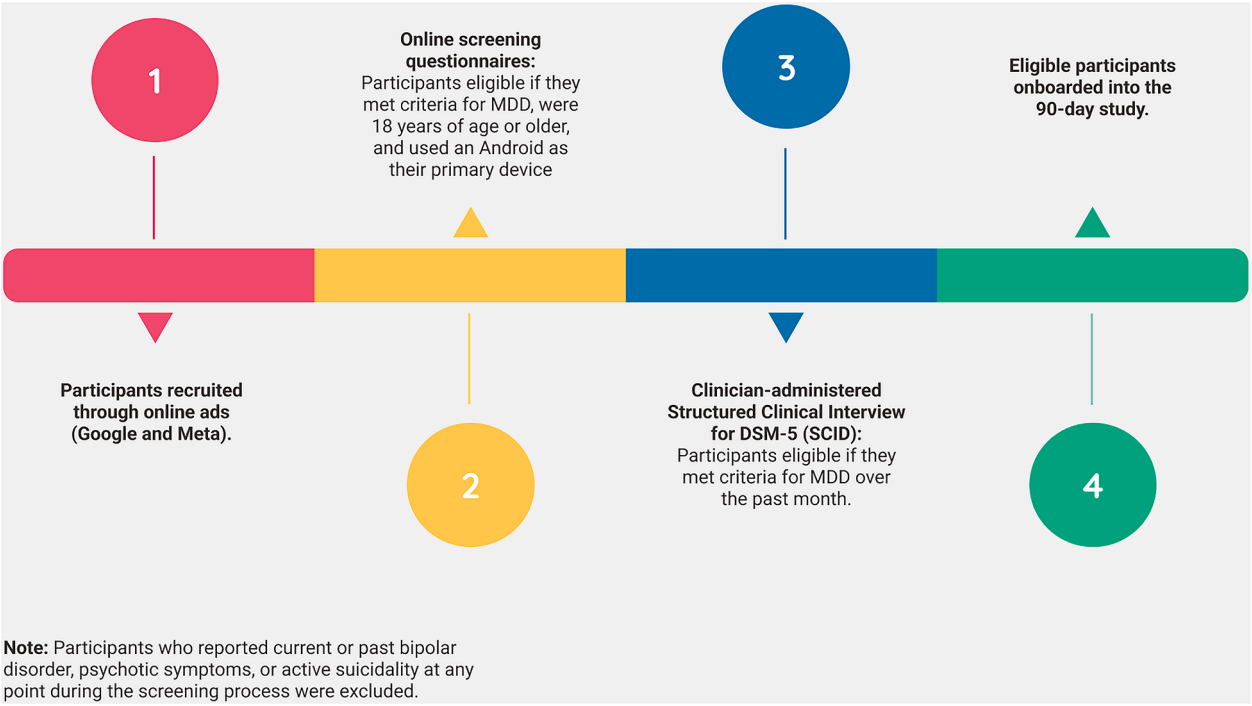

Fig. 1. Recruitment timeline.

Table 1
Cohort characteristics.

Attribute	Value	*n* (%)	Attribute	Value	*n* (%) or mean (sd)
Age	18–24 years	3 (5.5)	Ethnicity	Hispanic	5 (9.1)
	25–34 years	20 (36.4)		Non-Hispanic	50 (90.9)
	35–44 years	16 (29.1)	Income	Less than $20,000	13 (23.6)
	45–54 years	12 (21.8)		$20,000 – $39,999	10 (18.2)
	55–64 years	4 (7.3)		$40,000 – $59,999	9 (16.4)
Gender	Cisgender Women	45 (81.8)		$60,000 – $79,999	7 (12.7)
	Cisgender Men	3 (5.5)		$80,000 – $99,999	6 (10.9)
	Transgender Women	1 (1.8)		$100,000 – $149,999	7 (12.7)
	Transgender Men	1 (1.8)		$150,000 or more	3 (5.4)
	Transgender Non-binary	1 (1.8)	Depression	PHQ-9 Score	16.51 (2.76)
	Non-binary	3 (5.5)	Cannabis Use Disorder	CUDIT-R Score	6.24 (6.64)
	Other (prefer to self-describe)	1 (1.8)		Past CUD	7 (12.7)
Sexual Orientation	Heterosexual	26 (47.3)		Current CUD	7 (12.7)
	Homosexual	2 (3.6)	Alcohol Use Disorder	Past AUD	17 (30.9)
	Bi/pansexual	24 (43.6)		Current AUD	3 (5.5)
	Other (self-describe)	3 (5.5)	Cannabis and Alcohol Polysubstance Use Disorder	Past or Current CUD + Past or Current AUD	4 (7.3)
Race	White	44 (80.0)	Other Polysubstance Use Disorders	Past SUD	4 (7.3)
	Black or African American	4 (7.3)		Current SUD	0 (0.0)
	Asian	1 (1.8)			
	American Indian or Alaska Native	1 (1.8)			
	More than one race	5 (9.1)			
	Other (self-describe)	0 (0.0)			

Note. Percentages may not sum to 100 % due to rounding error. All past and present substance use disorder (SUD) counts are based on meeting the diagnostic threshold (2+ criteria) more than 12 months prior and within 12 months of the interview date, respectively. This was assessed with the Structured Clinical Interview for DSM-5 (SCID-5). Participants also completed the Cannabis Use Disorder Identification Test-Revised (CUDIT-R)—one of the most widely used measures to assess the severity of cannabis use problems (scores of 8+ indicative of hazardous use). Unlike the SCID-5, the CUDIT-R is an 8-item self-administered questionnaire that assesses the frequency of cannabis use behaviors and resultant problems (e.g., memory/concentration, spending several hours "stoned" each day). Bipansexual includes pansexual, bisexual, and bicurious. Other poly-SUDs include sedatives, stimulants (including cocaine), opioids, hallucinogens (including PCP), and inhalants. $N = 55$.

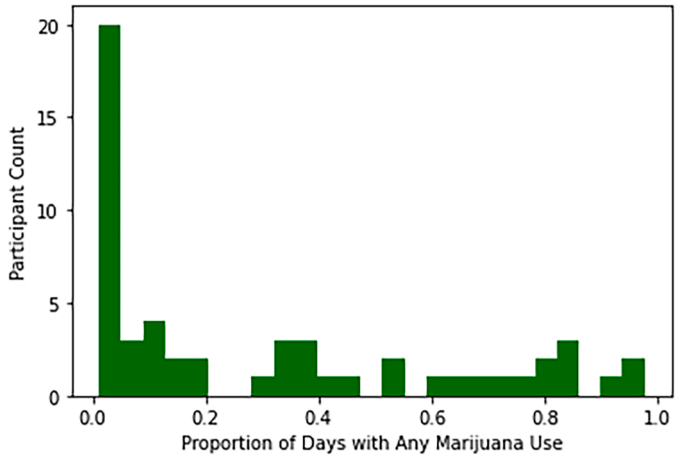

Fig. 2. Histogram of self-reported days of CU.

two ZI gaussian models were implemented to detect and predict daily CU. Day and uid variables were not included in the daily zero-inflation component of the models due to issues of convergence.

2.4.3. Sensitivity analyses

Of the 55 participants, 24 endorsed CU for at least 40 % of the 90 days (i.e., 3+ days of CU each week on average), and we will be referred to as "regular consumers" (McLellan et al., 1992). Alternatively, 29 participants ("low consumers") used cannabis for 20 % or less of the 90 days (i.e., 0-1 days of CU each week). Two participants did not fall within these parameters (i.e., endorsed CU 30–35 % of the time) and were excluded from our sensitivity analyses but are included in the full sample models. Across the entire sample, participants reported CU, on average, for 2.105 days in a week, whereas regular ($n = 24$) and low ($n = 29$) consumers endorsed an average of 4.206 and 0.414 days, respectively.

Given the heterogeneity of CU across our sample, we performed post-hoc sensitivity analyses to investigate differences between regular and low cannabis consumers. Thus, we ran the same six models outlined above for the regular and low cannabis consumers separately. We largely kept the formula specification the same; however, we omitted the ZI component for the regular consumers' models given that there were not a significant number of zeroes. Given the small samples in these subgroups, the sensitivity analyses are underpowered, but we conducted them to provide some insight into how MDD symptoms impact CU across different consumer groups. A brief discussion of sensitivity analyses is included; however, see Supplemental Materials for more detailed information.

2.4.4. Exploratory analyses

At the request of a reviewer, we ran exploratory analyses with all nine symptoms of MDD (as measured by the PHQ-9) as predictors in each of the models to investigate how individual symptoms may detect or predict CU. We also ran separate exploratory analyses with only the sum-score of the PHQ-9 as the predictor in the models. Given the number of current models and interpretations present in the current manuscript, we have added these models, and a description and interpretation of the results, to the Supplemental Materials in consideration of the manuscript length (Tables S7–S12).

3. Results

3.1. Weekly cannabis use

3.1.1. Number of days of use

Utilizing weekly count data (i.e., average number of days of *any* CU) in the overall sample, both anhedonia ($p = 0.020$) and depressed mood ($p = 0.002$; Table 2) were both associated with same-week cannabis use (CU). Specifically, lower, average anhedonia across a given week and higher, average depressed mood were associated with more days of CU in the same week. Time (week) was not significantly associated with same-week CU. No significant effects emerged within the zero-inflation (ZI) model: neither anhedonia, nor depressed mood were associated with an ability to signal for any non-zero amount of CU within the same week. Taken together, this pattern suggests that anhedonia and depressed mood were associated with varying levels of CU in the same week, but they were not associated with distinguishing between *any* or no CU.

Only weekly depressed mood was predictive of next-week CU ($p = 0.011$), indicating that higher levels of average depressed mood were predictive of using cannabis for more days in the following week. Anhedonia evidenced a non-significant association with CU ($p = 0.066$). Consistent with the detection model, time was not significantly associated with next week CU.

3.1.2. Average amount of use

Utilizing the weekly average use data (i.e., degree to which an individual's weekly use differed from their typical weekly CU), both weekly anhedonia ($p = 0.007$) and depressed mood ($p = 0.008$; Table 3) were both associated with average CU in the same week. Specifically, lower levels of average anhedonia across a given week and higher levels of average depressed mood were associated with using more cannabis than usual in the same week. Time was not significantly associated with CU. Participant (uid) was the only significant effect within the ZI model ($p = 0.026$), indicating that using any non-zero amount of cannabis within the same week was only driven by participant-specific variation.

Results indicated that both weekly anhedonia ($p = 0.011$) and depressed mood ($p = 0.014$) were also predictive of average CU in the following week, indicating that lower levels of average anhedonia and higher levels of average depressed mood predicted using more cannabis than usual in the next week. As before, time was not significantly associated with CU, and participant ID was the only significant effect within the ZI model ($p = 0.015$).

3.2. Daily cannabis use

Utilizing daily average use data (i.e., degree to which an individual's use in a day differed from their typical daily CU), results indicated that neither daily anhedonia nor depressed mood were associated with average CU in the same day (Table 4). Day of the week, however, was significantly associated with same-day CU ($p < 0.001$): days later in the week were associated with greater CU.

Compared to weekly models for the overall sample, the ZI results for the daily detection model yielded important insights. Indeed, lower depressed mood ($p < 0.001$) in a given day were both associated with using at least some amount of cannabis in the same day. Anhedonia was not significantly associated with CU in this model ($p = 0.068$). Interestingly, these directionalities were *opposite* of the patterns that emerged within the weekly models where lower anhedonia and higher depressed mood in a week were associated with using CU in the same week.

Results from the daily prediction model revealed a similar pattern for the overall sample: neither daily anhedonia nor depressed mood (Table 4) were predictive of average CU for the next day. In contrast to the detection model, day of the week was not predictive of next-day CU.

The ZI results for the prediction model yielded similar findings as in the detection model. Indeed, higher anhedonia ($p < 0.001$) and lower depressed mood ($p < 0.001$) in a given day were both associated with using at least some amount of cannabis during the following day for the overall sample.

Table 2
Number of days of CU across a given week.

Task	R^2	Conditional			Zero-Inflation		
		Variable	Estimate	*p*-value	Variable	Estimate	*p*-value
Detection (Same Week)	0.134	**PHQ1**	**−0.198**	**0.020**	PHQ1	−0.074	0.638
		PHQ2	**0.258**	**0.002**	PHQ2	−0.103	0.511
		week	−0.022	0.583	week	−0.042	0.615
Prediction (Next Week)	0.160	PHQ1	−0.155	0.066	PHQ1	0.018	0.912
		PHQ2	**0.215**	**0.011**	PHQ2	−0.235	0.154
		week	0.001	0.432	week	−0.069	0.432

Note. PHQ1 = Anhedonia; PHQ2 = Depressed Mood. Adjusted R^2 for zero-inflation models.

Table 3
Average CU across a given week.

Task	R^2	Conditional			Zero-Inflation		
		Variable	Estimate	*p*-value	Variable	Estimate	*p*-value
Detection	0.009	**PHQ1**	**−0.217**	**0.007**	PHQ1	−0.329	0.216
		PHQ2	**0.22**	**0.008**	PHQ2	−0.03	0.907
		week	−0.058	0.226	week	−0.104	0.443
					uid	**0.005**	**0.026**
Prediction	0.015	**PHQ1**	**−0.215**	**0.011**	PHQ1	−0.278	0.361
		PHQ2	**0.218**	**0.014**	PHQ2	−0.185	0.53
		week	−0.022	0.68	week	−0.126	0.42
					uid	**0.006**	**0.015**

Note. PHQ1 = Anhedonia; PHQ2 = Depressed Mood. Adjusted R^2 for zero-inflation models.

Table 4
Average CU across a given day.

Task	R^2	Conditional			Zero-Inflation		
		Variable	Estimate	*p*-value	Variable	Estimate	*p*-value
Detection	0.225	PHQ1	0.006	0.716	PHQ1	0.111	0.068
		PHQ2	−0.001	0.936	**PHQ2**	**−0.222**	**<0.001**
		day	**0.294**	**<0.001**			
Prediction	0.006	PHQ1	0.006	0.764	**PHQ1**	**0.204**	**<0.001**
		PHQ2	0.000	0.988	**PHQ2**	**−0.311**	**<0.001**
		day	0.002	0.906			

Note. PHQ1 = Anhedonia; PHQ2 = Depressed Mood. Adjusted R^2 for zero-inflation models.

3.3. Sensitivity analyses

3.3.1. Weekly cannabis use

3.3.1.3. Number of days of use. As discussed previously, we present an overview of our sensitivity analyses for the consumer subgroups here, and we direct the readers to Supplemental Materials for more details on the below findings. Among individuals with regular CU (i.e., >40 % of the time) anhedonia was similarly associated with same-week CU (p = 0.020), however depressed mood was not significantly associated (p = 0.066). Individuals with low CU did not demonstrate any significant conditional or ZI associations. In the prediction models (i.e., next week), anhedonia *was* associated with next-week CU in the regular consumer sample such that lower anhedonia was predictive of greater CU in the next week. No significant associations emerged in the low consumer sample for the prediction model.

3.3.1.4. Average amount of use. Regular consumers demonstrated the same patterns as the overall sample such that lower anhedonia (p = 0.004) and greater depressed mood (p = 0.039) in a given week were associated with greater average CU across the same week. but low consumers did not show any significant associations in either the conditional or ZI models. As seen in the detection model, regular cannabis consumers demonstrated a similar pattern for the prediction model: lower anhedonia ($p < 0.001$) and greater depressed mood (p = 0.007) were associated with greater average CU in the next week. There were no significant associations within the low cannabis consumers for the conditional and ZI models.

3.3.2. Daily cannabis use

The daily detection models revealed that, in the regular CU sample, anhedonia *was* significantly associated with same-day CU (p = 0.005), as was day (p = 0.003): lower anhedonia and days later in the week were associated with greater CU. In contrast, low cannabis consumers did not demonstrate significant associations with anhedonia or depressed mood in the conditional or ZI models. The daily prediction models for the regular consumers revealed that only anhedonia was predictive of average CU for the next day, such that lower anhedonia was associated with greater CU in the next day (p = 0.017). No significant associations emerged in the prediction model for low consumers. In addition, similar patterns to the detection model for the low CU sample were found for the ZI model: neither anhedonia nor depressed mood were significantly associated.

4. Discussion

In the current study, we sought to investigate how anhedonia and depressed mood were associated with daily and weekly cannabis use (CU) in a sample with MDD. Although most participants in the study did not meet criteria for current cannabis use disorder (CUD) or endorse problematic CU, the current findings provide important implications for persons with MDD and CU, despite the varying levels of CU from person

to person. Our constellation of findings suggest that anhedonia and depressed mood are independently associated with CU, and these associations vary at the weekly and daily level. While these findings largely support our hypotheses, we found that the associations between anhedonia and depressed mood with CU vary in their strength and directionality. Indeed, these rather complex associations, derived from investigations undertaken cross-sectionally and longitudinally, mirror inconsistent findings across the literature. Despite being underpowered for our sensitivity analyses, we also investigated these associations among different subgroups of cannabis consumers (i.e., regular and low CU) to provide additional insight into these findings. Importantly, these sensitivity analyses revealed different patterns between regular (i.e., CU for >40 % of the 90 days) and low (i.e., CU for <20 % of the 90 days) consumers for anhedonia and depressed mood with CU.

Our exploratory analyses with all nine symptoms in each model, as well as the overall severity of MDD in separate models, revealed unique patterns about how individual MDD symptoms and overall severity may impact CU. We briefly describe these findings here but emphasize our main aims of the study (i.e., anhedonia and depressed mood with CU), separately below. First, each symptom was associated with CU in at least one of the models. The most frequent symptoms, beyond anhedonia and depressed mood, that were associated with CU included fatigue, psychomotor difficulties, and suicidal ideation, which were associated with CU 4-5 times each. The least frequent symptoms, appetite difficulties and negative self-views, were only significantly associated with CU once. This suggests that greater severity of these three symptoms may be associated with greater daily or weekly CU, as evidenced by the conditional models. The zero-inflation models (ZI) revealed a slightly converging interpretation, however: lower severity of fatigue and psychomotor difficulties, and greater severity of suicidal ideation, were associated with using at least some amount of cannabis.

We also conducted exploratory analyses that only included the overall severity of MDD (i.e., not individual symptoms) as the predictor of daily or weekly CU. These findings revealed that overall MDD severity was only associated with CU in one of the models. Specifically, it only revealed a significant association with using cannabis at least once in the next week, with lower MDD severity predicting at least some CU. In sum, these exploratory models, as well as the main models discussed in more detail below, supports prior research and indicates that understanding the unique relationship between MDD and CU is likely better investigated using individual symptoms of MDD, rather than overall severity. Indeed, this provides evidence that investigating MDD as a heterogeneous construct can reveal further insight into how different persons use substances, such as cannabis.

4.1. Anhedonia and cannabis use

Our findings indicate that the association between anhedonia and CU can differ depending on a) the timeframe and b) the type of CU sample (i.e., overall sample, regular consumers, or low consumers). In the overall sample at the weekly level, lower levels of anhedonia were associated with, and predictive of, using more cannabis. While these findings support a temporal association between anhedonia and CU, the directionality differed from the hypothesized positive association. Specifically, lower anhedonia was related to increased engagement in CU. Acute effects of cannabis may enhance euphoria and contribute subsequently to alleviation of anhedonic symptoms. Indeed, this was supported by sensitivity analyses which revealed that this pattern of results was largely driven by regular consumers ($n = 24$). In contrast, there was no relationship between anhedonia and CU in low consumers ($n = 29$). This suggests that among regular cannabis consumers or those who use cannabis for at least 40 % of the time, anhedonia was lower and was associated with more CU during the same and subsequent week compared to individuals with low levels of cannabis consumption. This pattern may suggest a more chronic activation of pleasure over time, such that anhedonia levels remain relatively low given the chronic CU, and that regular consumers derive a continuous stream of pleasure from CU, supporting prior work (Skumlien et al., 2023).

At the daily level, anhedonia was not associated with the amount of CU on the same or next day; however, ZI models revealed higher levels of anhedonia were associated with using at least *some* amount of cannabis the same or next day. Stated differently, experiencing greater anhedonia may result in the decision to use cannabis in the same or next day, but *amount* of use in a given day is not impacted by anhedonia severity. However, sensitivity analyses for the regular consumers support this: anhedonia was lower and was associated with more CU during the same, and subsequent day compared to individuals with low levels of cannabis consumption. Taken together, these results may provide support for individuals using cannabis as a way to (1) cope with anhedonia (or reduced pleasure) and (2) derive pleasure from cannabis consumption, thus ultimately reinforcing daily CU. Moreover, the findings for anhedonia detecting and predicting CU were distinct from those patterns seen with depressed mood. We further detail these distinctions below and the clinical implications.

4.2. Depressed mood and cannabis use

The positive associations between depressed mood and CU were generally supported by our hypotheses. As with anhedonia, our findings elucidated associations between depressed mood and CU at both the weekly and daily levels. In contrast to anhedonia, higher levels of depressed mood were associated with more frequent CU during the same and next week in the overall sample. These weekly trends may signal the influence of chronic depressive symptomatology on CU, pointing to sustained efforts toward CU-mediated mood improvement. Sensitivity analyses support this: the association between depressed mood and CU were only seen for regular, and not low, consumers. As such, it may be that feeling depressed could result in someone using more CU to provide temporary relief; however, withdrawal may initiate a recurrence of depressed mood and result in further CU; thus, depressed mood may be maintained by chronic CU. Compared to the lower levels of anhedonia observed at the weekly level, it may also be the case that cannabis consumers with anhedonia derive greater benefit from smoking, while CU perpetuates depressive symptoms and motivates frequent use. Future work can investigate the opposite relationship: whether CU predicts depressed mood.

Although weekly models provided insights into the effect of depressed mood on CU, findings at the daily level were not entirely consistent with hypotheses, nor with what was observed at the weekly levels. Depressed mood was not associated with same-day or next-day CU, and thus did not provide significant insight into frequency and volume of CU compared to the weekly models. However, ZI models revealed that lower levels of depressed mood were associated with using at least *some* amount of cannabis the same or next day (i.e., non-zero), but did not provide insight into frequency and volume of CU compared to the weekly models. This finding may suggest that any amount of CU is associated with elevated mood during the same day, and next-day CU might indicate continued CU to reinforce and maintain lower depressed mood. Enabling a more protracted perspective, weekly models may be capable of detecting the effect of more persistent depressed mood states on CU, such that worsened depressed mood states motivate habitual CU (or vice versa) in an effort to alleviate MDD symptomatology (Lazareck et al., 2012). Meanwhile, the observed inverse association at the daily level for non-zero use, and non-significant associations for average daily use, reveals that cannabis consumers may have different experiences after CU, including that CU may only be beneficial for momentary relief from depressed mood for certain persons. However, future work should aim to replicate these findings in a larger sample of persons with regular CU to better understand who cannabis is helpful for regarding their MDD symptoms and why.

4.3. Clinical implications

Several clinical implications can be drawn from the complex temporal patterns found in this study. First, clinicians treating individuals with MDD should routinely assess changes in the frequency and amount of CU, which may serve as relevant clinical indicators for worsening MDD symptoms. Indeed, improvements in anhedonia or worsened depressed mood throughout a week may signal greater CU throughout that week and into the following week. Moreover, increased CU could elevate the risk of developing cannabis-related problems such as CUD particularly among regular consumers, which may complicate treatment for MDD. Additionally, this study supports that daily tracking of MDD symptoms and CU would provide rich data for both clinicians and clients to better understand how transient and persistent mood states influence a client's CU. In addition, the directionality of associations at the daily and weekly levels changed for both anhedonia and depressed mood. This could suggest that short-term efforts to manage MDD symptoms with CU are less effective when dealing with persistent negative mood states, and alternative coping strategies for both acute and persistent symptoms can be identified and implemented depending on the patient's presenting problem and course of their symptoms and behaviors during treatment.

Although several interventions exist to target MDD and SUDs (e.g., CUD), many interventions for co-occurring disorders are often sequential in nature and target one disorder at a time. These often include cognitive behavioral therapy (CBT) or a combination of CBT, contingency management, and/or motivational enhancement therapy (Budney et al., 2006; Carroll et al., 2006, 2012; Cuijpers et al., 2013; Mehta et al., 2021). Moreover, although CBT is particularly effective in reducing depressed mood, it may not be as effective in targeting anhedonia (Winer et al., 2019). As such, interventions that target anhedonia, including positive valence systems (PVS) interventions or behavioral activation (BA), may be more effective for persons with co-occurring MDD and SUDs who have a predominantly anhedonic presentation (Akeman et al., 2022; Taylor et al., 2017). In addition, integrative treatments that treat disorders simultaneously are more effective for treating co-occurring disorders than sequential interventions (Wolitzky-Taylor, 2023). Thus, interventions that have been created to target MDD specifically (i.e., CBT, PVS-based interventions, and BA) should be adapted to include psychoeducation and skills related to SUDs, which should be intertwined within each session, rather than simply adding these skills at the end of a treatment for MDD.

4.4. Strengths and limitations

This work is comprehensive in its employment of a multi-model approach to operationalize CU at two different levels of temporal resolution. It is also robust in its statistical treatment of the data, including the use of ZI models to account for high rates of no (zero) CU across measurement occasions and the application of sensitivity analyses to account for discrepancies between regular and low cannabis consumers. However, there are a few weaknesses that are important to discuss. First, this work aimed to model the associations of CU with core symptoms of MDD. Accordingly, the cohort is entirely clinical in nature (i.e., all participants had MDD), thus the generalizability of the findings are limited. Moreover, we did not assess for other symptoms that are often comorbid with MDD and CU (e.g., anxiety). This generalizability is further impacted by the fact that the cohort consisted of a cisgendered female and White racial majority. Second, this work utilized densely-collected longitudinal data for MDD symptoms; however, CU was assessed only once per week via the TLFB, and as such relied on participant recall that could have introduced bias and inaccuracies. Third, the necessity to implement more complex, ZI mixed-effects models, given the data, resulted in some issues with convergence, requiring the uid (participant) fixed effect to be excluded from two models. In addition, depressed mood and anhedonia are strongly correlated with each other, so including them both in the same model could contribute to multicollinearity and potentially impact the current results and their implications. However, additional analyses to investigate this further with each symptom as an individual predictor in each model further in issues with convergence. Relatedly, although the sensitivity analyses provide important insight into how MDD may impact CU in persons with different levels CU, the small sample sizes of these subgroups result in these analyses being underpowered, and the findings and implications should be interpreted with caution.

Fourth, our single-item measurement of anhedonia assesses "little interest or pleasure," which does not distinguish between drug- and non-drug related anhedonia. Prior research has suggested that a broad conceptualization of anhedonia may impact responses in a SUD sample (Stull et al., 2021). Future research should further investigate the associations between anhedonia and CU with more specific anhedonia measures, including those that assess non-drug rewards (Gard et al., 2006), or adapting such measures to assess drug-related anhedonia. Fifth, a small portion of the sample ($n = 14$) endorsed a history of CUD and may demonstrate unique associations between MDD symptoms and CU compared to their non-CUD counterparts; however, subgroup analyses based on CUD were not possible due to concerns with statistical power. Future studies could address this while also controlling for important clinical characteristics such as CU onset, duration of CUD, and treatment history. Lastly, it is important to note that we did not examine the bidirectional association between anhedonia, depressed mood, and CU, only the unidirectional association of MDD symptoms predicting CU. This decision was made for several reasons. First, our primary research question was focused on how anhedonia and depressed mood predict CU. Specifically, we aimed to investigate the impact of MDD symptoms on CU behaviors, rather than investigate the efficacy of cannabis on relieving MDD symptoms. Thus, the bidirectional association of CU predicting anhedonia and depressed mood is outside the scope of the current study. Second, the number of models included in the current study to investigate the associations between anhedonia, depressed mood, and other MDD symptoms with CU are large in quantity, and any additional models investigating the opposite directionality of these associations may make the scope of the current paper too large. Third, the efficacy of cannabis on MDD is best addressed with rigorous drug administration randomized controlled trials. Because this was a secondary analysis from a larger study that focused on MDD, substance use was collected only through a single self-report measure. As such, data on more nuanced cannabis behaviors (e.g., cannabinoid content, potency, route of administration, number of sessions of use, and dosage) were not collected and would make it difficult to properly interpret any potential models of CU predicting anhedonia and/or depressed mood.

Given the methodological decisions described above, we are unable to determine whether chronic CU is associated with future, lower levels of anhedonia and depressed mood. However, the impact of CU on MDD symptoms is of great importance to the literature, and future research can investigate the directionality of the associations, including with either non-clinical and community samples, clinical samples with MDD, and/or clinical samples with CUD. Moreover, given the complex patterns of CU behaviors in the general population, lab-based studies that are able to control for dosing, routes of administration, and product quality would also be important to more precisely evaluate how CU may impact subsequent mood states.

5. Conclusion

The current study extends prior work investigating the associations between MDD symptoms and CU. Taken together, our findings from a MDD sample with various levels of CU indicate that anhedonia and depressed mood both impact future CU across days and weeks. Moreover, these associations are complex, as evidenced by the variations in strength and directionality that were dependent on both the time frame assessed as well as the level of CU in the sample. Findings provide a more

fine-grained temporal analysis of these associations and implications for future explorations. Importantly, this work may be used to guide efforts that enhance our understanding of the impact of cardinal MDD symptoms on other substance use and co-use behaviors, including alcohol and tobacco.

CRediT authorship contribution statement

Amanda C. Collins: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **Damien Lekkas:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **Cara A. Struble:** Writing – review & editing, Writing – original draft. **Brianna M. Trudeau:** Writing – review & editing, Writing – original draft. **Abi D. Jewett:** Writing – review & editing, Writing – original draft. **Tess Z Griffin:** Writing – review & editing, Visualization, Project administration, Investigation. **Matthew D. Nemesure:** Writing – review & editing, Investigation. **George D. Price:** Writing – review & editing, Investigation. **Michael V. Heinz:** Writing – review & editing, Investigation. **Subigya Nepal:** Writing – review & editing, Software, Investigation. **Arvind Pillai:** Writing – review & editing, Software, Investigation. **Daniel M. Mackin:** Writing – review & editing, Investigation. **Andrew T. Campbell:** Writing – review & editing, Supervision, Software, Investigation. **Alan J. Budney:** Writing – review & editing. **Nicholas C. Jacobson:** Writing – review & editing, Supervision, Resources, Investigation, Funding acquisition.

Declaration of competing interest

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Supplementary materials

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