Motives for Microdosing Hallucinogens Among College Students

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Abstract

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Objective: Microdosing hallucinogens is generally defined as taking a small enough amount of a hallucinogen (e.g., LSD, psilocybin) with the purported intent of enchancing mood and cognition while avoiding hallucinating. Study aims were: 1) qualitatively identify college students' reasons for microdosing and 2) quantitatively explore associations between motives and use and related outcomes a year later. **Method:** Data were collected in a large randomized controlled trial (RCT) of non-medical prescription stimulant (NMPS) use. In aim 1, participants (N=150) who indicated NMPS use and microdosing hallucinogens in the past year were asked their reasons for microdosing and responses were qualitatively coded into motive categories. In aim 2, multiple regression examined associations between baseline (n=139) motives and microdosing frequency, consequences, mood (depression, anxiety), and cognitive enhancement (GPA) a year later. **Results:** In aim 1, frequent microdosing motives included experimentation/curiosity, avoid getting too high, have fun, enhance an event, alter perspective, social experience, enhance creativity, improve depression, mood, and anxiety. In aim 2, multiple regression analysis

revealed that the experimentation motive predicted increased frequency and fewer consequences a year later. Additionally, the motive to avoid getting too high predicted increased frequency, and the safety motive predicted decreased consequences a year later. The motive to enhance creativity predicted being above the diagnostic cut-off for anxiety and depression a year later. There were no associations between microdosing motives and GPA. **Conclusions:** Motives for microdosing hallucinogens predict microdosing use, consequences, and mood a year later. Future research should explore the associations with perceiving microdosing hallucinogens as an alternative low risk means of improving depression and anxiety.

Introduction

Two trends have been documented among college students in recent decades. One, the use of illicit substances, including nonmedical use of prescription stimulants (NMPS) such as Adderall and Ritalin, taken for the perceived benefit of enhancing cognitive performance, despite evidence that NMPS does not improve grade point average (GPA) over time (Arria et al., 2017). Two, that most college students who report experiencing issues like depressed mood do not seek help (Eisenberg et al., 2007). Aligned with these two trends, improved cognition and mental health are purported to result from microdosing hallucinogens, generally defined as the act of taking a small enough amount of a hallucinogen (e.g., LSD, psilocybin, mescaline) to avoid hallucinating. Microdosing hallucinogens has garnered recent media attention for a variety of reasons, including reports of use by high-performing professionals (Polito & Stevenson, 2019), small clinical trials supporting initial findings that "full"-dose hallucinogens improve mood and substance use behaviors (Carhart-Harris & Goodwin, 2017), the FDA granting psilocybin breakthrough therapy status in 2018 (Brauser & Deborah, 2018), and the recent decriminalization of hallucinogens across several US cities and states (Brauser & Deborah, 2018; Epstein, 2019). Given recent findings that 10% of college students at two large US universities are microdosing hallucinogens (Fossos-Wong et al., 2018), the current study examined: 1) college students' self-generated motives for microdosing hallucinogens, and 2) evaluated the relationship of motives to use and related consequences of microdosing as well as to mood (i.e., depression, anxiety), and a proxy for cognitive enhancement, academic performance as measured by grade point average (GPA).

Motives for Microdosing Hallucinogens

The only existing information on motives for microdosing hallucinogens come from observational surveys and interviews that recruited from online microdosing forums and identified microdosing motives related to improving mental health and cognition. Specifically, these studies identified 26-39% endorsing that microdosing motives include improving mood, mental health, or self-medicating (Anderson, Petranker, Christopher et al., 2019; Andersson & Kjellgren, 2019; Hutten et al., 2019; Lea et al., 2019; Lea, Amada, Jungaberle, Schecke, Scherbaum et al., 2020; Webb et al., 2019). Microdosing motives also included to improve depression (21%) (Lea et al., 2020) and to improve anxiety (4-7%) (Anderson et al., 2019; Lea et al., 2020). Moreover, a very wide range of 6 to 62% endorsed a varying combination of enhancing cognition, focus, work, and performance motives for microdosing (Anderson et al., 2019; Hutten et al., 2019; Lea et al., 2020). Participants further endorsed curiosity (13-15%) (Hutten et al., 2019; Lea et al., 2020) and creativity (13%) (Anderson et al., 2019; Andersson & Kjellgren, 2019; Lea et al., 2019; Webb et al., 2019) motives. Other microdosing motives included enhanced empathy/spirituality, physical health, self-efficacy, energy, and sociability (Anderson et al., 2019; Hutten et al., 2019; Lea et al., 2020; Webb et al., 2019). Given the the wide range of motives endorsed in these studies of online microdosing forums, often utilizing samples drawn from communities biased towards and advocating for microdosing, information is needed to understand the reasons people have for microdosing utilizing more representative samples.

Frequency of Microdosing Hallucinogens

The prevalence and frequency of microdosing is unknown, however, observational studies of microdosing forums identified common microdosing schedules. Across surveys of microdosing forums, specific microdosing schedules included microdosing one-day-on followed

by: 27-36% reporting two-days-off, 15-20% reporting three-days-off, and 11% reporting one-day-off (Lea et al., 2020; Rosenbaum et al., 2020). Further microdosing schedules included 14% daily, 18% weekly (Lea et al., 2020), two to three times/week (Johnstad, 2018), or every three to four days (Webb et al., 2019).

Among college students, while one study from a randomized and representative sample of college students reported the lifetime prevalence of microdosing at 10% (Fossos-Wong et al., 2018), data from Monitoring the Future indicates 9.1% of college students nationwide have engaged in hallucinogen use (without differentiating microdosing) in their lifetime, with 6.5% reporting LSD and 6.9% reporting other hallucinogen use (Schulenberg et al., 2020). A recent longitudinal prospective study of college students at a large public university reported 43% have had the opportunity to use hallucinogens, of which approximately half (18%) used hallucinogens (Allen et al., 2017), however, microdosing was not specified from "full" dose hallucinogen use. There may be regional differences in hallucinogen use, with data suggesting higher prevalence on the west coast and in larger cities (Johnston et al., 2021). While existing research shows that college students are engaging in hallucinogen use, if not also specifically microdosing hallucinogens, information is needed to understand what factors, including microdosing motives, may drive microdosing frequency.

Consequences of Microdosing Hallucinogens

With any substance use behavior, it is critical to understand what the resulting consequences are, if any, to inform decision making. Across RCTs of explicit microdoses of LSD and RCTs with doses of psilocybin <1 mg, which according to a review by Kuypers et. al. (2019) is a dose low enough to be considered a microdose (Kuypers et al., 2019), as well as across observational studies of online microdosing forums, there were reports of feeling "high"

or senstations that might be consistent with a hallucinogen-induced high, which is definitionally avoided when microdosing hallucinogens (Bershad et al., 2019a; Griffiths et al., 2016; Griffiths et al., 2017; Hasler et al., 2004; Lea, Amada, Jungaberle, Schecke, & Klein, 2020; Moreno et al., 2006; Yanakieva et al., 2019). This is notable given that 39% of people who had a "bad" trip rated it among the top five most challenging experiences of their lifetime (Carbonaro et al., 2016). Other consequences from microdosing hallucinogens include acute psychological effects, with 1–3% reporting these lasted for days (Hutten et al., 2019) as well as adverse physical experiences (Anderson et al., 2019; Cameron et al., 2020; Lea et al., 2019; Lea et al., 2020) such as physical discomfort after 3mg/70kg of psilocybin (Griffiths et al., 2016) mild to moderate headaches after 5-10μg of LSD (Family et al., 2019), and insomnia (Johnstad, 2018). Acknowledging these unwanted consequences from microdosing hallucinogens challenges the perception of microdosing as a low-risk means of mood and cognitive enhancement.

Mood and Mental Health Associations with Microdosing Hallucinogens

The existing evidence on associations between microdosing and mental health is inconsistently documented in controlled studies of healthy adult populations. While one RCT of microdoses of LSD found no relationship (Yanakieva et al., 2019), others found reports of increased vigor and decreased positive ratings of positive images (Bershad et al., 2019) and self-reported bliss (Bershad et al., 2020). In two RCTs investigating doses of psilocybin low enough to be considered a microdose, anxiety increased (Griffiths et al., 2011; Griffiths et al., 2016). Similarly, animal model studies showed mixed findings: microdoses of LSD reversed some depressive-like avoidance (Buchborn et al., 2014), whereas microdoses of psilocybin and DMT showed mixed anxiety findings (Cameron et al., 2019; Horsley et al., 2018).

Observational studies recruiting from online microdosing forums found mixed associations between microdosing and mood. While some of these studies found between 44-93% of respondants perceived microdosing improved their mood or mental health (Anderson et al., 2019; Cameron et al., 2020; Hutten et al., 2019; Lea et al., 2020), decreased stress (Polito & Stevenson, 2019), and decreased dysfunctional attitudes (Anderson, Petranker, Rosenbaum et al., 2019), still 7% indicated microdosing impaired mood (Anderson et al., 2019) and increased neuroticism (Polito & Stevenson, 2019). Moreover, observational studies recruiting from online microdosing forums found reports that microdosing decreased depression (Cameron et al., 2020; Johnstad, 2018; Polito & Stevenson, 2019), yet both decreased (Anderson et al., 2019; Cameron et al., 2020) and increased anxiety (Anderson et al., 2019). Taken together, these observational studies suggest an inconsistent relationship between microdosing and mental health.

Cognitive Associations with Microdosing Hallucinogens

The handful of controlled microdosing studies show mixed cognitive effects of microdosing hallucinogens. No RCTs of explicit microdoses of LSD found any significant change in cognition or focus (Bershad et al., 2019; Bershad et al., 2019b; Yanakieva et al., 2019). An open-label pre- post- assessment of a microdose of psilocybin among members of the Dutch Psychedelic Society, reported improved convergent and divergent thinking, but no change in fluid intelligence (Prochazkova et al., 2018). Of the RCTs that evaluated doses of psilocybin <1 mg, low enough to be considered a microdose, while one identified self-reported increases in perception and cognition (Griffiths et al., 2011), others identified no change in cognition (Family et al., 2019), a 50% decrease in attention (Hasler et al., 2004), and decreased vigilance (Family et al., 2019; Hasler et al., 2004).

Similarly, the cluster of observational microdosing studies recruiting from online microdosing forums found mixed cognitive findings. The evidence supporting cognitive enhancement consists of 6% reporting improved cognition (Anderson et al., 2019), attention (59%) (Cameron et al., 2020), performance (37%), memory (57%) (Cameron et al., 2020), creativity (Anderson et al., 2019; Lea et al., 2019; Webb et al., 2019), and work (Fadiman & Korb, 2019; Hutten et al., 2019; Lea et al., 2019; Webb et al., 2019). Conversely, the evidence supporting no effect, or a negative effect on cognition, consists of reports of cognitive interference (25%) (Anderson et al., 2019), impaired focus (9%) (Anderson et al., 2019), no effect on memory (47%) (Cameron et al., 2020), no changes in focus or productivity (Polito & Stevenson, 2019), no change in creativity (Polito & Stevenson, 2019), and that those microdosing LSD were more likely to report feeling overstimulated with difficulty concentrating at the end of the day (Lea et al., 2020). Differing from a media narrative of microdosing as a means of cognitive enhancement, the existing evidence both supports and refutes this claim.

Current Study

In sum, the small number of studies comprising the microdosing hallucinogens evidence base, the majority of which are observational studies recruiting from online microdosing forums, describe mood and cognitive enhacement motives for microdosing, and an emerging behavior of microdosing hallucinogens with associated psychological and physical consequences as well as both improved and dimished mood and cognition. To address the need for studies utilizing larger, randomized, and representative samples, the current study leveraged data from a large ongoing longitudinal RCT on NMPS use among college students. The current study was designed to address two primary aims. Our first aim was to qualitatively document and categorize open-ended self-reported motivations for microdosing among college students who

met past-year NMPS criteria for the larger RCT utilizing a methodological approach consistent with past research on motives for other risk behaviors (Lee et al., 2006; Neighbors et al., 2008). Though the microdosing motives coding procedure was largely exploratory, we expected several themes to arise from the coding of responses, including academic motives, motives related to attaining therapeutic benefits for depression and/or anxiety, and experimentation motives. In aim 2 of the current study, we then evaluated the longitudinal relationship of the baseline motives (coded in aim 1) to microdosing frequency, consequences, mental health (i.e., depression, anxiety), and cognition (i.e., GPA) at 12-month follow-up. For aim 2, given the exploratory nature of the research, while we did not hypothesize the direction of the associations, we hypothesized there would be significant associations between identification of the microdosing motives (in the qualitative analysis) and microdosing frequency, consequences, anxiety, depression, and GPA.

Method

All procedures were approved by the coordinating university institutional review board and a Certificate of Confidentiality was obtained from NIDA.

Participants and Procedures

Participants in this longitudinal secondary data analysis were recruited as part of a larger parent RCT on college students engaging in NMPS use (Fossos-Wong et. al. 2021, under development). Inclusion criteria for the parent study were: 1) reporting at least one occasion of NMPS over the previous year, 2) enrolled as an undergraduate student at one of the two participating universities, 3) between the ages of 18-25, and 4) had an anticipated graduation date at least 12 months in the future.

Recruitment and Screening

Participants in the parent RCT were screened from two US universities, in the northwest and mid-Atlantic regions, using the list of enrolled undergraduate students provided by the respective registrars' offices as well as recruiting from existing screening surveys for other studies at each campus. Participants across four cohorts recruited between fall 2018 and fall 2020 who met inclusion criteria for the parent RCT, were randomized, reported ≥ 1-day microdosing in the past year, and explained their reasons for microdosing at baseline, 6-months, and/or 12-months were included in the qualitative analysis for aim 1 (N=150). For aim 2, baseline microdosing motive categories present across n=139 participants predicting 5 outcomes at 12-month follow-up were included in the analysis. See Table 1 for participant demographics.

As part of the larger parent RCT on NMPS use, eligible participants were randomized to control (n=70) or a web-based brief intervention (n=69) targeting NMPS, alcohol, and marijuana use. Participants who completed baseline received a $20 Amazon.com electronic gift card in exchange for their participation. Baseline and 12-month follow-up, with 65% retention, included measures on depression, anxiety, and GPA. Participants who reported microdosing ≥ 1 day in the past year at screening also completed a measure of microdosing consequences at baseline and at 12-month follow-up.

Measures

Demographic Characteristics. Participants were asked to report their age, birth sex, race/ethnicity, and class standing.

Hallucinogen Use and Microdosing. Participants were asked to indicate whether they had ever used LSD, psilocybin (magic mushrooms), or mescaline (peyote) using a "check all that apply" response format developed for another secondary analysis of data from the parent research study (Fossos-Wong et. al. 2021, under developement). Participants were also allowed

to indicate “I have never used any of these substances.” Participants who indicated prior hallucinogen use were then asked “In your lifetime, on how many days have you microdosed a hallucinogen (LSD, psilocybin (magic mushrooms), mescaline (peyote))? Please estimate.” Participants were further provided with a definition of microdosing, or “the act of taking a low dose of a hallucinogenic substance.” Participants who indicated responses greater than “0” were further asked to report on their frequency of microdosing in the past 12 months.

Receiept of NMPS Use Intervention. As part of the larger parent RCT on NMPS use, eligible participants were randomized to a control or an NMPS intervention.

Microdosing Motives. The open-ended survey item “What are your reasons for microdosing? Please explain” was used to elicit self-generated motives for microdosing hallucinogens among individuals who reported ≥ 1-day microdosing hallucinogens in the past year. See the Data Analysis Plan for explanation of the motives coding procedure. For the multiple regression analyses, motives for microdosing hallucinogens were coded as “1=indicated” and “0= not indicated” in the qualitative responses.

Microdosing Consequences. Microdosing consequences were assessed with 15 items developed for another secondary analysis of data from the parent research study (Fossos-Wong et. al. 2021, under development). Participants were asked “As a result of taking a microdose of a hallucinogen (e.g., LSD, psilocybin (magic mushrooms), mescaline (peyote)), how often have you experienced the following in the PAST 12 MONTHS?” Items and scale response options were modelled after the Rutgers Alcohol Problem Index (White & Labouvie, 1989) and the Marijuana Consequence Checklist (Lee et al., 2020). Response options ranged from 0=“Never” to 4=“10 or more times.” Cronbach’s alpha was 0.83. Response options were recoded so that responses greater than “Never” equaled “1” and were summed to create a total score.

Depressions Symptoms. The Patient Health Questionnaire-2 (PHQ-2; (Kroenke et al., 2003) is a screening tool for depression that asks participants to report on their depressed mood and anhedonia over the past 2 weeks. Response options ranged from "0=Not at all" to "3=Nearly every day." Summed scores were created as an overall measure of depressed mood and were recoded so that scores of ≥ 3 indicated symptoms consistent with risk for a depression diagnosis (Löwe et al., 2005). Cronbach's alpha was 0.83.

Anxiety Symptoms. The Generalized Anxiety Disorder (GAD) 7-item Scale (Spitzer et al., 2006) assessed participants' self-reported anxiety symptoms. Participants were asked to rate how often they were bothered by each of 7 symptoms from 0="Not at all" to 3="Nearly every day." Example items included "Feeling nervous, anxious or on edge," "Being so restless that it is hard to sit still," and "Becoming easily annoyed or irritable." Summed scores were created as an overall measure of anxiety and were recoded so that scores ≥ 10 are indicative of likely GAD (Spitzer et al., 2006). Cronbach's alpha was 0.91.

Grade Point Average (GPA). Self-reported GPA integer (possible range: 0.0-4.0) was used to assess academic functioning.

Data Analysis Plan

The analysis occurred in two stages: 1) qualitative microdosing motive development and categorization (Aim 1), followed by 2) a series of multiple regressions to examine the relationship between endorsement of the microdosing motive categories to the microdosing motives question at baseline and each of five outcomes at 12-month follow-up: microdosing frequency, microdosing consequences, depression, anxiety, and GPA (Aim 2).

Qualitative Analysis. In Aim 1, all open-ended responses to the microdosing motives open-ended item were pooled across baseline, 6-month, and 12-month follow-up for a total of

238 responses, and were independently read by two project leads who generated motive categories and definitions. Then, a team of 5 coders independently determined how many, if any, of the motive categories were present or absent in each of the 238 participant responses. Two measures of inter-rater reliability, percent agreement and Light's kappa, were calculated for each motive category across the five sets of coder decisions. Final motive categorizations were determined by majority consensus (i.e., at least 3 of 5 coders agreed each motive category was either present or absent in each participant response).

Quantitative Analysis. In aim 2, baseline microdosing motives endorsed by at least 6 participants were used as predictors in multiple regression analyses, for a total of 10 microdosing motives included in the models (see Table 3). Multiple regression analyses evaluated the relationships between baseline motives and 12-month use, consequences, depression, anxiety, and GPA among participants who reported having microdosed at least one day in the past year at baseline (N = 139). The covariates in each regression model included sex, age (centered at 0), randomization status, and baseline past-year microdosing frequency. Given the outliers in the distribution of baseline past-year microdosing frequency, outliers were recoded to three times the standard deviation plus the mean. Accounting for positively skewed and zero-inflated microdosing frequency and microdosing consequences outcomes, assessing model fit with the Vuong test, BIC, and log likelihood statistics, a negative binomial model was selected for the microdosing frequency model and a zero-inflated Poisson (ZIP) model was selected for the microdosing consequences model. ZIP models are appropriate when the outcome has an excess of zeros including both structural zeros (e.g., someone abstaining from microdosing) and sampling zeros (e.g., someone who microdoses, but did not microdose in the sampled time period) common in count models of substance use (Atkins et al. 2013). The count portion of the

ZIP model, examines the number of consequences among those who microdose, and the zero-inflated portion of the ZIP model (i.e., the logit portion), examines the likelihood of a "certain zero," number of consequences, or not experiencing consequences. Binary logistic regression models were used to evaluate whether baseline microdosing motives predicted symptoms consistent with diagnostic cut-off for depression and anxiety at 12-months. Given the normal distribution of GPA, a linear model was used to evaluate the relationship between baseline microdosing motives predicting 12-month GPA, controlling for baseline GPA.

Results

Aim 1: Qualitative Motive Category Generation and Coding

Motive Classification and Reliability. Two project leads independently read all responses, pooled across baseline, 6-months, and 12-months, to the open-ended microdosing motives question, and independently generated motive categories and definitions. They then met to compare their motive categories and agreed to a set of 31 motive categories and definitions. Then, a team of 5 coders independently determined which of the 31 motive categories were present in each of the participant responses (i.e., indicated or not indicated), if any. For example, a participant reporting microdosing hallucinogens "provides mood and cognitive boost" was coded for both improve mood and cognitive enhancement motives. The team of 5 coders were instructed to revise the motive categories, or to generate new categories needed to capture a motive not otherwise represented, although after reviewing coding decisions, no revisions were made. As detailed in Table 3, the most frequent microdosing motive categories (≥ 10 instances out of 239 possible participant responses pooled over baseline, 6-month, and 12-month follow-up) had substantial to almost perfect inter-rater relaibility as measured by the Light's kappa

ranging from 0.7-1.0, which aligned with the percent agreement, another measure of inter-rater reliability, almost entirely above 90% (Landis & Koch, 1977).

Motive Frequency for Qualitative Categories. Across baseline, 6-months, and 12-month timepoints, the most frequently occurring motive was experimentation/curiosity (29.0%) followed by the motives to: avoid getting too high (14.7%), have fun (13.5%), enhance an event/entertainment (13.5%), and enhance or alter perspective/clarity/consciousness/mind expansion (10.9%). Motives for therapeutic benefit were split across four motive categories: depression (6%), panic/anxiety (4.2%), ADHD (0.4%) and improve mood (5.0%). The explicit academic motive was infrequent (1.7%), as were related motives: increase focus/alertness/concentration (4.2%), enhance productivity (3.4%) and cognition (2.9%) (see Table 3).

Aim 2: Quantitative Multiple Regression Analysis

Only 10 microdosing motives were endorsed in at least six open-ended responses at baseline, and were thus included as predictors in the multiple regression analyses. Overall, this resulted in only four baseline microdosing motives significantly predicting microdosing outcomes a year later.

Microdosing Frequency. Given that a substantial number of participants reported no microdosing within the past year, a negative binomial model with the set of aforementioned covariates and 10 baseline microdosing motives was used to predict microdosing frequency within the past-year at 12-month follow-up. Participants who indicated their motive for microdosing hallucinogens at baseline was experimentation/curiosity for the experience had 3.51 (95% CI: 1.25, 10.35) times the rate of microdosing hallucinogens in the past year at 12-month follow-up compared to people who did not indicate that motive. Additionally, participants who

indicated the motive to avoid getting too high or experiencing a trip, had 4.39 (95% CI: 1.14, 18.40) times the rate of microdosing hallucinogens in the past year at 12-month follow-up compared to people who did not indicate that motive. Lastly, participants who microdosed hallucinogens at baseline had a higher rate of microdosing hallucinogens in the past year at 12-month follow-up, and, participants who were randomized to control at baseline, had a lower the rate of microdosing hallucinogens in the past year at 12-month follow-up compared to those randomized to the NMPS intervention (Table 4).

Microdosing Consequences. More than half of participants reported experiencing no consequences within the past year at 12-month follow-up, thus a ZIP model was used. The count portion of the ZIP model revealed that at baseline, males significantly reported more microdosing consequences a year later compared to females, as did older participants compared to younger participants. Experimentation/curiosity for the experience and safer/lower risk than a full dose were the only baseline microdosing motives that significantly predicted a decrease in the number of microdosing consequences a year later. Specifically, holding all other variables constant, the expected number of consequences for participants who indicated that their motive for microdosing hallucinogens was experimentation/curiosity for the experience, is less than 0.39 (95% CI: 0.19, 0.81) times the expected number of consequences than those who did not indicate this microdosing motive. Similarly, those who indicated that their motive for microdosing was that it was safer/lower risk than a full dose, had a number of consequences less than 0.30 (95% CI: 0.12, 0.75) times the expected number of consequences than those who didn't indicate this motive (Table 5).

The zero-inflated portion of the ZIP model identified that males and those who were older exhibited with a higher odds of having a "certain zero" number of microdosing

hallucinogen consequences a year later. A negative association was found among those with greater microdosing frequency at baseline and those who indicated their motive for microdosing hallucinogens at baseline was experimentation/curiosity for the experience; both were associated with a lower odds of having a "certain zero" number of microdosing hallucinogen consequences a year later (Table 5).

Depression and Anxiety Diagnostic Cut-Off. When controlling for covariates, including baseline depression diagnostic cut-off (PHQ-2 score ≥ 3), a logistic regression of 10 baseline microdosing motives predicting depression at 12-month follow-up identified that participants who indicated their motive for microdosing hallucinogens was to enhance creativity had 21 times the odds of being above the depression diagnostic cut-off (PHQ-2 score ≥ 3) for depression a year later compared to those who did not indicate enhancing creativity as a motive for microdosing (Table 6). No other significant associations were found between microdosing motives and depression a year later.

Male sex and microdosing to enhance creativity were the only significant predictors in the logistic regression model of a set of covariates and 10 microdosing motives predicting diagnostic cut-off for anxiety (GAD-7 score ≥ 10) at 12-month follow-up (see Table 5). Men had 0.08 the odds of being above the GAD-7 diagnostic cut-off for anxiety a year later compared to women. Participants who indicated their motive for microdosing hallucinogens was to enhance creativity at baseline had 13 times the odds of being above the GAD-7 diagnostic cut-off (score ≥ 10) for anxiety a year later. However, when baseline GAD-7 diagnostic cut-off was controlled for, the baseline microdosing motive to enhance creativity was no longer a significant predictor of follow-up anxiety (Table 6).

GPA. The results of the linear regression indicated that when controlling for covariates, including the baseline GPA, and the set of 10 baseline microdosing motive predictors explained 17% of the variance (R^2 =.17, F(14,68)=1.02, p=0.45) in GPA at 12-month follow-up. Age was the only significant predictor, such that an increase in age at baseline significantly predicted a lower GPA one year later (β= -0.12, p<.05), however there was no statistical association between microdosing motives and GPA (Table 7).

Discussion

This study aimed to 1) qualitatively develop microdosing hallucinogen motives from an open-ended item on reasons for microdosing hallucinogens, and 2) to quantitatively use microdosing motives as predictors in a multiple regression analysis of five outcomes: microdosing frequency and consequences, depression, anxiety, and GPA. In total, the hypothesized motives of experimentation, academic, and therapeutic benefit emerged in participant responses to the microdosing motives open-ended question on reasons for microdosing. Substantial to almost perfect inter-rater reliability among a team of five independent coders was indicated by Light's kappa ranging from 0.70-0.98 and percent agreement above 80% for the 12 most frequently occurring (≥ 10 instances) microdosing motives categories.

Participants who indicated their motive for microdosing hallucinogens at baseline was experimentation/curiosity for the experience (the most frequently endorsed motive at 29%) significantly predicted increased microdosing frequency, yet decreased microdosing consequences at 12-month follow-up. Motives that we may conceptually group as specific to microdosing as opposed to "full" dose hallucinogen use, such as to avoid getting too high or experiencing a trip predicted increased frequency a year later, yet the motive safer/lower risk

than a full dose predicted decreased consequences at 12-month follow-up. Thus, although we anticipated that motives predicting increased microdosing frequency would also predict increased micrososing consequences, this was not uniformly the case. When microdosing hallucinogens, a definitional goal is generally to take a dose low enough to avoid a high and ostensibly other risky effects, so it's feasible that students microdosing at a higher frequency are more adept at finding a low enough dose to minimize unwanted consequences. This conceptually aligns with a qualitative study of members of online microdosing forums who perceived microdosing to be a safe means of taking care of their health and wellness, despite research that doesn't consistenly support this perception (Webb et al., 2019).

Despite uncertainty in the research, current ballot initiatives decriminalizing hallucinogens and ongoing "full"-dose hallucinogen clinical trials insinuate there may be a relationship between microdosing hallucinogens and lessening mental health symptoms (Carhart-Harris & Goodwin, 2017). However, in our study, there was a low prevalence of motives of therapeutic benefit spread across three categories: improve/treat depression (6%), anxiety/panic (4%), ADHD (0.4%) as well as potentially the motive category improve mood (5%). Only improving/treating depression was endorsed by at least 6 participants at baseline, enabling its inclusion in the multiple regression analyses. Surprisingly, logistic regression models found no association between the motive to improve/treat depression and either mental health outcome, depression or anxiety, at 12-month follow-up.

Moreover, an unanticipated finding was that the microdosing motive to enhance creativity significantly predicted a greater odds of being above diagnostic cut-off for depression (PHQ-2) and anxiety (GAD-7) at 12-month follow-up. While this effect held when baseline depression was included as a covariate for depression at 12-month follow-up, this effect did not

hold when baseline anxiety was included as a covariate for anxiety at 12-month follow-up. This inconsistency across the anxiety models reduces our confidence in the effect, as do the very wide confidence intervals for the significant findings that the enhancing creativity motive increases both depression and anxiety a year later. Future research is needed to better understand the relationship between microdosing to enhance creativity and mood states over time.

While not specific to enhancing creativity as a motive, clinical research on the association between creativity and mental health disorders is inconsistent (Baas et al., 2016). Bass, Nijstad, Boot & Dreu (2016) argued that creativity is influenced by differing approach vs. avoidance motivation systems, and therefore creativity should be reduced in avoidance-based conditions such as depression or anxiety and enhanced in approach-based conditions such as bipolar disorder. Perhaps the enhacing creativity microdosing motive significantly predicted increased depression and anxiety because participants experiencing these avoidance-based conditions are operating in a creativity deficit, and are therefore looking for a means of creativity enhancement via microdosing hallucinogens. Relatedly, despite a strong colloquial association between cannabis and creativity, in the cannabis literature, the limited set of studies on the association between cannabis and creativity find no association to impaired creativity resulting from cannabis use (Kowal et al., 2015) or that enhanced creativity resulting from cannabis use is an artifact of personality (LaFrance & Cuttler, 2017; Schafer et al., 2012). Moreover, in studies on cannabis motives, enhancing creativity does not surface as a frequent motive for cannabis use (Lee et al., 2006).

Given the lay media and observational research interest in microdosing hallucinogens as a means of cognitive enhancement, the absence of an association with cognitive enhancement, conceptualized as academic performance in this study, is a surprising finding. To improve

academic performance was a less frequent motive for microdosing hallucinogens at 2%, although several other motive categories may conceptually group with this motive, including increase focus/alertness/concentration (4%), enhance productivity (3%) and cognition (3%). Nevertheless, the academic microdosing motives were so infrequent that there were not even six participants at baseline, our very liberal cut-off for inclusion in the regression model, who endorsed these cognitive enhancement motives. Ultimately, there was no association between any of the motives for microdosing hallucinogens and GPA. The lack of any significant association between academic motives and microdosing is potentially an artifact of the open-ended nature of the questions assessing motives in this study, and perhaps it is possible that if presented with a list of multiple motives, we might see this motive endorsed more often.

Study Limitations

Limitations of this research relate to the novelty of the measures and generalizability of the sample. Specifically, none of the microdosing hallucinogen measures were validated in previous research, which is a direct result of how new the research on microdosing hallucinogens is. However, the open-ended exploratory framework allowed participants to report motives for microdosing hallucinogens without biasing their responses by not imposing a predefined set of motives on participants. Additionally, self-report measures inherently risk recall bias and potential hesitancy to report illegal drug use, although participants were provided assurances of confidentiality, anonymity, as well as no consequences for their responses, which would mitigate illegality concerns (Lynch et al., 2019). The microdosing study sample was selected from the large parent RCT on NMPS use, and thus identified a sample of those engaging in microdosing hallucinogens that is likely a more high risk group engaging in polysubstance use. Lastly, the low sample size and 65% retention from baseline to 12-month follow-up is a limitation of the

multiple regression analyses. Future research with a larger sample size may afford more power to detect associations between microdosing motives and a variety of outcomes. Future research should recruit samples specific to microdosing hallucinogens only, as opposed to polysubstance use, and should recruit from clinical samples engaging in microdosing hallucinogens.

Conclusions

This exploratory study suggests that college students engaging in both NMPS use and microdosing hallucinogens who say they microdose hallucinogens for experimentation or safety and avoiding a high appear to be microdosing more frequently with less consequences, despite students who say they microdose to enhance creativity experiencing increased depression and anxiety. Taken together, these findings contribute longitudinal information on microdosing hallucinogens utilizing a representative college sample as well as a sample engaged in other substance use (NMPS). Moreover, this study complicates a dominant narrative that motives for microdosing hallucinogens include its status as a low risk substance that improves mood and cognition. On the one hand, the findings supported that motives aligned with microdosing as a low risk substance use behavior (i.e., avoid getting too high, safe) were associated with less consequences a year later. On the other hand, motives around improving mood and congition were not the most frequent motives, save the motive to enhance creativity, which predicted being above diagnostic cut-off for anxiety and depression diagnoses a year later. Further research is warranted given the increasing legislative efforts decriminalizing hallucinogens in Oregon, Washington DC, and likely in other areas with a growing public perception of microdosing hallucinogens as a low-risk cognition and mood enhancer.

References

Allen, H. K., Caldeira, K. M., Bugbee, B. A., Vincent, K. B., O'Grady, K. E., & Arria, A. M. (2017). Drug involvement during and after college: Estimates of opportunity and use given opportunity. *Drug and Alcohol Dependence, 174*, 150-157. 10.1016/j.drugalcdep.2017.01.025

Anderson, T., Petranker, R., Christopher, A., Rosenbaum, D., Weissman, C., Dinh-Williams, L., Hui, K., & Hapke, E. (2019). Psychedelic microdosing benefits and challenges: an empirical codebook. *Harm Reduction Journal, 16*(1), 43. 10.1186/s12954-019-0308-4

Anderson, T., Petranker, R., Rosenbaum, D., Weissman, C. R., Dinh-Williams, L., Hui, K., Hapke, E., & Farb, N. A. S. (2019). Microdosing psychedelics: personality, mental health, and creativity differences in microdosers. *Psychopharmacology (Berlin, Germany), 236*(2), 731-740. 10.1007/s00213-018-5106-2

Andersson, M., & Kjellgren, A. (2019). Twenty percent better with 20 micrograms? *Harm Reduction Journal, 16*(1) http://urn.kb.se/resolve?urn=urn:nbn:se:kau:diva-75976

Arria, A. M., Caldeira, K. M., Vincent, K. B., O'Grady, K. E., Cimini, M. D., Geisner, I. M., Fossos-Wong, N., Kilmer, J. R., & Larimer, M. E. (2017). Do college students improve their grades by using prescription stimulants nonmedically? *Addictive Behaviors, 65*, 245-249. 10.1016/j.addbeh.2016.07.016

Baas, M., Nijstad, B. A., Boot, N. C., & De Dreu, Carsten K. W. (2016). Mad Genius Revisited: Vulnerability to Psychopathology, Biobehavioral Approach-Avoidance, and Creativity. *Psychological Bulletin, 142*(6), 668-692. 10.1037/bul0000049

Bershad, A. K., Schepers, S. T., Bremmer, M. P., Lee, R., & de Wit, H. (2019a). Acute Subjective and Behavioral Effects of Microdoses of Lysergic Acid Diethylamide in Healthy Human Volunteers. *Biological Psychiatry (1969), 86*(10), 792-800. 10.1016/j.biopsych.2019.05.019

Bershad, A., Van Hedger, K., Keedy, S., Bremmer, M., & de Wit, H. (2020). Individuals With High Trait Negative Emotionality are More Sensitive to the Subjective Effects of a Microdose of LSD [Abstract]. *Neuropsychopharmacology, 44*(08) 136-137.

Bershad, A. K., Preller, K. H., Lee, R., Keedy, S., Wren-Jarvis, J., Bremmer, M. P., & de Wit, H. (2019b). Preliminary Report on the Effects of a Low Dose of LSD on Resting-State Amygdala Functional Connectivity. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 5*(4), 461-467. 10.1016/j.bpsc.2019.12.007

Brauser, & Deborah. (2018). *FDA Permits Psilocybin to Be Tested for Refractory Depression.* https://www.medscape.com/viewarticle/904159

Buchborn, T., Schröder, H., Höllt, V., & Grecksch, G. (2014). Repeated lysergic acid diethylamide in an animal model of depression: Normalisation of learning behaviour and hippocampal serotonin 5-HT2 signalling. *Journal of Psychopharmacology, 28*(6), 545-552. 10.1177/0269881114531666

Cameron, L. P., Benson, C. J., DeFelice, B. C., Fiehn, O., & Olson, D. E. (2019). Chronic, Intermittent Microdoses of the Psychedelic N, N-Dimethyltryptamine (DMT) Produce Positive Effects on Mood and Anxiety in Rodents. *ACS Chemical Neuroscience, 10*(7), 3261-3270. 10.1021/acschemneuro.8b00692

Cameron, L. P., Nazarian, A., & Olson, D. E. (2020). Psychedelic Microdosing: Prevalence and Subjective Effects. *Journal of Psychoactive Drugs, 52*(2), 1-10. 10.1080/02791072.2020.1718250

Carbonaro, T. M., Bradstreet, M. P., Barrett, F. S., MacLean, K. A., Jesse, R., Johnson, M. W., & Griffiths, R. R. (2016). Survey study of challenging experiences after ingesting psilocybin mushrooms: Acute and enduring positive and negative consequences. *Journal of Psychopharmacology (Oxford), 30*(12), 1268-1278. 10.1177/0269881116662634

Carhart-Harris, R. L., & Goodwin, G. M. (2017). The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future. *Neuropsychopharmacology (New York, N.Y.), 42*(11), 2105-2113. 10.1038/npp.2017.84

Eisenberg, D., Golberstein, E., & Gollust, S. E. (2007). Help-Seeking and Access to Mental Health Care in a University Student Population. *Medical Care, 45*(7), 594-601. 10.1097/MLR.0b013e31803bb4c1

Epstein, K. (2019). *Oakland decriminalizes 'magic mushrooms' and other natural psychedelics.* Washington Post. https://www.washingtonpost.com/nation/2019/06/05/oakland-decriminalizes-magic-mushrooms-other-natural-psychedelics/

Fadiman, J., & Korb, S. (2019). Might Microdosing Psychedelics Be Safe and Beneficial? An Initial Exploration. *Journal of Psychoactive Drugs, 51*(2), 118-122. 10.1080/02791072.2019.1593561

Family, N., Maillet, E. L., Williams, L. T. J., Krediet, E., Carhart-Harris, R. L., Williams, T. M., Nichols, C. D., Goble, D. J., & Raz, S. (2019). Safety, tolerability, pharmacokinetics, and pharmacodynamics of low dose lysergic acid diethylamide (LSD) in healthy older volunteers. *Psychopharmacology (Berlin, Germany), 237*(3), 841-853. 10.1007/s00213-019-05417-7

Fossos-Wong, N., Lee, H., Vincent, K., Abdallah, D. A., Dashtestani, K. S., Cimini, M. D., Sokolowski, K., Subramaniam, G., & Geisner, I. M. (2018). 1.13 Microdosing of Hallucinogens Among College Students: Frequency, Correlates, and Consequences. *Journal of the American Academy of Child & Adolescent Psychiatry, 57*(10), S139. 10.1016/j.jaac.2018.09.029

Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., Cosimano, M. P., & Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *Journal of Psychopharmacology, 30*(12), 1181-1197. 10.1177/0269881116675513

Griffiths, R. R., Johnson, M. W., Richards, W. A., Richards, B. D., Jesse, R., MacLean, K. A., Barrett, F. S., Cosimano, M. P., & Klinedinst, M. A. (2017). Psilocybin-occasioned mystical-type experience in combination with meditation and other spiritual practices

produces enduring positive changes in psychological functioning and in trait measures of prosocial attitudes and behaviors. *Journal of Psychopharmacology (Oxford), 32*(1), 49-69. 10.1177/0269881117731279

Griffiths, R., Johnson, M., Richards, W., Richards, B., McCann, U., & Jesse, R. (2011). Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects. *Psychopharmacology, 218*(4), 649-665. 10.1007/s00213-011-2358-5

Hasler, F., Grimberg, U., Benz, M. A., Huber, T., & Vollenweider, F. X. (2004). Acute psychological and physiological effects of psilocybin in healthy humans: a double-blind, placebo-controlled dose?effect study. *Psychopharmacology (Berlin, Germany), 172*(2), 145-156. 10.1007/s00213-003-1640-6

Horsley, R., Páleníček, T., Kolin, J., & Valeš, K. (2018). Psilocin and ketamine microdosing: effects of subchronic intermittent microdoses in the elevated plus-maze in male Wistar rats. *Behavioural Pharmacology, 29*(6), 530-536. 10.1097/FBP.0000000000000394

Hutten, N. R., Mason, N. L., Dolder, P. C., & Kuypers, K. P. C. (2019). Motives and Side-Effects of Microdosing With Psychedelics Among Users. *The International Journal of Neuropsychopharmacology, 22*(7), 426-434. 10.1093/ijnp/pyz029

Johnstad, P. G. (2018). Powerful substances in tiny amounts. *Nordic Studies on Alcohol and Drugs, 35*(1), 39-51. 10.1177/1455072517753339

Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Patrick, M. E. (2021). *Monitoring the Future national survey results on drug use 1975-2020: Overview, key findings on adolescent drug use.*

Kowal, M. A., Hazekamp, A., Colzato, L. S., Steenbergen, H. v., Wee, N. J. A. van der, Durieux, J., Manai, M., & Hommel, B. (2015). Cannabis and creativity: highly potent cannabis impairs divergent thinking in regular cannabis users. http://hdl.handle.net/1887/100226

Kroenke, K., Spitzer, R. L., & Williams, J. (2003). The Patient Health Questionnaire-2: validity of a two-item depression screener. 10.1097/01.MLR.0000093487.78664.3C

Kuypers, K. P., Ng, L., Erritzoe, D., Knudsen, G. M., Nichols, C. D., Nichols, D. E., Pani, L., Soula, A., & Nutt, D. (2019). Microdosing psychedelics: More questions than answers? An overview and suggestions for future research. *Journal of Psychopharmacology,* , 26988111985720-269881119857204. 10.1177/0269881119857204

LaFrance, E. M., & Cuttler, C. (2017). Inspired by Mary Jane? Mechanisms underlying enhanced creativity in cannabis users. *Consciousness and Cognition, 56*, 68-76. 10.1016/j.concog.2017.10.009

Landis, J. R., & Koch, G. G. (1977). The measurement of observer agreement for categorical data. *Biometrics,*

Lea, T., Amada, N., & Jungaberle, H. (2019). Psychedelic Microdosing: A Subreddit Analysis. *Journal of Psychoactive Drugs, 52*(2), 1-12. 10.1080/02791072.2019.1683260

Lea, T., Amada, N., Jungaberle, H., Schecke, H., & Klein, M. (2020). Microdosing psychedelics: Motivations, subjective effects and harm reduction. *International Journal of Drug Policy,* , 1-9. https://doi.org/10.1016/j.drugpo.2019.11.008

Lea, T., Amada, N., Jungaberle, H., Schecke, H., Scherbaum, N., & Klein, M. (2020). Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders. *Psychopharmacology (Berlin, Germany), 237*(5), 1521-1532. 10.1007/s00213-020-05477-0

Lee, C. M., Kilmer, J. R., Neighbors, C., Cadigan, J. M., Fairlie, A. M., Patrick, M. E., Logan, D. E., Walter, T., & White, H. R. (2020). A Marijuana Consequences Checklist for Young Adults with Implications for Brief Motivational Intervention Research. *Prev Sci,* doi: 10.1007/s11121-020-01171-x

Lee, C. M., Neighbors, C., & Woods, B. A. (2006). Marijuana motives: Young adults' reasons for using marijuana. *Addictive Behaviors, 32*(7), 1384-1394. 10.1016/j.addbeh.2006.09.010

Löwe, B., Kroenke, K., & Gräfe, K. (2005). Detecting and monitoring depression with a two-item questionnaire (PHQ-2). *J Psychosom Res,* 10.1016/j.jpsychores.2004.09.006.

Lynch, E., McGovern, R., Elzerbi, C., Breckons, M., Deluca, P., Drummond, C., Alam, M. F., Boniface, S., Coulton, S., Gilvarry, E., McArdle, P., Patton, R., Russell, I., Strang, J., & Kaner, E. (2019). Adolescent perspectives about their participation in alcohol intervention research in emergency care: A qualitative exploration using ethical principles as an analytical framework. *PloS One, 14*(6)https://doi.org/10.1371/journal.pone.0217855

Moreno, F. A., Wiegand, C. B., Taitano, E. K., & Delgado, P. L. (2006). Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients With Obsessive-Compulsive Disorder. *The Journal of Clinical Psychiatry, 67*(11), 1735-1740. 10.4088/jcp.v67n1110

Neighbors, C., Geisner, I. M., & Lee, C. M. (2008). Perceived Marijuana Norms and Social Expectancies Among Entering College Student Marijuana Users. *Psychology of Addictive Behaviors, 22*(3), 433-438. 10.1037/0893-164X.22.3.433

Polito, V., & Stevenson, R. J. (2019). A systematic study of microdosing psychedelics. *PLoS One, 14*(2), e0211023. 10.1371/journal.pone.0211023

Prochazkova, L., Lippelt, D., Colzato, L., Kuchar, M., Sjoerds, Z., & Hommel, B. (2018). Exploring the effect of microdosing psychedelics on creativity in an open-label natural setting. *Psychopharmacology, 235*(12), 3401-3413. 10.1007/s00213-018-5049-7

Rosenbaum, D., Weissman, C., Anderson, T., Petranker, R., Dinh-Williams, L., Hui, K., & Hapke, E. (2020). Microdosing psychedelics: Demographics, practices, and psychiatric comorbidities. *Journal of Psychopharmacology (Oxford), 34*(6), 026988112090800-622. 10.1177/0269881120908004

Schafer, G., Feilding, A., Morgan, C. J. A., Agathangelou, M., Freeman, T. P., & Valerie Curran, H. (2012). Investigating the interaction between schizotypy, divergent thinking and cannabis use. *Consciousness and Cognition, 21*(1), 292-298. 10.1016/j.concog.2011.11.009

Schulenberg, J. E., Johnston, L. D., O'Malley, P. M., Bachman, J. G., Miech, R. A., & Patrick, M. E. (2020). Monitoring the Future national survey results on drug use, 1975–2017:

Volume II, College students and adults ages 19–60. http://monitoringthefuture.org/pubs.html#monographs

Spitzer, R. L., Kroenke, K., Williams, J., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med,* https://doi.org/10.1001/archinte.166.10.1092

Webb, M., Copes, H., & Hendricks, P. S. (2019). Narrative identity, rationality, and microdosing classic psychedelics. *The International Journal of Drug Policy, 70*, 33-39. 10.1016/j.drugpo.2019.04.013

White, H. R., & Labouvie, E. W. (1989). Towards the assessment of adolescent problem drinking. *Journal of Studies on Alcohol,* https://doi.org/10.15288/jsa.1989.50.30

Yanakieva, S., Polychroni, N., Family, N., Williams, L., Luke, D., & Terhune, D. (2019). The effects of microdose LSD on time perception: a randomised, double-blind, placebo-controlled trial. *Psychopharmacology, 236*(4), 1159-1170. 10.1007/s00213-018-5119-x

Table 1. Baseline Demographic Characteristics

	Baseline (n=139)
	n (%)
Sex	
Male	64 (46%)
Female	75 (54%)
Age	
18-20	104 (75%)
21-25	35 (25%)
Race	
Asian/Asian American	40 (29%)
Black/African American	5 (4%)
White	77 (55%)
More than one	9 (6%)
Other	8 (6%)
Student Class Standing	
Year 1	23 (17%)
Year 2	38 (27%)
Year 3	64 (36%)
Year 4	7 (5%)
Receipt of NMPS PFI	
NMPS PFI	69 (50%)
Control	70 (50%)

Table 2. Outcome Descriptive Statistics

	Baseline (n=139)		**12-Month Follow-Up** (n=90)	
	n (%)	**mean (SD)**	**n (%)**	**mean (SD)**
# Days Past Year Microdosing	139 (100%)	4.04 (5.34)	71 (51%)	1.68 (3.07)
# Past Year Microdosing Consequences	128 (92%)	2.86 (2.79)	72 (52%)	2.48 (3.11)
PHQ-2	139 (100%)	1.71 (1.63)	85 (61%)	1.87 (1.73)
Below diagnostic cut-off (score ≤ 2)	107 (77%)	-	65 (72%)	-
Above diagnostic cut-off (score ≥ 3)	32 (23%)	-	20 (22%)	-
GAD-7	138 (99%)	6.97 (5.26)	84 (60%)	7.2 (6.16)
Below diagnostic cut-off (score ≤ 9)	98 (71%)	-	59 (66%)	-
Above diagnostic cut-off (score ≥ 10)	40 (29%)	-	25 (28%)	-
GPA	139 (100%)	3.3 (0.44)	89 (64%)	3.29 (0.39)

Table 3. Motives for Microdosing Hallucinogens

Microdosing Motive - Definition	**Motive Endorsement Frequency**		**Inter-Rater Reliability**	
	pooled count (%)[a]	baseline count (%)[b]	Light's Kappa	% Agreement
Experimentation/curiosity for the experience - experimentation, curiosity, or wanting to try or to experience microdosing	69 (29.0%)	32 (28.8%)	0.8	80.7%
Avoid getting too high or experiencing a trip - avoiding a full high/trip/hallucination	35 (14.7%)	16 (14.4%)	0.8	90.7%
To have fun - experiencing enjoyment, and/or to have fun; fun as a desired outcome	32 (13.5%)	18 (16.2%)	0.9	94.5%
Enhancing an event/entertainment - heightening or more intensely experiencing an event (e.g., camping, hiking) or entertainment (e.g., concert, rave)	32 (13.5%)	14 (12.6%)	0.8	91.9%
Enhance or alter perspective/clarity/consciousness/mind expansion - heightening, increasing, enhancing, more intensely experiencing, or altering a sense of perspective, clarity, consciousness, or mind expansion	26 (10.9%)	15 (13.5%)	0.8	91.9%
For a social experience - social experiences (e.g., hanging out, with a group) or being in a social setting	23 (9.7%)	8 (7.2%)	0.8	93.7%
Enhance creativity - enhancing or causing creative feelings, thoughts, or way of being	20 (8.4%)	9 (8.1%)	1.0	99.1%
Improve/ treat depression - treatments for or used to help with depression	13 (5.5%)	8 (7.2%)	1.0	99.6%
Improve mood - treatments for or used to help with mood, mental health, or emotions without specifically mentioning depression, panic, or anxiety. Statements assume baseline low mood and using microdosing to improve mood state.	12 (5.0%)	5 (4.5%)	0.7	93.2%
Improve/treat panic, anxiety - treatments for or used to help with panic and/or anxiety	10 (4.2%)	5 (4.5%)	0.9	98.7%
Heighten senses - heightening or more intensely experiencing visuals, sounds (e.g., music), or time	10 (4.2%)	6 (5.4%)	0.9	97.5%
Increase focus/alertness/concentration - increasing or heightening focus, alertness or concentration on a task or idea, focusing attention	10 (4.2%)	5 (4.5%)	0.7	94.9%
Available - microdosing because it was available, offered, or gifted	9 (3.8%)	2 (1.8%)	0.8	95.9%
Safer/lower risk than a full dose - having a lower risk/safer experience	9 (3.8%)	7 (6.3%)	0.4	88.6%
Enhance productivity - heightening, increasing, enhancing, or more intensely experiencing productivity and being able to get more done or getting more higher quality stuff done	8 (3.4%)	5 (4.5%)	0.9	97.5%
Low cost or small amount - saving money, paying less, or low cost of microdosing, and/or specifying it was a small amount of hallucinogen	8 (3.4%)	3 (2.7%)	0.7	94.5%

Because of social pressure - social pressure to microdose from the people in that social setting	7 (2.9%)	4 (3.6%)	0.7	97.0%
Enhance self-knowledge/self-exploration - heightening, increasing, enhancing, or more intensely experiencing self-knowledge, exploring one's self, one's life, or feeling more connected to one's self	7 (2.9%)	3 (2.7%)	0.7	96.6%
Enhance cognition - enhancing, increasing, or causing improved thinking/cognition, ability to process information	7 (2.9%)	3 (2.7%)	0.7	96.2%
Makes things more interesting/stimulating - making things more interesting/stimulating (not as in energy level or concentration)	7 (2.9%)	3 (2.7%)	0.6	94.1%
Enhance energy - increasing, heightening, or enhancing/sustaining physical energy, or being boosted	6 (2.5%)	4 (3.6%)	0.7	96.6%
To get high - intending to get high, trip, or hallucinate	6 (2.5%)	4 (3.6%)	0.5	92.8%
To study, improve academic performance - studying, preparing for class, attending class, and/or academic performance	4 (1.7%)	3 (2.7%)	0.9	99.2%
To feel good - microdosing to feel good; microdosing to attain a desired "good feeling." Assumes a normal baseline mood state.	4 (1.7%)	1 (0.9%)	0.5	94.5%
Improve health - treatments for general/physical health or wellbeing, without specifically mentioning, mental/emotional health or depression, panic, anxiety, or ADHD	3 (1.3%)	1 (0.9%)	0.5	97.1%
Increase motivation - increasing or heightening motivation	2 (0.8%)	0 (0%)	0.9	99.6%
Improve/ treat ADHD - using or considering microdosing as an alternative to prescription stimulants (e.g., Adderall, Ritalin) or other treatments for ADHD. Explicit statements about microdosing being used to help with ADHD symptoms.	1 (0.4%)	1 (0.9%)	NA	99.6%
It's natural - microdosing as natural or from the Earth	1 (0.4%)	1 (0.9%)	0.5	99.2%
Boredom - boredom or lack of alternative things to do	1 (0.4%)	1 (0.9%)	0.8	98.7%
To have a spiritual experience - having a spiritual experience	1 (0.4%)	0 (0%)	0.7	98.3%
Increase mindfulness - increasing or heightening mindfulness; being in the present moment	1 (0.4%)	0 (0%)	0.6	96.6%

Note. Only motives with > 5 responses at baseline were included in the multiple regressions

[a] The number of open-ended responses to the microdosing motives questions pooled over time was 238

[b] The baseline number of responses to the microdosing motives questions was 111

Table 4. Negative Binomial Regression Model for Number of Past Year Days Hallucinogens were Microdosed at 12-month Follow-up

	B (SE)	Rate Ratio Exp (B) (95% CI)
Intercept	-0.63 (0.66)	0.53 (0.14, 1.98)
Male Sex	-0.19 (0.42)	0.82 (0.34, 1.95)
Age	-0.01 (0.19)	0.99 (0.68, 1.46)
Baseline # Days Past Year Microdosing Hallucinogens	0.10 (0.03)***	1.11 (1.05, 1.19)
Receipt of NMPS PFI	-1.00 (0.38)**	0.37 (0.16, 0.81)
Motives for Microdosing:		
Experimentation/curiosity for the experience	1.26 (0.47)**	3.51 (1.25, 10.35)
To have fun	-0.10 (0.51)	0.90 (0.32, 2.59)
Enhancing an event/entertainment	0.63 (0.60)	1.87 (0.50, 7.15)
Avoid getting too high or experiencing a trip	1.48 (0.63)*	4.39 (1.14, 18.40)
Enhance or alter perspective/clarity/consciousness/mind expansion	0.69 (0.73)	1.99 (0.44, 10.53)
Improve/treat depression	1.07 (0.59)	2.91 (0.90, 10.51)
Enhance creativity	0.36 (0.71)	1.44 (0.34, 6.25)
For a social experience	0.47 (0.73)	1.60 (0.35, 7.66)
Safer/lower risk than a full dose	0.19 (0.65)	1.20 (0.31, 4.74)
Heighten senses	0.04 (0.89)	1.05 (0.14, 7.32)

Note. *p<0.05, **p<0.01, ***p<0.001. n=69.
Motives for Microdosing hallucinogens were coded as "1=indicated" and "0= not indicated."
Abbreviations: NMPS PFI = Non-Medical Perscription Stimulant Use Personalized Feedback Intervention

Table 5. Zero-Inflated Poisson Regression Model for Sum of Past Year Consequences from Microdosing Hallucinogens at 12-month Follow-up

	Count Model		Zero-Inflated Model	
	B (SE)	**IRR (95% CI)**	**B (SE)**	**OR (95% CI)**
Intercept	0.80 (0.62)	2.23 (0.66, 7.57)	-0.47 (1.70)	0.63 (0.02, 17.61)
Male Sex	1.02 (0.45)*	2.78 (1.15, 6.71)	2.82 (1.37)*	16.72 (1.14, 244.38)
Age	0.50 (0.26)*	1.65 (1.00, 2.72)	2.00 (0.76)**	7.37 (1.65, 32.81)
Baseline # Days Past Year Microdosing Hallucinogens	-0.01 (0.02)	0.99 (0.94, 1.04)	-0.73 (0.27)**	0.48 (0.28, 0.81)
Receipt of NMPS PFI	-0.36 (0.32)	0.70 (0.37, 1.31)	1.97 (1.10)	7.18 (0.84, 61.82)
Motives for Microdosing:				
Experimentation/ curiosity for the experience	-0.95 (0.37)*	0.39 (0.19, 0.81)	-3.76 (1.60)*	0.02 (0.00, 0.53)
To have fun	0.19 (0.45)	1.21 (0.50, 2.92)	0.04 (1.25)	1.04 (0.09, 12.15)
Enhancing an event/ entertainment	0.15 (0.56)	1.17 (0.39, 3.48)	-1.23 (1.42)	0.29 (0.02, 4.69)
Avoid getting too high or experiencing a trip	0.07 (0.50)	1.08 (0.40, 2.88)	-1.22 (1.91)	0.30 (0.01, 12.41)
Enhance or alter perspective/ clarity/ consciousness/ mind expansion	0.01 (0.63)	1.01 (0.30, 3.43)	-0.21 (2.67)	0.81 (0.00, 152.79)
Improve/treat depression	-0.20 (0.60)	0.82 (0.25, 2.65)	0.07 (2.00)	1.07 (0.02, 53.75)
Enhance creativity	-0.27 (0.53)	0.77 (0.27, 2.16)	-1.32 (1.59)	0.27 (0.01, 6.11)
For a social experience	-0.16 (0.60)	0.85 (0.26, 2.72)	-3.20 (1.65)	0.04 (0.00, 1.04)
Safer/lower risk than a full dose	-1.19 (0.46)**	0.30 (0.12, 0.75)	-3.24 (2.25)	0.04 (0.00, 3.24)
Heighten senses	-0.87 (0.95)	0.42 (0.07, 2.67)	-1.35 (2.87)	0.26 (0.00, 71.33)

Note. *p<0.05, **p<0.01, ***p<0.001. n=70.
Motives for Microdosing hallucinogens were coded as "1=indicated" and "0= not indicated."
Abbreviations: IRR = Incident Rate Ratio, OR = Odds Ratio, NMPS PFI = Non-Medical Perscription Stimulant Use Personalized Feedback Intervention

Table 6. Logistic Regression Models for Diagnostic Cut-Off for Depression PHQ-2 and Anxiety GAD-7 at 12-month Follow-up

	Depression Diagnosis (PHQ-2 Score ≥ 3) at 12-month follow-up		Anxiety Diagnosis (GAD-7 Score ≥ 10) at 12-month follow-up[a]	
	B (SE)	**OR (95% CI)**	**B (SE)**	**OR (95% CI)**
Intercept	-2.14 (1.09)	0.12 (0.01, 0.93)	-0.77 (0.95)	0.46 (0.07, 2.93)
Male Sex	-1.32 (0.92)	0.27 (0.03, 1.41)	-2.51 (0.84)**	0.08 (0.01, 0.36)
Age	0.66 (0.40)	1.93 (0.91, 4.48)	0.17 (0.31)	1.18 (0.64, 2.25)
Baseline # Days Past Year Microdosing Hallucinogens	-0.01 (0.13)	0.99 (0.70, 1.18)	0.01 (0.08)	1.01 (0.80, 1.15)
Receipt of NMPS PFI	-0.69 (0.74)	0.50 (0.11, 2.11)	-0.90 (0.63)	0.41 (0.11, 1.38)
Baseline Depression Diagnosis	0.80 (0.83)	2.22 (0.43, 11.54)	-	-
Motives for Microdosing:				
Experimentation/ curiosity for the experience	-0.62 (0.98)	0.54 (0.07, 3.58)	1.53 (0.84)	4.63 (0.94, 26.59)
To have fun	-0.45 (0.93)	0.64 (0.09, 3.72)	-0.87 (0.85)	0.42 (0.07, 2.15)
Enhancing an event/ entertainment	0.32 (0.94)	1.38 (0.21, 8.93)	1.04 (0.86)	2.82 (0.54, 16.10)
Avoid getting too high or experiencing a trip	-0.90 (1.50)	0.41 (0.01, 5.62)	-0.07 (1.05)	0.93 (0.10, 7.08)
Enhance or alter perspective/ clarity/ consciousness/ mind expansion	1.74 (1.26)	5.72 (0.49, 80.93)	1.65 (1.17)	5.20 (0.54, 60.41)
Improve/treat depression	1.31 (1.60)	3.69 (0.10, 76.46)	-1.54 (1.68)	0.21 (0.00, 3.67)
Enhance creativity	3.05 (1.38)*	21.05 (1.78, 449.67)	2.58 (1.18)*	13.22 (1.46, 166.14)
For a social experience	0.46 (1.42)	1.58 (0.10, 33.80)	0.13 (1.15)	1.14 (0.10, 11.52)
Safer/lower risk than a full dose	-16.46 (2237.98)	0.00 (NA, 2.26e+58)	0.84 (1.12)	2.32 (0.22, 22.11)
Heighten senses	-0.52 (1.71)	0.60 (0.02, 15.36)	-0.06 (1.47)	0.95 (0.05, 16.75)

Note. *p<0.05, **p<0.01, ***p<0.001. Motives for Microdosing hallucinogens were coded as "1=indicated" and "0= not indicated."

The sample size for the PHQ-2 diagnostic cut-off at 12-month follow-up model is n=80.

The sample size for the GAD-7 diagnostic cut-off at 12-month follow-up is n=79.

[a] When baseline GAD-7 diagnosis is controlled, the significance of the motive "enhance creativity" does not hold.

Abbreviations: NMPS PFI = Non-Medical Perscription Stimulant Use Personalized Feedback Intervention

Table 7. Linear Regression Model for GPA at 12-month Follow-up

	B (SE)	B 95% CI	β	t-value	p-value
Intercept	3.61 (0.14)***	3.33, 3.90	-	25.35	0.00
Male Sex	-0.01 (0.09)	-0.20, 0.18	-0.02	-0.14	0.89
Age	-0.12 (0.05)*	-0.21, -0.03	-0.33	-2.64	0.01
Baseline # Days Past Year Microdosing Hallucinogens	-0.01 (0.01)	-0.03, 0.00	-0.18	-1.51	0.14
Receipt of NMPS PFI	-0.03 (0.09)	-0.21, 0.15	-0.05	-0.38	0.70
Motives for Microdosing:					
Experimentation/curiosity for the experience	-0.05 (0.11)	-0.26, 0.17	-0.06	-0.43	0.67
To have fun	0.03 (0.12)	-0.21, 0.26	0.03	0.22	0.82
Enhancing an event/entertainment	0.02 (0.14)	-0.25, 0.29	0.02	0.15	0.88
Avoid getting too high or experiencing a trip	-0.06 (0.15)	-0.36, 0.24	-0.06	-0.38	0.70
Enhance or alter perspective/ clarity/ consciousness/mind expansion	-0.13 (0.18)	-0.48, 0.23	-0.11	-0.70	0.48
Improve/treat depression	-0.01 (0.17)	-0.35, 0.33	-0.01	-0.05	0.96
Enhance creativity	0.03 (0.16)	-0.29, 0.35	0.02	0.18	0.86
For a social experience	-0.30 (0.18)	-0.66, 0.07	-0.21	-1.61	0.11
Safer/lower risk than a full dose	0.19 (0.17)	-0.15, 0.54	0.14	1.11	0.27
Heighten senses	-0.07 (0.22)	-0.52, 0.37	-0.05	-0.34	0.74

Note. *p<0.05, **p<0.01, ***p<0.001, n= 83.
Motives for Microdosing hallucinogens were coded as "1=indicated" and "0= not indicated."
Abbreviations: NMPS PFI = Non-Medical Perscription Stimulant Use Personalized Feedback Intervention