Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

# Age moderates the relationship between psychedelics use and mental health in naturalistic settings

**Giammarco Di Gregorio**
Durham University
**Sophia Basset**
Durham University
**Harjot Manmohan**
Durham University
**Warren C. Nixon**
Durham University
**Amrutha Pogaku**
Durham University
**Jing Zhou**
Durham University
**David J. Sanderson**
Durham University
**Michael L. Lengieza**
Durham University
**Marco Bocchio**
marco.bocchio@durham.ac.uk

Durham University

**Article**

**Keywords:** psychedelics, age, anxiety, depression, mental health

**Posted Date:** March 10th, 2026

**DOI:** https://doi.org/10.21203/rs.3.rs-9022170/v1

**License:** This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

**Additional Declarations:** No competing interests reported.

# Abstract

Depression and anxiety affect one in five adults, with age affecting prevalence. While clinical trials suggest classic psychedelics (e.g., psilocybin, LSD) and non-classic psychedelics (e.g., MDMA, ketamine) may alleviate these symptoms, it remains unclear how these relationships function in naturalistic settings or how they vary across the lifespan. We conducted a cross-sectional survey of 1,088 adults (18–55 + years) to assess how lifetime psychedelic use - categorized as classic, non-classic, or mixed - relates to mental health. Using structural equation modeling, we found that age significantly moderates the relationship between psychedelic use and mental health outcomes. Specifically, classic psychedelic use was linked to lower depression and anxiety among younger adults, but these effects diminished with age - even reversing for anxiety in older participants. These age-related effects persisted independently of drug-use parameters - including dosage, frequency, and recency of use - and were moderated by mystical experiences for depression, but not for anxiety. Our findings suggest that age may be a meaningful moderator of mental health outcomes from psychedelic use. This underscores the potential value of age-stratified research to optimize the efficacy and safety of psychedelic-assisted interventions, including in aging populations.


# Introduction

Depression and anxiety affect approximately one in five adults worldwide and show age-related variation across the lifespan. While prevalence of depression and anxiety appears to decrease with aging (GBD 2019 Mental Disorders Collaborators) substantial burden persists in later life. For instance, meta-analytic estimates indicate global prevalence of approximately 19% for depression and 16% for anxiety among older adults[3]. Thus, understanding how mental health interventions operate across different stages of adulthood has become increasingly important, particularly as the global population ages.

Among the most promising of these are “classic psychedelics”, psychoactive substances capable of altering multiple aspects of consciousness and influencing mood. These substances primarily act as agonists of 5-$HT_{2A}$ receptors and include compounds such as psilocybin, lysergic acid diethylamide (LSD) and N,N-dimethyltryptamine (DMT;[4]. Other compounds such as ketamine, MDMA or ibogaine, often labelled as “non-classic psychedelics”, show some overlap in experiential effects and similarly powerful ability to trigger neuroplasticity[5], but differ in their neuropharmacology.

Classic and non-classic psychedelics have received increasing clinical attention for their potential therapeutic benefits. In controlled, supervised settings, they have shown promise in treating a range of psychiatric conditions[6], including depression[7–9]. While classic psychedelics show potential for reducing anxiety[10], the existing clinical evidence remains constrained by methodological challenges: (1) small sample sizes, and (2) a focus on highly specific populations, such as patients with terminal cancer[11,12]. Among non-classic psychedelics, ketamine has demonstrated rapid and robust antidepressant effects[13] and is now prescribed in several countries. However, its efficacy for anxiety disorders remains

uncertain[14]. Evidence concerning other non-classic psychedelics, such as MDMA, and their associations with anxiety or depression is even more limited.

As public and scientific interest in psychedelic substances continues to grow, questions about the mental health consequences of their naturalistic (i.e., recreational) use have become increasingly important. As we are witnessing an upsurge in naturalistic use of these compounds [15], concerns remain around the potential adverse effects and long-term psychological harm associated with recreational use[16]. Evidence in the literature remains mixed. Numerous retrospective and prospective studies have linked naturalistic psilocybin use with improvements in mood[17–20], though contrasting findings—while less common—have also been reported[21]. Evidence regarding non-classic psychedelics is even more limited. Heavy or frequent recreational ketamine use has been associated with elevated anxiety and depression[22], but the consequences of moderate or occasional use, as well as the naturalistic use of other non-classics such as MDMA, remain poorly characterized.

Given the mixed evidence, there is a pressing need to identify individual-level predictors of mental health outcomes associated with psychedelic use. Age represents a particularly strong yet often overlooked candidate[23]. Younger users appear more susceptible to certain adverse acute effects. For instance, individuals under 25 report higher rates of psychologically challenging experiences and may be at greater risk of persistent perceptual disturbances (e.g. hallucinogen persisting perception disorder - HPPD) than older adults[24,25]. Conversely, younger users appear to benefit from qualitatively different psychedelic experiences, including more frequent and intense mystical experiences and ego dissolution (Kettner et al., 2024; Russ et al., 2019), both of which have been linked to therapeutic benefits in clinical settings[28]. An age-related shift in the psychedelic experience is biologically plausible as it aligns with both individual neuroimaging studies[29] and meta-analyses[30] reporting a reduction of 5-$HT_{2A}$ receptor density in the neocortex of healthy aging adults. Whether these age-related differences in subjective experience translate into differential mental health outcomes, however, remains largely unknown.

To our knowledge, no study has systematically examined how age moderates the mental health correlates of psychedelic use in naturalistic settings, nor how such effects may vary as a function of time since last use. This gap likely reflects: (1) the exclusion of older individuals from clinical trials, often due to medical risk considerations[23], (2) the predominance of younger participants in observational studies of recreational use, and (3) insufficient sample sizes for robust age-stratified analyses. To address these limitations, the present study employed a cross-sectional, naturalistic design to access an age-diverse sample, capture ecologically valid patterns of polydrug use and outcomes beyond conventional follow-up periods. Participants were classified as classic-only, non-classic-only, mixed classic–non-classic users, or non-users, enabling theoretically motivated comparisons while controlling for general drug-use propensity. We addressed two primary questions. First, is naturalistic use of classic and non-classic psychedelics associated with differences in anxiety, depression, wellbeing, and life satisfaction relative to non-users? Second, do the mental health correlates of psychedelic use change across the adult lifespan?

## Methods

# Study design

The present observational study used an online platform (Qualtrics) to deliver a cross-sectional, international survey designed to assess participants' mental health and naturalistic psychedelic use. Inclusion criteria for participants were: (1) at least 18 years old and (2) fluent in English language.

## Participant enrollment and ethical approval

Participants were recruited between November 2024 and August 2025. The study was conducted on a fully anonymous basis, with no personally identifying information collected (including location or IP address). Ethical approval was obtained from the Department of Psychology Ethics Committee at Durham University (study #2570). Recruitment was conducted through multiple channels, including the online research platform Prolific (www.prolific.com), the university's participant pool, online platforms, social media, word-of-mouth, email, and snowball sampling (e.g., referrals from participants to others in their social networks). Multi-channel recruitment was used to ensure a balanced proportion of psychedelic users, enhance demographic and psychological diversity, and capture complex, heterogeneous patterns of polydrug use. A total of 1270 individuals enrolled in the study. Of these, 182 did not complete the full survey, resulting in a final sample of 1088 participants.

## Demographics and psychedelics use

Participants first provided demographic information, including age and gender. Next, participants were then asked whether they had ever used psychedelics at any point in their lives. Those who reported no psychedelic use were directed to complete subsequent mental health questionnaires (see below). Participants who reported lifetime use were asked to indicate which substances they had taken from a list including (LSD, psilocybin, DMT, ayahuasca, mescaline, MDMA, ketamine, or other—with option to include free text). Psychedelic users then provided additional details on their use patterns, including age at first use, frequency of use across life stages ("1–2 times," "3–5 times," "6–10 times," "10 times +"), typical dosage (microdose, mild, moderate, high, or varies), and reasons for use (recreational, therapeutic, spiritual, or other—with option to include free text). They also reported whether use was for mental health purposes (self-medication), occurred with or without a guide, involved concurrent substances use, and whether they ever had a mystical experience during psychedelic use.

## Mystical experience

Participants who reported mystical experiences completed a checklist (yes/no) adapted from the Revised Mystical Experience Questionnaire (MEQ-30[31], covering the following items: (1) sense of unity or openness, (2) transcendence of time and space, (3) ego dissolution, (4) encounter with the divine or a

higher power, (5) profound emotional insight or healing, (6) sacred geometry or visions, (7) feelings of love and compassion, (8) mystical or religious revelations, (9) awe and wonder, and (10) experiences of rebirth or renewal.

## Mental health questionnaires

Anxiety symptoms were assessed with the 7-item Generalized Anxiety Disorder Scale (GAD-7; Spitzer et al., 2006), which evaluates symptom frequency over the past two weeks. It assesses seven core symptoms: nervousness, inability to control worrying, excessive worry, restlessness, difficulty relaxing, irritability, and fear that something awful might happen. Each item is rated on a four-point scale from “not at all” to “nearly every day,” producing a total score ranging from 0 to 21. Higher values reflect greater levels of anxiety.

Depression symptoms were assessed with the 9-item Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001), which evaluates symptom frequency over the past two weeks. Each item is rated on a four-point scale from “not at all” to “nearly every day,” yielding a total score between 0 and 27. Higher values reflect greater levels of depressive symptoms.

General wellbeing was assessed with the World Health Organization 5-item Well-Being Index (WHO-5; World Health Organization, 2020), which measures positive mood, vitality, and general interest over the past two weeks. Items are rated on a six-point scale from “at no time” (0) to “all of the time” (5), generating a raw score between 0 and 25. This score is multiplied by four to produce a percentage score (0–100), with higher values reflecting greater wellbeing.

Life satisfaction was measured with the Satisfaction with Life Scale (SWLS; Diener et al., 1985), which consists of five items assessing global cognitive judgments of life satisfaction. Each item is rated on a seven-point scale from “strongly disagree” (1) to “strongly agree” (7), yielding a total score ranging from 5 to 35. Higher scores indicate greater satisfaction with life.

Internal consistency was high across all scales. Cronbach’s α was .92 for the GAD-7, .89 for the PHQ-9, .90 for the WHO-5, and .91 for the SWLS, indicating excellent reliability for all measures. For all four scales, if only one item was missing, its value was imputed using the participant’s mean score on the remaining items. Participants with two or more missing items were excluded from analyses for that scale.

# Classification of psychedelic drugs

Participants were classified according to the pharmacological profiles of the substances they reported using. Classic psychedelics, defined by primary 5-$HT_{2A}$ receptor agonism, included psilocybin/psilocin (magic mushrooms), lysergic acid diethylamide (LSD), N,N-dimethyltryptamine (DMT), mescaline (peyote, San Pedro), ayahuasca, 4-AcO-DMT, and LSD analogues. Non-classic psychedelics comprised

dissociatives (ketamine, phencyclidine [PCP], methoxetamine [MXE], dextromethorphan/dextrorphan [DXM/DXO], nitrous oxide), entactogens (3,4-methylenedioxymethamphetamine [MDMA], 3,4-methylenedioxyamphetamine [MDA], 6-APB), and oneirogenics (ibogaine, noribogaine). Atypical serotonergic psychedelics reported as free text (DOx series, 2C-x series, NBOMe derivatives, 5-MeO compounds, and LSA-containing seeds) were not considered classic psychedelics because, despite their 5-HT2A agonism, they exhibit broader serotonergic activity and less established safety or therapeutic profiles. Substances reported in free-text responses but excluded from analysis were those lacking a clear psychedelic, neuroplastic, or therapeutic profile, acting primarily as stimulants, or serving only as facilitators in psychedelic mixtures; these included salvia divinorum, mephedrone, cannabis, and harmala alkaloids. For statistical comparisons, participants were grouped into three mutually exclusive categories: (1) Non-Classic Only (exclusive use of non-classic psychedelics), (2) Classic Only (exclusive use of classic psychedelics), and (3) Classic+ (use of classic psychedelics in combination with non-classic and/or atypical serotonergic psychedelics).

## Estimated use patterns

To estimate *cumulative lifetime use*, for each participant, categorical responses within each of six age bands were converted into numeric midpoints (“1–2 times” = 1.5, “3–5 times” = 4, “6–10 times” = 8, “10 times+” = 10) and summed to create a cumulative estimate of lifetime psychedelic use. To estimate *years since last use*, we identified the most recent age band in which a participant reported use, assigned a representative midpoint to each age band (“Under 18” = 16, “18–25” = 21, “26–34” = 30, “35–44” = 40, “45–54” = 50, “55+” = 60), and subtracted that midpoint from each participant’s current age to yield an approximate number of years since last psychedelic use.

# Data analysis

We tested a series of structural equation models (SEMs) using robust standard errors and a Satorra–Bentler correction (“MLM” in *Lavaan* 0.6.19; Rosseel, 2012). In these models, each latent variable of interest (anxiety [GAD-7], depression [PHQ-9], life satisfaction [SWLS], and wellbeing [WHO-5]) was regressed onto orthogonal contrast codes representing psychedelic drug type, age, and their interaction. Using orthogonal contrasts allowed us to test theoretically motivated comparisons while ensuring that each contrast captured unique variance, facilitating clearer interpretation compared with other tests that do not target specific hypotheses. In addition, modelling latent variables in SEM has the advantage of reducing measurement error and individual-level variability, providing more reliable estimates than analyses based on raw observed scores.

For initial full-sample models (including both psychedelic users and non-users), the orthogonal contrasts tested were: (A) the difference between individuals who had ever used classic psychedelics versus those who had never used classic psychedelics (Classic-only = − 1, Classic+ = −1, Non-classic-only = + 1, Non-users = + 1); (B) the difference between individuals who had used only classics versus those who had used both classics and non-classics (Classic-only = − 1, Classic+ = +1, Non-classic-only = 0, Non-users =

0); (C) the difference between users of only non-classics versus non-users (Classic-only = 0, Classic + = 0, Non-classic-only = − 1, Non-users = + 1).

Follow-up analyses were conducted to evaluate whether additional variables characterizing psychedelic-use history (e.g., *cumulative lifetime use, age at first use, typical dosage*, and *recency of use*) altered associations. Because these variables were not available for non-users, models included only users and the contrasts tested in this subsample were: (A) the difference between individuals who had ever used classic psychedelics versus those who had only used non-classic psychedelics (Classic-only = − 1, Classic+ = −1, Non-classic-only = + 2); (B) the difference between individuals who had used only classics versus those who had used both classics and non-classics (Classic-only = + 1, Classic+ = −1).

Significant interactions were probed using simple-slopes analyses at the mean and ± 1 SD of age. When interactions approached significance ($p > 0.05$ and $< 0.10$) in simple-slope analyses, Floodlight (Johnson–Neyman) procedures were applied to determine the specific age ranges at which group differences reached statistical significance. Finally, age-related variation in mystical experience was examined using logistic regression. The likelihood of reporting a mystical experience was regressed onto age, psychedelic-use contrasts, and their interactions. Simple slopes were probed at the mean and ± 1 SD of age to determine whether age moderated group differences in the probability of experiencing mystical effects.

## Results

# Participant demographics and psychedelic use characteristics

Table 1 shows demographic characteristics of the 1008 adults who completed the full survey. Of these, 562 reported no lifetime use of psychedelic substances, 90 reported exclusive use of non-classic psychedelics (“Non-classic-only”), 126 reported exclusive use of classic psychedelics (“Classic-only”), and 310 reported use of classic psychedelics in combination with non-classic and/or atypical serotonergic psychedelics (“Classic+”; see Methods for full criteria on classification).

Psychedelic use characteristics across drug groups are presented in Table 2. Most psychedelic users reported initiating use between the ages of 18 and 25 years. Recreational motives were predominant across all groups (77–93%), followed by therapeutic intentions (6–20%). Reported dosages were broadly comparable across groups. Most participants (83–86%) indicated using psychedelics without the presence of a guide. Lifetime mystical experiences were reported by 60% of Classic-only users and 73% of Classic+ users, whereas substantially fewer Non-classic-only users (35%) reported such experiences.

Table 1
Demographic characteristics of the sample by psychedelic-use group.

| Characteristic | Non-users | Non-classic only | Classic only | Classic+ |
|---|---|---|---|---|
| **Age** | | | | |
| 18–25 | 184 (32.7) | 35 (38.9) | 28 (22.2) | 88 (28.4) |
| 26–34 | 105 (18.7) | 19 (21.1) | 32 (25.4) | 77 (24.8) |
| 35–44 | 95 (16.9) | 21 (23.3) | 28 (22.2) | 62 (20.0) |
| 45–54 | 92 (16.4) | 12 (13.3) | 13 (10.3) | 57 (18.4) |
| 55+ | 86 (15.3) | 3 (3.3) | 25 (19.8) | 26 (8.4) |
| **Gender** | | | | |
| Male | 210 (37.4) | 32 (35.6) | 72 (57.1) | 181 (58.4) |
| Female | 343 (61.0) | 56 (62.2) | 49 (38.9) | 119 (38.4) |
| Non-binary / third gender | 8 (1.4) | 2 (2.2) | 4 (3.2) | 9 (2.9) |
| Prefer not to say | 1 (0.2) | 0 (0.0) | 1 (0.8) | 1 (0.3) |

Cells show number of participants (column %) within each group.

Table 2
Psychedelic-use characteristics.

| Characteristic | Metric | Non-classic only | Classic only | Classic+ |
|---|---|---|---|---|
| **Cumulative lifetime use** | Mean (SD) | 6.7 (4.8) | 7.4 (6.8) | 15.0 (10.1) |
| **Years since last use** | Mean (SD) | 8.9 (10.2) | 15.9 (14.7) | 14.5 (12.9) |
| **Age at first use** | n (%) | | | |
| < 18 | | 16 (17.8) | 23 (18.3) | 108 (34.8) |
| 18–25 | | 54 (60.0) | 67 (53.2) | 155 (50.0) |
| 26+ | | 20 (22.2) | 36 (28.6) | 46 (14.8) |
| **Typical dosage** | n (%) | | | |
| Microdose | | 12 (13.3) | 9 (7.1) | 13 (4.2) |
| Mild dose | | 32 (35.6) | 34 (27.0) | 39 (12.6) |
| Moderate dose | | 37 (41.1) | 56 (44.4) | 141 (45.5) |
| High dose | | 2 (2.2) | 16 (12.7) | 56 (18.1) |
| Varies | | 7 (7.8) | 11 (8.7) | 60 (19.4) |
| **Intent** | n (%) | | | |
| Recreational | | 70 (77.8) | 97 (77.0) | 289 (93.2) |
| Therapeutic | | 18 (20.0) | 28 (22.2) | 18 (5.8) |
| Spiritual | | 0 (0.0) | 1 (0.8) | 1 (0.3) |
| Other | | 2 (2.2) | 0 (0.0) | 1 (0.3) |
| **Guide present** | n (%) | 15 (16.7) | 21 (16.7) | 44 (14.2) |
| **Mystical experience** | | 32 (35.6) | 76 (60.3) | 227 (73.2) |
| **Perceived Long-term effect** | | | | |
| Positive | | 18 (20.0) | 48 (38.1) | 160 (51.6) |
| Negative | | 4 (4.4) | 5 (4.0) | 10 (3.2) |
| No long-term effects | | 67 (74.4) | 73 (57.9) | 139 (44.8) |

Cells show number of participants (column %) within each group.

# Age moderates associations between type of psychedelic use and mental health outcomes

To disentangle theoretically distinct comparisons between psychedelic-use groups while avoiding redundant tests, we fitted structural equation models incorporating orthogonal contrasts (see Methods). These contrasts tested: (1) a main effect of classic psychedelic use (Classic [only/+] vs Non-users/Non-classic); (2) whether use of classic psychedelics alone differs from use in combination with non-classic or atypical serotonergic substances (Classic-only vs Classic+); and (3) a main effect of non-classic psychedelic use (Non-classic-only vs Non-users). All models showed good fits (Table S1) and included gender as a covariate to account for group imbalances (Table 1).

We first examined the association between psychedelic-use group and anxiety (GAD-7). In the first-order model, age showed a negative association with anxiety ($\beta = -0.151$, $p < 0.001$; Table S2). There was also a significant main effect of using Classic psychedelics, with lower anxiety among classic-psychedelic users (Classic-only and Classic+) compared with Non-users and Non-classic-only users ($\beta = 0.093$, $p = 0.014$) (Fig. 1A). The other contrasts were not significant (Classic-only vs Classic+: $\beta = -0.001$, $p = 0.975$; Non-classic-only vs Non-users: $\beta = 0.038$, $p = 0.291$). In the second-order model, a significant age × Classic vs Non-classic/Non-users interaction ($\beta = -0.147$, $p < 0.001$) indicated that the association between classic psychedelic use and anxiety varied with age. To characterize this moderation, we probed simple slopes at three representative age groups: younger adults (− 1 SD, 23 years), mean age (36 years) and older adults (+ 1 SD, 50 years). These analyses showed that classic psychedelic use was associated with lower anxiety in younger adults ($\beta = 0.227$, $p < 0.001$; Fig. 2A), that this association attenuated at the sample mean age ($\beta = 0.083$, $p = 0.023$), and that it was absent in older participants ($\beta = -0.06$, $p = 0.201$). Next, we examined the association between psychedelic use group and depression (PHQ-9). Age showed a negative association with depressive symptoms ($\beta = -0.222$, $p < 0.001$; Table S2). There was no significant main effect of psychedelic-use group, although the contrast comparing classic-psychedelic users (Classic-only and Classic+) with participants who had never used classic psychedelics (Non-classic-only and Non-users) was close to significance ($\beta = 0.073$, $p = 0.052$, Fig. 1B). Depression outcomes nonetheless showed a significant interaction between age and whether participants used or not classic psychedelics (Classic-only/Classic + vs Non-classic-only/Non-users, $\beta = -0.089$, $p = 0.017$). Simple-slopes analyses indicated that Classic-only/Classic+ were associated with lower depression only among younger adults ($\beta = 0.148$, $p = 0.009$; Fig. 2B), with no significant association at the mean age or at older ages.

For wellbeing (WHO-5), we found no significant main effect of psychedelic use category or interactions with age (Table S2, Fig. 1C). In contrast, life satisfaction (SWLS) showed both a main effect and an age-moderated association, but with a different pattern from anxiety and depression. Non-classic-only users reported higher life satisfaction than Non-users ($\beta = -0.084$, $p = 0.019$; Table S2, Fig. 1D), whereas other contrasts between psychedelic-use categories were not significant. Life satisfaction also showed a significant interaction between age and classic-psychedelic use (Classic-only/Classic + vs Non-classic-only/Non-users; $\beta = 0.087$, $p = 0.039$), while the Non-classic-only vs Non-user contrast did not interact with age ($p = 0.328$). Simple-slopes analyses (Fig. 2C) indicated no significant differences between Classic-only/Classic+ users and Non-classic-only/Non-users at younger or average ages, but a trend toward lower life satisfaction for Classic-only/Classic+ users emerged among older participants ($\beta =$

0.114, p = 0.057). To more precisely identify potential ages at which classic-psychedelic use was associated with lower life satisfaction, we conducted a floodlight (Johnson–Neyman) analysis. This analysis revealed that Classic-only/Classic+ users reported significantly lower life satisfaction compared with Non-classic-only/Non-users at 53 years of age (p = 0.047).

Overall, these results indicate that age moderates associations between type of psychedelic use and mental health outcomes: classic psychedelic use was linked to lower anxiety and depression in younger adults, use of non-classic psychedelics was associated with higher life satisfaction overall, and classic-psychedelic use was associated with lower life satisfaction in older adults.

# Age-dependent associations of classic psychedelics with anxiety and depression are not explained by use patterns

We next asked whether the age-dependent associations could reflect obvious confounds in drug-use patterns. For example, older participants may have used psychedelics longer ago (so effects could have faded), accumulated more lifetime exposure, or younger and older users may differ in typical dosages. To account for effects of psychedelic use patterns, we generated a fresh set of structural models with orthogonal contrasts including psychedelic users only (n = 562).

Confirming the full-sample findings, age significantly moderated the association between psychedelic-use type and both anxiety and depression for the Classic-only/Classic + vs Non-classic-only contrast (Table S3). Simple-slopes analyses indicated that younger Classic-only/Classic+ exhibited lower anxiety scores than Non-classic-only (β = 0.158, p = 0.017; Fig. 3A), whereas no differences were observed at the mean age. In older users, the pattern was reversed, with classic users showing higher anxiety scores than non-classic users (β = −0.116, p = 0.038). Depression displayed a qualitatively similar age-related trend for the Classic-only/Classic + vs Non-classic-only contrast, although none of the comparisons reached statistical significance within any of the three age groups (Fig. 3B).

With the substantive full-sample pattern replicated in the user-only analyses, we then tested whether specific aspects of psychedelic use could account for these age-related effects. Controlling for *years since last use* (Table S4) preserved the significant Age × Classic-only/Classic + vs Non-classic-only interaction for both anxiety (β = −0.138, p = 0.002) and depression (β = −0.097, p = 0.024). Adjusting for *dosage* produced the same result (anxiety: β = −0.148, p = 0.001; depression: β = −0.105, p = 0.025). Likewise, accounting for *cumulative lifetime use* left the interaction intact for both anxiety (β = −0.144, p = 0.001) and depression (β = −0.096, p = 0.031). This indicates that the age-related pattern linking classic-psychedelic use to anxiety and depression is not explained by how recently, how often, or at what dosage participants used these substances.

# Mystical experience accounts for age-related effects on depression but not on anxiety

Given that differences in drug-use patterns did not account for age-related associations between classic-psychedelic use with depression and anxiety, we next asked whether results could be explained by factors known to vary with age. Mystical experience was a prime candidate, as prior research shows younger adults are more likely than older adults to report these experiences (Kettner et al., 2024). Using logistic regression, we modelled the likelihood of reporting a prior mystical experience based on age and psychedelic drug type. (Fig. 4, Table S5). Consistent with prior evidence[37], participants who had used classic psychedelics (Classic Only and Classic+ combined) were more likely to report mystical experiences than those who had used only non-classic psychedelics (OR = 1.560, $p < 0.001$, Fig. 4A). As expected, higher doses were associated with higher likelihood of mystical experience (OR = 1.70, $p < 0.001$), aligning with established evidence that high doses are needed to induce these experiences [38]. Interestingly, participants who had used combinations of classic and non-classic or atypical serotonergic psychedelics (Classic+) were more likely to report mystical experiences than those who had used only classic psychedelics (OR = 0.746, $p = 0.009$).

Consistent with prior work (Kettner et al., 2024), both the Age × Classic (only/+) vs Non-classic-only contrast and the Age × Classic + vs Classic-only contrast showed significant interactions with age (OR = 0.984, $p = 0.024$; OR = 1.973, $p = 0.002$, respectively). Dose did not account for these effects (Table S5), indicating that age-related differences in mystical experience could not be explained by dosage.

Simple-slopes analyses for the Classic (only/+) vs Non-classic-only contrast showed that younger adults (23 years) and participants at the mean age (36 years) who had used classic psychedelics (Classic Only or Classic+) were significantly more likely to report mystical experiences than Non-classic-only users (Younger: OR = 0.523, $p < 0.001$; Mean: OR = 0.649, $p < 0.001$; Fig. 4A). By contrast, at older ages (50 years), the effect was nonsignificant (OR = 0.807, $p = 0.122$), indicating a decline in the ability of classic psychedelics to induce mystical experiences with age. For the Classic-only vs Classic+ contrast, we found similar likelihood of mystical experiences in younger participants (OR = 0.861, $p = 0.405$), a non-significant trend toward higher likelihood in Classic+ users at mean age (OR = 1.260, $p = 0.054$), and significantly higher likelihood in older Classic+ users (OR = 1.830, $p < 0.001$; Fig. 4B).

Given the age-related decline in mystical experiences associated with Classic psychedelics, we tested whether controlling for the mystical experience eliminated the age-dependent associations between Classic-psychedelic use and mental health. Controlling for mystical experience rendered the Age × Classic (only/+) vs Non-classic interaction non-significant for depression ($\beta = -0.084$, $p = 0.064$), consistent with prior evidence linking mystical experience to antidepressant outcomes[39]. In contrast, the interaction for anxiety remained significant ($\beta = -0.124$, $p = 0.006$; Fig. S4). Overall, these results suggest that age-related differences in mystical experience mediate the association between classic-psychedelic use and lower depression in younger adults, but do not explain age-dependent effects on anxiety, leaving the latter largely unexplained by any of the control variables tested.

# Discussion

Our study identifies age as a central moderator of mental-health associations with psychedelic use. Classic psychedelics were linked to lower anxiety and depression only among younger adults. Interestingly, the pattern for anxiety reversed in later adulthood, with non-classic psychedelics showing more favorable anxiety outcomes than classic compounds. These age-related effects were not explained by factors such as recency, typical dose, age at first use, or cumulative exposure, and instead appear to reflect chronological age itself. This same age-related pattern emerged regarding life satisfaction, where classic psychedelic use was associated with higher levels in younger participants but lower levels in older users. Furthermore, the likelihood of reporting mystical-type experiences declined with age and explained the age-dependent association between classic psychedelic use and depression but not anxiety, suggesting that the therapeutic importance of the mystical experience may be symptom-specific.

# Divergent mental health correlates of classic psychedelic use across the adult lifespan

The observed association between classic psychedelic use and positive mental health outcomes aligns with prospective and retrospective naturalistic studies reporting improvements in depression and anxiety with psilocybin[17–20]. While previous research has compared wellbeing changes following psilocybin use across two age groups (Kettner et al., 2024), to our knowledge no study had jointly examined depression, anxiety, and life satisfaction, nor formally tested age as a moderator of these outcomes.

We report here, for the first time, that age moderates the association between classic psychedelic use and mental health outcomes: specifically, younger users exhibited lower anxiety and depression scores compared with non-users, a pattern not observed in older participants. These findings align with observations from independent clinical trials, where younger cohorts[41] have historically reported more pronounced reductions in depressive symptoms compared to older populations[11,12]. While a formal systematic comparison of these disparate trials has remained absent from the literature, our study provides the first direct evidence within a single, age-diverse sample to suggest that age-related responses to psychedelic may not be uniform.

Our finding of age moderation may also help account for divergent results across recent naturalistic studies. For example, a recent study reported higher levels of mixed anxiety and depression among psilocybin users in a sample with a mean age of approximately 48 years[21]. This age group is comparable to our older participant group, which showed mental health scores similar to non-users. In contrast, studies reporting beneficial effects of psilocybin[17–20] examined younger samples, with mean ages of 27 and 38 years, respectively, closely aligning with the age groups in which we observed lower anxiety and depression relative to non-users. Taken together, our findings suggest that age is a critical variable in psychedelic outcomes. Although the cross-sectional nature of the present study warrants caution, these results underscore the need for future clinical research to formally examine age as a key factor influencing the efficacy of psychedelic interventions.

Several converging processes may account for the observed age-related pattern. At the molecular level, the intensity of psychedelic experiences - and their associations with mental health - depends on 5-HT2A receptor activation[42,43]. 5-HT2A receptor density declines substantially with age[29,30], which is likely to reduce the brain's capacity to enter profound psychological states that facilitate emotional recalibration. Consistent with this account, the age-related reduction in mystical-type experiences observed in our sample, from approximately 75% in younger participants to around 50% in the older cohort, broadly matches the expected decline in 5-HT2A receptor availability, estimated at 7–17% per decade across the adult lifespan[29,30]. Together, these findings support the idea that age-related molecular changes may contribute to attenuated psychedelic responsiveness. Beyond molecular mechanisms, age is associated with reduced neural plasticity and cognitive flexibility[44,45], as well as a shift toward more segregated and stable brain network architecture from mid-adulthood onwards[46]. These factors may limit the brain's ability to reorganize in response to salient experiences, making the integration of psychedelic states (and their mental health correlates) less pronounced in older adults. Psychologically, older adults possess more mature ego structures[47], which may resist the temporary state of ego dissolution often invoked by classic psychedelics[48], further constraining the potential impact of these experiences. Taken together, pharmacological, neural, and psychological factors likely converge to produce the age-dependent patterns observed in our study, highlighting chronological age as a critical moderator of mental health associations with classic psychedelic use.

# Distinct outcomes associated with classic and non-classic psychedelics

The inclusion of a distinct group of non-classic psychedelic users, a design choice previously unimplemented in naturalistic research, was a key element of our analysis. This structure served two key purposes: first, it provided a stringent comparison group to control for a general 'openness' to altered states; second, it enabled a direct examination of the pharmacological divergence between classic and non-classic substances. This latter objective is particularly salient given the partially overlapping, yet mechanistically distinct, neuroplasticity-enhancing properties of classic and non-classic substances[5]. A notable finding was that non-classic psychedelics showed more favorable anxiety outcomes in older adults. Mechanistically, these age-related differences likely reflect the stability of specific neurotransmitter systems. For instance, the main molecular targets of non-classic psychedelics show a weaker age-related decline in density than 5-HT2A[30,49,50]. This raises the possibility that non-classic compounds may have greater therapeutic utility in older populations, particularly as classic psychedelics may also present increased cardiovascular risks in these cohorts[51].

For anxiety and depression, Classic-only and Classic+ users showed similar trends and appeared distinct from Non-classic-only, suggesting that use of classic psychedelics, regardless of co-use, may be the primary driver of these associations. However, Classic+ users were more likely to report mystical-type experiences in older age than those who had used only classic substances. It is possible that co-use patterns may shape subjective experiences and potentially mental health outcomes. However, we cannot

fully rule out the possibility that some of the associations in the present study reflect differing baseline psychological traits between psychedelic class users. Future studies should determine whether the observed associations are driven by specific compounds, especially within the pharmacologically heterogeneous non-classic category (e.g., MDMA vs ketamine) or by interactions between specific substances.

# Different associations of psychedelic use across mental health domains

In line with recent and ongoing clinical trials showing anxiolytic properties of psilocybin and LSD[10,12], our study demonstrates that these associations persist in naturalistic settings. Furthermore, our findings indicate that mystical experiences may be more crucial for depression than anxiety. Introducing mystical experiences in the statistical model abolished the *age x drug type* interaction for depression, whereas the interaction for anxiety remained. This suggests that the psychological mechanisms through which naturalistic psychedelic experiences influence mental health outcomes may differ between these two conditions.

Psychedelics use did not influence broader wellbeing. This dissociation suggests that positive affect and general wellbeing may be more stable traits and less sensitive to episodic psychedelic use than negative affect. An alternative explanation is methodological: many participants reported high wellbeing, raising the possibility of ceiling effects, and the WHO-5 offers a limited assessment of this multi-dimensional construct. By contrast, non-classic psychedelics were positively associated with life satisfaction. Their common use in relational, social, or therapeutic environments may enhance interpersonal connection and positive autobiographical memory - factors closely tied to life satisfaction. Distinguishing whether these effects reflect drug pharmacology, contextual factors, or user characteristics will require more granular future work.

# Methodological considerations

Several methodological issues warrant caution when interpreting the findings. The cross-sectional design precludes causal inference and is vulnerable to selection and self-selection bias. Systemic differences in psychological traits, including emotional stability, personality, and risk tolerance may exist between individuals open to classic psychedelic use and those who are not. Consequently, the observed associations may partially reflect preexisting psychological resilience or a higher baseline for openness among those inclined toward psychedelic use, rather than the effects of the substances themselves. However, the use of a 'Non-classic-only' comparison group, which includes individuals with similar risk profiles and psychological openness to users of classic psychedelics, partially addresses this potential selection bias. Furthermore, all outcome measures relied on self-reporting, and the study did not account for socioeconomic factors, which may influence both psychedelic use and mental health outcomes.

Nonetheless, our large and age-diverse sample enabled robust modelling of age-by-drug-class interactions. Examining psychedelic use within real-world polydrug patterns increases ecological validity

and captures naturalistic use rather than artificially isolating compounds. Moreover, cross-sectional designs avoid expectancy issues inherent to prospective psychedelic studies.

# Implications and future directions

While the cross-sectional nature of this study precludes definitive causal inferences, our findings suggest that chronological age is a pivotal moderator of the relationship between psychedelic use and mental health in naturalistic settings. These results underscore the necessity for longitudinal research and age-stratified clinical trials to determine if tailoring substance selection to a patient's neurobiological age can optimize treatment efficacy and safety. For example, could the management of depression in older adults via classic psychedelics be complicated by a decline in the likelihood of mystical-type experiences - a key psychological mediator of antidepressant effects? Similarly, do the more favorable anxiety outcomes associated with non-classic psychedelics in older cohorts suggest that these compounds offer a potentially viable pharmacological pathway for older populations? Ultimately, clarifying if and why classic psychedelics show diminishing, and eventually unfavorable, associations with mental health in older ages will be a critical step toward developing personalized strategies for the management of mental health across the lifespan.

# Declarations

Author contributions

Conceptualization: MB, GDG, MLL; Methodology: GDG, MLL, MB; Software: GDG; Formal analysis: GDG; Investigation: GDG, SB, HM, WCN, AP, JZ, MB; Data curation: GDG; Visualization: GDG; Writing – original draft: MB, GDG; Writing – review and editing: MB, GDG, MLL, DJS; Supervision: MB, MLL, DJS; Funding acquisition: MB. All authors have read and agreed to the published version of the manuscript.

Statements and declarations

Ethical considerations

The study was conducted on a fully anonymous basis, with no personally identifying information collected (including location or IP address). Ethical approval was obtained from the Department of Psychology Ethics Committee at Durham University (study #2570).

Consent to participate

Participants provided informed consent before starting the survey. Consent was obtained electronically via the online platform, and participation was voluntary.

Declaration of conflicting interest

The authors declare no conflict of interest

Funding

M.B. was supported by an Academy of Medical Sciences Springboard Award.

Data availability

The data supporting the findings of this study, as well as the analysis codes, will be deposited in an open-access repository and made publicly available upon publication.

# References

1. Terlizzi, E. & Zablotsky, B. *Symptoms of Anxiety and Depression Among Adults: United States, 2019 and 2022*. https://stacks.cdc.gov/view/cdc/164018 (2024). 10.15620/cdc/164018
2. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019 - The Lancet Psychiatry. https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(21)00395-3/fulltext
3. Jalali, A. et al. Global prevalence of depression, anxiety, and stress in the elderly population: a systematic review and meta-analysis. *BMC Geriatr.* **24**, 809 (2024).
4. Nichols, D. E. & Psychedelics *Pharmacol. Rev.* **68**, 264–355 (2016).
5. Olson, D. E. & Psychoplastogens A Promising Class of Plasticity-Promoting Neurotherapeutics. *J. Exp. Neurosci.* **12**, 1179069518800508 (2018).
6. Vargas, M. V., Meyer, R., Avanes, A. A., Rus, M. & Olson, D. E. Psychedelics and Other Psychoplastogens for Treating Mental Illness. *Front Psychiatry* **12**, (2021).
7. Carhart-Harris, R. L. et al. Psilocybin with psychological support for treatment-resistant depression: An open-label feasibility study. *Lancet Psychiatry*. **3**, 619–627 (2016).
8. Müller, F. et al. Efficacy and safety of low- versus high-dose-LSD-assisted therapy in patients with major depression: A randomized trial. *Med* **6**, 100725 (2025).
9. Palhano-Fontes, F. et al. Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial. *Psychol. Med.* **49**, 655–663 (2019).
10. Robison, R. et al. Single Treatment With MM120 (Lysergide) in Generalized Anxiety Disorder: A Randomized Clinical Trial. *JAMA* **334**, 1358–1372 (2025).
11. Griffiths, R. R. et al. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *J. Psychopharmacol.* **30**, 1181–1197 (2016).
12. Ross, S. et al. Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. *J. Psychopharmacol.* **30**, 1165–1180 (2016).

13. Nikolin, S. et al. Ketamine for the treatment of major depression: a systematic review and meta-analysis. *eClinicalMedicine* 62, (2023).
14. Tully, J. L., Dahlén, A. D., Haggarty, C. J., Schiöth, H. B. & Brooks, S. Ketamine treatment for refractory anxiety: A systematic review. *Br. J. Clin. Pharmacol.* **88**, 4412–4426 (2022).
15. Rockhill, K. M. et al. The Rise of Psilocybin Use in the United States: A Multisource Observational Study. *Ann. Intern. Med.* **178**, 1052–1054 (2025).
16. Evans, J. et al. On Minimizing Risk and Harm in the Use of Psychedelics. *Psychiatr Res. Clin. Pract.* **7**, 4–8 (2025).
17. Bălăeţ, M., Trender, W., Lerede, A., Hellyer, P. J. & Hampshire, A. Naturalistic use of psychedelics is associated with longitudinal improvements in anxiety and depression during global crisis times. *J. Psychopharmacol.* **39**, 957–967 (2025).
18. Nayak, S. M. et al. Naturalistic psilocybin use is associated with persisting improvements in mental health and wellbeing: results from a prospective, longitudinal survey. *Front Psychiatry* **14**, (2023).
19. Nygart, V. A. et al. Antidepressant effects of a psychedelic experience in a large prospective naturalistic sample. *J. Psychopharmacol.* **36**, 932–942 (2022).
20. Raison, C. L., Jain, R., Penn, A. D., Cole, S. P. & Jain, S. Effects of Naturalistic Psychedelic Use on Depression, Anxiety, and Well-Being: Associations With Patterns of Use, Reported Harms, and Transformative Mental States. *Front. Psychiatry*. **13**, 831092 (2022).
21. Abramsky-Sze, S., Marseille, E., Matzopoulos, R., Morlock, R. & Lerer, L. Characteristics and mental health of psychedelic mushroom and multi-psychedelic users relative to non-psychedelic users in American adults, 2020–2021. *Front Psychiatry* **16**, (2025).
22. Van Amsterdam, J. & Van Den Brink, W. Harm related to recreational ketamine use and its relevance for the clinical use of ketamine. A systematic review and comparison study. *Exp. Opin. Drug Saf.* **21**, 83–94 (2022).
23. Aday, J. S., Carhart-Harris, R. & Boehnke, K. F. Blunted psychedelic drug effects in older adults. *Preprint at.* https://doi.org/10.31234/osf.io/yz4cd_v2 (2025).
24. Izmi, N., Carhart-Harris, R. L. & Kettner, H. Psychological effects of psychedelics in adolescents. *Front Child. Adolesc. Psychiatry* **3**, (2024).
25. Ko, K., Carter, B., Cleare, A. J. & Rucker, J. J. Predicting the Intensity of Psychedelic-Induced Mystical and Challenging Experience in a Healthy Population: An Exploratory Post-Hoc Analysis. *NDT* 19, 2105–2113 (2023).
26. Kettner, H., Roseman, L., Gazzaley, A., Carhart-Harris, R. L. & Pasquini, L. Effects of Psychedelics in Older Adults: A Prospective Cohort Study. *Am. J. Geriatric Psychiatry*. **32**, 1047–1059 (2024).
27. Russ, S. L., Carhart-Harris, R. L., Maruyama, G. & Elliott, M. S. States and traits related to the quality and consequences of psychedelic experiences. *Psychol. Consciousness: Theory Res. Pract.* **6**, 1–21 (2019).

28. Ko, K., Knight, G., Rucker, J. J., Cleare, A. J. & Psychedelics Mystical Experience, and Therapeutic Efficacy: A Systematic Review. *Front Psychiatry* **13**, (2022).
29. Sheline, Y. I., Mintun, M. A., Moerlein, S. M. & Snyder, A. Z. Greater Loss of 5-HT2A Receptors in Midlife Than in Late Life. *Am. J. Psychiatry*. https://doi.org/10.1176/appi.ajp.159.3.430 (2002).
30. Karrer, T. M., McLaughlin, C. L. & Guaglianone, C. P. Samanez-Larkin, G. R. Reduced serotonin receptors and transporters in normal aging adults: a meta-analysis of PET and SPECT imaging studies. *Neurobiol. Aging*. **80**, 1–10 (2019).
31. Barrett, F. S., Johnson, M. W. & Griffiths, R. R. Validation of the revised Mystical Experience Questionnaire in experimental sessions with psilocybin. *J. Psychopharmacol.* **29**, 1182–1190 (2015).
32. Spitzer, R. L., Kroenke, K., Williams, J. B. W. & Löwe, B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch. Intern. Med.* **166**, 1092–1097 (2006).
33. Kroenke, K., Spitzer, R. L. & Williams, J. B. The PHQ-9: validity of a brief depression severity measure. *J. Gen. Intern. Med.* **16**, 606–613 (2001).
34. World Health Organization. WHO-Five Well-being Index. (2020). https://doi.org/10.1037/t36093-000
35. Diener, E., Emmons, R. A., Larsen, R. J. & Griffin, S. The Satisfaction With Life Scale. *J. Pers. Assess.* **49**, 71–75 (1985).
36. Rosseel, Y. lavaan: An R Package for Structural Equation Modeling. *J. Stat. Softw.* **48**, 1–36 (2012).
37. Strickland, J. C., Garcia-Romeu, A. & Johnson, M. W. The Mystical Experience Questionnaire 4-Item and Challenging Experience Questionnaire 7-Item. *Psychedelic Med. (New Rochelle)*. **2**, 33–43 (2024).
38. Griffiths, R. R. et al. Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects. *Psychopharmacol. (Berl)*. **218**, 649–665 (2011).
39. Roseman, L., Nutt, D. J. & Carhart-Harris, R. L. Quality of Acute Psychedelic Experience Predicts Therapeutic Efficacy of Psilocybin for Treatment-Resistant Depression. *Front. Pharmacol.* **8**, 974 (2017).
40. Kettner, H., Roseman, L., Gazzaley, A., Carhart-Harris, R. L. & Pasquini, L. Effects of Psychedelics in Older Adults: A Prospective Cohort Study. *Am. J. Geriatr. Psychiatry*. **32**, 1047–1059 (2024).
41. Davis, A. K. et al. Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder: A Randomized Clinical Trial. *JAMA Psychiatry*. **78**, 481–489 (2021).
42. Kometer, M. et al. Psilocybin biases facial recognition, goal-directed behavior, and mood state toward positive relative to negative emotions through different serotonergic subreceptors. *Biol. Psychiatry*. **72**, 898–906 (2012).
43. Quednow, B. B., Kometer, M., Geyer, M. A. & Vollenweider, F. X. Psilocybin-induced deficits in automatic and controlled inhibition are attenuated by ketanserin in healthy human volunteers. *Neuropsychopharmacology* **37**, 630–640 (2012).
44. Gopnik, A. et al. Changes in cognitive flexibility and hypothesis search across human life history from childhood to adolescence to adulthood. *Proceedings of the National Academy of Sciences* 114,

7892–7899 (2017).

45. Marzola, P., Melzer, T., Pavesi, E., Gil-Mohapel, J. & Brocardo, P. S. Exploring the Role of Neuroplasticity in Development, Aging, and Neurodegeneration. *Brain Sci.* **13**, 1610 (2023).
46. Mousley, A., Bethlehem, R. A. I., Yeh, F. C. & Astle, D. E. Topological turning points across the human lifespan. *Nat. Commun.* **16**, 10055 (2025).
47. Loevinger, J. & Blasi, A. *Ego Development: Conceptions and Theories* (Jossey–Bass, 1976).
48. Carhart-Harris, R. L. & Goodwin, G. M. The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future. *Neuropsychopharmacology* **42**, 2105–2113 (2017).
49. Cruz-Muros, I. et al. Deglycosylation and subcellular redistribution of VMAT2 in the mesostriatal system during normal aging. *Neurobiol. Aging*. **29**, 1702–1711 (2008).
50. Magnusson, K. R., Brim, B. L. & Das, S. R. Selective Vulnerabilities of N-methyl-D-aspartate (NMDA) Receptors During Brain Aging. *Front. Aging Neurosci.* **2**, 11 (2010).
51. Nahlawi, A., Ptaszek, L. M. & Ruskin, J. N. Cardiovascular effects and safety of classic psychedelics. *Nat. Cardiovasc. Res.* **4**, 131–144 (2025).

# Figures

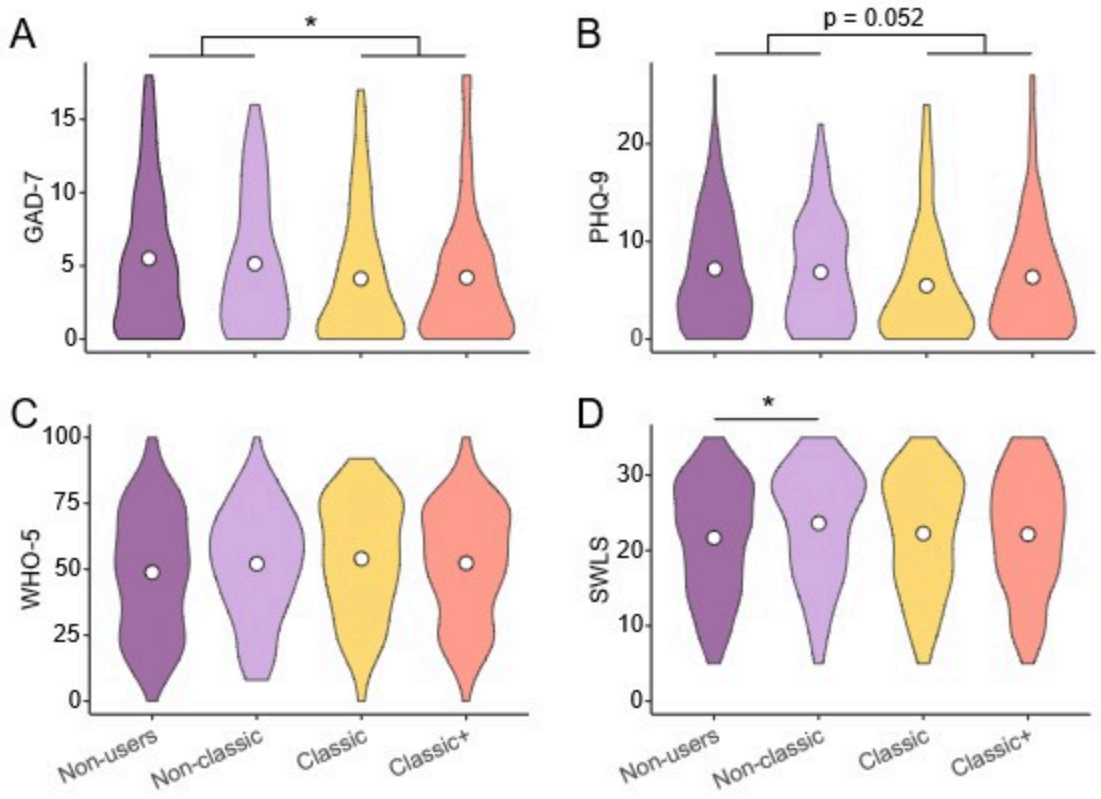



**Figure 1**

**Mental health measures across psychedelic-use groups.** Distributions of GAD-7 (A), PHQ-9 (B), SWLS (C), and WHO-5 (D) scores by psychedelic group. Violin plots show score distributions; white points mark group means. * p < 0.05

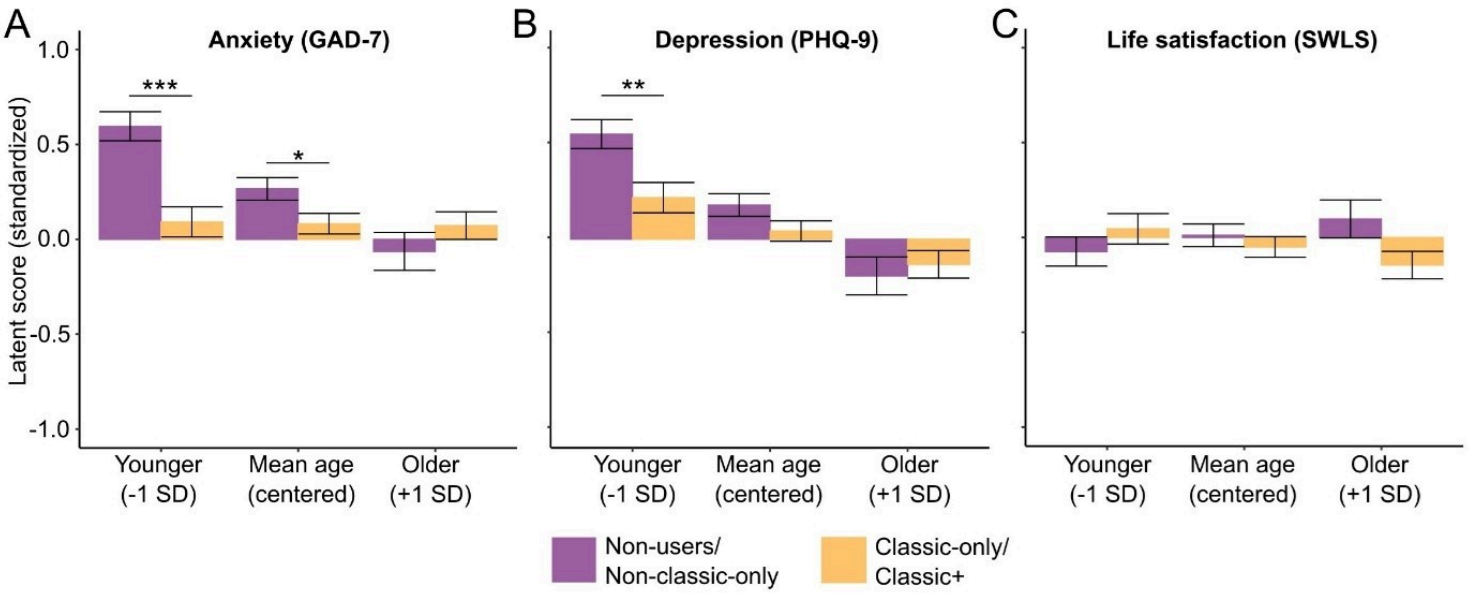



**Figure 2**

**Age-related variation in anxiety, depression, and life satisfaction across psychedelic-use groups.** Predicted latent anxiety (GAD-7; A), latent depression (PHQ-9; B), and latent life satisfaction (SWLS; C) as a function of age (−1 SD, mean age, +1 SD) and psychedelic drug type (Classic only/+ vs Non-user/Non-classic), estimated via SEM. Error bars represent the fitted value plus or minus one Standard Error for each *Age × Drug Type* combination. Younger (−1 SD) = 23 years; Average age = 36 years; Older (+1 SD) = 50 years. * p < 0.05; ** p < 0.01; *** p< 0.001.

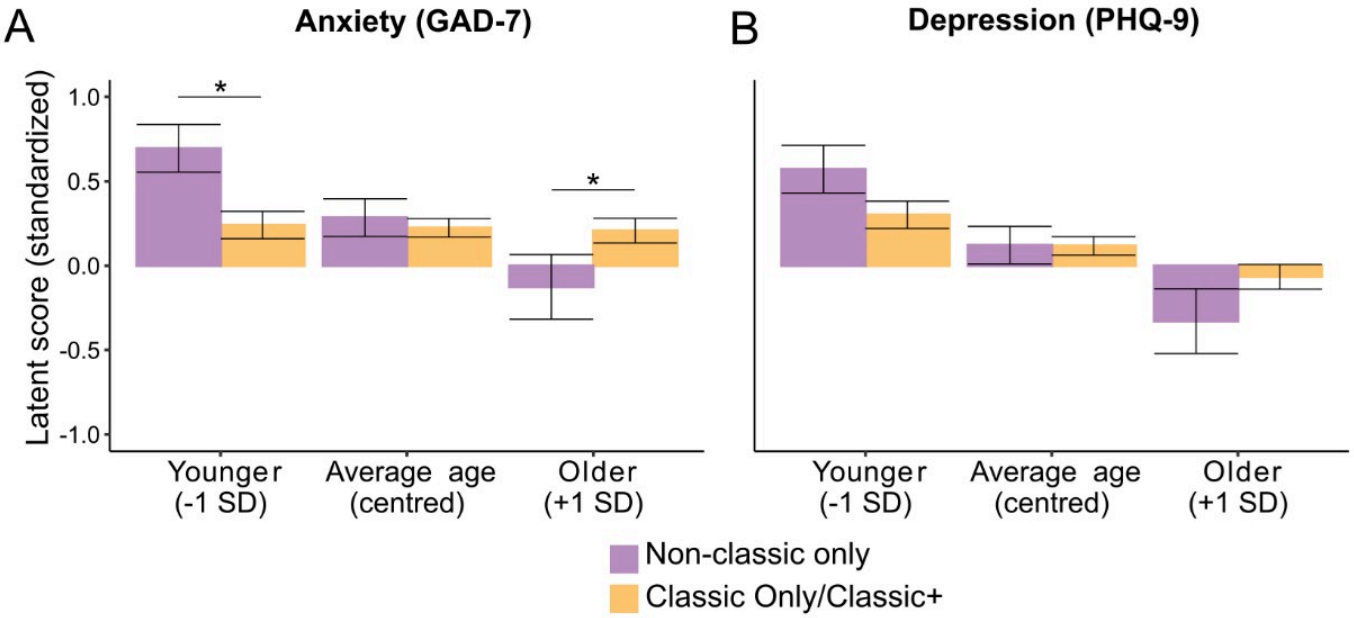



**Figure 3**

**Age-related variation in anxiety and depression among classic and non-classic psychedelic users**. Predicted latent anxiety (GAD-7; A) and latent depression (PHQ-9; B) as a function of age (−1 SD, mean age, +1 SD) and psychedelic-use drug type (Classic only/$^{+}$ vs Non-classic only) in the user-only subsample, estimated via SEM. Error bars represent the fitted value plus or minus one Standard Error for each *Age × Drug Type* combination. Younger (−1 SD) = 23 years; Average age = 36 years; Older (+1 SD) = 50 years. * $p < 0.05$.

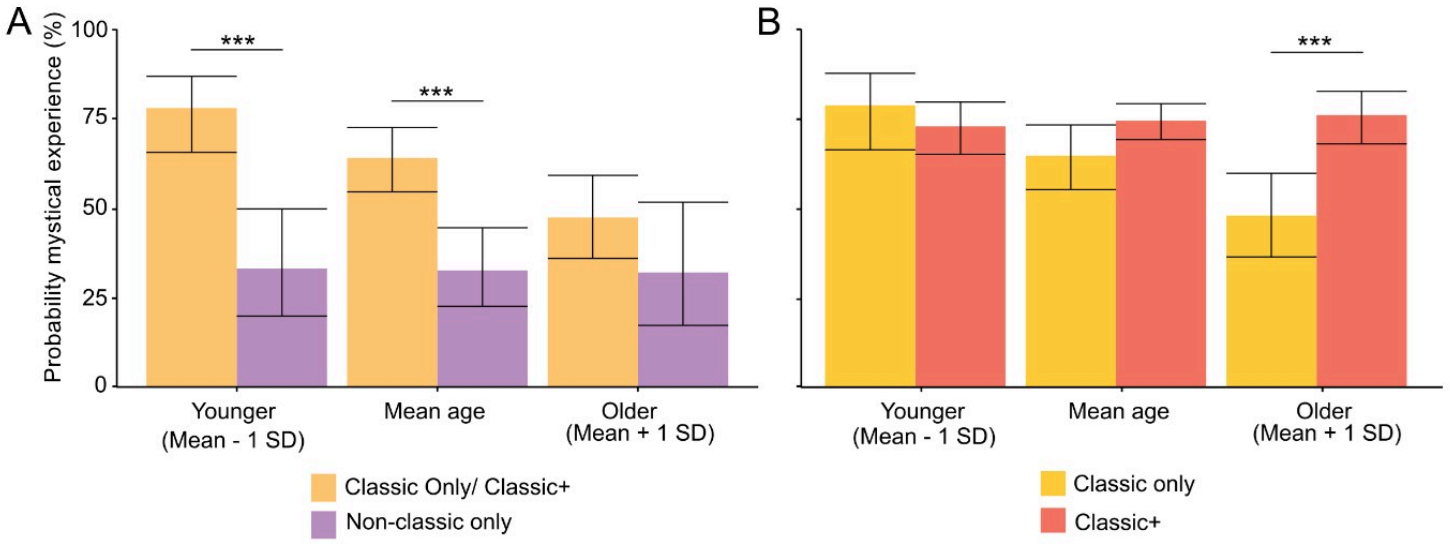



**Figure 4**

**Age-related variation in predicted mystical experience across psychedelic-use groups.** Predicted Mystical experience by age for the contrast (A) Classic (only/+) vs Non-Classic Only and (B) Classic Only and Classic$^{+}$. Error bars = 95% CI from logistic model. *** p < 0.001.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- DiGregorioetalAgemoderatesSupplementalMaterial.pdf