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Exploring the potential psychological predictors associated with changes in depression, anxiety, and well-being following naturalistic psychedelic use

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A B S T R A C T

Although research shows that psychedelic use may lead to improvement in mental health and well-being, the underlying changes in psychological predictors associated with these improvements remain unclear. 161 participants were recruited in a prospective online survey assessing naturalistic psychedelic use. We used lasso regression to assess how 19 distinct changes in psychological variables (e.g., meaning in life, mindfulness) were linked to future changes in depression, anxiety, and well-being changes. We found increases in *meaning in life* ($\beta = 0.229$, 95 % CI [0.101, 0.357], $p < 0.01$), *agreeableness* ($\beta = 0.193$, [0.077, 0.361], $p < 0.05$), *mindfulness* ($\beta = 0.174$, [0.022, 0.383], $p < 0.05$), and *extraversion* ($\beta = 0.135$, [0.002, 0.246], $p = 0.046$) to be the variables most strongly associated with future increases in *well-being*. Increases in *mindfulness* ($\beta = -0.347$, [−0.481, −0.220], $p < 0.001$), *emotional stability* ($\beta = -0.158$, [-0.279, −0.020], $p < 0.05$), and *extraversion* ($\beta = -0.147$, [0.022, 0.383], $p < 0.05$) were the most strongly associated with future decreases in *anxiety*. Lastly, increases in *self-esteem* ($\beta = -0.216$, [−0.365, −0.056], $p < 0.05$) were most strongly associated with changes in *depression*. Changes in *mindfulness* and *emotional stability* were also associated with *depression*; however, they were not significant. Mindfulness was the sole predictor that ranked within the top three across all outcomes. These findings suggest that these differing predictors may underpin the observed psychological improvements following naturalistic psychedelic use.

1. Introduction

Classic psychedelics are psychoactive substances that can alter states of consciousness and induce changes in mood. Acting primarily as agonists to serotonin 5-HT 2 A receptors, these substances include naturally occurring or naturally derived compounds such as psilocybin, lysergic acid diethylamide (LSD), N,N-dimethyltryptamine (DMT), mescaline, peyote, and ayahuasca (Nichols, 2016). Numerous civilizations and indigenous communities have used psychedelics as healing agents for many millennia. In the current context of Western science, clinical trials are examining classic psychedelics for treating numerous mental health disorders, including depression (Carhart-Harris et al., 2021; Carhart-Harris et al., 2016; Davis et al., 2021; Palhano-Fontes et al., 2019; Sanches et al., 2016), anxiety (Gasser et al., 2014; Griffiths et al., 2016; Grob et al., 2011; Ross et al., 2016), OCD (Kelmendi et al., 2022; Moreno et al., 2006), and alcohol use disorder (Bogenschutz et al., 2022). Additional epidemiological studies have linked naturalistic psychedelic use with lowered odds of social impairment, suicidality, crime arrests, and substance use disorders (Jones et al., 2022; Jones, 2023; Jones and Nock, 2022a, 2022b; Nayak et al., 2023). Despite their medicinal promise, psychedelics' therapeutic effects remain poorly understood, particularly the psychological processes that drive these improvements.

To our knowledge, no studies have directly compared multiple psychological predictors associated with improved mental health following psychedelic use to determine which are most influential. Most prior studies have examined only a few predictors in isolation (Van Elk and Yaden, 2022), providing important preliminary insights but failing to identify which factors best explain post-psychedelic mental health improvements. Hence, the goal of this study is to assess and compare numerous plausible drivers of change, as this comparison can help us to develop a more comprehensive understanding of the key factors driving positive mental health outcomes following psychedelic use.

Research has provided clues as to which psychological traits may

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drive improvements in mental health that result from psychedelic use. First, increased mindfulness—a mental quality characterized by nonjudgmental awareness of the present moment—may strongly contribute to the enduring therapeutic effects of psychedelics, yet its role has not been systematically compared to other predictors. Changes in mindfulness have repeatedly been linked to improvements in mental health in non-psychedelic studies (Enkema et al., 2020; Keng et al., 2011; Schuman-Olivier et al., 2020), and numerous studies have demonstrated that psychedelics can increase mindfulness. In a double-blind study examining a five-day meditation retreat, a single dose of psilocybin significantly enhanced state mindfulness compared to the placebo group (Smigielski et al., 2019); however, this study did not assess mindfulness alongside other potential predictors, nor did it evaluate mental health changes. Similarly, two psilocybin studies showed sustained increases in trait mindfulness three months after administration, even in the absence of explicit mindfulness instruction (Madsen et al., 2020; Søndergaard et al., 2022). A study on naturalistic use of 5-MEO-DMT also found that this compound increased trait mindfulness one month post-administration (Uthaug et al., 2019). Yet, this study only evaluated one other potential predictor – satisfaction with life (Uthaug et al., 2019). Despite growing evidence that psychedelics enhance mindfulness, research has yet to systematically compare its role to other plausible predictors of post-psychedelic mental health improvements.

Personality changes may also help explain the improvements seen after psychedelic use; however, as with mindfulness, the role of personality has not been rigorously evaluated alongside other plausible psychological predictors. A meta-analysis examining personality changes throughout therapeutic interventions found that, regardless of intervention type, treatment was associated with substantial reductions in neuroticism, modest increases in extraversion, and minimal increases in conscientiousness and agreeableness (Roberts et al., 2017). Relatedly, research has demonstrated that psilocybin may increase extraversion and conscientiousness and decrease in neuroticism over the long-term (Erritzoe et al., 2018; Weiss et al., 2023), suggesting personality changes as a potential driver of mental health benefits. Notably, studies have not yet tested whether personality changes in the context of psychedelic use are directly associated with clinical improvements, nor have they compared personality shifts to other potential mechanisms of change. Hence, there are major limitations in our understanding of how changes in personality contribute to post-psychedelic improvements.

Several other studies have documented psychological changes associated with psychedelic use that may also contribute to their therapeutic effects, yet the relative influence of these factors remains unclear. Cross-sectional and longitudinal studies suggest that psychedelic use may increase self-compassion (Fauvel et al., 2023), nature relatedness (Kettner et al., 2019; Newton and Moreton, 2023; Nour et al., 2017), non-physicalist beliefs (Timmermann et al., 2021), cognitive flexibility (Nayak et al., 2023), emotion regulation (Nayak et al., 2023), and social connectedness (Kettner et al., 2021). While these findings highlight the breadth of potential psychological predictors, existing research has yet to quantitatively compare multiple mechanisms in the same study. This gap in the literature limits our understanding of which processes are most strongly linked to therapeutic improvements in mental health.

Hence, the current study seeks to address limitations of prior research by leveraging longitudinal data to examine multiple plausible drivers of change simultaneously. Specifically, this study builds off Mans et al. (2021), which found that psychedelics had a sustained positive impact on well-being in a prospective, naturalistic sample. To extend these findings, we assess the specific psychological variables that are most strongly associated with changes in self-reported well-being, depression, and anxiety following naturalistic psychedelic use. Overall, this work can provide critical insights into the psychological mechanisms underlying the potential therapeutic effects of psychedelics.

2. Methods

2.1. Procedures

Design. This study utilized observational data from a prospective, opportunity-sampled online survey platform called "Psychedelic Survey" (www.psychedelicsurvey.com). Advertisements for the survey were posted online through social media platforms including Twitter, Facebook, online drug forums, and email newsletters. Before filling out surveys, individuals who intended to use classic psychedelics provided informed consent. Participants then entered their email address, name, and the expected date of their upcoming psychedelic experience. Surveys inquiring about subjective experiences were emailed based on participants' expected date of psychedelics experience and were administered both before and after consuming classic psychedelics. Inclusion criteria required participants to be 18 years or older, have adequate English comprehension, and express intent to take classic psychedelics (psilocybin/magic mushrooms/truffles, LSD/1 P-LSD, ayahuasca, DMT/5-MeO-DMT, salvia divinorum, mescaline, iboga/ibogaine) in the near future. The study received approval from the Joint Research Compliance Office at Imperial College London and was favorably reviewed by the Imperial College Research Ethics Committee. The dataset was originally collected for a broader study aimed at reducing uncertainty about individual responses to psychedelics in uncontrolled settings (for full description, see Haijen et al. (2018)). The present analysis is a secondary analysis of these data to address our specific research question.

Timepoints. The sample sizes for each survey were N = 658 (T1, one week before psychedelic use), N = 316 (T4, two weeks after), and N = 220 (T5, four weeks after), respectively. 75.53 % of participants dropped out before completing the final survey at the four-week time point (T5). Hübner et al. (2021) examined factors contributing to attrition in this sample, finding that education, age, and personality traits (i.e., conscientiousness and extraversion) predicted non-completion, whereas baseline advocacy of psychedelics and intensity of challenging experiences did not. Prior to analysis, rows with missing values were removed through case-wise deletion. The final sample included 161 participants within all three time points.

Measures. Variables were selected based on expert knowledge of constructs related to mental health. The dependent variables were delta scores (T1-T5)—reflecting changes from one week before (T1) minus four weeks after psychedelic use (T5)—in three psychological outcomes: well-being, anxiety, and depression. Well-being was measured using the Warwick-Edinburgh Mental Well-being Scale (Tennant et al., 2007); anxiety, by the Spielberger State–Trait Anxiety Inventory (Marteau and Bekker, 1992); and depression, through the 16-item Quick Inventory of Depressive Symptomatology (Rush et al., 2003). The independent variables consisted of delta scores (T1-T4)—or changes from one week before (T1) to two weeks after psychedelic use (T4)—from nineteen potential predictors: extraversion, agreeableness, conscientiousness, emotional stability, openness to experience, self-esteem, empathy, gratitude, social connectedness, resilience, presence of meaning in life, search for meaning in life, mindfulness, absorption, nature relatedness, suggestibility, magical ideation, delusional thinking, and political perspectives. The scales that measured these constructs are detailed in Supplementary Table 1.

2.2. Data analysis

Lasso regression. Lasso extends upon Ordinary Least Squares (OLS) by adding a regularization term, which helps perform variable selection (Tibshirani, 1996). By incorporating this term into the OLS loss function, lasso mitigates overfitting by penalizing the absolute values of the regression coefficients. This penalty term shrinks the coefficients of predictors, with some being reduced to exactly zero. Predictors with larger coefficients are deemed to have a stronger relationship with the

outcome variable, while smaller coefficients or coefficients that are dropped to 0 are interpreted as having a weaker relationship. The penalty strength, controlled by the regularization parameter lambda, is typically selected through *k*-fold cross-validation. In this process, the data is split into *k* groups, with the model iteratively trained on *k*-1 groups and tested on the remaining group. This iterative evaluation helps identify the optimal value for the regularization parameter.

Data Preparation. We included the covariate sex, a binary categorical variable (i.e., male or female). All continuous and ordinal variables, including covariates such as age, education, and prior psychedelic use, were standardized to have a mean of zero and a standard deviation of one. This standardization is important in lasso regression to prevent variables with larger scales from disproportionately influencing the model and to be able to compare the relative effect size of the coefficients.

Statistical Methods. We used Lasso regression with 23 predictor variables—19 representing changes in psychological mechanisms (T1-T4) and 4 covariates—to identify the independent variables most associated with changes in psychological well-being (T1-T5). We performed this analysis using the *glmnet* package in R (Friedman et al., 2010). We conducted 10-fold cross-validation to determine the optimal tuning parameter, lambda, by selecting the value that minimized the mean squared error (MSE). Importantly, predictor variables with higher absolute coefficients were interpreted as being more strongly associated with changes in the dependent variables.

In addition, to obtain confidence intervals and p-values, we used the *selectiveInference* package in R, which accounts for the variable selection process inherent in lasso regression (Lee et al., 2016; Taylor and Tibshirani, 2018). However, while this approach helps mitigate bias introduced by variable selection, it does not completely eliminate it. As a result, the p-values and confidence intervals should be interpreted with caution and used only as complementary metrics; the ordering of coefficients remains the primary basis for interpreting our results. All analyses were conducted using R version 4.4.0.

Assumptions. Normal QQ-plots, residual fitted plots, and the Shapiro-Wilk test were used to examine the distribution of residuals, non-linearity, and heteroscedasticity.

3. Results

3.1. Demographics of sample

Participant demographics (i.e., age, education, sex and prior psychedelic use) are illustrated in Table 1.

Table 1
Demographics of sample.

Characteristics	Participants (N = 161)	
	Mean	SD
Age	31.71	11.7
Education	**n**	**%**
Left school before age 16 without qualifications	5	3.11
Some high school level (in UK)	14	8.7
High school diploma/A-level education	15	9.32
Some university	26	16.15
Bachelor's degree	63	39.13
Post-graduate degree	38	23.6
Sex	**n**	**%**
Male	112	69.57
Female	49	30.43
Prior Psychedelic Use	**n**	**%**
Never	14	8.7
Only once	10	6.21
2-5 times	43	26.71
6-10 times	22	13.66
11-20 times	23	14.29
21-50 times	30	18.63
51-100 times	7	4.35
More than 100 times	12	7.45

3.2. Lasso regression results

Table 2 shows the inferential statistics of the well-being lasso regression, which was performed with 23 variables to predict changes in psychological well-being. Increases in the "presence" subscale of meaning in life (T1-T4) were most strongly associated with increases in psychological well-being (T1-T5). Significant associations were also observed for increases (T1-T4) in agreeableness, mindfulness, and extraversion (all $p < 0.05$). The remaining variables were shrunk to zero and so are not shown in Table 2. The R-squared of the model was 0.43, indicating that approximately 43 % of the variance in well-being scores was explained by the predictors selected.

Table 3 shows the inferential statistics of the anxiety lasso regression. Changes in mindfulness (T1-T4) were most strongly associated with future decreases in anxiety (T1-T5). Increases in emotional stability and extraversion were also strongly associated (T1-T4) with future decreases in anxiety. The R-squared of the model was 0.34.

Table 4 shows the inferential statistics of the depression lasso regression using the same 23 predictor variables. Self-esteem (T1-T4) was the most strongly associated variable with future decreases in depression (T1-T5), and this association was the only one that reached significance. The R-squared of the model was 0.21.

To avoid issues with multicollinearity – which occurs when independent variables are excessively correlated with one another – we assessed the variance inflation factors (VIF) of all 23 independent variables. In short, VIF is a metric used to quantify possible issues of excessive correlations between variables. No predictor variable had a VIF higher than 1.72, indicating acceptable levels of correlations between variables. We also plotted a Pearson correlation heatmap to visually inspect the extent to which each significant predictor was correlated with each outcome, as shown in Fig. 1.

4. Discussion

In the present study, we used lasso regression to identify the most influential predictors of improvements in mental health among individuals using psychedelics in a naturalistic context. Improvements in the "presence" subscale of meaning in life was the single strongest individual predictor of subsequent improvement in psychological well-being, followed by increases in trait agreeableness and trait mindfulness.Enhances in mindfulness was the strongest predictor of reduced anxiety, followed by increases in emotional stability and extraversion. Regarding depression reduction, positive change in self-esteem emerged as the strongest predictor; changes in emotional stability and

Table 2
Lasso regression Well-being results.

Predictors	Coefficient estimate	Lower CI	Higher CI	P value
Meaning in life - presence	0.229	0.101	0.357	0.002**
Agreeableness	0.193	0.077	0.361	0.005**
Mindfulness	0.174	0.022	0.383	0.031**
Extraversion	0.135	0.002	0.246	0.046**
Emotional Stability	0.119	−0.034	0.245	0.095
Self-Esteem	0.126	−0.051	0.258	0.113
Nature Relatedness	0.090	−0.082	0.202	0.184
Absorption	0.088	−0.088	0.20	0.197
Magical Ideation	0.084	−0.090	0.195	0.205
Resilience	0.076	−0.117	0.188	0.258
Interpersonal Reactivity	0.045	−0.284	0.211	0.493
Gratitude	0.019	−0.841	0.104	0.798

Predictors are listed from the top down by largest coefficient. Predictor coefficients that were set to 0 were not listed. Significance of p values: **: <0.05; ***: <0.001.

Table 3
Lasso regression Anxiety results.

Predictors	Coefficient estimate	Lower CI	Higher CI	P value
Mindfulness	−0.347	−0.481	−0.22	<0.001***
Emotional Stability	−0.158	−0.279	−0.020	0.031**
Extraversion	−0.147	−0.262	−0.018	0.032**
Self-Esteem	−0.111	−0.25	0.088	0.169
Agreeableness	−0.100	−0.211	0.060	0.141
Meaning in life - search	0.077	−0.127	0.190	0.267
Meaning in life - presence	−0.052	−0.169	0.296	0.498

Predictors are listed from the top down by largest coefficient. Predictor coefficients that were set to 0 were not listed. Significance of p values: **: <0.05; ***: <0.001.

Table 4
Lasso regression Depression results.

Predictors	Coefficient estimate	Lower CI	Higher CI	P value
Self-Esteem	−0.216	−0.365	−0.056	0.015**
Emotional Stability	−0.124	−0.258	0.064	0.13
Mindfulness	−0.123	−0.264	0.081	0.15
Resilience	−0.092	−0.216	0.114	0.224
Meaning in life - presence	−0.086	−0.224	0.183	0.31
Social Connectedness	−0.068	−0.193	0.219	0.387

Predictors are listed from the top down by largest coefficient. Predictor coefficients that were set to 0 were not listed. Significance of p values: **: <0.05; ***: <0.001.

mindfulness were also strongly predictive of depression. Mindfulness was the sole predictor that ranked in the top three across all outcomes.

Prior research indicates that psychedelics can induce positive psychological change; there is a growing research base suggesting that psychedelic use may improve mental health (Nutt and Carhart-Harris, 2021; Yao et al., 2024) and lead to personal and spiritual growth (Amada and Shane, 2022; Schutt et al., 2024; St. Arnaud and Sharpe, 2023). Supporting this view, Spangemacher et al. (2024) suggest that psychedelics may not only reduce symptoms but also strengthen broader dimensions of well-being. However, there is presently less clarity as to the mechanisms by which psychedelic experiences can improve mental health. This study aimed to lay the foundation for future studies designed to identify psychological mechanisms through which naturalistic psychedelic use may enhance mental health. To do so, we sought to satisfy Hill's temporality criterion for causal inference, which asserts that the *cause* must precede the *effect* (Fedak et al., 2015). While we do not interpret our findings as evidence of causality, we examined changes in psychological predictors (T1–T4) that preceded changes in mental health outcomes (T1–T5) to demonstrate that the observed relationships are temporally ordered—one necessary condition for causal interpretation. Our findings offer preliminary evidence that builds upon existing models of change theorizing into which specific psychological changes that may be driving the health-promoting aspects of psychedelic use (Kočárová et al., 2021). Supporting this view, Spangemacher et al. (2024) suggest that psychedelics may not only alleviate symptoms but also strengthen broader dimensions of health. Taken together, these perspectives provide a foundation for situating our findings within the wider psychedelic literature on adaptive and transformative psychological change. Below, we consider key implications of our findings, discuss study limitations, and suggest several potentially fruitful directions for future research.

4.1. Well-being, "presence" of meaning in life, and mindfulness

Given the litany of prior theoretical and empirical work indicating a deep connection between perceived meaning in life and subjective well-being, it is perhaps unsurprising that the former emerged as the strongest predictor of well-being improvement in the context of naturalistic psychedelic use. Meaning has long been conceptualized as a foundation of psychological well-being (Seligman, 2011, 2018; Viktor, 1992), and empirical studies have consistently shown a strong correlation between meaning and well-being (Li et al., 2021; Zika and Chamberlain, 1992). Our results are consistent with research indicating that naturalistic psychedelic use is associated with persistent improvements in subjective well-being (Griffiths et al., 2008; Nayak et al., 2023), and that these improvements are mediated in part by deeply meaningful mystical experiences (Yaden and Griffiths, 2021). Our work builds on these findings in suggesting that psychedelics may improve well-being by catalyzing existential or reflective processes that lead to the generation or realization of meaning. While not a causal relationship, the fact that changes in the "presence" subscale of meaning in life from one week before through two weeks post-psychedelic use predicted changes in well-being from one week before through four weeks post-use could imply that the process of well-being cultivation may persist long after the acute psychedelic experience. As such, may be influenced by formal integration practices that can help individuals process and assimilate insights from their psychedelic experiences into their broader lives (Bathje et al., 2022; Gorman et al., 2021).

Mindfulness also emerged as one of the strongest predictors of well-being, and was the only variable that emerged as a top-three predictor for all outcomes within our study (the effect for depression being non-significant). Multiple clinical and non-clinical studies have linked psychedelic use to improvements in mindfulness (Jones et al., 2024; Madsen et al., 2020; Smigielski et al., 2019; Søndergaard et al., 2022); further, mindfulness is a well-established predictor of improved psychological functioning and mental health (Keng et al., 2011; Wielgosz et al., 2019; Zollars et al., 2019). Relatedly, studies have demonstrated that engaging more frequently in meditation and other spiritual practices is a predictor of more enduring salutary effects from psychedelics (Griffiths et al., 2018). Others have shown that psychedelics can serve as a conduit to enhanced engagement with meditation as well as higher trait mindfulness, even among experienced meditators (Smigielski et al., 2019). Future observational and clinical studies should aim to directly explore mindfulness as a core potential mechanism underlying positive psychological changes post-psychedelic use.

4.2. Anxiety, mindfulness, and personality

The present findings also build on prior research exploring how psychedelics can lead to persisting improvements in anxiety (Agin-Liebes et al., 2020; Griffiths et al., 2016; Nayak et al., 2023). Mindfulness emerged as the most important predictor of reduced anxiety. This finding is consistent with studies showing that dispositional mindfulness—particularly the *Nonjudgment* and *Act with Awareness* facets—have been associated with lower anxiety among both healthy and clinical samples (Carpenter et al., 2019; Eleftheriou and Thomas, 2021). This study suggests that mindfulness may be a key mechanism of change driving anxiety reduction after psychedelic use.

Increases in emotional stability and extraversion were also related to lower anxiety. Systematic reviews have demonstrated that psychedelics are linked to improvements in emotional processing (Solaja et al., 2024); our findings add to this literature, and suggest that psychedelic users who experience greater improvements in emotional stability become less prone to experiencing unmanageable levels of anxiety. Additionally, our finding on extraversion is consistent with prior studies showing that psychedelic use may engender persistent and beneficial long-term shifts in personality (Nayak et al., 2023). However, the path via which higher extraversion leads to lower anxiety among psychedelic users is less clear.

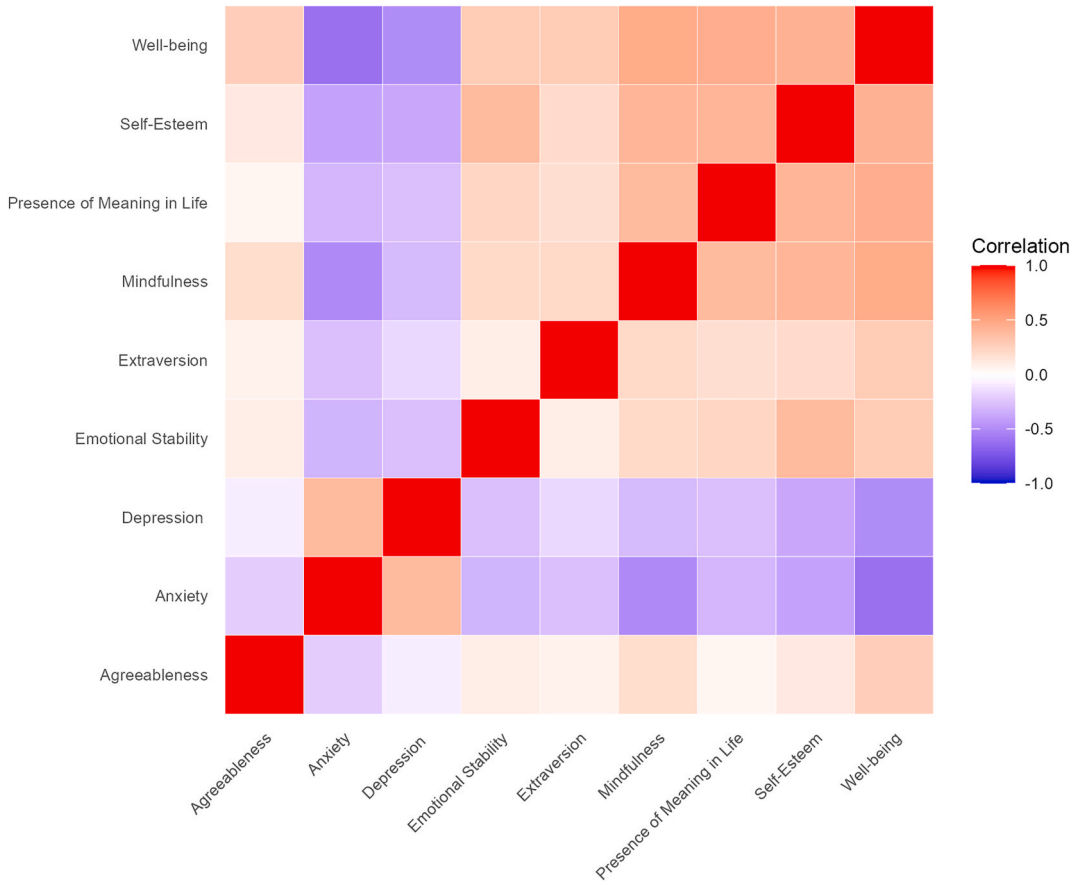

Fig. 1. Heatmap of Pearson correlation coefficients between significant predictors and mental health outcomes.
Note. Pearson correlation coefficients are shown between significant predictors from the lasso model (T1–T4) and outcomes of depression, anxiety, and well-being (T1–T5). Positive correlations appear in red; negative correlations appear in blue.

It may be that increased extraversion enhances social connectedness, engagement in the world, and/or more frequent experiences of positive emotion, all of which might buffer against negative emotional states such as anxiety (Fredrickson, 2004; Gunnar and Hostinar, 2015).

4.3. *Depression and self-esteem*

Our model predicting reductions in depressive symptoms had one significant predictor: self-esteem. Low self-esteem is a core feature of major depression (American Psychiatric Association, 2013) and has been identified as a vulnerability factor for future depressive symptoms (Sowislo and Orth, 2013). Prior work has shown that naturalistic psychedelic use is associated with improvements in self-esteem both for adults (Mans et al., 2021) and adolescents (Izmi et al., 2024), and the present work underscores the importance of increases in self-esteem as a potential mechanism of depression reduction in the context of psychedelic use.

It is presently unknown *how* psychedelics might engender higher self-esteem. One possibility is that psychedelic use may directly enhance an individual's self-image. Alternatively, psychedelics may alter one's relationship with "the self" in general. Psychedelics, particularly in higher doses, can lead to subjective experiences of ego dissolution (Letheby and Gerrans, 2017) and self-transcendence (Yaden et al., 2017) that may then encourage a variety of positive changes, including a shift towards less egocentric values (Kähönen, 2023), reduced self-referential processing (Sacchet et al., 2024), and contextualization of the self as part of a much larger whole (Kähönen, 2023). All of the above self-related processes may possibly reduce depression.

5. Limitations

Our study is subject to several important limitations. First, this sample was derived via online opportunity sampling (aka "convenience sampling") and, as such, our findings may not generalize to the broader population of naturalistic psychedelic users, many of whom may be reluctant to report past use of illicit substances. Further, due to our observational study design and our sampling method, we had no active or waitlist control condition, and had no control over either the type of psychedelic substance(s) used, or the dosages taken. We likewise had no control over participants' use expectations, intentions, and overall emotional state (i.e., "set"), the settings in which they used psychedelics, and the types of post-experience integration activities that were undertaken. Additionally, other psychological mechanisms—such as increased empathy or improved cognitive functioning—have been linked to the salutary effects of psychedelics (Jungwirth et al., 2025; Sayalı and Barrett, 2023) and may underlie our findings, yet they were not examined in the current study. Importantly, our claims are not causal given we did meet key assumptions for causal interpretations (e.g., experimental evidence, consistency across multiple studies, etc.) (Fedak et al., 2015).

All constructs were measured via self-report, opening the possibility of common method bias—a form of measurement error that arises when data are collected using the same method (e.g., self-report)—leading to the artificial overinflation of associations between constructs (Podsakoff et al., 2003). Another limitation is that our sample suffered from attrition over the course of the study; over half of our baseline (T1) sample did not complete the two-week post-use follow-up survey (T4), and just one third of baseline participants completed the one-month follow-up

survey (T5). As this attrition is not random and is linked to certain demographic factors (e.g., age, demographics) (Hübner et al., 2021), differential attrition may have shaped our results. As numerous prior studies have demonstrated that demographic factors may shape the associations between psychedelic use and mental health (Jones, 2023, 2025; Jones et al., 2023, 2024, 2025; Jones and Nock, 2022c), future studies should examine how drivers of psychedelic change may vary based on an individual's demographic background.

In addition, as mentioned in our Methods section, the methods we used to derive confidence intervals and p-values for our lasso analyses have limitations. Although we leveraged validated approaches by Lee et al. (2016), these methods do not completely eliminate the bias introduced by lasso's variable selection process. Our resulting coefficient estimates are influenced by the lasso method, which may differ from other approaches (e.g., ordinary least squares, ridge). However, biased coefficients are more concerning in the presence of multicollinearity, which we ruled out.

5.1. Future directions

Our findings raise several questions and suggest potential future research directions on the mechanisms and timescales through which psychedelics foster psychological change. For example, when considering perceived meaning in life, we might ask: do psychedelic experiences cause meaning in life to be realized immediately or gradually—over subsequent days, weeks, or months—through a process of integration? Given reports of both immediate meaning generation through psychedelic use and more long standing—potentially challenging—periods of integration (Evans et al., 2023), it is likely the case that perceived meaning does not follow a universal trajectory among users. As change for some variables (e.g., higher trait mindfulness) may be more immediate than others (e.g., higher trait agreeableness), future studies that incorporate experience-sampling methods can elucidate these change processes at a higher temporal resolution (Sznitman et al., 2025). Researchers could design clinical trials that include ecological momentary assessment to better illustrate how changes in hypothesized psychological mechanisms contribute to improved mental health. Furthermore, to enhance external validity of this future trial, this study could include a more diverse sample of participants (i.e., additional people of color, women, etc.) in order to maximize the generalizability of the findings.

Future work on the impact of naturalistic psychedelic use might also incorporate additional self-report measures to test a wider range of variables and also incorporate measures from the text of reports and integration sessions using natural language processing. Lastly, it may be useful to explore whether psychedelics tend to induce specific salutary beliefs about self, others, or the world. Prior work has found that psychedelic use can shift worldviews away from physical explanations of reality towards belief systems that view consciousness as a fundamental property of the universe (Timmermann et al., 2021), which might confer both benefits and risks regarding psychological well-being.

6. Conclusion

The present work used a longitudinal research design to investigate the predictors of positive psychological change among individuals using psychedelics in naturalistic contexts. We found that different forms of positive psychological change (i.e., enhancements in well-being and reductions in depression and anxiety) were predicted by change in distinct psychological constructs (e.g., perceived meaning in life; mindfulness; self-esteem) in the wake of psychedelic experiences. Perceived meaning in life was the single strongest predictor of enhanced well-being, whereas mindfulness was the strongest predictor of reduced anxiety, and increased self-esteem the strongest predictor of lowered depression. Though the present work does not establish definitive mechanisms by which psychedelics cause distinct forms of psychological change, our findings shed light on the possible pathways by which psychedelic experiences may foster meaningful shifts in key psychological variables that ultimately reduce human suffering and facilitate our flourishing.

CRediT authorship contribution statement

Felipe M. Herrmann: Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Formal analysis, Data curation. **Grant Jones:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Daniel M. Low:** Writing – review & editing, Visualization, Validation, Software, Formal analysis, Data curation. **James M. Zech:** Writing – review & editing, Writing – original draft. **Robin L. Carhart-Harris:** Writing – review & editing, Supervision, Resources, Investigation, Funding acquisition. **Hannes Kettner:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Methodology, Investigation, Data curation, Conceptualization.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Grant Jones reports financial support was provided by Massachusetts General Hospital. Hannes Kettner reports financial support was provided by Maya Health. Daniel Low reports financial support was provided by National Institute of Mental Health. Robin Carhart-Harris reports financial support was provided by Tryp Therapeutics, MindState, Osmind, and Otsuka. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2025.09.007.

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