

Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Perkins, D;Opaleye, ES;Simonova, H;Bouso, JC;Tófoli, LF;Galvão-Coelho, NL;Schubert, V;Sarris, J

Title:

Associations between ayahuasca consumption in naturalistic settings and current alcohol and drug use: Results of a large international cross-sectional survey

Date:

2022-01-01

Citation:

Perkins, D., Opaleye, E. S., Simonova, H., Bouso, J. C., Tófoli, L. F., Galvão-Coelho, N. L., Schubert, V. & Sarris, J. (2022). Associations between ayahuasca consumption in naturalistic settings and current alcohol and drug use: Results of a large international cross-sectional survey. *Drug and Alcohol Review*, 41 (1), pp.265-274. <https://doi.org/10.1111/dar.13348>.

Persistent Link:

<https://hdl.handle.net/11343/298778>

Associations between ayahuasca consumption in naturalistic settings and current alcohol and drug use: results of a large international cross-sectional survey

Daniel Perkins¹, Emerita Opaleye², Hana Simonova, José Carlos Bouso³, Luís Fernando Tófoli⁴, Nicole Leite Galvão-Coelho⁵, Violeta Schubert¹, Jerome Sarris^{6,7}

¹School of Social and Political Science, University of Melbourne, Melbourne, Australia

²Department of Psychobiology, Universidade Federal de São Paulo, São Paulo, Brazil

³International Center for Ethnobotanic Education, Research & Service, Barcelona, Spain

⁴Interdisciplinary Cooperation for Ayahuasca Research and Outreach, School of Medical Sciences, University of Campinas, Campinas, Brazil

⁵Department of Physiology and Behavior, Federal University of Rio Grande do Norte, Natal, Brazil

⁶NICM Health Research Institute, Western Sydney University, Sydney, Australia

⁷Professorial Unit, The Melbourne Clinic, Department of Psychiatry, University of Melbourne, Melbourne, Australia

Daniel Perkins PhD, Research Fellow, Emerita Opaleye PhD, Senior Researcher, Hana Simonova M.Psych, Psychologist, José Carlos Bouso PhD, Scientific Director, Luís Fernando Tófoli PhD, Professor, Nicole Leite Galvão-Coelho PhD, Professor, Violeta Schubert PhD, Senior Lecturer, Jerome Sarris PhD, Professor.

Correspondence to: Dr Daniel Perkins, School of Social and Political Science, 420 John Medley Building, University of Melbourne, Parkville, Victoria 3010, Australia. Tel: +61 414620666; Email: d.perkins@unimelb.edu.au

Running header: Drug and alcohol use among ayahuasca drinkers

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1111/dar.13348](https://doi.org/10.1111/dar.13348)

This article is protected by copyright. All rights reserved.

Abstract

Introduction: Emerging evidence suggests that psychedelic compounds, including the Amazonian botanical decoction ayahuasca, may provide clinical benefit in the treatment of alcohol or other drug use disorders. This study investigates associations between ayahuasca consumption in naturalistic settings and current alcohol and other drug use.

Methods: Online cross-sectional study of people who have consumed ayahuasca in religious, traditional and non-traditional settings in over 40 countries. A total of 8629 participants (53% male, average age 40 years) were included in the analysis. Logistic regressions were used to explore associations between ayahuasca drinking variables and the current use of alcohol and other drugs, as well as the influence of confounding factors such as church or community membership.

Results: The number of times ayahuasca had been consumed was strongly associated with increased odds of never or rarely drinking alcohol, never or rarely engaging in 'risky drinking' and having not consumed a range of drugs in the past month, with these effects greater for those with a prior substance use disorder compared to those without. The strength of ayahuasca drinkers subjective spiritual experience, number of personal self-insights obtained and drinking ayahuasca with an ayahuasca church were also associated with lower substance use in some models.

Discussion and Conclusions Consumption of ayahuasca in naturalistic settings is associated with lower self-reported current consumption of alcohol and other drugs for those with and without prior substance use disorders, with such effects present after adjusting for religious or social group effects.

Key words: ayahuasca; psychedelics; alcohol consumption; substance use; substance use disorder; illicit drugs

Introduction

After many decades of inattention, a resurgence of interest in the potential clinical application of various psychedelic substances for the treatment of mental health and substance use disorders is now underway [1]. The primary focus of contemporary research in this area is the so-called classic psychedelics (psilocybin, ayahuasca and LSD/Lysergic acid diethylamide), which have their chief mode of action via the 5-HT_{2A} receptors, as well as the entactogen and indirect serotonergic agonist, MDMA (3,4-Methylenedioxymethamphetamine) [1]. Although preliminary, mounting evidence relating to the use of these substances is encouraging, and both psilocybin and MDMA have recently been granted 'breakthrough therapy' status by the United States Food and Drug Administration for major depressive disorder and post-traumatic stress disorder respectively [2,3].

There is also strong interest in the use of psychedelic compounds in addiction treatment [4,5]. Two recent reviews (one systematic review and one meta-analysis) of older LSD research (undertaken between 1966 and 1973) have reported a beneficial effect of LSD versus placebo for alcohol misuse [odds ratio (OR) 1.96; $P < 0.001$], and the first modern addiction studies with psilocybin have identified significant improvements in tobacco and alcohol dependence [6-10]. Another trial using psilocybin for the treatment of cocaine dependence is underway (NCT02037126), as well as a pilot study of MDMA for the treatment of alcohol dependence [11]. A recent systematic review examining the effects ayahuasca on substance use and dependence identified improvement in addiction related biochemical or behavioural parameters in animals and reductions in dependence symptoms in human studies[12].

Here we focus specifically on ayahuasca, a traditional botanical decoction of the *Banisteriopsis caapi* and *Psychotria viridis* or *Dypllopterys cecbrerara* plants containing DMT (N,N-Dimethyltryptamine) and harmala alkaloids. Ayahuasca has been used as a traditional medicine by indigenous groups in South America for centuries and was adopted as a religious sacrament by several Brazilian Christian based syncretic churches in the middle of the 20th century [13]. Recent decades have seen a global expansion of ayahuasca use via the international spread of these ayahuasca churches, the growth of ayahuasca tourism in South American countries, particularly Peru, and the increasing popularity of neo-shamanic healing ceremonies using ayahuasca across North America, Europe and Australia [14-16].

The ayahuasca churches differ from traditional and neo-shamanic ayahuasca groups in being structured religious organisations, which use ayahuasca on a regular ongoing basis in all usual services, and in Brazil have a large middle class and professional membership [17,18]. This long-term

organisational use has presented an unusual opportunity for research, with studies undertaken reporting no adverse impacts on neuropsychological functioning and apparent positive effects on mood and wellbeing, in addition to either a complete remission or significant reduction in drug and alcohol use among church members identifying prior dependence or abuse [19-26]. Studies of ayahuasca drinkers in other naturalistic settings have reported similar findings relating to reduced problematic substance use, as well as improved health behaviours, and a range of psychological or emotional effects suggested to be able to support recovery and relapse prevention [27-34]. Although the potential for emotional or psychological difficulties post-use has also been noted [16,27].

Relevant mechanisms of action for the classic psychedelics, such as DMT and psilocybin, involve the modulation of the serotonergic, dopaminergic and glutamatergic systems (related largely to interactions with 5-HT_{2A} receptors), promotion of structural and functional plasticity in the pre-frontal cortex, and agonism at the 5-HT_{2C} receptors [35-38]. Additional pathways specific to ayahuasca that have been suggested to support anti-addictive effects include the activation by DMT of the sigma-1 (σ 1) and trace amine-associated receptors, and apparent anti-addictive effects of the brew's harmala alkaloids, particularly harmine [39-41]. Psychotherapeutic mechanisms such as self-insights are also suggested to be important [42,43].

It is also important to note that the community or religious contexts in which ayahuasca is often drunk may provide a potential benefit for psychiatric or substance use disorders, independently of the ayahuasca itself [44]. In addition, in a range of studies with psychedelics extra-pharmacological factors, such as an individual's mental state prior to consumption, the context of consumption and the strength of participants' subjective mystical experience during the acute phase, have been identified as being important and predictive of a positive therapeutic response [45-48].

Anonymous online surveys have particular utility for accessing hidden populations, such as users of scheduled substances, and have been previously used to gain a broader understanding of potential risks and benefits, which can inform drug and health policy and potential clinical trials [49-52]. A further strength of samples obtained online is that these provide a perspective different to substance use research involving individuals in clinical settings or the criminal justice system [52]. Online cross-sectional surveys similar to the current study have also been successfully used to assess self-reported change in alcohol consumption associated with other plant based substances such as medicinal cannabis [53].

This exploratory study uses the largest dataset ever collected relating to ayahuasca drinking (n=10,836), to explore associations between ayahuasca consumption and participants current use of alcohol and other drugs, and the extent to which this may be influenced by patterns of use, aspects of the acute subjective experience and potential confounding factors such as church or community membership. Differences in associations for those with and without prior substance use disorders are also investigated.

Methods

Study design

Data analysed were from the Global Ayahuasca Project, an international online cross-sectional survey (n=10,836) of ayahuasca drinkers conducted between April 2017 and May 2019 that collected data from individuals (18+ years) who had consumed ayahuasca at least once. The survey was translated into five languages other than English (Portuguese, Spanish, German, Italian and Czech). A non-random sampling strategy was chosen due to the hidden nature of the ayahuasca drinking population in most countries and the benefits associated with obtaining a large sample size. Participation was promoted via email and websites of relevant organisations, ayahuasca churches and retreat centres, as well as Facebook. No financial incentives were provided for participation. Data was cross-checked to remove suspected duplicate responses, and partially completed surveys were retained. Ethics approval was provided by the University of Melbourne Human Research Ethics Committee (HREC number 1545143.3), with data collected via the University's Limesurvey survey platform. For the present publication, only participants who provided responses to at least one of the alcohol and drug items in the survey were included in the analysis (n=8629) (Table 1).

Demographic data collected included age, education and country of residence. Detailed data regarding ayahuasca drinking was obtained including history and patterns of drinking, and any adverse effects experienced. Subjective spiritual experience (during all ayahuasca experiences) was assessed using the spirituality component of the Persisting Effects Questionnaire (PEQ-S) [54], a six-point scale (ranging from not at all significant to the single most spiritually significant experience of my life); and an adapted version of the nine item Short Index of Mystical Orientation (SIMO) scale, a unidimensional instrument intended to capture seven defining characteristics of mysticism: ineffability, noesis, transiency, passivity, oneness, timelessness and true ego [55]. SIMO items are scored 1 (not at all) to 10 (very much), giving a total score range of 9-90. This adapted version of the SIMO displayed a good level of internal consistency ($\alpha = 0.85$).

Several customised questions were developed from the ayahuasca literature. Number of 'self-insights' during your ayahuasca experiences utilised a list of seven commonly reported personal insights such as new understanding of childhood events, your physical body function and care, and the purpose and direction of your life. This variable displayed a good level of internal consistency ($\alpha = 0.80$). Such insights are often reported to be one of the most profound aspects of the ayahuasca experience [31]. A single item question was used to measure the extent to which extreme fear or panic had been experienced during an ayahuasca session, scored from 0 "Not at all" to 10 "Very much". Individuals were also asked if they have a "close community or network of people" with whom they drink ayahuasca, with responses, Not at all, slightly, moderately, or very much.

Respondents were also asked to identify from a list any lifetime mental health diagnoses received from a health professional, including alcohol dependence/abuse and drug dependence/abuse, as well as whether they had been experiencing the mental health disorder at the time of drinking ayahuasca (on any occasion). Number of emotional or psychological 'integration difficulties' in the weeks or months after drinking ayahuasca was based on the Patient Health Questionnaire for Depression and Anxiety (PHQ-4) [56] plus five additional items such as 'Nightmares, or disturbing thoughts, feelings, or sensations', and 'Feeling disconnected or alone'. The integration difficulties variable displayed a good level of internal consistency ($\alpha = 0.86$). Information was also collected on the frequency of current alcohol consumption, frequency of 'risky' alcohol consumption (see Table 1), defined as more than 4 standard drinks on one occasion, as well as the lifetime, past year and past month use of a range of drugs.

Statistical analyses

Pearson's χ^2 test and Independent samples t-test were used to assess differences between categorical and continuous variables. Multivariate models utilised binary logistic regressions and were performed using STATA 16. To minimise potential bias associated with participants not completing certain questions/sections within the survey we utilised multiple imputation for the imputation of missing data for all independent variables in multivariate models. We used the mi impute chained command in STATA 16 with imputations undertaken using the regress command for continuous variables, the ologit command for ordinal variables, and logit command for categorical variables with 20 datasets ($m=20$) imputed for the analysis. The maximum proportion of missing cases imputed was 9%. Statistical significance was considered as a P value of <0.05 .

Results

Sample characteristics

Respondent characteristics, split by ayahuasca church/non-ayahuasca church due to notable differences outlined above, are reported in Table 1. For both groups the average age was 41 years, with a greater proportion of males (53%) and high levels of university education. There were several differences revealed between respondents who had last drunk with an ayahuasca church and those who had drunk in other contexts, with the latter group being significantly less likely to live in Brazil, but more likely to have a lifetime mental health diagnosis, have higher current alcohol and drug use, a higher lifetime number of different drugs used, and to have consumed ayahuasca fewer times (Table 1). Around 10% of both groups reported having a prior drug use disorder (total n=792) (difference not significant), while a similar number (total n=800) reported a prior alcohol use disorder (11.2% ayahuasca church vs 9.6% other contexts ($\chi^2 (1) 5.3$; $P=0.02$).

-----TABLE 1 ABOUT HERE-----

Current alcohol and drug use

Table 2 shows the results of bivariate logistic regression models investigating associations between alcohol and drug use and ayahuasca drinking variables. Regressions were performed separately for individuals with and without a prior alcohol or drug use disorder for the three dependent variables rarely/never drinking alcohol, rarely/never engaging in risky drinking and having no recent consumption of any drugs (of the 11 drugs listed in Table 3, plus heroin). A consistent and strong positive association was observed between the number of times ayahuasca has been consumed (10 categories) and the likelihood of lower alcohol and drug use. This included increased odds of rarely/never consuming any alcohol [No prior alcohol use disorder (AUD) OR 1.26, 95% confidence interval (CI) 1.22-1.30; Prior AUD OR 1.36, 95% CI 1.22-1.51], rarely/never engaging in risky drinking (No prior AUD OR 1.05, 95% CI 1.01-1.10; Prior AUD OR 1.18, 95% CI 1.01-1.38) and having consumed no drugs (other than alcohol) in the past month [No prior drug use disorder (DUD) OR 1.16, 95% CI 1.12-1.19; Prior DUD OR 1.40, 95% CI 1.26-1.56]. Drinking ayahuasca with an ayahuasca church was also strongly associated lower alcohol and drug use other than rarely/never engaging in risky drinking for people with a prior AUD, where there was no significant association.

A higher rated subjective mystical experience, measured via the PEQ-S, was associated with 11% (OR 1.11, 95% CI 1.04-1.18) and 28% (OR 1.28, 95% CI 1.03-1.59) increases in the odds of no recent drug use for those with and without a prior drug use disorder respectively. However, the second spiritual experience measure, SIMO score, had a marginal negative association with rarely/never engaging in

risky drinking (OR 0.99, 95% CI 0.99-1.00) for people with no prior AUD, and having no recent drug use (OR 0.99, 95% CI 0.99-1.00) for people with no prior DUD. A modest negative association was also identified for integration difficulties and no recent drug use for those with a prior DUD (OR 0.90, 95% CI 0.83-0.98), as well as weak negative associations between experiencing extreme fear and never/rarely drinking alcohol for those with no prior AUD (OR 0.98, 95% CI 0.96-1.00), and the number of years since ayahuasca was last consumed and rarely/never engaging in risky drinking for people with no prior AUD (OR 0.97, 95% CI 0.95-1.00). By contrast, each additional year since ayahuasca was last consumed was associated with 12% increase in the odds of no recent drug use for people with a prior DUD (OR 1.12, 95% CI 1.02-1.24).

Models investigating the odds of recent use of specific drugs (for those with lifetime use) are presented in Table 3. Again, the most consistent association between ayahuasca drinking variables and current drug use was for the number of times ayahuasca had been consumed, with this association present for 7 out of the 11 drugs for which data was available. Each additional category of lifetime ayahuasca consumption was associated with a reduction in the odds of recent use of 10-19% for these drugs, with the strongest association present for cocaine (OR 0.81, 95% CI 0.74-0.89). Of the four drugs where this association was not present, recent use of one, non-medical use of tranquilisers, was negatively associated with the PEQ-S (OR 0.86, 95% CI 0.75-1.00) and number of self-insights attained (OR 0.89, 95% CI 0.83-0.97). The PEQ-S and self-insights were also negatively associated with recent use of cannabis (OR 0.92, 95% CI 0.86-0.97) and cocaine respectively (OR 0.92, 95% CI 0.85-0.99). However, number of self-insights was associated with a slight increase in the odds of recent cannabis use (OR 1.03, 95% CI 1.00-1.07). Our other spirituality measure, SIMO score, also marginally increased (by 1%) the odds of recent cannabis (OR 1.01, 95% CI 1.01-1.01) and LSD (OR 1.01, 95% CI 1.00-1.02) use.

Significant negative associations were present for drinking with an ayahuasca church and recent use of five of 11 individual drugs. Experiencing extreme fear was associated with slightly reduced odds of recent cannabis (OR 0.97, 95% CI 0.95-0.99) and LSD use (OR 0.95, 95% CI 0.92-0.99), while there were no significant associations with integration difficulties, or drinking ayahuasca with a strong community of people and recent use of any individual drugs. As with the previous models there was little apparent time effect (years since drunk) other than a modest negative association with recent magic mushroom use (OR 0.94, 95% CI 0.90-1.00).

-----TABLE 3 ABOUT HERE-----

We undertook further analysis of the associations between the number of times ayahuasca had been consumed and recent use of individual drugs by prior DUD status, adjusting for age, sex and drinking with an ayahuasca church (See Table S1). This revealed stronger negative associations between times consumed and current drug use for people with, compared to those without, a prior DUD, for all of the seven drugs for which this was significant for the whole sample, other than magic mushrooms (not significant for either group), and novel psychoactive substances, which was significantly negatively associated for the prior DUD group only (OR 0.57, 95% CI 0.39-0.83).

Discussion

In the context of both expanding naturalistic use and academic research interest in the therapeutic use of ayahuasca, our dataset of 8629 ayahuasca drinkers from more than 40 countries provides a unique opportunity to investigate associations between ayahuasca consumption in naturalistic settings and the use of alcohol and other drugs. We identified a strong positive association between the consumption of ayahuasca and the likelihood of never or rarely drinking alcohol, never or rarely engaging in risky drinking (>4 standard drinks on one occasion) and having not consumed a range of drugs in the past month. Multivariate models revealed the number of times ayahuasca was consumed to be consistently and strongly associated with low or no current consumption of alcohol and drugs.

A further notable aspect of our results is to highlight associations between aspects of the acute ayahuasca experience and current alcohol and drug use. The role of the subjective spiritual experience has been well documented in other research with classic psychedelics. Here the PEQ-S was associated with substantial increases in the odds of lower alcohol consumption and no recent use of any drug use for those with a prior AUD or DUD respectively [1]. We also identify modest associations between the number of self-insights attained and current drug and alcohol use. This concept has been noted by other authors in the form of experiences that enable participants to identify negative thought patterns related to their addiction, provide understanding of the origins and dynamics of their addiction, and contribute to the healing of traumas that underlie many addictive disorders [42,57-59]. The contextual factor of drinking ayahuasca with an ayahuasca church was found to be strongly associated with lower current alcohol and drug use. Interestingly there was little evidence of a diminishing of the association between ayahuasca drinking variables and alcohol and other drug use over time (which for some respondents had been several years).

Our findings suggesting anti-substance use effects are consistent with those reported in several smaller studies. Analysis of outcomes for 36 patients at the Takiwasi (therapeutic community) drug

treatment centre in Peru which uses ayahuasca along with other traditional plants, identified significant decreases in addiction severity outcomes for drug and alcohol use, as well as reduced emotional distress and enhanced wellbeing [60]. Similarly, an observational study of First Nations young people in Canada provided with ayahuasca-assisted treatment for problematic substance use reported psychological and wellbeing benefits as well as reductions in tobacco, alcohol and cocaine use at 6 months [30]. A global survey of drug users, including 527 ayahuasca drinkers, found this group to have lower problematic alcohol consumption than other psychedelic users, but not non-psychedelic users, however heterogeneity of groups was noted [61]. A number of studies have also reported lower rates of alcohol and other drug use among members of ayahuasca churches in Brazil, when compared to a comparison group or the Brazilian population, with these effects visible even among samples with a higher lifetime incidence of illicit drug use or dependence [21,22,62,63]. However, it is unclear to what extent these outcomes are related to ayahuasca consumption per se vs broader group membership and social connection benefits [44]. Ours is the first study to investigate these effects separately and shows that ayahuasca drinking variables remain robustly associated with reduced alcohol and drug use after adjusting for ayahuasca church and community membership.

Strengths of this study include the large sample and cross-cultural sampling frame, however several limitations are also important to note. In particular, the non-random, self-selected sample, which risks bias towards respondents who have had a positive experience with ayahuasca and are motivated to spend time completing a survey, versus those with negative or neutral experiences that may prefer non-involvement. All data collected was self-reported, and several items involved retrospective assessments of things that may have occurred some time ago. The cross-sectional study design also means that we do not have data relating to historical alcohol and drug use to confirm apparent reductions in alcohol and other drug use. Around (29%) of respondents also did not complete the alcohol and drug sections of the survey and were excluded from the analysis. This group may differ from the included sample, resulting in further selection bias. We also note limitations in comparative data relating to prior diagnoses of alcohol and drug use disorders and other mental health conditions, which is likely to be influenced by mental health system capacity for Brazil in particular [64]. However, the high average education level of the Brazilian sample (higher than drinkers from all other regions), is likely to mitigate this effect. Finally, we note that multivariate models reported nominal p-values that were not adjusted for multiple-hypothesis testing [65,66].

In conclusion, this study identified a robust negative association between the consumption of ayahuasca and low current use of alcohol and other drugs for those with and without prior

substance use disorders, in a large cross-national sample of ayahuasca drinkers. We note several aspects of the ayahuasca drinking experience that appear to contribute to this association, and that these associations remain strong even after adjusting for ayahuasca church and community membership. The results add further support to the current academic interest in the potential use of classic psychedelics as agents for the treatment of addictive disorders, and provide important data to support the development of experimental treatment protocols for use in controlled clinical studies.

Acknowledgements

Thanks are extended to the survey participants. JS is supported by a National Health and Medical Research Council Clinical Research Fellowship (APP1125000). NLGC is supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) - Brazil (Finance Code 001 Research Fellowship 88887.466701/2019-00) and National Science and Technology Institute for Translational Medicine (INCT-TM Fapesp 2014/50891-1; CNPq 465458/2014-9).

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

NLGC is supported by CAPES Foundation from Brazilian Ministry of Education (Research Fellowship 88887.466701/2019-00) and JS is supported by a National Health and Medical Research Council Clinical (Fellowship APP1125000).

References

1. Reiff CM, Richman EE, Nemeroff CB, Carpenter LL, Widge AS, Rodriguez CI, et al. Psychedelics and Psychedelic-Assisted Psychotherapy. *Am J Psychiatry* 2020;175:391-410.
2. Jerome L, Feduccia AA, Wang JB, Hamilton S, Yazar-Klosinski B, Emerson A, et al. Long-term follow-up outcomes of MDMA-assisted psychotherapy for treatment of PTSD: a longitudinal pooled analysis of six phase 2 trials. *Psychopharmacology (Berl)* 2020;237:2485-97.
3. Agin-Liebes GI, Malone T, Yalch MM, Mennenga SE, Ponté KL, Guss J, et al. Long-term follow-up of psilocybin-assisted psychotherapy for psychiatric and existential distress in patients with life-threatening cancer. *J Psychopharmacol* 2020;34:155-66.
4. Sessa B, Johnson MW. Can psychedelic compounds play a part in drug dependence therapy? *Br J Psychiatry* 2015;206:1-3.
5. Bogenschutz MP, Forcehimes AA. Development of a Psychotherapeutic Model for Psilocybin-Assisted Treatment of Alcoholism. *J Humanist Psychol* 2016;57:389-414.
6. Johnson MW, Garcia-Romeu A, Cosimano MP, Griffiths RR. Pilot study of the 5-HT_{2A}R agonist psilocybin in the treatment of tobacco addiction. *J Psychopharmacol* 2014;28:983-92.
7. Johnson MW, Garcia-Romeu A, Griffiths RR. Long-term follow-up of psilocybin-facilitated smoking cessation. *Am J Drug Alcohol Abuse* 2017;43:55-60.
8. Bogenschutz MP, Forcehimes AA, Pommy JA, Wilcox CE, Barbosa PCR, Strassman RJ. Psilocybin-assisted treatment for alcohol dependence: a proof-of-concept study. *J Psychopharmacol* 2015;29:289-99.
9. Krebs TS, Johansen P-Ø. Lysergic acid diethylamide (LSD) for alcoholism: meta-analysis of randomized controlled trials. *J Psychopharmacol* 2012;26:994-1002.
10. Fuentes JJ, Fonseca F, Elices M, Farré M, Torrens M. Therapeutic use of LSD in psychiatry: A systematic review of randomized-controlled clinical trials. *Front Psychiatry* 2020;10:943.
11. Sessa B, Sakal C, O'Brien S, Nutt D. First study of safety and tolerability of 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy in patients with alcohol use disorder: preliminary data on the first four participants. *BMJ Case Rep* 2019;12:e230109.
12. Nunes AA, Dos Santos RG, Osório FL, Sanches RF, Crippa JAS, Hallak JEC. Effects of ayahuasca and its alkaloids on drug dependence: A systematic literature review of quantitative studies in animals and humans. *J Psychoactive Drugs* 2016;48:195-205.
13. Tupper KW. The globalization of ayahuasca: harm reduction or benefit maximization? *Int J Drug Policy* 2008;19:297-303.
14. Trichter S. Ayahuasca beyond the amazon: the benefits and risks of a spreading tradition. *Journal of Transpersonal Psychology* 2010;42:131-48.
15. Tupper KW. Ayahuasca healing beyond the Amazon: the globalization of a traditional indigenous entheogenic practice. *Global Networks* 2009;9:117-36.
16. Kavenská V, Simonová H. Ayahuasca tourism: Participants in Shamanic rituals and their personality styles, motivation, benefits and risks. *J Psychoactive Drugs* 2015;47:351-9.
17. Henman AR. Ayahuasca use in a religious context: The case of the União do Vegetal in Brazil 2009. Available at: https://erowid.org/chemicals/ayahuasca/ayahuasca_article2.shtml.
18. Ference J. Balancing Discretion and Expansion in the União do Vegetal. *Journal of Undergraduate Research*. 2020;20.
19. Grob CS, McKenna DJ, Callaway JC, Brito GS, Neves ES, Oberlaender G, et al. Human psychopharmacology of hoasca, a plant hallucinogen used in ritual context in Brazil. *J Nerv Ment Dis* 1996;184:86-94.
20. Halpern JH, Sherwood AR, Passie T, Blackwell KC, Ruttenber AJ. Evidence of health and safety in American members of a religion who use a hallucinogenic sacrament. *Med Sci Monit* 2008;14:SR15-SR22.

21. Barbosa PCR, Tófoli LF, Bogenschutz MP, Hoy R, Berro LF, Marinho EAV, et al. Assessment of alcohol and tobacco use disorders among religious users of ayahuasca. *Front Psychiatry* 2018;9:136.
22. Fábregas JM, González D, Fondevila S, Cutchet M, Fernández X, Barbosa PCR, et al. Assessment of addiction severity among ritual users of ayahuasca. *Drug Alcohol Depend* 2010;111:257-61.
23. Bouso JC, González D, Fondevila S, Cutchet M, Fernández X, Ribeiro Barbosa PC, et al. Personality, psychopathology, life attitudes and neuropsychological performance among ritual users of ayahuasca: A longitudinal study. *PLoS One* 2012;7:e42421.
24. Barbosa PCR, Strassman RJ, da Silveira DX, Areco K, Hoy R, Pommy J, et al. Psychological and neuropsychological assessment of regular hoasca users. *Compr Psychiatry* 2016;71:95-105.
25. Bouso JC, Palhano-Fontes F, Rodríguez-Fornells A, Ribeiro S, Sanches R, Crippa JAS, et al. Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans. *Eur Neuropsychopharmacol* 2015;25:483-92.
26. Franquesa A, Sainz-Cort A, Gandy S, Soler J, Alcázar-Córcoles MÁ, Bouso JC. Psychological variables implied in the therapeutic effect of ayahuasca: A contextual approach. *Psychiatry Res* 2018;264:334-9.
27. Loizaga-Velder A, Verres R. Therapeutic effects of ritual ayahuasca use in the treatment of substance dependence—Qualitative results. *J Psychoactive Drugs* 2014;46:63-72.
28. Schmid JT, Jungaberle H, Verres R. Subjective theories about (self-)treatment with ayahuasca. *Anthropology of Consciousness* 2010;21:188-204.
29. Ross S. Serotonergic hallucinogens and emerging targets for addiction pharmacotherapies. *Psychiatr Clin North Am* 2012;35:357-74.
30. Thomas G, Lucas P, Capler NR, Tupper KW, Martin G. Ayahuasca-assisted therapy for addiction: results from a preliminary observational study in Canada. *Curr Drug Abuse Rev* 2013;6:30-42.
31. Shanon B. The antipodes of the mind : charting the phenomenology of the ayahuasca experience: Oxford University Press; 2002.
32. Giovannetti C, Garcia Arce S, Rush B, Mendive F. Pilot evaluation of a residential drug addiction treatment combining traditional amazonian medicine, ayahuasca and psychotherapy on depression and anxiety. *J Psychoactive Drugs* 2020;52:472-81.
33. Soler J, Elices M, Franquesa A, Barker S, Friedlander P, Feilding A, et al. Exploring the therapeutic potential of ayahuasca: acute intake increases mindfulness-related capacities. *Psychopharmacology (Berl)* 2016;233:823-9.
34. Joaquim S, Matilde E, Elisabeth D-C, Juan CP, Amanda F, Mayte N-G, et al. Four weekly ayahuasca sessions lead to increases in “acceptance” capacities: A comparison study with a standard 8-week mindfulness training program. *Front Pharmacol* 2018;9:224.
35. Higgins GA, Fletcher PJ. Therapeutic potential of 5-HT_{2C} receptor agonists for addictive disorders. *ACS Chem Neurosci* 2015;6:1071-88.
36. Bogenschutz MP, Johnson MW. Classic hallucinogens in the treatment of addictions. *Prog Neuropsychopharmacol Biol Psychiatry* 2016;64:250-8.
37. Canal CE. Serotonergic psychedelics: Experimental approaches for assessing mechanisms of action. *Handb Exp Pharmacol* 2018;252:227-60.
38. Ly C, Greb AC, Cameron LP, Wong JM, Barragan EV, Wilson PC, et al. Psychedelics promote structural and functional neural plasticity. *Cell Reports* 2018;23:3170-82.
39. Owaisat S, Raffa RB, Rawls SM. In vivo comparison of harmine efficacy against psychostimulants: Preferential inhibition of the cocaine response through a glutamatergic mechanism. *Neurosci Lett* 2012;525:12-6.
40. Brierley DI, Davidson C. Developments in harmine pharmacology - Implications for ayahuasca use and drug-dependence treatment. *Prog Neuropsychopharmacol Biol Psychiatry* 2012;39:263-72.
41. Aricioglu-Kartal F, Kayir H, Tayfun Uzbay I. Effects of harman and harmine on naloxone-precipitated withdrawal syndrome in morphine-dependent rats. *Life Sciences* 2003;73:2363-71.

42. Liester MB, Prickett JI. Hypotheses regarding the mechanisms of ayahuasca in the treatment of addictions. *J Psychoactive Drugs* 2012;44:200-8.
43. Breeksema JJ, Niemeijer AR, Krediet E, Vermetten E, Schoevers RA. Psychedelic treatments for psychiatric disorders: A systematic review and thematic synthesis of patient experiences in qualitative studies. *CNS drugs* 2020;34:925-46.
44. Room R. Spirituality, intoxication and addiction: Six forms of relationship. *Subst Use Misuse* 2013;48:1109-13.
45. Hartogsohn I. Constructing drug effects: A history of set and setting. *Drug Science, Policy and Law*. 2017;3:2050324516683325.
46. Haijen ECHM, Kaelen M, Roseman L, Timmermann C, Kettner H, Russ S, et al. Predicting Responses to Psychedelics: A Prospective Study. *Front Pharmacol* 2018;9:897.
47. Griffiths R, Richards W, Johnson M, McCann U, Jesse R. Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *J Psychopharmacol* 2008;22:621-32.
48. Griffiths RR, Johnson MW, Richards WA, Richards BD, Jesse R, MacLean KA, et al. Psilocybin-occasioned mystical-type experience in combination with meditation and other spiritual practices produces enduring positive changes in psychological functioning and in trait measures of prosocial attitudes and behaviors. *J Psychopharmacol* 2018;32:49-69.
49. Barratt MJ, Ferris JA, Zahnow R, Palamar JJ, Maier LJ, Winstock AR. Moving on from representativeness: Testing the utility of the Global Drug Survey. *Subst Abuse* 2017;11:1178221817716391.
50. Garcia-Romeu A, Davis AK, Erowid F, Erowid E, Griffiths RR, Johnson MW. Cessation and reduction in alcohol consumption and misuse after psychedelic use. *J Psychopharmacol* 2019;33:1088-1101.
51. Davis AK, Barsuglia JP, Lancelotta R, Grant RM, Renn E. The epidemiology of 5-methoxy- N, N-dimethyltryptamine (5-MeO-DMT) use: Benefits, consequences, patterns of use, subjective effects, and reasons for consumption. *J Psychopharmacol* 2018;32:779-92.
52. Miller PG, Sønderlund AL. Using the internet to research hidden populations of illicit drug users: a review. *Addiction* 2010;105:1557-67.
53. Lucas P, Boyd S, Milloy MJ, Walsh Z. Reductions in alcohol use following medical cannabis initiation: results from a large cross-sectional survey of medical cannabis patients in Canada. *Int J Drug Policy* 2020;86:102963.
54. Griffiths R, Richards W, McCann U, Jesse R. Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology* 2006;187:268-83.
55. Francis LJLSH. A Short Index of Mystical Orientation (SIMO): A study among Roman Catholic priests. *Pastoral Psychol* 2004;53:49-51.
56. Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics* 2009;50:613-21.
57. Argento E, Capler R, Thomas G, Lucas P, Tupper KW. Exploring ayahuasca-assisted therapy for addiction: A qualitative analysis of preliminary findings among an Indigenous community in Canada. *Drug Alcohol Rev* 2019;38:781-9.
58. Fernández X, Fábregas JM. Experience of Treatment with Ayahuasca for Drug Addiction in the Brazilian Amazon. In: Labate BC, Cavnar C, editors. *The therapeutic use of ayahuasca*: Heidelberg: Springer, 2014.; 2014.
59. Perkins D, Sarris J. Ayahuasca and Childhood Trauma: Potential Therapeutic Applications. In: Labate BC, Cavnar C, editors. *Ayahuasca Healing & Science*: Springer; 2021.
60. Berlowitz I, Walt H, Ghasarian C, Mendive F, Martin-Soelch C. Short-Term Treatment Effects of a Substance Use Disorder Therapy Involving Traditional Amazonian Medicine. *J Psychoactive Drugs* 2019;51:323-34.
61. Lawn W, Hallak JE, Crippa JA, Dos Santos R, Porffy L, Barratt MJ, et al. Well-being, problematic alcohol consumption and acute subjective drug effects in past-year ayahuasca users: a large, international, self-selecting online survey. *Sci Rep* 2017;7:15201.

62. Doering-Silveira E, Grob CS, de Rios MD, Lopez E, Alonso LK, Tacla C, et al. Report on psychoactive drug use among adolescents using ayahuasca within a religious context. *J Psychoactive Drugs* 2005;37:141-4.
63. Halpern JH, Sherwood AR, Passie T, Blackwell KC, Ruttenber AJ. Evidence of health and safety in American members of a religion who use a hallucinogenic sacrament. *Med Sci Monit* 2008;14:15-22.
64. WHO. Geneva: World Health Organisation; 2019. Available at: <https://apps.who.int/gho/data/view.main.HWF11v>.
65. Althouse AD. Adjust for multiple comparisons? It's not that simple. *Ann Thorac Surg* 2016;101:1644-5.
66. Eggenberger P, Bürgisser M, Rossi RM, Annaheim S. Body Temperature Is Associated With Cognitive Performance in Older Adults With and Without Mild Cognitive Impairment: A Cross-sectional Analysis. *Front Aging Neurosci* 2021;13:585904s.

Table 1. Sample characteristics and alcohol and drug use variables by context of use^{a,b}

	Non-ayahuasca church ^c	Ayahuasca church	Statistical test
	% (n)	% (n)	
<i>Sex</i>	(4351)	(3955)	$\chi^2=0.1$ $P=0.000$
Female	47.3	47.0	
Male	52.7	53.0	
<i>Age^d</i>	(4346)	(3935)	$T(8279)=-0.5$ $P=0.596$
Mean age (SD)	40.6 (11.5)	40.7 (12.9)	
<i>University education</i>	(4358)	(3959)	$\chi^2=1.2$ $P=0.281$
Yes	63.2	64.3	
<i>Region of residence</i>	(4091)	(3954)	$\chi^2=3.8e+03$ $P=0.000$
Brazil	15.6	84.1	
Other Latin America	9.8	0.5	
Europe	42.2	7.1	
North America	23.6	7.5	
Australia and New Zealand	7.5	0.7	
Asia and Middle East	1.3	0.1	
<i>Lifetime mental health diagnosis</i>	(4248)	(3822)	$\chi^2=112.2$ $P=0.000$
Any	42.7	31.2	
Number (SD) ^d	0.9 (1.3)	0.5 (0.9)	$T(7,3456)=39.9$; $P=0.000$
<i>Times drunk ayahuasca (lifetime)</i>	(4326)	(3653)	$\chi^2=4.0e+03$ $P=0.000$
1	12.4	1.8	
2-3	19.8	2.6	
4-5	14.6	1.5	
6-10	16.1	3.1	
11-20	12.8	3.8	
21-50	12.3	9.6	
51-100	5.9	10.8	
101-200	2.9	12.0	
201-500	2.0	27.7	
500-5000	1.3	27.3	
<i>Any past month drug use</i>	(3897)	(3450)	$\chi^2=1.2e+03$ $P=0.000$
Yes	38.2	9.6	
<i>Lifetime number of different drugs used</i>	(3897)	(3450)	$T(7,3456)=39.9$ $P=0.000$
Mean number (SD) ^d	4.4 (2.9)	1.9 (2.3)	
<i>Alcohol consumption (any)</i>	(3904)	(3455)	$\chi^2=2.4e+03$ $P=.000$
Every day	2.3	0.2	
5 or 6 days per week	3.4	0.6	
3 or 4 days per week	7.9	1.5	
1 or 2 days per week	16.1	3.5	
2 or 3 days per month	12.9	3.2	
Rarely	35.4	12.7	
Never	22.2	78.5	
<i>Alcohol consumption (>4 standard drinks – among alcohol drinkers only)</i>	(2991)	(718)	$\chi^2=23.7$ $P=.000$
At least twice a week	8.86	6.27	
Once a week	8.63	6.82	
2 or 3 times a month	11.13	7.38	
About once a month	12.67	11.84	
Less than monthly	34.34	38.02	
Never	24.37	29.67	
<i>Prior alcohol use disorder</i>	(3978)	(3216)	$\chi^2=5.3$ $P=0.021$
Yes	9.6	11.2	

<i>Prior drug use disorder</i>	(3978)	(3620)	$\chi^2=0.45$ $P=0.500$
Yes	10.4	9.9	

^a Percentages may not sum to 100.0% due to rounding; ^b “(n)” indicates valid (non-missing) sample for each item; ^c ‘non-ayahuasca church’ includes traditional, non-traditional, mixed and other contexts ^d Independent sample T-test.

Table 2. Associations between demographic and ayahuasca drinking variables and low/no recent alcohol and drug use (bivariate logistic regression models)

Dependent variable	Consumes any alcohol ^a				Risky drinking (alcohol drinkers only) ^b				Drug consumption in last month (among those with any lifetime use) ^c			
Coding	1=never/rarely, 0=more than rarely				1=never/rarely, 0=more than rarely				1=none, 0=at least once			
Group	No prior AUD (n=6821)		Prior AUD (n=721)		No prior AUD (n=3528)		Prior AUD (n=283)		No prior DUD (n=6813)		Prior DUD (n=711)	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Covariates												
Age (decades)	0.91 (0.86; 0.96)	0.001	0.91 (0.76; 1.1)	0.338	1.24 (1.16; 1.33)	0.000	1.1 (0.84; 1.44)	0.489	1.13 (1.07; 1.19)	0.000	1.03 (0.85; 1.25)	0.752
Female	1.41 (1.25; 1.60)	0.000	1.27 (0.84; 1.91)	0.251	1.54 (1.33; 1.77)	0.000	1.75 (1.03; 2.97)	0.038	1.33 (1.17; 1.5)	0.000	1.43 (0.95; 2.14)	0.086
University education	0.67 (0.59; 0.76)	0.000	0.66 (0.45; 0.99)	0.042	0.95 (0.82; 1.1)	0.504	1.24 (0.73; 2.12)	0.430	1.22 (1.08; 1.38)	0.002	0.93 (0.64; 1.36)	0.721
Lifetime MH diagnoses ^d	1.11 (1.04; 1.18)	0.001	0.98 (0.86; 1.12)	0.740	1.02 (0.95; 1.09)	0.542	1 (0.85; 1.19)	0.963	0.95 (0.89; 1)	0.056	0.88 (0.77; 1.00)	0.057
Ayahuasca drinking												
Number of times drunk ^e	1.26 (1.22; 1.30)	0.000	1.36 (1.22; 1.51)	0.000	1.05 (1.01; 1.10)	0.010	1.18 (1.01; 1.38)	0.038	1.16 (1.12; 1.19)	0.000	1.40 (1.26; 1.56)	0.000
Ayahuasca church ^f	3.04 (2.53; 3.64)	0.000	2.81 (1.64; 4.81)	0.000	1.26 (1.03; 1.54)	0.023	0.87 (0.43; 1.78)	0.709	2.81 (2.38; 3.33)	0.000	2.35 (1.47; 3.76)	0.000
Ayahuasca community ^g	1.01 (0.95; 1.08)	0.736	1.03 (0.83; 1.27)	0.801	1.04 (0.96; 1.11)	0.330	1.16 (0.87; 1.54)	0.322	0.98 (0.92; 1.05)	0.635	1.08 (0.86; 1.34)	0.516
SIMO total	1.00 (0.99; 1.00)	0.402	1.00 (0.99; 1.02)	0.816	0.99 (0.99; 1.00)	0.023	1.00 (0.98; 1.02)	0.672	0.99 (0.99; 1.00)	0.000	1.00 (0.99; 1.01)	0.942
PEQ-S	1.00 (0.94; 1.06)	0.958	1.20 (0.97; 1.49)	0.088	1.01 (0.95; 1.09)	0.699	1.34 (0.98; 1.84)	0.066	1.11 (1.04; 1.18)	0.001	1.28 (1.03; 1.59)	0.027
Self-insights	1.05 (1.01; 1.08)	0.004	1.04 (0.94; 1.16)	0.459	1.03 (0.99; 1.07)	0.124	1.18 (1.00; 1.39)	0.044	0.97 (0.94; 1.00)	0.055	1.06 (0.95; 1.19)	0.280
Extreme fear	0.98 (0.96; 1.00)	0.032	0.94 (0.89; 1.01)	0.075	1.00 (0.98; 1.03)	0.783	0.99 (0.91; 1.07)	0.821	1.01 (0.99; 1.03)	0.216	1.02 (0.96; 1.09)	0.487
Years since drunk ^h	0.99 (0.97; 1.01)	0.389	1.07 (0.96; 1.19)	0.236	0.97 (0.95; 1.00)	0.031	1.19 (1.00; 1.41)	0.053	0.99 (0.98; 1.01)	0.520	1.12 (1.02; 1.24)	0.017
Integration difficulties	0.98 (0.95; 1.01)	0.222	0.97 (0.89; 1.06)	0.495	0.98 (0.95; 1.01)	0.237	1.05 (0.94; 1.18)	0.346	0.97 (0.94; 1.00)	0.051	0.90 (0.83; 0.98)	0.013

^a Rarely/never = once a month or less ; ^b Rarely = less than monthly; ^c includes the 11 drugs listed in Table 3, plus heroin, ^d Number of lifetime mental health diagnoses; ^f lifetime uses of ayahuasca (categories as per Table 1); ^f last drank with an ayahuasca church; ^g drink ayahuasca with a close community; ^h number of years since last drank ayahuasca. CI, confidence interval; OR, odds ratio.

Table 3. Odds (95% confidence interval) of recent drug use by drug¹ (among those with lifetime use) (logistic regression models)

Dependent variable (N with lifetime use) (1=recent use, 0=no recent use)	Cannabis (5622)	Cocaine (3052)	Meth/speed (1503)	Ecstasy (2975)	LSD (3205)	Magic mushrooms (3402)	Non-med tranquilisers (1339)	Non-med opiates (631)	Opium (767)	Ketamine (946)	NPS (597)
(% of total sample/% of lifetime users with recent use)	(75.0/28.4)	(41.5/2.6)	(20.6/1.6)	(40.5/4.3)	(43.6/4.7)	(46.5/6.6)	(18.3/3.2)	(8.7/1.3)	(10.6/1.3)	(13.1/1.6)	(8.2/0.6)
Covariates											
Age (decades)	0.88* (0.84; 0.93)	0.68* (0.58; 0.80)	0.62* (0.50; 0.77)	0.77* (0.68; 0.88)	0.69* (0.61; 0.78)	0.88** (0.80; 0.96)	0.98 (0.85; 1.13)	0.77 (0.50; 1.18)	0.94 (0.75; 1.18)	0.66** (0.51; 0.85)	1.09 (0.79; 1.5)
Female	0.78* (0.69; 0.88)	0.71*** (0.52; 0.97)	0.77 (0.51; 1.15)	0.74*** (0.58; 0.95)	0.66** (0.52; 0.85)	0.81*** (0.66; 1.00)	1.06 (0.78; 1.44)	0.24*** (0.08; 0.75)	0.78 (0.48; 1.28)	0.88 (0.57; 1.35)	0.44*** (0.20; 1.00)
University education	0.83** (0.74; 0.94)	0.87 (0.64; 1.18)	1.23 (0.81; 1.85)	0.93 (0.73; 1.20)	1.11 (0.87; 1.42)	0.84 (0.69; 1.03)	0.98 (0.72; 1.34)	1.43 (0.59; 3.49)	1.06 (0.66; 1.69)	1.52 (0.96; 2.41)	0.79 (0.41; 1.53)
Lifetime MH diagnoses^a	1.05*** (1.00; 1.00)	1.03 (0.92; 1.15)	1.15*** (1.02; 1.30)	0.96 (0.87; 1.06)	0.89*** (0.81; 0.98)	1.04 (0.96; 1.12)	1.05 (0.95; 1.16)	1.24 (0.97; 1.57)	1.21** (1.05; 1.38)	1.05 (0.90; 1.22)	1.16 (0.95; 1.42)
Ayahuasca drinking											
Number of lifetime uses^b	0.86* (0.83; 0.89)	0.81* (0.74; 0.89)	0.89*** (0.79; 1.00)	0.84* (0.78; 0.91)	0.86* (0.80; 0.92)	0.90* (0.85; 0.95)	1.02 (0.94; 1.11)	0.92 (0.73; 1.16)	0.89 (0.78; 1.02)	0.83** (0.73; 0.94)	0.85 (0.70; 1.05)
Ayahuasca church^c	0.42* (0.35; 0.49)	0.58*** (0.34; 0.98)	0.59 (0.3; 1.16)	0.58** (0.38; 0.87)	0.43* (0.29; 0.64)	0.40* (0.28; 0.58)	0.92 (0.60; 1.41)	1.20 (0.35; 4.17)	0.49 (0.18; 1.30)	0.55 (0.24; 1.28)	0.85 (0.26; 2.79)
Ayahuasca community^d	1.00 (0.94; 1.06)	0.94 (0.80; 1.09)	0.85 (0.70; 1.05)	1.08 (0.95; 1.23)	1.01 (0.89; 1.14)	1.04 (0.94; 1.16)	0.96 (0.82; 1.13)	1.16 (0.73; 1.85)	0.96 (0.76; 1.20)	1.13 (0.91; 1.39)	1.00 (0.71; 1.41)
SIMO total	1.01* (1.01; 1.01)	1.00 (0.99; 1.01)	1.01 (1; 1.02)	1.00 (0.99; 1.00)	1.01*** (1.00; 1.02)	1.00 (1.00; 1.01)	1.00 (0.99; 1.01)	0.95 (0.64; 1.41)	1.01 (0.79; 1.29)	1.03 (0.84; 1.26)	0.99 (0.97; 1.01)
PEQ-S	0.92** (0.86; 0.97)	0.97 (0.84; 1.12)	0.85 (0.71; 1.01)	0.92 (0.82; 1.04)	0.91 (0.81; 1.03)	1.05 (0.94; 1.16)	0.86*** (0.75; 1.00)	0.99 (0.96; 1.02)	0.99 (0.98; 1.01)	0.99 (0.98; 1.01)	0.76 (0.56; 1.02)
Insights - self	1.03*** (1.00; 1.07)	0.92*** (0.85; 0.99)	0.91 (0.82; 1.01)	0.95 (0.89; 1.02)	0.99 (0.93; 1.05)	1.06 (1.00; 1.11)	0.89** (0.83; 0.97)	0.85 (0.69; 1.05)	0.98 (0.87; 1.1)	0.94 (0.85; 1.05)	1.01 (0.85; 1.19)
Extreme fear	0.97** (0.95; 0.99)	1.00 (0.95; 1.05)	0.97 (0.91; 1.03)	0.99 (0.95; 1.03)	0.95*** (0.92; 0.99)	0.98 (0.95; 1.01)	1.02 (0.97; 1.07)	1.00 (0.87; 1.14)	1.05 (0.98; 1.12)	0.99 (0.93; 1.06)	1.06 (0.95; 1.17)
Years since drunk^e	1.00 (0.98; 1.02)	1.01 (0.96; 1.07)	0.96 (0.87; 1.06)	0.98 (0.93; 1.04)	0.98 (0.93; 1.03)	0.94*** (0.90; 1.00)	1.02 (0.99; 1.06)	0.66 (0.41; 1.08)	0.93 (0.83; 1.03)	1.05 (0.97; 1.14)	1.03 (0.93; 1.14)
Integration difficulties^f	1.03 (1.00; 1.06)	1.03 (0.95; 1.10)	1.04 (0.95; 1.13)	1.01 (0.95; 1.06)	1.03 (0.97; 1.08)	1.01 (0.97; 1.06)	0.99 (0.93; 1.06)	1.17 (0.99; 1.38)	0.94 (0.84; 1.05)	0.93 (0.84; 1.04)	0.97 (0.83; 1.12)

* $P < 0.001$, ** $P < 0.01$, *** $P < 0.05$. ¹ Data was collected on heroin use but this model was not run as only 3 of 317 (0.95%) respondents with lifetime heroin use had used in the last month; ^a

number of lifetime mental health diagnoses; ^b lifetime uses of ayahuasca (categories as per Table 1); ^c last drank with an ayahuasca church; ^d drink ayahuasca with a close community; ^e

number of years since last drank ayahuasca, ^f number of integration difficulties. MH, mental health; NPS, new psychoactive substances; PEQ-S, Persisting Effects Questionnaire; SIMO, Short Index of Mystical Orientation.