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Research Paper

Ayahuasca use and reported effects on depression and anxiety symptoms: An international cross-sectional study of 11,912 consumers

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ABSTRACT

Background: Ayahuasca is a psychoactive Amazonian brew which has emerging data indicating that it has antidepressant and anxiolytic properties.

Methods: This paper uses data from the Global Ayahuasca Project (GAP), which was undertaken across 2017–2020 and involved 11912 people, to examine the perceived effects of Ayahuasca consumption on affective symptoms. The study focused on the subsample reporting depression or anxiety diagnoses at time of Ayahuasca consumption.

Results: Of participants reporting depression ($n = 1571$) or anxiety ($n = 1125$) at the time of consuming Ayahuasca, 78% reported that their depression was either 'very much' improved (46%), or 'completely resolved' (32%); while 70% of those with anxiety reported that their symptoms were 'very much' improved (54%), or 'completely resolved' (16%). A range of factors were associated with greater reported affective symptoms improvement, including subjective mystical experience, number of Ayahuasca sessions, and number of personal psychological insights experienced. 2.7% and 4.5% of drinkers with depression or anxiety, respectively, reported worsening of symptoms.

Limitations: This study is recognized as a cross-sectional analysis which cannot assess treatment efficacy. Selection bias may exist due to survey-respondents with favorable experience being potentially biased towards participation.

Conclusions: Drinkers of Ayahuasca in naturalistic settings perceived remarkable benefits for their affective symptoms in this survey assessment. There is no obvious evidence of negative mental health effects being associated with long-term consumption. Additional randomized controlled trial evidence is required to establish the efficacy of Ayahuasca in affective disorders, and to understand the worsened symptoms reported by a small percentage of drinkers.

Abbreviations: K-10, Kessler Psychological Distress Scale; SIMO, Short Index of Mystical Orientation; GAP, Global Ayahuasca Project; LSD, Lysergic acid diethylamide; DMT, N,N-Dimethyltryptamine; PEQ, Persisting Effects Questionnaire.

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1. Introduction

Ayahuasca is an Amazonian brew made primarily with *Psychotria viridis* (or *chakropanga* species) and *Banisteriopsis caapi* (Palhano-Fontes et al., 2014), which has had a central place in traditional healing for centuries among indigenous cultures in the Amazon Basin. From the 1930s the tea was adopted as a religious sacrament by a number of Brazilian syncretic religions – the Santo Daime, União do Vegetal (UDV) and Barquinha. Both the Santo Daime and the UDV have experienced rapid growth since the 1980s and are now present in in all major cities in Brazil as well as Europe, the United States, and Australia Tupper (2009). The last two decades has seen use expand further via a dramatic increase in the number of Westerners traveling to South America to participate in Ayahuasca rituals (Prayag et al., 2015); as well as indigenous styled neo-shamanic Ayahuasca ceremonies taking place in many countries including Australia, New Zealand, North America Tupper (2009), and Europe Horák and Verter (2019).

This psychedelic plant medicine has also been subject of increasing research interest, in particular examining its effects on mood and addiction (although exploration of the neurobiological effects is still in its relative infancy), including open-label and double-blind trials revealing antidepressant or anti-addictive effects (de Almeida et al., 2019; Dos Santos et al., 2011; Galvao et al., 2018; Nunes et al., 2016; Osorio Fde et al., 2015; Palhano-Fontes et al., 2017; Palhano-Fontes et al., 2019; Zeifman et al., 2019). For example, Ayahuasca has been assessed in a recent double-blind placebo-controlled trial for treatment-resistant depression (n = 28) compared to healthy controls (n = 45). In patients with depression, a significant reduction of C-reactive protein (CRP) levels occurred across time in both patients and controls treated with a single session of Ayahuasca (but not with placebo); with a significant correlation (rho = 0.57) between greater reductions of CRP and lower depressive symptoms (Galvão-Coelho, N.L. et al., 2020b).

The psychoactive compounds of Ayahuasca are regarded as N, N-Ditmethyltryptamine (DMT), which is present in *Psychotria viridis* or other related species, and three main β-carbolines (harmine, harmaline and tetrahydroharmine) which are found in *Banisteriopsis caapi*. These β-carbolines are reversible inhibitors of monoamine oxidase (MAOI), while the tetrahydroharmine is an inhibitor of serotonin reuptake (Palhano-Fontes et al., 2014). The MAOI function of β-carbolines inhibits N, N-DMT degradation in the gastrointestinal system allowing this substance to reach the brain, where it activates serotonergic pathways via 5HT 2A receptor interaction (Riba et al., 2003). Additionally, research has indicated that harmine could have a central role in Ayahuasca's anti-addictive effects, including reducing recidivism to alcohol, cocaine and methamphetamine (Aricioglu-Kartal et al., 2003; Brierley and Davidson, 2012; Owaisat et al., 2012).

To address a need for further research into the use of this psychoactive plant combination via a large sample, The Global Ayahuasca Project (GAP) was undertaken across 2017–2020, involving 11,912 people from across the world who had experience with Ayahuasca use across both traditional ethnobotanical, syncretic religious, and Western settings. GAP took a multi-disciplinary approach, aiming to inform drug and health policy relating to the consumption and regulation of Ayahuasca; to identify risks and impacts on health; and explore the transmission, modification, and adoption of traditional Ayahuasca practices globally.

One of the key outcomes explored within GAP was the use of Ayahuasca for the amelioration of depression and anxiety. Thus, the aim of this specific publication from GAP is to report retrospective cross-sectional data from participants reporting a depression or anxiety diagnosis at time of Ayahuasca consumption. Specifically, we assessed the degree of self-reported benefit (or worsening) that respondents experienced in their affective symptoms in response to Ayahuasca drinking, and whether sociodemographic or use variables (such as use context, degree of mystical experience, psychological adverse events), were related to these reported effects. We also investigated whether any negative mental health effects occurred in association with the consumption of the plant medicine.

2. Methods

2.1. Overview

A cross-sectional survey was implemented, utilizing online survey tools, with questions developed from the Ayahuasca research literature and drawn from a range of existing psychological scales and survey instruments. Extensive consultation was undertaken with both academic researchers and Ayahuasca practitioners (as individuals or part of Ayahuasca-using churches) during development. The survey was initially available in English and then translated into Brazilian Portuguese, Spanish, Czech, German, and Italian. The LimeSurvey survey system was used to develop the online survey, with an installation hosted by the University of Melbourne.

2.2. Assessments

A range of validated psychological assessment scales were employed, including the Kessler-10 (K-10) Psychological Distress Scale (used to measure affective symptoms, with a higher number indicating worse mental health) (Kessler et al., 2003), as well as other standardized assessments (not reported here). The degree of spiritual significance of ceremonies was reported using the spirituality component of the Persisting Effects Questionnaire (Griffiths et al., 2011) that involved a six-point scale (ranging from not at all significant to the single most spiritually significant experience of my life), and the Short Index of Mystical Orientation (adapted version; SIMO, used to assess perceived mystical experiences) with nine items rated on 1 to 10 scale where 1 was equal to "Not at all" and 10 "very much" Francis and Louden (2004). Internal consistency for the SIMO was acceptable (Cronbach's $\alpha = 0.85$). Patients were asked to identify whether they had been experiencing anxiety or depression (that had been diagnosed by a health professional), prior to drinking Ayahuasca on any occasion. A six level Patient Global Impression of Change measure (a patient-focused version of the Clinical Global Impressions Scale) Hurst and Bolton (2004) was used to identify any effects they believed their Ayahuasca drinking had on their symptoms. Possible responses were 'much worsened', 'a bit worsened', 'no change', 'a bit improved', 'much improved' or 'completely improved'.

Several customized questions were developed from the Ayahuasca literature. The 'number of insights', which was created based on a list of 15 commonly reported psychological, emotional, philosophical or spiritual insights, such as "Understanding patterns and dynamics in your intimate relationships" or "Increased sense of connection to the natural world", which are often reported by drinkers to be one of the most profound aspects of their experience Shanon (2002). The number of insights variable was assessed to be internally consistent (Cronbach's $\alpha = 0.80$). "Psychosocial difficulties" in the weeks or months after drinking Ayahuasca, was assessed via the Patient Health Questionnaire for Depression and Anxiety (PHQ-4) (Kroenke et al., 2009) plus five additionally created items, while a single item question was developed to measure the extent to which extreme fear or panic was experienced during the Ayahuasca session.

2.3. Recruitment and procedure

An online self-report methodology was employed to access a large sample size to capture a greater breadth of issues for extensive sub-group analysis. For note, this approach is particularly useful given the hidden nature of psychedelic-using populations in Western countries. Email invitations containing a weblink to participate in the research were distributed by Ayahuasca-related organizations, and via online forums and flyers at conferences and lectures. Web advertisements were also placed on Facebook. No financial incentives were provided for participation.

Data was cross-checked to remove suspected repeat responses, while data from incomplete surveys was still utilized. The study received ethics approval from Melbourne University Health Research Committee (HREC number 1545143.3). For the present publication, only participants who provided responses to the mental health sections of the questionnaire (specifically those related to prior diagnoses of mood or anxiety disorders) were included in the analysis.

2.4. Data analysis

Between-group comparisons of continuous measures were conducted with independent samples *t*-tests when data were approximately normally distributed, or Mann-Whitney U tests when data was not normally distributed. Categorical variables were compared using Chi-squared tests of independence. For correlations between continuous variables, Pearson's (r) and Spearman's (rho) correlations were used, where appropriate.

To assess the association between demographic and Ayahuasca drinking variables and reported effects on anxiety and depression symptoms; proportional odds models (appropriate for the analysis of Likert scale outcomes) were employed. Such models assume equal log-odds ratios across the *k*-thresholds (i.e., in our case, category 1 versus category 2,3,4 & 5; category 1 & 2 vs category 3,4 & 5 and so on) of the outcome for each predictor variable – allowing for one regression coefficient to be estimated for each predictor Ananth and Kleinbaum (1997). This assumption was assessed for each variable using the Brant test. For variables with marked deviation from this assumption of proportionality, they were included as nominal variables without ordering (i.e. odds ratios were estimated for each individual threshold). For these models, response categories 'much worsened' and 'a little worsened' were combined due to low counts. For analysis of continuous outcomes, such as total K10 score, a linear regression analysis was used. The association between categorical predictors and continuous outcomes was assessed using ANOVA models with post-hoc comparisons assessed using Tukey's honestly significant difference (HSD) procedure. All statistical analyses were performed using R (R Foundation, Austria) and STATA (StataCorp LP, College Station, Texas, USA).

3. Results

3.1. Participant characteristics

The total sample of respondents from over 50 countries of residence in GAP was 11,912 (52% male; mean age 40.8, SD 12.2). A total of 7785 (65%) provided responses to the mental health section of the questionnaire and were included in the present analysis. Participants who did not respond to the mental health section of the questionnaire did not materially differ in the distribution of sex, age, education, country of residence or number of total Ayahuasca doses to those who did complete this part of the survey (data not shown). Of the included respondents, 49% were living in Brazil, 25% in Europe, 16% North America, 5% Latin America (excluding Brazil), 4% Australia and New Zealand, and the remainder in Asia and the Middle East (or an unidentified location), which totaled approximately 5%. Participants were largely highly educated, with 87% having at least a post-high school diploma or university level education, and the majority (61%) identifying as being in a professional or managerial role. A total of 62% were married/partnered. For respondents whose last context of drinking was within the Ayahuasca churches - including UDV, Santo Daime and Barquinha or related ceremonies (84% of these were from Brazil) - the median number of Ayahuasca doses was 270 (interquartile range [IQR]: 480). Median lifetime use by respondents not associated with Ayahuasca churches was six doses (IQR: 17; Table S1 in supplementary material). The motivations for using Ayahuasca diverged between traditional Ayahuasca church drinkers and those in other contexts, with 26% of those in churches using the plant medicine to 'deal with emotional issues' and 9% for 'healing for mental illness', compared to 52% and 35%, respectively, for drinkers in other contexts. Further information on use context is contained in Table S1 (see supplementary material).

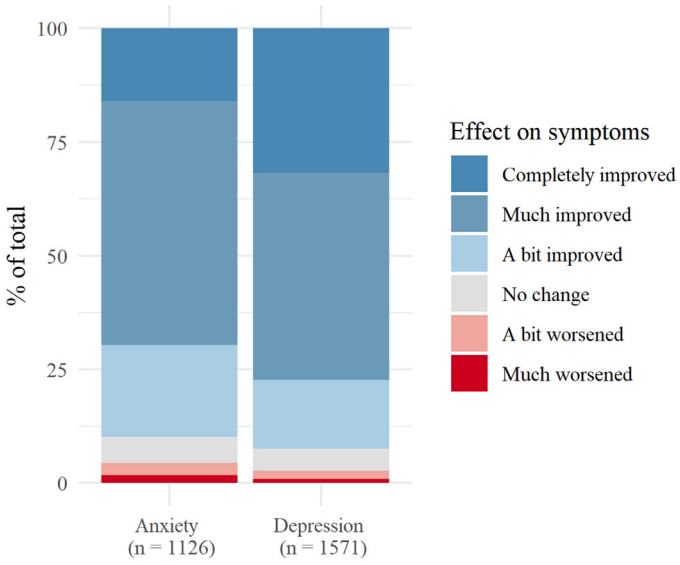

Fig. 1. Effect of Ayahuasca on anxiety and depression symptoms.

A total of 2,011 (17%) individuals identified as having had a depressive and/or an anxiety disorder (882 depression alone, 431 anxiety alone, and 698 both) diagnosed by a health professional at the time of drinking Ayahuasca (any occasion). Comparing the subsample with a prior diagnosis of anxiety and/or depression to those without such diagnoses revealed that the depression/anxiety subsample had a higher proportion of females (53.5%), relative to those without depression/anxiety (45.6%; X^2 [1, N=7735] = 37.2, $p < 0.001$). Furthermore, there were differences in marital status, with the proportion married or cohabiting lower in those who reported depression/anxiety (married/cohabitating in those with illness 44.8%, married/cohabiting in others 56.5%; X^2[4, $N = 7670$]= 81.5, $p < 0.001$). The median K10 score of the subsample identifying either depression or anxiety at time of Ayahuasca consumption was higher (median 14; IQR = 6), than others (median 12; IQR = 4, $p < 0.001$). The two subsamples did not substantially differ on other sociodemographic variables.

3.2. Affective symptoms and mental health outcomes

Of the participants reporting depression or anxiety at time of drinking Ayahuasca, 94% believed that their depression had improved either 'a bit' (15%), 'very much' (46%), or was 'completely resolved' (32%) due to their consumption of the brew. With respect to anxiety, this effect was even more pronounced, with 90% reporting an improvement in symptoms either 'a bit' (20%), 'very much' (54%), or 'completely improved/resolved' (16%); See Fig. 1. A small proportion of people with depression or anxiety reported a worsening of symptoms, which they attributed to Ayahuasca. Fifteen (1%) with depression, reported that their symptoms were 'much worsened', and 28 (1.8%) 'a bit worsened', with these numbers slightly higher among the anxiety group, 1.8% 'much worsened' ($n = 20$) and 2.7% ($n = 30$) 'a bit worsened'.

Consistent with participants self-reported benefits of Ayahuasca, those who reported a greater degree of benefit tended to have better mental health, assessed via the total K-10, at the time of survey completion (depression: rho: -0.52, $p < 0.001$; anxiety: rho: -0.51, $p < 0.001$; see Fig. 2). In addition, analysis of current mental health status based on K-10 categories adopted in previous studies (10–19 "likely to be well", 20–24 "likely to have a mild mental disorder", 25–29 "likely to have moderate mental disorder, and 30–50 "likely to have a severe mental

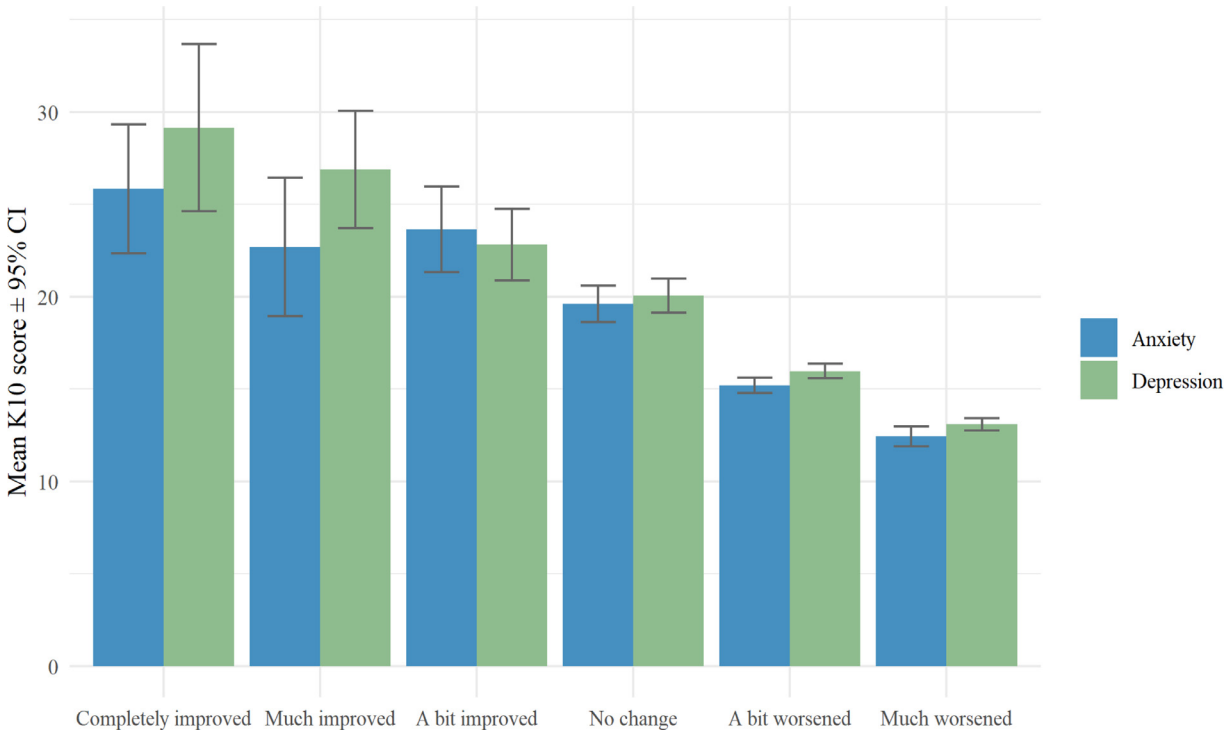

Fig. 2. Current mental health by self-reported effects of Ayahuasca drinking on depression and/or anxiety symptoms.

disorder") (Lee et al., 2008; Sopheab et al., 2020), revealed large differences in current mental health status corresponding to the self-reported level of improvement in depression and anxiety in response to drinking ($X^2[15, N = 1412] = 401.1$, $p < 0.001$ and $X^2[15, N = 1412] = 215.7$, $p < 0.001$, respectively; see Fig. 3). For those reporting complete improvement/resolution of their condition, 94.5% of the depression group and 95.2% of the anxiety group were classified as "likely to be well" at the survey date. Similarly, 82% (depression) and 86% (anxiety) of those reporting their condition "much improved" were considered "likely to be well" at the time of completing the survey (Fig. 3).

To explore the extent to which these changes may be reflecting the severity of mental health symptoms pre-Ayahuasca (i.e. people with the least severe conditions reporting the greatest improvement and better current mental health), we used the number of lifetime mental health diagnoses as a proxy for severity, and for both groups found that the small number of people reporting symptoms to be 'much worsened' had the highest mean number of lifetime mental health diagnoses. This difference in means was however not significant for the anxiety group $F(5,1120) = 1.88$, $p = 0.09$), but was borderline for the depression group ($F(5,1120)=2.23$, $p=0.05$), where those reporting complete improvement/resolution of their depression also had a lower mean number of lifetime mental health diagnoses than all other response categories (Table S2; see supplementary material). However, pairwise comparison of means using Tukey's HSD procedure identified no significant comparisons. Further analysis of differences in lifetime mental health diagnoses by whether respondents reported that they intended to drink Ayahuasca again or not (or were unsure) identified no differences for the depression $F(2,1556) = 0.01$, $p = 0.99$) or anxiety $F(2,1111) = 1.44$, $p = 0.23$) groups.

Bivariate associations between reported changes in anxiety and depression and Ayahuasca drinking variables and demographic variables are displayed in Table S3 (see supplementary material). Several differences were observed, the largest of which was a substantially greater likelihood of much improvement/complete resolution of anxiety or depression being identified by those reporting that their Ayahuasca experiences were in the top five or single most spiritually significant experience of their lives. Respondents with a higher number of uses were more likely to report improvement/resolution of their condition, as were members of Ayahuasca churches. For depression only, individuals who were under 35 or who were working fulltime were more likely to identify that their depression was completely resolved/improved.

3.3. Perceived mystical experience and mental health outcomes

Compared to the sample without an affective disorder at time of Ayahuasca consumption, the depression/anxiety subgroup reported a similar degree of mystical experience (as per total SIMO score) in their Ayahuasca use (mean = 70.1 ± 17.5 for depression/anxiety subgroup, mean = 68.6 ± 17.0 for others). The depression/anxiety subgroup, however, reported a greater number of total insights during the drinking experience (median = 11, IQR = 6) than others (median = 9, IQR = 6; $p < 0.001$). Greater mystical experience and a greater number of insights experienced during Ayahuasca drinking were each associated with better mental health at survey date for the affective disorders sample (assessed K10 total score), albeit somewhat weakly (r = -0.15, $p < 0.001$ and r = -0.071, $p < 0.001$, respectively). Interestingly, the degree of mystical experience was non-monotonically related to the reported effect of Ayahuasca on affective symptoms (see Fig. S1). Those who self-reported 'no change' in their symptoms of depression and/or anxiety in response to the plant medicine reported the least mystical experience, while those reporting complete improvement reported the greatest degree of mystical experience.

Table 1.

3.4. Use characteristics and mental health outcomes

For both the depression and anxiety groups a greater amount of lifetime Ayahuasca use was associated with lower average current K10 scores, with an average decrease of 0.57 points (95%CI: 0.73, 0.42) and 0.60 (95%CI: 0.72, 0.48) per increased consumption category for the anxiety and depression groups, respectively (See Figure S2). The lowest K10 score was in those in the highest use category

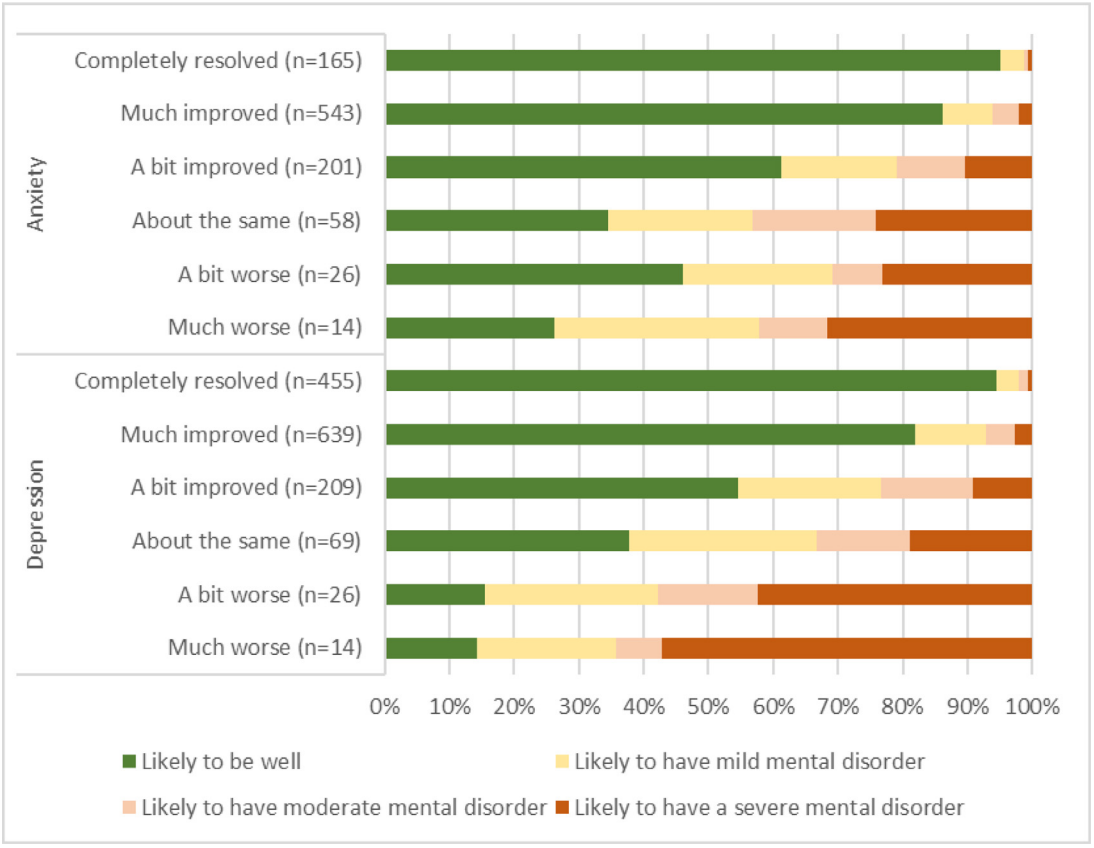

Fig. 3. Current mental health for Ayahuasca users by the degree of self-reported improvement in depression/anxiety symptoms.

(500–9999 uses; mean = 13.7, SD = 4.7 anxiety, and mean = 13.3, SD = 4.0 depression), while the highest K-10 score was in single-time drinkers for those with depression (mean = 18.9, SD = 7.8), and in those that had drunk 2–3 times for the anxiety group (mean = 19.5, SD = 8.5).

A partial proportional odds regression analysis (multivariable model) identified a group of demographic and Ayahuasca use variables which were significantly associated with reported effects on pre-existing depression and anxiety (Table 2). For the depression model, greater number of times Ayahuasca was drunk, greater mystical experience (as per total SIMO score), greater number of insights, greater degree of spiritual significance (assessed on the Persisting Effects Questionnaire [PEQ] spirituality subscale), as well as female sex were each associated with greater odds of a more highly beneficial response. Conversely, experiencing immense fear, panic or feeling they would die during the Ayahuasca experience, greater number of mental health difficulties in weeks after drinking, requiring support for mental health adverse events were each associated with lower odds of a more highly beneficial response, along with university education (see Table 2). In the case of requiring support for mental health adverse events, this variable was associated with substantially lower odds of greater response at all except the final threshold. A greater number of years since drinking was also associated with lower odds of reporting a more highly beneficial response, albeit quite weakly. Similar variables were predictors of reported change in anxiety symptoms (see Table 3). In contrast to the findings for depression, however, older age was associated with greater odds of a more highly beneficial response while unemployment/looking for work was associated with substantially lower odds of reporting greater benefit from drinking (see Table 3). For both depression and anxiety, drinking within an Ayahuasca church was not notably predictive of self-reported improvement in symptoms after controlling for demographic and other consumption factors.

A multiple linear regression model identified the same set of variables to be significantly associated with mental health status at survey date (measured via the K-10) for the people reporting depression ($F(13,1267)=26.4$, $p < 0.001$, $R^2 = .21$) or anxiety ($F(12,900)=20.3$, $p < 0.001$, $R^2 = .23$) at the time of drinking Ayahuasca (see Table S4; see supplementary material). For both groups, SIMO total score and self-rated spiritual significance on the PEQ spirituality subscale of their Ayahuasca experiences were negatively associated with a lower (less psychological distress) K-10 score, independently of the number of times the plant medicine was drunk, although number of times drunk was also predictive of a lower K-10 score, as was drinking within an Ayahuasca church and older age (depression only). Variables predictive of a higher K-10 score included the number of mental health/emotional difficulties experienced in the weeks after consumption, and experiencing extreme fear, panic or that they may die during the Ayahuasca session, for both groups, while time since last drinking was predictive for the anxiety group only, and requiring professional support for difficulties in weeks after drinking for depression only.

3.5. Safety

While not the specific focus of this paper (an in-depth safety analysis is being prepared separately), it is important to note that despite the overwhelmingly positive reports, there was a small minority of people with depression or anxiety who considered their condition worsened after taking Ayahuasca, 2.7% and 4.4%, respectively. In addition, difficulties with integration and assimilation of the experiences in the ensuing weeks were not uncommon. Among the depression/anxiety subgroup, experiences most commonly reported as increasing during the weeks/months following consumption were: feeling disconnected or alone (31.4% $n = 504$), feeling nervous, anxious or on edge (26.7% $n = 515$), and feeling down depressed or hopeless (25.1% $n = 482$). Of

Table 1
Sociodemographic characteristics of the sample.

Sex, n (%)	
Male, n (%)	4028 (52.1%)
Female	3684 (47.6%)
Age at survey date, mean (SD)	41.80 (12.2)
Highest level of education, n (%)	
None/primary	46 (0.6%)
Lower secondary/high school	943 (12.2%)
Vocational/diploma	1794 (23.2%)
Undergraduate degree	2315 (29.9%)
Post-graduate degree	2646 (34.2%)
Current occupation, n (%)	
Professionals	3430 (44.6%)
Managers	1255 (16.3%)
Community and personal service workers	863 (11.2%)
Technicians and trades workers	646 (8.4%)
Clerical and administrative workers	601 (7.8%)
Sales workers	423 (5.5%)
Other	480 (6.2%)
Marital or partnership status, n (%)	
Married/cohabiting	4100 (53.5%)
Single	2107 (27.5%)
Partnered, not living together	688 (9.0%)
Divorced or separated	710 (9.3%)
Region, n (%)	
Brazil	3693 (49.2%)
Europe	1852 (24.7%)
North America	1190 (15.9%)
Other Latin America	378 (5.0%)
Australia and New Zealand	327 (4.4%)
Asia and Middle East	59 (0.8%)

respondents who reported such events most indicated these were minor and transient, however, 267 (13.9%) reported seeking professional support (e.g. counsellor, psychiatrist, or traditional healer) to help deal with these effects.

4. Discussion

Currently there is a resurgence of interest by the public, clinicians, academics, and the media in the use of psychedelics in the treatment of psychiatric disorders, or for psychospiritual purposes (Chi and Gold, 2020; Dos Santos et al., 2018; Reiff et al., 2020; Schenberg, 2018). Due to this, it is of importance to capture the 'lived experience' of people consuming classical psychedelics such as Ayahuasca, which is often used within both traditional and non-traditional contexts. Although not designed to assess treatment efficacy, the present GAP data revealed a strong association between Ayahuasca use and self-reported benefits in affective symptoms. Further, we found a strong positive association between the level of subjective mystical experience (measured via both the PEQ spirituality subscale, and the total SIMO score), and perceived improvement of depression and anxiety outcomes, with both measures also being predictive of better current mental health on the K10, albeit marginally non-significantly for the depression group. The number of insights gleaned from the Ayahuasca ceremony was also positively associated with perceived improvement in symptoms, as well as being associated with better mental health at survey date.

These latter findings are consistent with previous research. A recent study reported a correlation between lower MADRS (Montgomery–Åsberg Depression Rating Scale) scores after Ayahuasca drinking and a higher score on the MEQ30 transcendence of time and space sub-scale, although interestingly no associations were evident on the other subscales ineffability, mystical, and positive mood (Palhano-Fontes et al., 2019). Further, a previous longitudinal survey assessment of 654 adults utilizing psychedelics for psychological well-being found that higher levels of "mystical-type experience" were associated with greater improvement in well-being in response to the treatments (Haijen et al., 2018). Finally, our results reflect a previous 2015-2016 online, self-selecting, global survey examining patterns of drug use, from which a sub-sample of 527 reported Ayahuasca use (Lawn et al., 2017). This data revealed that users reported an even greater level of wellbeing than both classic psychedelic users e.g. LSD or psilocybin (n = 18,138) and non-psychedelic drug-using respondents (n = 78,236).

A renewal of research is occurring across the range of classic psychedelics including psilocybin, and DMT (which is often consumed via traditional Ayahuasca preparations), lysergic acid diethylamide (LSD) and mescaline (Luoma et al., 2020). To highlight this, and place our GAP data within this context, our recent meta-analysis combined and evaluated data from 12 double-blind randomized controlled trials investigating the efficacy of classic serotonergic psychedelics (psilocybin, Ayahuasca and LSD) on mood state and depressive symptoms (between 3 hours and 60 days after administration). We observed highly significant moderate effect sizes for acute and long-term reduc-

Table 2
Proportional odds regression: Reported change in depression symptoms and demographic and Ayahuasca drinking variables.

	Proportional odds			Non-proportional odds[1]			
	OR	2.5%	97.5%	W vs NC, ALI, MI, CI	W, NC, vs ALI, MI, CI	W, NC, ALI vs MI, CI	W, NC, ALI, MI vs CI
Variables meeting proportional odds assumption				OR	OR	OR	OR
Female	1.27*	1.03	1.57				
Not working or looking for work	0.757	0.442	1.29				
Number of times drunk - grouped	1.16***	1.10	1.22				
University education	0.759*	0.610	0.944				
Lifetime mental health diagnoses	0.912*	0.836	0.995				
Ayahuasca church	0.867	0.645	1.16				
SIMO total score (per SD)	1.40***	1.22	1.60				
Number of insights	1.13***	1.09	1.17				
Spiritual significance	1.15*	1.03	1.30				
Time since last drink (years)	0.960*	0.926	1.00				
Drinking motivated by healing for mental health	1.03	0.812	1.31				
Immense fear, panic, or feeling that would die	0.955**	0.925	0.987				
Variables considered nominal							
Age (per SD)				1.30	0.971	1.09	0.816**
Requiring support for mental health adverse events				0.382*	0.406**	0.511**	0.978
No. mental health/emotional difficulties in weeks after				0.639***	0.800***	0.874***	0.877***

[1] W = worsened, NC = no change, ALI = a little improved, MI = much improved, CI = completely improved.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

Table 3
Partial proportional odds regression: Reported change in anxiety symptoms and demographic and Ayahuasca drinking variables.

	Proportional odds			Non-proportional odds[1]			
	OR	2.5%	97.5%	W vs NC, ALI, MI, CI	W, NC, vs ALI, MI, CI	W, NC, ALI vs MI, CI	W, NC, ALI, MI vs CI
Variables meeting proportional odds assumption				OR	OR	OR	OR
Age (per SD)	1.19*	1.02	1.39				
Female	1.09	0.842	1.40				
Not working or looking for work	0.415*	0.212	0.815				
Number of times drunk - grouped	1.13***	1.06	1.20				
University education	0.866	0.667	1.12				
Lifetime mental health diagnoses	1.01	0.914	1.12				
Ayahuasca church	0.949	0.687	1.31				
SIMO total score (per SD)	1.33***	1.13	1.56				
Spiritual significance	1.20**	1.05	1.38				
Number of insights	1.13***	1.08	1.18				
Time since last drink (years)	0.918**	0.865	0.969				
Drinking motivated by healing for mental health	1.24	0.935	1.65				
Immense fear, panic, or feeling that would die	0.971	0.934	1.01				
Variables considered nominal							
Requiring support for mental health adverse events				0.170***	0.263***	0.439***	1.05
No. mental health/emotional difficulties in weeks after				0.763***	0.907	0.898**	0.782***

[1] W = worsened, NC = no change, ALI = a little improved, MI = much improved, CI = completely improved.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

tions of negative mood, compared to placebo (Galvão-Coelho, N. et al., 2020a). For depressive symptoms, a large effect size was detected from a medium-term assessment, and a moderate effect size for both acute and long-term outcomes. This present GAP publication supports such findings by providing additional evidence of the self-reported effects of Ayahuasca, in a large sample and across a range of use contexts.

We found several contextual, demographic and Ayahuasca use factors to be strongly associated with the reported effects of its use on change in anxiety and depression symptoms. One such factor revealed that a greater amount of lifetime usage was strongly associated with improved anxiety and depression, with odds of a more highly beneficial response increasing by approximately 15% for each increased category of consumption. This is however acknowledged to potentially reflect reverse-causality as those who have a beneficial response may be more inclined to continue use. Women were found to report greater odds of greater benefit in depressive symptoms (which incidentally is more prevalent in females) although this did not extend to anxiety. A greater amount of time since last Ayahuasca use was similarly related to lower odds of experiencing a greater benefit from drinking, although the effect was relatively small (<10% decrease in odds per year since drinking). Finally, drinking within an Ayahuasca church was associated with greater improvement in depression and anxiety in bivariate analyses but did not have any marked effect on response after adjusting for other contextual and use variables. It can also be noted that those attending Ayahuasca churches will have the confounding element of significant community and social support in this context.

Strengths of this study include the large sample size and cross-cultural sampling frame. Regardless, several limitations are recognized. The first is that this study was not a prospective randomized controlled trial and was not designed to assess treatment efficacy. Our findings rather describe the patterns and self-reported benefits or hazards of the use of an emergent therapy and aim to identify and describe the variables which predict such response. Secondly, the assessment of the effects of Ayahuasca on mental health symptoms used a self-reported metric which relied on accurate recall by participants. Despite this, there was a strong association between reported benefits of the plant medicine on anxiety and depressive symptoms and mental health (K-10 score) at the survey date. As such, the self-reported degree of response was corroborated by mental health at survey date. Thirdly, as this is a cross-sectional survey, we do not have data on the severity of mental health symptoms before the intervention, and our proxy measure of number of lifetime mental health diagnoses may not be a completely satisfactory substitute. For this reason, there remains some doubt about the extent to which those with more or less severe symptoms may be receptive to beneficial effects. Another principal limitation concerns selection bias. The solicitation of survey respondents through non-random means (such as online forums) is likely to lead to the selection of a sample which is biased towards the reporting of positive effects of Ayahuasca, while those with minimal or negative effects may preference non-involvement. This selection bias is particularly acknowledged also in that it primarily involved Westernized people, with limited participation of traditional indigenous users of the plant medicine. A substantial minority of survey respondents (35%) also did not respond to the mental-health section of the survey and could not be included in the present analysis. Although this subsample of non-respondents did not substantially differ from responding participants in key sociodemographic or Ayahuasca use variables, they may have differed in other ways, such as mental health features, which we were not able to assess.

4.1. Conclusions

In conclusion, drinkers of Ayahuasca self-reported a marked perceived benefit for their affective symptoms in this survey analysis. This effect may also reflect potential benefits of a traditional healing model within naturalistic contexts. The apparent success of such practices raises interesting questions about potential therapeutic applications within a supportive psychological/medical care framework, and whether this may be able to further reduce adverse mental health effects occurring in a small percentage of drinkers who in particular may be unlikely to continue using the plant medicine. Therefore, our findings motivate further systematic research on Ayahuasca in controlled settings to examine its safety, tolerability, and efficacy in the treatment of affective symptoms in clinical populations.

Role of funding source

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.

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Author contributions

DP coordinated the study. DP, VS, JS, EO and LFT contributed to the design of the study. JS wrote the first draft of the manuscript, and JS and DP designed the data analysis which was conducted by LC and DP. Survey translations were undertaken by LFT, EO, JCB, MS, HA, HS, MH, and DP LFT, EO, JB, MS, HA, HS, MH contributed to the survey recruitment and promotion globally. All authors reviewed and edited the manuscript prior to publication.

Declaration of Competing Interest

The authors 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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Supplementary materials

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