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Subjective Effects of a Single Dose of Ayahuasca among College Students with Harmful Alcohol Use: Qualitative Analysis of Participant Accounts

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Abstract: Alcohol is the recreational drug most frequently consumed, and its high frequency of use can lead to worsening social, psychological, and domestic issues. The age group most susceptible to alcohol dependence is 18- to 24-year-old youths, demanding interventional tools to target early involvement risks. Ayahuasca seems to be a promising therapeutic tool since evidence suggests it presents potential for the treatment of depression, anxiety, and substance abuse, among other disorders. This study aimed to analyze subjective reports of university students with harmful alcohol use participating in a single-blind study evaluating the effects of one ayahuasca dose (1 mL/kg). Twenty-one days after ayahuasca administration, semi-structured interviews were conducted (n = 6) to identify peer psychological elements linked to its therapeutic potential. Subsequently, content analysis methodology was employed to define the main categories: Self-perception of experience, Positive Impacts (PI), Substances Use Pattern (SUP), Insights (I), Visual Effects, Transient Derealization, and Sleep Pattern. Among these, the most pertinent categories for this study were PI, SUP, and I, as, together, they suggest a potential link between insights and/or positive emotions and reduced alcohol consumption due to their internal transformation potential, which could be linked to a decrease in consumption.

Keywords: harmful alcohol use; ayahuasca; youth; university students; subjective reports

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1. Introduction

Ayahuasca is a botanical psychedelic/hallucinogen prepared by the prolonged decoction of macerated parts of the Banisteriopsis caapi vine together with the Psychotria viridis leaves [1,2]. *B. caapi* is abundant in harmine and tetrahydroharmine (THH), presenting small concentrations of other β-carbolines such as harmaline, harmol, and harmalol. *P. viridis* leaves are rich in N,N-dimethyltryptamine (DMT), a hallucinogenic tryptamine considered the main psychoactive substance in ayahuasca [2]. Harmine, THH, and harmaline are reversible inhibitors of the monoamine oxidase-A (MAO-A) enzyme, with THH also exhibiting selective serotonin reuptake inhibition activity [2]. DMT acts as an agonist to 5-HT2A/2C/1A serotonergic receptors, but when ingested orally, it does not have psychoactive effects due to its degradation by peripheral MAO-A. However, peripheral

inhibition of MAO-A by β-carbolines, especially harmine, allows DMT to reach the central nervous system (CNS) [2].

Ayahuasca is currently being investigated as a new pharmacological tool to treat mental health disorders. Preclinical and clinical studies indicate that ayahuasca has antidepressant and anxiolytic properties [3–5]. Furthermore, case reports and observational studies carried out around the world suggest beneficial effects on the harmful use of psychoactive substances, especially alcohol [6–8]. It should be noted that alcohol is the drug with the highest prevalence of frequent (11.7%) and heavy (6.7%) use in Brazil [9,10]. Around 23% of the Brazilian adult population has some type of problem (social, work-related, familiar, physical, legal, and related to violence) associated with alcohol use [10]. Consumption onset usually takes place during adolescence and youth [10], and 34.3% of adolescents are ingesting alcoholic beverages at least once a year [11]. The highest incidence of harmful alcohol use is present among young people, especially university students, comprising individuals aged 18 to 24 years old, followed by the 25- to 34-year-old group (4.1% and 4%, respectively) [10,11]. Moreover, males have greater lifetime use and dependence on alcohol than females in all age groups [10,11]. The high prevalence of alcohol consumption among young people highlights the need for new interventions.

Most of the research regarding hallucinogen use in psychological treatment is in the domain of psychiatry [12]. However, it also involves the field of psychology since the therapeutic result from the hallucinogenic experience also seems to rely on the subjective effects of these substances. Still, analysis of subjective reports from studies' volunteers is scarce. Regarding drug-related disorders, two studies explored the subjective reports of patients with alcohol use disorder that received psilocybin [13,14] and two others explored the reports of patients with tobacco use disorder that also received psilocybin [15,16]. Patients with alcohol use disorder reported lasting changes in their perceptions of themselves and in their relationship with alcohol, catharsis, forgiveness, and self-compassion [13,14]. Regarding studies related to smoking, volunteers reported feelings of gratitude, humility, and increased spirituality; vivid insights into self-identity; and experiences of interconnection, wonder, and curiosity [15,16]. However, there is no study that specifically investigates the effects of ayahuasca. Hence, the aim of this study was to evaluate the subjective reports through a semi-structured interview of university students with harmful alcohol use who received a single dose of ayahuasca in a single-blind trial. The interview aimed to understand the possible impacts of this experience on participants alcohol use patterns. The same questions were made to all participants to allow the identification of possible similarities between these reports and a generalization of the results.

2. Materials and Methods

2.1. Participants

The presented analysis was performed on six volunteers who participated in a single-blind trial assessing the effects of ayahuasca on alcohol consumption among university students. The sample size was based on previous literature with psilocybin [13–16]. The quantitative data collected in this trial will be published elsewhere. Here, only data regarding the subjective reports of participants will be considered. Volunteers were recruited through researchers' contacts, advertisements on the University of São Paulo campus in Ribeirão Preto, university parties, university digital portals, harm reduction collectives, and in the social media at Ribeirão Preto Medical School (FMRP-USP).

Inclusion criteria consisted of being an undergraduate student at a university, having harmful alcohol use assessed by the Alcohol Use Disorder Identification Test (AUDIT) (minimum score of 8 points) [17,18], and signing the informed consent form. Exclusion criteria were the presence of cardiovascular, hepatic, or neurological diseases; any psychiatric diagnosis (except alcohol-related disorder, with anxiety and depression disorders as comorbidities) assessed through the Structured Clinical Interview for DSM-V (SCID-V—clinical version); score above 1.8 on the Risk Detection Questionnaire for Serious Adverse Reactions to Hallucinogens (the Wave test [19], translated from the original in Spanish to Portuguese

by our group); pregnant or lactating women; previous experience (>2 lifetime uses) with ayahuasca (we did not restrict the use of other hallucinogens and other recreational drugs); and use of psychiatric medications (antidepressants, mood stabilizers, anxiolytics, and antipsychotics).

2.2. Drug

We administered a single oral dose of 1 mL/kg of ayahuasca containing 0.61 ± 0.22 mg/mL of DMT, 1.90 ± 0.57 mg/mL of harmine, 1.39 ± 0.78 mg/mL of THH, and 0.20 ± 0.07 mg/mL of harmaline. Ayahuasca was donated by the Centro de Regeneração Espiritual Casa de Jesus e Lar de Frei Manuel, which is a religious institution in Rondônia State, Brazil. Ayahuasca was stored at −20 °C, and alkaloid stability was analyzed over time using UPLC-ESI-MS/MS (for details on the methods, see Supplementary Materials). The dose of 1 mL/kg was chosen based on safety evidence from previous studies in our group [4,19]. Since volunteers had a mean weight of 73.2 kg, they ingested a mean ayahuasca dose of 73.2 mL, with a mean alkaloid dose of 44.6 mg DMT, 139.1 mg harmine, 101.7 mg THH, and 14.6 mg harmaline.

2.3. Procedure

Ayahuasca administration was carried out following a single-blind protocol, where volunteers were instructed that they could receive ayahuasca or a psychoactive placebo, but only researchers knew that all volunteers would receive ayahuasca. Ayahuasca was administered on the first day of the protocol, which had three weekly follow-ups (days 7, 14, and 21). As in our previous studies, we recommended abstinence from alcohol, tobacco, and caffeinated drinks 24 h before the experimental sessions. In addition, volunteers were instructed to fast before the session and not to ingest tyramine-containing foods/drinks 24 h before and 12 h after the experimental session to avoid possible interactions with the β-carbolines in ayahuasca, which are reversible inhibitors of the monoamine oxidase enzyme type A. We offered volunteers a standardized breakfast (crackers, cream cheese, butter, strawberry and guava jellies, and 300 mL of natural orange juice) before baseline measurements (around 7:30 AM). After breakfast, baseline measurements were collected. At around 8:00 AM (or around half an hour after breakfast), volunteers received ayahuasca.

It was suggested that volunteers wear comfortable clothes and avoid using cell phones/social media during the experimental sessions. Reading was allowed (volunteers could bring their own reading). Music and movies were not allowed, so the environment during the effects of ayahuasca was kept as quiet and neutral as possible. No specific psychotherapeutic intervention was used before, during, or after the experiments, as in our previous studies [4,20]. Our protocol included (1) the creation of trust with the volunteers before the experiment, (2) the use of a nondirective supportive approach during drug sessions, and (3) follow-up encounters from some days to weeks after the session. Before each session, volunteers were informed about the general effects of ayahuasca. During the sessions, simple instructions were given: "remain as quiet and introspective as possible, with your eyes opened or closed, while focusing on your body, thoughts, and emotions". In the days and weeks after the experimental session, volunteers freely described their experiences, but no specific integration technique was used. During the experimental session, volunteers remained seated in a comfortable reclining chair in a quiet, dimly lit room. Researchers stayed in a room next to the room where the volunteers were and assessed their well-being during the data collection points (from baseline to +300 min). The experiment was conducted in six individual sessions. Quantitative primary data (alcohol use) and other secondary quantitative measures (psychometric tests and safety data) were collected in this trial but will be published elsewhere.

At the end of the experimental session, volunteers were offered a meal, and their general condition was evaluated. After this, they were discharged if they were feeling well. Volunteers were offered R$20.00 (approximately $4.00) for going to the laboratory in the experimental and follow-up sessions, totaling R$60.00 (approximately $12.00).

The interview was conducted on day 21. The interview was recorded with the participant's consent, and it was clarified that the recording would be only for scientific purposes, preserving anonymity. The study was evaluated and approved by the Ethics Committee of FMRP-USP.

2.4. Subjective Reports Evaluation

Bardin's content analysis methodology was used to create content categories. The category arrangement followed the criteria highlighted by the author: exhaustion of the subject without omission of any part, representativeness, homogeneity, relevance, and exclusivity [21]. To achieve this, the interviews were fully transcribed without omitting any content. The interview script was planned to collect participants subjective reports. Hence, the relevance criteria were supported by their alignment with the goals of the current study. The exclusivity criterion was meticulously preserved when categorizing the obtained data. The following script was employed:

1. Could you describe your experience with the substance used in the experiment?
2. Do you think this experience has had an impact on your current alcohol consumption? What about your life quality?
3. Was this experience important in your life?
    - 3.1. How much?
    - 3.2. Why?
    - 3.3. Which aspects of the experience were more relevant to you?

The chosen questions were meant to be open-ended, allowing the subject to freely talk about their experience and to highlight the points they considered more relevant.

2.5. Data Analysis

Data were first analyzed following Bardin qualitative methodology [21], using content analysis as a reference, which is divided into three stages: pre-analysis, material exploration, and results treatment [21]. All interviews were recorded, with participants' consent, using a Redmi Note 9s smartphone. All obtained interviews were fully transcribed without omitting any part. Then, interviews were organized, and the first hypotheses were formulated based on the literature on subjective reports of volunteers with substance use disorders who use psychedelics in clinical trials (basically, psilocybin for alcohol and tobacco use disorders). Therefore, we hypothesized that volunteers' reports would refer to revelations about patterns of substance use, self-analysis, compassion, catharsis, and motivations to change.

After reading the material, the data were coded based on a systematic process of aggregating data into registration units concerning volunteers' subjective experience. Registration units are components to be coded, which can be either a theme, a word, or a phrase. The data coding process, however, is restricted by the chosen registration units; therefore, this process addresses the focus that will be given to the research [21]. Then, we registered the frequency with which a registration unit appeared and its intensity (measured through verbal tenses, adverbs, and adjectives, using criteria such as positive, neutral, or negative). That way, units' content can be allocated to a category [21]. Bardin [21] recommends some criteria that could be adopted when the units created during the systematic organization of data are not clear enough: semantic (themes), syntactic (verbs, adjectives, and pronouns), lexical (sense and meaning of words), and expressive (variations in language). The present work creates categories based on semantic content criteria. Finally, after a thorough and in-depth study of the data using the theoretical framework whenever necessary, a proposition was made based on a semantic-categorized analysis of the nondirective interviews. At all stages, another professional with knowledge of the topic was consulted before each decision was taken to avoid a limited, unilateral, and biased view.

3. Results

3.1. Demographic

All six participants were male (by chance). Four of them declared themselves as being white and two as being black. Age varied between 21 and 30 years old (mean: 26 and SD ± 3.6). Table 1 describes in further detail the sociodemographic and diagnostic information about each participant.

Table 1. Sociodemographic characteristics and clinical diagnosis.

Participant	Age	Weight (kg)	AUDIT Score	Psychiatric Diagnosis	Family Income [1]	Personal Income [1]	Education	Occupation	Marital status	Ethnicity
1	22	90	24	Mild AUD	1 to 4 minimum wages	1 to 2 minimum wages	High school diploma	Undergraduate	Single	White
2	27	77	19	Mild MDD	3 to 6 minimum wages	1 to 3 minimum wages	High school diploma	Undergraduate	Single	White
3	27	75	14	-	6 to 9 minimum wages	1 to 4 minimum wages	Bachelor's degree	Graduate student	Single	White
4	21	57	20	-	3 to 6 minimum wages	1 to 2 minimum wages	High school diploma	Undergraduate	Single	Black
5	29	70	18	-	6 to 9 minimum wages	1 to 3 minimum wages	Bachelor's degree	Graduate student	Single	White
6	30	70	17	Mild AUD	3 to 6 minimum wages	1 to 2 minimum wages	Bachelor's degree	Graduate student	Single	Black

AUD: alcohol use disorder; AUDIT: Alcohol Use Disorders Identification Test; MDD: major depressive disorder. [1] Values calculated based on the minimum wage in Brazil in 2019 (R$ 1006.00/month) that, considering an exchange rate of USD 1 = R$ 0.2, would amount around USD 201.2/month.

3.2. Categories

Ten main categories were defined based on interview reports from the six participants. Table 2 depicts the main categories, the number of reports containing each category, and the frequency of each category appearing in participants' reports. The categories more frequently mentioned (≥50% of reports) were Self-perception of experience, Positive impacts, Substances use pattern, Insights, Visual effects, Transient derealization, and Sleep pattern.

Table 2. Categories, subcategories, respondents, and report frequency for each category (n = 6).

Category	Subcategories	Respondents	Category Frequency (%)
1. Self-perception of experience	1.1. Uniqueness	V5 V6	100%
	1.2. Positive	V1	
	1.3. Valid	V2	
	1.4 Safety	V3	
	1.5. Switch Effect	V3	
	1.6. Lightness	V4	
	1.7. Scary, but decreased anxiety	V5	
	1.8. Regret during peak moments	V6	
	1.9. Discomfort due to a lack of control	V6	
2. Positive impacts	2.1. Decrease in anxiety	V2 V4 V5	83.33%
	2.2. Tranquility	V1 V4	
	2.3. Therapeutic effects duration	V1 V2	
	2.4. Lightness	V2 V3	
	2.5. Shift in the mental pattern	V2 V4	
	2.6. Increased openness to close people	V3	
	2.7. Self-acceptance	V4	
	2.8. Purification	V5	
	2.9. Contact with yourself	V5	
3. Substance use pattern	3.1. Alcohol—Ambivalence	V1	83.33%
	3.2. Decrease in alcohol intake	V2 V4 V5	
	3.3. Decrease in tobacco use	V4 V5	
	3.4. Decrease in marijuana use	V4	
	3.5. Unchanged	V6	

Table 2. *Cont.*

Category	Subcategories	Respondents	Category Frequency (%)
4. Insights	4.1. Significant	V1 V2	83.33%
	4.2. Life choices insights	V1 V6	
	4.3. Nonspecific	V3 V6	
	4.4. Happiness as an event	V2	
	4.5. Enjoyment of living processes	V2	
	4.6. Contact with anxiety × decrease in anxiety	V4	
	4.7. Fighting anxiety is like fighting ocean waves	V4	
5. Visual effects	5.1. Increased visual effects with closed eyes	V3 V4 V5 V6	66.67%
	5.2. First pleasant view	V4	
	5.3. Hallucinations	V4	
6. Transient derealization	6.1. Spectator feeling	V3	50.00%
	6.2. Loss of sense of reality	V5	
	6.3. Impact on spatial perception	V6	
7. Sleep pattern	7.1. Ambivalence	V4	33.33%
	7.2. Unchanged	V1	
8. Life quality	8.1. Unchanged	V4	33.33%
	8.2. Increased	V5	
9. Physical symptoms	-	V4 V5	33.33%
10. Synesthesia	-	V4	16.67%

3.3. Subcategories

Some of the main categories comprise subcategories mentioned in reports from two or more participants. The first main category, Self-perception of Experience, encloses only one subcategory (Experience uniqueness); five subcategories can be pointed out from the Positive Impacts category (Anxiety reduction, tranquility, therapeutic effects duration, lightness, shift in the mental pattern); the category Substance Use Pattern can be further divided into two subcategories (Decrease in alcohol intake, Decrease in tobacco use); the Insights category comprises three subcategories (Significant, life choices insights, nonspecific); only one subcategory can be pointed out from the Visual Effects category (Increased visual effects with closed eyes). Therefore, twelve subcategories are composed of five main categories, and the five main categories do not include any subcategory (Physical symptoms, Transient derealization, Sleep pattern, Life quality, and Synesthesia) (Table 2).

3.3.1. Self-Perception of Experience

Experience Uniqueness

Two participants, V5 and V6, reported that ayahuasca consumption was a unique experience.

> *"Well, the experience was unique. Before participating on the trial, I had tried other substances [. . .] but, in my opinion, this (ayahuasca) was the only one capable of, during its maximal effect, make me lose. . . sense of reality" (V5).*

> *"But, like, it was a unique experience, I had not guessed how one would behave during the session. . . If you would forget about using a substance, where you were, what you used, the other people in the room [. . .] and you are conscious about what you used, you know, to be feeling this" (V6).*

3.3.2. Positive Impacts

Anxiety Reduction

Two volunteers, V2 and V5, reported that the experience decreased the anxiety they were used to feeling.

> *"I noticed that it helped with my anxiety, and I think it's a psychological effect of keeping me in control, for example, I have the habit of biting my nails [. . .] since the beginning of the protocol I have been basically 20 days without biting them" (V2).*

> *"I am very anxious and until now my anxiety improved a lot. For example, I have an issue, usually I would be sitting here constantly shaking my legs. And I am still not doing this anymore" (V5).*

Tranquility

Participants V1 and V4 described a positive experience of tranquility.

> *"These last few days I [. . .] had a lot of activities [. . .] had tense obligations, like tests, and I believe that in other situations like these, that I have been through in the past, even recently, I did not feel as calm as I have been in the past few weeks [. . .] my mood was so much better, I think I dealt with things very calmly, and my anxiety did not worsened" "I feel more willing after I used it (ayahuasca), like, I guess my tranquility is related to my willingness. I am calmer, I am more willing" (V1).*

> *"It was, like, a mentality change. It feels like I calmed down a lot after the experience, so this was very, very good" (V4).*

Therapeutic Effects Duration

V1 and V2 reported that a positive effect of the experience was the medium-to-long-term duration of these effects.

> *"[. . .] and I believe that in other situations like these, that I have been through in the past, even recently, I did not feel as calm as I have been in the past few weeks, so it is very interesting, my mood was so much better [. . .]. I feel more tolerant with situations" (V1).*

> *"Effects that last a long time, I feel like I am in a lighter state, calmer, for at least 15 to 20 days" (V2).*

Lightness

Two participants, V2 and V3, reported a sense of lightness as a positive impact of the experience.

> *"I feel more at ease [...]. In the first days, I was even scared of becoming an esoteric boy [. . .]" (V2).*

> *"I left feeling very light and feeling well about my life. Generally speaking, it was very nice" (V3).*

Shift in Mental Patterns

Volunteers V2 and V4 reported that a shift in their mental patterns was positive.

> *"But I already feel like the context changed, even if the context changed unconsciously, maybe this makes more sense" (V2).*

> *"More comfortable with my choices and so, I felt more comfortable in general. I feel like this shift in mentality, bigger and calmer, was very important. Especially because of that, because I left with more positive thoughts, I was having very negative thoughts before. And it is not that I do not have them anymore, sometimes I feel very negative, but I feel more at ease. It was a very introspective experience, you know? Then I felt more comfortable with myself and prepared to begin a path to be more comfortable with myself [. . .]" (V4)*

3.3.3. Substance Use Pattern

Decrease in Alcohol Intake

This subcategory comprises the reports of three volunteers who noticed a decrease in alcohol intake after the experiment. The quotes below refer to volunteers V2, V4, and V5, respectively.

> *"But I actually felt like sometimes I got more moderate [. . .] before I used to drink almost every day, almost like a habit. I got home, opened a bottle, and drank; I opened I can and drank, I would drink a few routinely. In the last weeks it has become more like a social experience, during moments when I am with other people" (V2).*

> *"My alcohol intake is decreasing, my tobacco use as well. I decided this, I am decreasing my use of drugs in general. I was already considering this, already thinking about this, but dependence is very hard, it is something that comes and go. But now my mentality is much more willing to this" (V4).*

> *"My point was, like, drinking on weekends, right? Like, drinking a lot. So, in this first week, I also drank, right? You know, when I went out. But I drank less, not in an exaggerated way, compared to before" (V5).*

Decrease in Tobacco Use

Two participants, V4 and V5, also reported a decrease in tobacco use.

> *"My tobacco use decreased a lot" (V4).*

> *"In this first week I decreased smoking a lot" (V5).*

3.3.4. Insights

Significant

Regarding this category, participants V1 and V2 reported being deeply affected by what they experienced during the session and communicated that they will keep these insights with them for the rest of their lives.

> *"I have got really thoughtful sometimes, it was really outstanding and will be forever engraved in my memory" (V1).*

> *"Small insights that I have got, that arose during the experimental session, in some way will be taken with me for the rest of my life" (V2).*

Life Choices Insights

Concerning the insights category, two participants, V1 and V6, highlighted insights they had regarding their life choices.

> *"I reflected on my college degree, the place where I live and my relationship with my girlfriend" (V1).*

> *"So, there is this reflection I had in the beginning, you know, during the peak of effects. I still cannot understand why, I cannot fully interpretate, but it is about the reason I practice so many sports. It looks like I am trying no to be a burden to anyone in the future" (V6).*

Nonspecific

Two participants, V3 and V6, were not able to report specific insights.

> *"But it was a pleasant experience, I had a few insights" (V3).*

> *"During the substance effects, I have got these stories, these thoughts. . ." (V6)*

3.3.5. Visual effects

Increased Visual Effects with Closed Eyes

Four participants, V3, V4, V5, and V6, described that visual effects were more intense when they closed their eyes.

> *"I just closed my eyes and even with my eyes closed I saw many imaging patterns, kind of psychedelic motifs, it looked like a kaleidoscopic [. . .] when I opened my eyes there was a lot less patterns, the best part was keeping my eyes closed" (V3).*

> *"So, my sight was normal, and my hearing as well, but when I closed my eyes, I began to have visions" (V4).*

> *"When I closed my eyes, I went back to this trip, this religious experience" (V5).*

> *"There was a lot of visual effects. . . They had specific formats, but they were mainly focused on the hospital bed. . . Later I saw abstract shapes and a lot of color" (V6).*

3.3.6. Physical Symptoms

Two volunteers, V4 and V5, reported experiencing physical symptoms during the session.

> *"I went to the bathroom, and I had diarrhea. I went to the bathroom several times. . ." (V4)*

> *"I only know that at some point she (entity) asked me, something like, that in order to continue the purification process I would have to throw up. . . And I was embarrassed to throw up in here" (V5).*

4. Discussion

This study aimed to analyze subjective reports of university students with harmful alcohol use participating in a single-blind study evaluating the effects of one ayahuasca dose. In our analysis, the categories of substance use pattern, positive impacts, and insights were the most relevant ones and seemed to be related to the self-reported decrease in alcohol (and other drugs) consumption among some participants. Specifically, three volunteers reported a decrease in drug consumption (considering alcohol, tobacco, and cannabis), that is, 50% of the sample. Participants V2, V4, and V5 reported a decrease in alcohol intake after the experimental session. Additionally, V4 and V5 reported a reduction in tobacco use, and V4 noticed a decrease in cannabis use. Participant V1 did not associate his participation in the trial with the observed decrease in alcohol use, V6 was already decreasing alcohol use prior to the experiment, and the report of V3 did not include this category. Thus, two participants did not attribute the decrease to the experiment (33.34%), and one did not mention his use pattern during the report (16.66%).

These results differ from those found in Bogenschutz et al. [13], which had a smaller sample size (n = 3) and, although consumption profiles varied across the sample, all participants achieved a reduction in alcohol intake. This difference could be associated with the smaller sample size and/or differences in the research protocol, since it was a double-blinded protocol lasting 12 weeks and including two drug sessions (4 and 8 weeks) associated with psychotherapy. In comparison, Nielson et al. [14], in an open-label, pilot study assessing the effects of psilocybin in adults with alcohol use disorder, reported results like ours. Of 10 participants, 4 reported a complete reduction in heavy drinking days (40% of the sample). Six participants reported a reduction that ranged from 0 to 42.84%. As in the present study, consumption patterns were more evenly divided between those who reduced and those who did not reduce alcohol intake, which could be associated with a larger sample size. Recent results from Garcia-Romeu et al. [15], in an open-label, pilot study on psilocybin-facilitated treatment associated with cognitive behavioral therapy (CBT) for smoking cessation, showed that 12 of 15 participants (80%) achieved smoking cessation after 6 months of the experimental session. This difference may be due to the included therapeutic elements, such as CBT, and the longer intervention protocol (15 weeks).

Regarding the "positive impacts" category, five volunteers covered this topic in their reports, V1, V2, V3, V4, and V5 (83.33% of the total sample). Each participant noticed different types of positive impacts. In the "decreased anxiety" subcategory, V2 and V5 reported a noticeable reduction in their anxiety after the experimental session (33.33% of the total sample). This decrease was not mentioned as one of the main results in similar studies [13–16]. Another theme that does not appear significant in these studies was brought up by two other volunteers, V1 and V5 (33.33%), who reported a feeling of greater tranquility after the experimental session. V1 and V2 observed that the positive effects they perceived were medium-to-long-term. This finding is in line with results reported by Bogenschutz et al. [13], in which volunteers observed lasting changes in their perceptions of themselves. Finally, two volunteers highlighted the shift in their mental patterns as a positive impact of the experience. V2 described it as something subconscious, and V4 as something introspective. This finding is similar to the findings described by Bogenschutz et al. [13], in which participants noticed an increase in the quality of their basic consciousness. Only the report for V6 did not include the "positive impacts" category (16.67%).

The Insights category appeared in the reports of five volunteers, V1, V2, V3, V4, and V6 (83.33%). This theme also appears as a highlight in Noorani et al. [16], in which volunteers reported having vivid insights into self-identity. Moreover, a recent international cross-sectional study of ayahuasca users reported that insights were "almost universally reported as part of the ayahuasca experience", were highly valued by ayahuasca users, and were "strongly predictive of subsequent beneficial life and lifestyle changes" [22]. In the present study, three subcategories include the reports of two or more volunteers. Two participants, V1 and V2, reported that the insights they had during the experiment were so significant that they will be taken for the rest of their lives. V1 and V6 reported having had insights regarding their life choices, while two other volunteers (V3 and V6) reported having insights they were unable to specify. The report by V4 could not be classified among any of those subcategories, but he had his own insights. First, he mentioned that dealing with anxiety leads to an anxiety decrease: "but I also felt really light but, at the same time, it was something that increased my anxiety and decreased at the same time". Second, he stated that fighting against anxiety is like fighting against ocean waves: "I remember mentioning that not being anxious was impossible, it was like fighting against the ocean waves". Only the V5 report was not part of this category (16.67%).

From a psychology point of view, it is interesting that volunteers who reported having insights, even if nonspecific, noticed a reduction in anxiety or an increase in feelings of tranquility and/or lightness and, in some cases, even a decrease in substance consumption. This was the case for V1, V2, V3, and V4 reports. Although V1 had an ambiguous substance consumption evaluation, he reported an increase in tranquility feelings that were medium-to-long-term, as well as relevant insights he had during the experiment. Besides the insights previously mentioned, V2 reported an increase in feelings of lightness that were also medium-to-long-term, and a decrease in alcohol intake. Although V3 insights were nonspecific, he also noticed an increase in lightness and increased openness to close people. Lastly, V4 noticed as positive impacts of the experience an increase in tranquility, self-acceptance, and a shift in the mental pattern. Additionally, he was the only participant reporting a reduction in all substances he used (alcohol, tobacco, and cannabis). Of the five volunteers that had insights, four reported a reduction in substance consumption and/or an increase in positive feelings, like tranquility and lightness. This is in line with the observations of naturalistic ayahuasca use [22].

Insight is an innovative idea about something that is already known; therefore, it is speculated that those volunteers who accessed new perspectives on issues in their daily lives managed to benefit from the experience, either by reducing substance consumption or by increasing positive feelings. According to the literature, it is possible that insight acts as a potentially important mechanism of change for psychology [23]. Hypothetically, this result may result from a relationship between contact with a new idea—insight—and

a reduction in anxiety, an increase in feelings such as tranquility and lightness, and/or a decrease in substance consumption. The age range of 18 to 25 years old is a period of great importance regarding substance consumption, as it is a time of emotional transition in which the process of 'becoming an adult' begins [24]. Specifically for university students, this is a period in which they leave parental supervision and enter a new environment where substance use is often encouraged [24]. Furthermore, many adolescents have not yet developed the necessary skills to deal with the pressure resulting from this transition while maintaining close contact with people who turn to drugs as a way of dealing with stressful situations [25]. However, when coming into contact with this new perspective, even if it is through nonspecific insights, it may be that the volunteers were able to give new meaning to internal issues and, therefore, managed to get something positive out of the experiment (even if not necessarily a reduction in consumption), such as the reduction in anxiety resulting from social pressures that typically occurs in this phase [23,24]. This decrease can be subjectively observed as just a reduction in anxiety or as an increase in feelings of tranquility and lightness.

5. Conclusions

In summary, the categories Substances use pattern, Positive impacts, and Insights, seemed to be associated with a reduction in alcohol use among our sample. Reduced anxiety, increased feelings of tranquility/lightness, a shift in mental pattern, and the durability of positive effects also seemed to play a role in this reduction. It is interesting to note the intersection of these categories in the participants' reports, as volunteers who reported insights also reported a reduction in substance use and/or an increase in positive feelings. Insights may have transformative potential, as they allow contact with new perspectives. Evidently, more studies are needed to explore this possible relationship, which the present study launches as a possible explanation behind the therapeutic potential of the experience with ayahuasca: insights as drivers of a process, even unconscious, that provides internal changes in the subject.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/psychoactives2040022/s1, Chemical Analysis of Ayahuasca.

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References

1. dos Santos, R.G.; Landeira-Fernandez, J.; Strassman, R.J.; Motta, V.; Cruz, A.P.M. Effects of ayahuasca on psychometrc measures of anxiety, panic-like and hopelessness in Santo Daime members. *J. Ethnopharmacol.* **2007**, *112*, 507–513. [CrossRef] [PubMed]
2. dos Santos, R.G.; Balthazar, F.M.; Bouso, J.C.; Hallak, J.E.C. Current state of research on ayahuasca: A systematic review of human studies assessing psychiatric symptoms, neuropsychological functioning, and neuroimaging. *J. Psychopharmacol.* **2016**, *30*, 1230–1247. [CrossRef] [PubMed]
3. dos Santos, R.G.; Osório, F.L.; Crippa, J.A.S.; Hallak, J.E.C. Antidepressive and anxiolytic effects of ayahuasca: A systematic literature review of animal and human studies. *Braz. J. Psychiatry* **2016**, *38*, 65–72. [CrossRef] [PubMed]
4. Sanches, R.F.; Osório, F.L.; dos Santos, R.G.; Macedo, L.R.; Maia-de-Oliveira, J.P.; Wichert-Ana, L.; de Araujo, D.B.; Riba, J.; Crippa, L.A.S.; Hallak, J.E.C. Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A SPECT study. *J. Clin. Pharmacol.* **2016**, *36*, 77–81. [CrossRef] [PubMed]
5. Palhano-Fontes, F.; Barreto, D.; Onias, H.; Andrade, K.C.; Novaes, M.M.; Pessoa, J.A.; Mota-Rolim, S.A.; Osório, F.L.; Sanches, R.; Dos Santos, R.G.; et al. Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: A randomized placebo-controlled trial. *Psychol. Med.* **2019**, *49*, 655–663. [CrossRef] [PubMed]
6. Grob, C.S.; McKenna, D.J.; Callaway, J.C.; Brito, G.S.; Neves, E.S.; Oberlaender, G.; Saide, O.L.; Labigalini, E.; Tacla, C.; Miranda, C.T.; et al. Human psychopharmacology of hoasca, a plant hallucinogen used in ritual context in Brazil. *J. Nerv. Ment. Dis.* **1996**, *184*, 86–94. [CrossRef] [PubMed]
7. Barbosa, P.C.R.; Tófoli, L.F.; Bogenschutz, M.P.; Hoy, R.; Berro, L.F.; Marinho, E.A.V.; Areco, K.N.; Winkelman, M.J. Assessment of Alcohol and Tobacco Use Disorders Among Religious Users of Ayahuasca. *Front. Psychiatry* **2018**, *9*, 136. [CrossRef] [PubMed]
8. Lawn, W.; Hallak, J.E.C.; Crippa, J.A.; dos Santos, R.G.; Porffy, L.; Barratt, M.J.; Ferris, J.A.; Winstock, A.R.; Morgan, C.J. 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. [CrossRef] [PubMed]
9. Dalgalarrondo, P. *Psicopatologia e Semiologia dos Transtornos Mentais*, 3rd ed.; Artmed Ed: Porto Alegre, Brasil, 2000; pp. 19–866.
10. da República, P.; Duarte, P.C.A.V.; Stempliuk, V.A.; Barroso, L.P. *Relatório Brasileiro Sobre Drogas/Secretaria Nacional de Políticas Sobre Drogas*; IME USP. SENAD: Brasília, Brasil, 2009; pp. 9–362.
11. Bastos, F.I.P.M.; Vasconcellos MT, L.D.; De Boni, R.B.; Reis NB, D.; Coutinho CF, D.S. *III Levantamento Nacional Sobre o uso de Drogas pela População Brasileira*; FIOCRUZ/ICICT: Rio de Janeiro, Brasil, 2017; p. 528.
12. Horton, D.M.; Morrison, B.; Schmidt, J. Systematized review of psychotherapeutic components of psilocybin-assisted psychotherapy. *Am. J. Psychother.* **2021**, *74*, 140–149. [CrossRef] [PubMed]
13. Bogenschutz, M.P.; Podrebarac, S.K.; Duane, J.H.; Amegadzie, S.S.; Malone, T.C.; Owens, L.T.; Ross, S.; Mennenga, S.E. Clinical interpretations of patient experience in a trial of psilocybin-assisted psychotherapy for alcohol use disorder. *Front. Pharmacol.* **2018**, *9*, 100. [CrossRef] [PubMed]
14. Nielson, E.M.; May, D.G.; Forcehimes, A.A.; Bogenschutz, M.P. The psychedelic debriefing in alcohol dependence treatment: Illustrating key change phenomena through qualitative content analysis of clinical sessions. *Front. Pharmacol.* **2018**, *9*, 132. [CrossRef] [PubMed]
15. Garcia-Romeu, A.R.; Griffiths, R.; Johnson, M.W. Psilocybin-occasioned mystical experiences in the treatment of tobacco addiction. *Curr. Drug Abuse Rev.* **2014**, *7*, 157–164. [CrossRef] [PubMed]
16. Noorani, T.; Garcia-Romeu, A.; Swift, T.C.; Griffiths, R.R.; Johnson, M.W. Psychedelic therapy for smoking cessation: Qualitative analysis of participant accounts. *J. Psychopharmacol.* **2018**, *32*, 756–769. [CrossRef] [PubMed]
17. Babor, T.F.; Caetano, R. Evidence-based alcohol policy in the Americas: Strengths, weaknesses, and future challenges. *Rev. Panam. Salud Pública* **2005**, *8*, 327–337. [CrossRef] [PubMed]
18. Lima, C.T.; Freire, A.C.C.; Silva, A.P.B.; Teixeira, R.M.; Farrell, M.; Prince, M. Concurrent and construct validity of the AUDIT in an urban Brazilian sample. *Alcohol. Alcohol.* **2005**, *40*, 584–589. [CrossRef] [PubMed]
19. Oña, G. Elaboración y validación de un cuestionario para detección del riesgo de reacciones adversas graves por empleo de drogas psicodélicas en terapia. *IJP&PT* **2020**, *20*, 211–222.
20. Dos Santos, R.G.; Osório, F.L.; Rocha, J.M.; Rossi, G.N.; Bouso, J.C.; Rodrigues, L.S.; de Oliveira Silveira, G.; Yonamine, M.; Hallak, J.E.C. Ayahuasca improves self-perception of speech performance in subjects with social anxiety disorder: A pilot, proof-of-concept, randomized, placebo-controlled trial. *J. Clin. Pharmacol.* **2021**, *41*, 540–550. [CrossRef] [PubMed]
21. Bardin, L. *Análise de Conteúdo*, 3rd ed.; Edições 70: Lisboa, Portugal, 2004; pp. 7–274.
22. Perkins, D.; Opaleye, E.; Bouso, J.C.; Tófoli, L.F.; Sarris, J.; Schubert, V.; Ruffell, S.; Simonova, H. Insights, Life Changes and Lifestyle Changes Reported by Individuals Consuming Ayahuasca in Naturalistic Settings: Nature, Frequency and Associations with Mental Health and Wellbeing. *Psychoactives* **2023**, *2*, 256–286. [CrossRef]
23. Castonguay, L.G.; Hill, C.E. *Insight in Psychotherapy*, 1st ed.; American Psychological Association: Worcester, MA, USA, 2007; p. 448.

24. Prendergast, M.L. Substance Use and Abuse among College Students: A Review of Recent Literature. *J. Am. Coll. Health* **1994**, *43*, 99–113. [CrossRef] [PubMed]
25. Doering-Silveira, E.; Grob, C.S.; de Rios, M.D.; Lopez, E.; Alonso, L.K.; Tacla, C.; Da Silveira, D.X. Report on Psychoactive Drug Use among Adolescents Using Ayahuasca within a Religious Context. *J. Psychoact. Drugs* **2005**, *37*, 141–144. [CrossRef] [PubMed]