Available online at www.sciencedirect.com

ScienceDirect

Comprehensive Psychiatry 71 (2016) 95–105

COMPREHENSIVE PSYCHIATRY

www.elsevier.com/locate/comppsych

Psychological and neuropsychological assessment of regular hoasca users

Paulo Cesar Ribeiro Barbosa[a,b,*], Rick J. Strassman[a], Dartiu Xavier da Silveira[c], Kelsy Areco[c], Robert Hoy[a], Jessica Pommy[a], Robert Thoma[a], Michael Bogenschutz[a,d]

[a]*University of New Mexico Center for Psychiatric Research, 1101 Yale Blvd NE, Albuquerque, NM 87106, USA*

[b]*Departamento de Filosofia e Ciências Humanas, Universidade Estadual de Santa Cruz, Campus Soane Nazaré de Andrade, Rodovia Jorge Amado, km 16, Bairro Salobrinho, Ilhéus, BA CEP 45662-900, Brazil*

[c]*Departamento de Psiquiatria da Universidade Federal de São Paulo, Rua Borges Lagoa, n° 570, São Paulo, SP CEP 04038-020, Brazil*

[d]*New York School of Medicine, 550 1st Avenue, New York, NY 10016, USA*

Abstract

Background: Hoasca (also called *ayahuasca*) is a *N*,*N*-dimethyltryptamine (DMT) – containing psychedelic brew originally used for magico-religious purposes by Amerindian populations of the Amazon Basin. Recently, Brazilian syncretic churches have helped spread the ritual use of hoasca to Western societies. The aim of this study was to evaluate substance use, and neuropsychological and psychological functioning of regular hoasca users within a religious setting.

Methods: Assessment of socio-economic status, mood, personality traits, impulsiveness, drug use, quality of life, extrinsic and intrinsic religiosity, and neuropsychological function was performed on 30 volunteers from a U.S. branch of União do Vegetal (UDV), a Brazilian religion which uses hoasca ritually. We also assessed 27 non-hoasca-using control subjects matched by socio-demographic profile and church attendance. Mann–Whitney *U*, chi-squared and Fisher tests were used to analyze differences between groups. Spearman's association and simple logistic regression tests were used to analyze the impact of frequency of hoasca use on dependent variables.

Results: Relative to the control group, the UDV group demonstrated lower scores for depression ($p = 0.043$, $r = .27$) and confusion ($p = 0.032$, $r = .29$) as assessed by the Profile of Mood States (POMS); higher scores on the instrument Big Five Inventory (BFI) for the personality traits agreeableness ($p = 0.028$, $r = .29$) and openness ($p = 0.037$, $r = .28$); higher scores on the quality life domain role limitations due to physical health as determined by the instrument Medical Outcomes Study Short Form-36 – SF-36 ($p = 0.035$, $r = .28$); less recent use of alcohol ($p < 0.001$, $\varphi_c = .57$), greater past use of alcohol to intoxication ($p = 0.007$, $\varphi_c = .36$) and past use of cannabis ($p = 0.001$, $\varphi_c = .45$) as measured by the Addiction Severity Index (ASI), 5th edition; better score on a measure of memory vulnerability to proactive interference as measured by the California Verbal Learning Test – CVLT ($p = 0.040$, $r = .27$). Lifetime use of hoasca was positively correlated with role limitations due to physical health ($p = 0.032$, $r_s = .39$) and negatively associated with lifetime heavy alcohol use ($p = 0.034$, $OR = 0.979$).

Conclusions: The findings indicate that religious use of hoasca does not adversely affect neuropsychological functioning and may have positive effects on substance abuse and mood.

1. Introduction

Hoasca is the name for a decoction made from the bush *Psychotria viridis*, which contains *N,N*-dimethyltryptamine (DMT), and the liana *Banisteriopsis caapi*, which contains the β-carboline alkaloids harmine, harmaline, and tetrahydroharmine (THH). DMT is a tryptamine hallucinogen which is thought to act primarily at $5HT_{2A}$, $5HT_{2C}$, and $5HT_{1A}$ receptors. DMT is orally inactive due to its breakdown by monoamine oxidase activity in the gastrointestinal tract.

This study was funded by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) from Brazilian Ministry of Education. Processo BEX 3584 10-0.

No conflicts of interest have been declared.

* Corresponding author at: Departamento de Filosofia e Ciências Humanas, Universidade Estadual de Santa Cruz, Campus Soane, Nazaré de Andrade, Rodovia Jorge Amado, km 16, Bairro Salobrinho, Ilhéus, BA CEP 45662900, Brazil. Tel.: +55 031 73 98826 8898.

E-mail address: pcrbarbosa@uesc.br (P.C.R. Barbosa).

http://dx.doi.org/10.1016/j.comppsych.2016.09.003

0010-440X/

The β-carboline alkaloids in the hoasca are monoamine oxidase inhibitors (MAOI) and render the DMT orally psychoactive [1–3]. The hoasca tea is used sacramentally by the União do Vegetal (UDV), a Brazilian religion that combines Christian and reincarnation beliefs with the ritual use of the psychedelic brew.

The acute effects of hoasca begin 30 to 60 min after ingestion, reach maximum intensity between 60 and 120 min, and are marked by dose-dependent effects on perceptual, cognitive, affective, and kinesthetic function [4–6]. Acute adverse reactions such as anxiety, nausea and vomiting have also been described [7–9]. Single photon emission tomography (SPECT) and functional magnetic resonance imaging (fMRI) studies have detected acute activation of occipital, temporal, and frontal cortices that are involved in a wide array of cognitive functions. The reported phenomenological effects of hoasca include enhanced inner awareness, and changes in subjective feeling states and emotional arousal. Users also commonly report changes in visual perception, memory, and intention [10,11].

β-Carboline alkaloids' plasma concentrations peak later than DMT, with THH showing a markedly longer course than the other hoasca alkaloids [12]. Cardiovascular responses (i.e., heart rate and blood pressure) to hoasca are modest, and most psychological and physiological parameters return to baseline levels by 4 to 6 h [5].

Hoasca was originally used for magico-religious purposes by Amerindian and Mestizo populations of the western Amazon Basin [13]. During the last decades the expansion of religions such as the União do Vegetal and Santo Daime, and the increasing popularity of hoasca use in less overtly religious contexts, made the brew available to non-Amazonian populations throughout Latin and North America, and parts of Europe, Oceania, and Asia [14].

Hoasca-using religious groups have come under scrutiny by regulatory agencies, because DMT is classified as a controlled substance [15], and in part due to reports of exploitation and harmful effects experienced by people interacting with purported "healers" in Amazon area [16]. However, use of ayahuaca for religious purposes has resulted in its being judged more favorably in Brazil [14,17–19]. In the United States, the judicial appeals of UDV reached the US Supreme Court, which, in 2006, affirmed the right of the UDV to have returned to them the hoasca seized previously by the government [20,21]. This decision was based on the lack of convincing evidence that religious use of hoasca causes social harm or injury to individuals that might outweigh religious freedom [22,23]. There are few rigorous studies of long-term safety and/or persisting effects of hoasca. Further studies are warranted in order to make well-informed decisions regarding effects of hoasca on mental health.

Existing data from scientific studies suggest that there are no persisting adverse effects on neuropsychological functioning [24], and that religious use of hoasca may have beneficial effects on substance abuse, and on psychological, spiritual, and physical wellbeing [4,25–28].

The present research was designed as a cross-sectional, case-controlled study of the psychological and neuropsychological characteristic of a group of UDV members who drink hoasca regularly during religious services. Previous studies failed to properly control for the religious attendance variables in the evaluations of religious hoasca users [4,24]. Evidence suggests that social support and encouragement of healthy behavior provided by religious organizations can improve mental health status [29]. In order to address this gap, we compared the UDV group to a group of socio-economic status matched non-hoasca users from other religious denominations in the same geographical locations, and carefully evaluated religious attendance variables from both groups.

2. Methods

2.1. Background information: União do Vegetal

According to UDV's official documents, this religion was founded in 1961 by Jose Gabriel da Costa – known in UDV as "Mestre Gabriel" [30]. In 2012, there were estimated to be approximately 16,500 UDV members in South and North America and Europe. The UDV subscribes to Christian principles in addition to beliefs regarding reincarnation. Regular hoasca sessions are held twice a month, but higher ranking members – those who are more committed to the organization – may drink the brew more frequently. Hoasca rituals last approximately 4 h, the tea being served at the beginning of the ceremony with additional available mid-session. UDV leadership believes that spiritual and health benefits of UDV may result from three interdependent factors: regular sessions with the tea as a religious sacrament, transmission of the doctrine and teachings of the UDV within these sessions, and the community practice of these teachings both in and out of sessions.

2.2. Sample

Thirty UDV members in the United States and 27 control subjects from the same geographic area who were members of other organized religious groups were evaluated. Both UDV and control subjects had to be at least 18 years of age and able to provide informed consent. Controls were matched by age (±2 years) and gender to a UDV study participant, and had no exposure to hoasca. Current use of psychiatric or neurological medication was an exclusion criterion. All subjects were fluent English speakers. This research was reviewed and approved by the Human Subjects Protections Office at the University of New Mexico Health Sciences Center.

2.3. Recruitment

UDV subjects were recruited through an invitation presented to the congregation of the local UDV church. Prospective subjects contacted the group's leadership, who

made the formal referral. Control subjects were recruited through public presentations in churches, flyers, and advertisements, and with the assistance of local priests and ministers. Prospective subjects were pre-screened for eligibility and those who met all criteria, and could be matched with an UDV subject, were enrolled in the study.

2.4. Procedures and instruments

Evaluations took place at the Center for *Psychiatric Research* of the University of New Mexico and in a quiet area near the UDV church in which privacy could be assured. Subjects were instructed not to consume alcohol-containing beverages for two days before their evaluations, and to avoid caffeine, tobacco, or any stimulant for an hour before their evaluation. UDV subjects were also instructed to refrain from drinking hoasca for at least 6 days before their assessment.

2.5. Socio-economic variables

Age, sex, years of education, and marital and employment status were evaluated through the University of New Mexico Center on Alcoholism, Substance Abuse, and Addiction (CASAA) standardized SES (socio-economic status) assessment questionnaire [31].

2.6. Religiosity and hoasca ritual attendance variables

A questionnaire was designed to characterize subjects' religious history and hoasca ceremony attendance. All subjects were asked about religion of birth, current religious affiliation, and attendance at services during the previous 12 months. UDV subjects were also asked to provide a history of total lifetime months of regular attendance at hoasca rituals (i.e., at a frequency of at least twice a month) as well as number of hoasca ceremonies attended during the previous 12 months.

We used the Duke University Religion Index (DUREL), a five-item self-administered instrument that evaluates involvement in communal "organizational religious activity" (ORA); "non-organizational religious activity" (NORA) performed in private, such as prayer, meditation, and Bible study; and "intrinsic religiosity" (IR), a measure of commitment to religious principles and feelings of God's presence [32].

We also administered the Daily Spiritual Experience Scale (DSES), a 16-item self-report measure that assesses spiritual experiences, such as feeling thankful for one's blessings and asking for God's help in the midst of daily activities [33].

2.7. Quality of life, and psychological and substance use assessments

We administered the Medical Outcomes Study Short Form-36 (SF-36) to evaluate eight dimensions of quality of life: 1) physical functioning; 2) role-physical – impairments in daily life caused by physical health problems; 3) bodily pain; 4) general health; 5) vitality; 6) social functioning; 7) role-emotional – limitations in daily life caused by emotional problems; and 8) mental health [34].

Subjects' mood was evaluated using a shortened version of the Profile of Mood States (POMS), a 30-item questionnaire assessing tension, depression, anger, fatigue, and confusion [35].

Personality traits were evaluated using the Big Five Inventory (BFI), a 44-item questionnaire assessing: 1) extraversion – the tendency to be outgoing and energetic; 2) agreeableness – related to pro-social and altruistic orientation towards others; 3) conscientiousness – the tendency to show self-discipline and act dutifully; 4) neuroticism – the tendency to experience unpleasant emotions such as anger and anxiety; and 5) openness – the tendency to be inventive and appreciate art and unusual ideas [36].

We administered the Barratt Impulsiveness Scale (BIS-11), a 30-item questionnaire that assesses three domains of impulsivity: 1) attentional impulsivity, marked by the tendency to make quick decisions; 2) motor impulsivity, acting without thinking; and 3) non-planning impulsivity, noted by a lack of forethought [37].

Recent and past uses of alcohol and drugs were evaluated using the drug/alcohol section of the Addiction Severity Index (ASI), 5th edition [38]. Recent use was defined as any substance use during the 30 previous days. Past use was defined as a history of substance use two days or more per week for at least one year. We evaluated alcohol use, alcohol use to intoxication, and cannabis use as separate categories, and grouped the remaining ASI list of substances (heroin, methadone, other opiates/analgesics, barbiturates, other sedatives, hypnotics and tranquilizers, cocaine, amphetamines, hallucinogens, inhalants) in a single category "other drugs."

2.8. Neuropsychological evaluation

The American version of the Nelson Adult Reading Test (AMNART) [39] estimates premorbid intelligence through pronunciation of 45 irregularly-spelled words.

A standard formula (118.2 − .89 (AMNART errors + .64 (years of Education))) was applied to raw scores to compute an estimate of verbal intelligence.

The Trail Making Test (TMT) [40], with the time-based score on Part A assesses speed of visual scanning and psychomotor speed. Scores on Part B reflect executive functioning and cognitive flexibility. A third score is the total time required to complete both parts [41].

The Stroop Color and Word Test, Golden Version (Stroop Test) [42] also examines executive functioning by assessing cognitive flexibility, processing speed, inhibitory control, and selective attention. The number of item subjects can read within 45 s for each of three trials were recorded and the difference between the color (C) and color–word (CW) scores were used to compute an interference score (interference = color (C) minus color–word (CW)). Lower interference score indicates less interference effect.

The Conners' Continuous Performance Test, Second Edition (CPT II V.5) [43] was used as a measure of sustained

attention. Multiple sub-score values are also generated, including measures of omissions (targets that are not responded to), commissions (responses to non-targets), average speed of correct response, hit reaction time, standard error, variability of hit reaction time standard error, detectability (d'), "response style indicator" (ß), perseverations, hit reaction time by block change, standard error by block, reaction time by inter-stimulus interval, and standard error by inter-stimulus interval.

The California Verbal Learning Test (CVLT) [44] assesses verbal retention, retrieval, recognition, and vulnerability to proactive interference. The Rey–Osterrieth Complex Figure Test (ROCF) [45] assesses visual memory, and provides additional sub-scores pertaining to fine motor skills and visuospatial-constructional ability.

2.9. Statistical analyses

Statistical analyses were performed using IBM SPS statistics 20.0 for Windows. Analyses of categorical variables were done using chi-squared (χ^2) and Fisher tests. The majority of the continuous variables did not meet normality assumptions (Shapiro–Wilk = $p \leq 0.05$). Therefore the continuous variables were analyzed using the Mann–Whitney U test. Effect sizes of chi-squared and Mann–Whitney U were calculated using the Cramer's V and the standard formula $r = Z/\sqrt{N}$, respectively.

The effect of hoasca ceremony attendance variables – total lifetime months of regular attendance at hoasca rituals and the number of hoasca rituals attended during the previous 12 months – on the significant differences of the UDV group relative to control was further explored. If the differences occurred on continuous variables, we used the Spearman's correlation within the UDV sample to determine the relationship between these variables and the hoasca ceremony attendance variables. Also, binomial regression analyses were used to assess the prediction of the hoasca ceremony attendance variables on dichotomous dependent variables. Here, we used the Box-Tidwell [46] procedure to assess the linearity assumption of the independent variables with respect to the logit of the dependent variables and studentized residual with a cut-off to identify outliers ($\geq \pm 2.5$). We adopted $p \leq 0.05$ as the level of significance.

3. Results

Table 1 presents demographic, religious affiliation, masses, services and hoasca ritual attendance data. Subjects were 30 members of the UDV and 27 control members from Catholic, Protestant, and Unitarian Universalist communities.

There were no significant differences between the UDV and control groups in term of gender, age, years of education, or annual family income. Additional SES variables including marital and employment status are also described. Protestants included Baptists ($N = 6$), Episcopalians ($N = 3$), Presbyterians ($N = 2$), Methodists ($N = 1$), and Pentecostals ($N = 1$).

The UDV group consisted of 14 individuals at the beginners rank, and 16 subjects from the upper ranks. Only two UDV subjects attended less than 24 hoasca ceremonies during the previous year – this being the minimum number of church-required ceremonies held in a calendar year. Controls varied by denomination in their church attendance during the preceding 12 months, Baptists were the highest attendees (range 40–112), followed by the Catholics (range 30–80), Presbyterians (range 36–45), Episcopalians (range 24–25) and Unitarians (range 6–30). The Methodist subject attended 48 services and the Evangelical subject attended 10. The UDV group scored significantly lower on the Duke Religious Index (DUREL)-assessed Organizational Religious Activity (ORA) scale, indicating fewer church attendance to rituals and other public religious activities than controls ($U = 107$, $p < 0.001$, $r = .69$).

A positive correlation was found between number of hoasca sessions attended in the previous 12 months and DUREL-assessed Organizational Religious Activity [r_s ($N = 30$) = .39, $p = 0.034$] (Table 2).

Regarding past and present use of substances, on the Addiction Severity Index (Table 3), the UDV group scored significantly higher on measures of lifetime past use of alcohol to intoxication (χ^2 (1) = 7.402, $p = 0.007$, $\varphi_c = .36$) and lifetime cannabis use (χ^2 (1) = 11.315, $p = 0.001$, $\varphi_c = .45$). However, UDV group scores were significantly lower for use of alcohol over the previous 30 days (χ^2 (1) = 18.192, $p < 0.001$, $\varphi_c = .57$).

We performed simple logistic regressions to ascertain the effects of total lifetime months of regular attendance at hoasca rituals and the number of hoasca rituals attended during the previous 12 months on ASI-assessed drug use variables. Both continuous hoasca attendance rituals independent variables were found to be linearly related to the logit of the ASI-assessed drug use dependent variables.

All cases studentized residuals were less than ±2 standard deviations, indicating there were no significant outliers in the models.

Increasing total lifetime months of regular attendance at hoasca rituals age was associated with a decreased likelihood of lifetime past use of alcohol to intoxication ($B = -.022$; $p = 0.034$; $OR = 0.979$).

This negative association indicates that more experienced UDV subjects were less likely to have a past history of alcohol abuse than the newer UDV subjects.

The number of UDV subjects who had used alcohol during the previous 30 days did not provide an appropriate sample size to run logistic regressions (two of 30).

However, it is worth noting that these two subjects were under the 25th quartile of the total lifetime months of regular attendance at hoasca rituals and under the 10th quartile of the number of hoasca rituals attended during the previous 12 months.

With regard to self-reported general health, the UDV group had significantly higher scores on Medical Outcomes Study Short Form-36 (SF-36)-assessed role limitations due

Table 1
Sociodemographic variables.

	UDV				Control				Statistics		
	N (%)	Median	Min	Max	N (%)	Median	Min	Max	*U*	*p*	*r*
Matching variables											
Gender											
Men	16 (53.3)				14 (51.9)						
Women	14 (46.7)				13 (48.2)						
Age		42.5	22.0	67.0		45.0	20.0	64.0	398	0.91	.015
Years of education		16.0	13.0	22.0		18.0	13.0	26.0	344	0.43	.11
Annual family income		58,000	5000	110,000		62,500	12,000	180,000	322	0.25	.15
Religious variables											
Religious affiliation											
UDV	30 (100)										
Catholics					11 (40.7)						
Protestants					13 (48.2)						
Unitarian universalist					3 (11.1)						
Frequency of ceremonies											
During the last 12 months	30	32,5	20.0	62.0	27	45.0	6.00	112	308	0.12	.21
Months of regular attendance	30	60.0	12.0	192	27	360	24.0	684	151	<0.001**	.54
Additional sociodemographic variables											
Marital status											
Single, never been married	6 (20.0)				11 (40.7)						
Legally married	18 (60.0)				11 (40.7)						
Cohabiting with partner (but not married)	2 (6.67)				2 (7.41)						
Separated but still married	2 (6.67)				1 (3.70)						
Divorced	2 (6.67)				2 (7.41)						
Employment status											
Work 40 h or more a week	15 (50.0)				18 (66.7)						
Work fewer than 40 h a week	14 (46.7)				5 (18.5)						
Retired	1 (3.33)				–						
Unemployed	–				4 (14.8)						
Duke Religious Index											
Organizational religious activity	30	4.00	4.00	6.00	27	5.00	4.00	6.00	107	<0.001**	.69
Non-organizational religious activity	30	5.00	1.00	6.00	27	5.00	1.00	6.00	339	0.27	.15
Intrinsic religiosity	30	15.0	10.0	15.0	27	14.0	7.00	15.0	307	0.080	.23
Daily Spiritual Experiences											
Scale 1	25	36.0	16.0	52.0	25	34.0	16.0	66.0	306	0.90	.018
Scale 2	30	3.00	2.00	4.00	26	3.00	1.00	4.00	341	0.34	.13

** Significant at 0.01 level.

to physical health item, indicating fewer role limitations due to health problems than controls ($U = 311$, $p = 0.035$, $r = .28$).

With regard to self-reported mental health status, the lower scores of UDV on the Profile of Mood States (POMS)-assessed depression and confusion scales indicated lower levels of depressive ($U = 270$, $p = 0.043$, $r = .27$) and confusion ($U = 273$, $p = 0.032$, $r = .29$) states than control group. UDV scored significantly higher than controls on the Big Five Inventory (BFI)-assessed personality factors agreeableness ($U = 268$, $p = 0.028$, $r = .29$) and openness ($U = 275$, $p = 0.037$, $r = .28$) (Table 4).

SF-36-assessed role limitations due to physical health correlated positively with total of months of regular use of hoasca, [r_s ($N = 30$) = .39, $p = 0.032$], indicating that longer lifetime attendance to hoasca sessions was associated with lower impairments in daily life caused by physical health problems (Table 2).

There were no group differences across neuropsychological variables with one exception; the UDV group scored higher on CVLT interference list, indicating they were less susceptible to proactive interference than controls during verbal learning ($U = 279$, $p = 0.040$, $r = .27$) (Table 5). CVLT list B was not correlated with the total lifetime months of regular attendance at hoasca rituals nor the number of hoasca rituals attended during the previous 12 months (Table 2).

4. Discussion

4.1. General findings

Overall, no deleterious effects of regular ritual consumption of hoasca were found relative to a control group matched for age, gender, SES and regularity of church attendance.

The UDV group did not differ relative to controls in multiple neuropsychological measures. These included intellectual functioning, attention, memory, visuospatial ability, executive functioning, and fine motor control. Despite scoring higher on lifetime alcohol and cannabis

Table 2
The effect of hoasca ceremony attendance variables on the differences of the UDV group relative to control.

Spearman's correlation	Number of hoasca rituals attended during the previous 12 months		Total lifetime months of regular attendance at hoasca rituals	
	Corr. coef	*p*	Corr. coef	*p*
DUREL assessed – organizational religious activity	.39	0.034*	.24	0.20
SF-36 assessed – role limitations due to physical health	.11	0.57	.39	0.032*
POMS assessed – depression	.072	0.70	−.13	0.49
POMS assessed – confusion	−.22	0.25	−.19	0.32
BIG 5 assessed – agreeableness	−.12	0.54	−.15	0.44
BIG 5 assessed – openness	−.14	0.46	−.11	0.55
CVLT – interference list	−.064	0.74	.094	0.62

Simple logistic regression							95% C.I. for EXP (B)	
	B	S.E.	Wald	*df*	*Sig.*	OR	Lower	Upper
ASI assessed – alcohol to intoxication at least one year during lifetime								
Total lifetime months of regular attendance at hoasca rituals	−.022	0.010	4.507	1	0.034*	0.979	0.959	0.998
Constant	1.719	0.814	4.46	1	0.035*	5.577		
ASI assessed – cannabis use at least one year during lifetime								
Total lifetime months of regular attendance at hoasca rituals	−.014	0.008	2.887	1	0.089	0.986	0.97	1.002
Constant	1.82	0.795	5.234	1	0.022*	6.17		
ASI assessed – alcohol to intoxication at least one year during lifetime								
Number of hoasca rituals attended during the previous 12 months	−.075	0.040	3.605	1	0.058	0.928	.858	1.002
Constant	2.824	1.453	3.777	1	0.052	16.850		
ASI assessed – cannabis use at least one year during lifetime								
Number of hoasca rituals attended during the previous 12 months	−.013	0.034	.144	1	0.704	0.987	.923	1.055
Constant	1.162	1.303	.795	1	0.373	3.196		

* Significant at 0.05 level.

use, the UDV group consumed less alcohol in the previous 30 days, and their cannabis use did not differ from that of controls.

The UDV demonstrated better status than controls on the SF-36-assessed role limitations due to health and this status was positively associated with increasing lifetime attendance to hoasca sessions.

The UDV group demonstrated healthier scores on self-assessments of current mood state; i.e., less depression and confusion. They scored higher on the Big Five personality factors of agreeableness and openness. Previous studies [47–49] suggested that higher scores for these three are negatively correlated with alcohol and substance use, anxiety, depression, and antisocial personality disorders. In the present study, the UDV group's lower DUREL-assessed organizational religious activity was expected due to the more frequent ceremonies held by the control religious groups – weekly vs twice a month for the UDV. Interestingly, DUREL-assessed organizational religious activity had a significant positive association with the number of hoasca ceremonies attended during the previous 12 months but not with the longer term hoasca variable total lifetime months of regular attendance at hoasca rituals.

Table 3
Substance use.

	UDV ($N = 30$)		Control ($N = 27$)		*p*	Test	Cramer's V
Alcohol and drug use							
Alcohol							
Any use previous 30 days	2	(6.7%)	16	(59.3%)	$p < 0.001$**	χ^2	.57
At least one year lifetime	21	(70.0%)	14	(51.9%)	$p = 0.16$	χ^2	.19
Alcohol to intoxication							
Any use previous 30 days	1	(3.3%)	2	(7.4%)	$p = 0.60$	Fisher	.09
At least one year lifetime	16	(53.3%)	5	(18.5%)	$p = 0.007$**	χ^2	.36
Cannabis							
Any use previous 30 days	1	(3.33%)	–		$p = 1.0$	Fisher	.13
At least one year lifetime	20	(66.7%)	6	(22.2%)	$p = 0.001$**	χ^2	.45
Other drugs							
At least one year lifetime	2	(6.7%)	3	(11.1%)	$p = 0.66$	Fisher	.08

** Significant at 0.01 level.

Table 4
Quality of life, profile of mood states, personality traits and impulsivity.

	UDV				Control				Statistics		
	N	Median	Min	Max	N	Median	Min	Max	*U*	*p*	*r*
SF-36 quality of life											
Physical functioning	30	97.5	80.0	100	27	100	40.0	100	375	0.60	.069
Role limitations due to physical health	30	100	25.0	100	27	100	0	100	311	0.035*	.28
Role limitations due to emotional problems	30	100	0	100	27	100	0	100	335	0.14	.20
Energy/fatigue	29	70.0	45.0	100	27	60.0	0	85.0	306	0.16	.19
Emotional well being	30	84.0	60.0	100	27	84.0	28.0	96.0	352	0.39	.12
Social functioning	30	100	50.0	100	27	87.5	37.5	100	343	0.28	.15
Pain	30	90.0	57.5	100	27	90.0	45.0	100	362	0.48	.095
General health	30	85.0	65.0	100	27	80.0	40.0	95.0	312	0.13	.20
Profile of Mood States											
Depression	30	1.00	0	9.00	26	2.50	0	12.0	270	0.043*	.27
Anger	30	1.00	0	8.00	26	2.00	0	10.0	292	0.096	.22
Vigor	29	13.0	2.00	20.0	26	11.5	0	17.0	310	0.25	.16
Tension	30	3.00	0	9.00	26	4.00	0	11.0	281	0.069	.24
Fatigue	30	5.00	0	13.0	27	5.00	0	17.0	381	0.69	.053
Confusion	30	2.50	1.00	6.00	27	4.00	1.0	16.0	273	0.032*	.29
Big five personality traits											
Extraversion	30	3.63	1.25	4.88	27	3.63	2.38	5.00	364	0.51	.087
Agreeableness	30	4.22	3.56	5.00	27	3.89	2.78	4.89	268	0.028*	.29
Conscientiosness	30	4.22	3.33	4.89	27	4.00	2.78	5.00	293	0.071	.24
Neuroticism	30	2.31	1.00	3.88	27	2.50	1.25	4.00	338	0.28	.14
Openness	30	4.10	3.40	5.00	27	3.90	2.10	4.80	275	0.037*	.28
Barratt Impulsiveness Scale											
Attentional	30	12.0	9.00	22.0	27	15.0	9.00	24.0	293	0.070	.24
Motor	30	20.0	16.0	24.0	27	21.0	16.0	32.0	340	0.30	.14
Nonplanning	30	20.0	14.0	27.0	25	22.0	12.0	30.0	293	0.16	.19
Impulsiveness global	30	53.5	44.0	65.0	25	57.0	37.0	86.0	272	0.081	.24

* Significant at 0.05 level.

4.2. Substance use and psychological functioning

We found that the UDV group, while evincing greater past use of alcohol to intoxication, also drank less than the controls during the preceding 30 days. This suggests that ritual use of hoasca reduces alcohol use and abuse. Previous studies comparing ritual hoasca users to controls reported similar data [4,26,28,50]. The UDV group's lower scores on POMS-assessed negative mood states are consistent with previous case-control and cross-sectional evaluations that found greater psychiatric health in hoasca-using groups than control groups and normative data [24,25,51].

Organizational aspects of the UDV might be contributing to our results. For example, there was no difference in recent cannabis use between the UDV members and controls. This finding differs from that of Fabregas et al. [26] who reported greater use in their hoasca group compared to controls. This most likely because the authors evaluated other hoasca-using groups, one of which sanctions cannabis use. This contrasts with the stricter attitude of the UDV towards cannabis use.

Only past use of alcohol to intoxication was significantly correlated with one ritual hoasca attendance variable; that is, total lifetime months of regular attendance at hoasca rituals. The lack of significant correlations between any other drug use, psychological and neuropsychological measures and UDV ritual attendance, as well as the UDV group's better scores on measures of mood and personality, indicates possible selection-bias. For example, those with greater openness may be more likely to search for a psychedelic-based religion and to successfully integrate this altered state into their everyday lives. Those with lower confusion levels may be less prone to adhere to the UDV's rigorous discipline regarding one's behavior. It may be that newcomers to the UDV who have higher levels of confusion and who do not possess prominent traits of openness do not continue in the church and therefore are missed in cross-sectional studies.

However, previous studies demonstrated that hoasca use may involve a powerful combination of experiential processes and pharmacological properties that results in dramatic short-term changes on mood, personality and substance use. For example, experiential effects have been demonstrated in a clinical research with the DMT-like compound psilocybin that indicated that the intensity of a psychedelic-induced "mystical experience" is associated with relatively stable increases in the personality trait of openness [52]. Further, a recent study of psilocybin-assisted psychotherapy for alcohol dependence demonstrated a relationship between the intensity and mystical quality of the altered state experienced and improvement of drinking outcomes [53].

Regarding pharmacological mechanisms, Osório et al. [54] reported acute antidepressant effects that lasted three weeks after a single administration of hoasca. A possible mechanism suggested by the authors is harmine-induced

Table 5
Neuropsychological function.

	UDV				Control				Statistics		
	N	Median	Min	Max	N	Median	Min	Max	*U*	*p*	*r*
AMNART											
AMNART	24	120	107	130	27	118	105	130	323	0.99	.003
Stroop											
Word	29	97.0	68.0	120	27	98.0	71.0	130	351	0.51	.089
Color	29	76.0	49.0	92.0	27	73.0	46.0	97.0	353	0.53	.085
Incongruent word/color	29	48.0	29.0	64.0	27	43.0	30.0	62.0	283	0.075	.24
Interference effect	29	25.0	16.0	51.0	27	28.0	4.00	42.0	328	0.30	.14
California Verbal Learning Test											
Trial 1	29	8.00	3.00	12.0	27	8.00	4.00	11.0	386	0.93	.013
Trial 2	30	11.0	6.00	14.0	27	11.0	7.00	15.0	361	0.47	.096
Trial 3	30	12.0	8.00	16.0	27	13.0	7.00	16.0	339	0.29	.14
Trial 4	30	12.5	8.00	16.0	27	13.0	8.00	16.0	393	0.85	.026
Trial 5	29	13.0	9.00	16.0	27	14.0	8.00	16.0	369	0.70	.051
Sum trials 1–5	28	54.5	39.0	70.0	27	59.0	36.0	71.0	377	0.98	.004
Sum intrusions 1–5 trials CVLT	28	.00	0	5.00	27	1.00	0	7.00	313	0.23	.16
Interference list	30	8.00	5.0	12.0	27	7.00	5.00	11.0	279	0.040*	.27
Short delay free recall	30	12.5	6.00	16.0	27	13.0	7.00	16.0	388	0.78	.038
Short delay cued recall total	29	13.0	7.00	16.0	27	13.0	8.00	16.0	377	0.80	.034
Long delay free recall	29	13.0	7.00	16.0	27	13.0	6.00	16.0	376	0.80	.035
Long delay cued recall total	30	14.0	7.00	16.0	27	13.0	8.00	16.0	399	0.92	.013
Long delay cued recall intrusions	30	.000	0	5.00	27	.00	.00	5.00	399	0.90	.017
Recognition	29	15.0	12.0	16.0	27	15.0	13.0	16.0	386	0.92	.014
Proactive interference	29	0.20	−.42	1.00	27	−.11	−.29	.50	285	0.080	.23
Trail Making Test											
TMT A	30	25.5	14.0	83.0	27	26.0	18.0	48.0	355	0.42	.11
TMT B	30	59.5	35.0	123	27	60.0	34.0	119	349	0.37	.12
TMTB minus TMTA	30	30.0	17.0	73.0	27	35.0	11.0	82.0	338	0.28	.14
Rey–Osterrieth Complex Figure											
Copy	30	34.0	22.5	36.0	27	34.0	25.0	36.0	386	0.75	.042
Immediate recall	29	24.0	10.0	36.0	27	23.0	5.00	33.0	315	0.21	.17
Delayed recall	30	23.5	8.00	34.0	27	20.0	12.0	34.0	347	0.35	.12
Connners Continuous Performance Test											
Omissions	30	.000	0	9.00	27	1.00	0	17.0	375	0.60	.070
Commissions	30	11.5	2.00	26.0	27	11.0	3.00	32.0	398	0.90	.016
Hit reaction time	30	329	271	569	27	367	285	438	338	0.28	.14
Hit reaction time standard error	30	4.44	3.38	7.73	27	5.27	3.07	9.38	301	0.096	.22
Variability	30	5.42	2.81	12.1	27	5.70	3.22	17.6	350	0.38	.12
Detectability (d′)	30	.55	.17	2.18	27	.66	−.060	1.35	402	0.96	.008
Response style indicator (ß)	30	.34	0	2.12	27	.38	0	1.08	404	0.98	.004
Perseverations	30	.000	0	23.0	27	.000	0	24.0	378	0.58	.075
Hit reaction time by block change	30	.000	−.030	.060	27	.000	−.060	.050	361	0.48	.095
Standard Error by Block	30	−.020	−.12	.18	27	.000	−.18	.23	333	0.25	.15
Reaction time by inter-stimulus interval	30	.050	−.020	.090	27	.050	.010	.13	347	0.35	.13
Standard error by inter-stimulus interval	30	.010	−.18	.24	27	.020	−.26	.22	337	0.28	.15

* Significant at 0.05 level.

elevation of brain-derived neurotrophic factor (BDNF) levels. Finally, another research group found out that hoasca inhibits ethanol-induced locomotion and prevents ethanol sensitization in mice models [55]. The pathways involved in these models are thought to share the same mesolimbic dopaminergic pathways that underlie human craving and compulsive use of abused substances [56].

These studies are consistent with qualitative reports from members of the UDV who state that the visionary experiences induced by hoasca are essential to the positive behavioral effects associated with church membership [4] and with a prospective study found that the mood of novice hoasca-church members mood improved after their first session [7,27]. Thus, it may be that data regarding experienced hoasca users reflect longer-term, and relatively stable effects of hoasca use, and miss more dramatic changes occurring in the earlier phases.

4.3. Neuropsychological functioning

The results from the interference list task of the California Verbal Learning Test (CVLT) indicated that there were

overall no group differences in verbal memory ability. However, the UDV group achieved better scores a measure of proactive interference than controls suggesting that controls were more susceptible to the effects of prior learning when trying to learn new and similar information [57]. This is consistent with previous results using a similar instrument – the World Health Organization Auditory Verbal Learning Test – demonstrating better learning performance in adult UDV members than in controls [4].

One possible reason for this finding is that UDV teachings are communicated during hoasca sessions during which members are encouraged to pay attention and memorize verbal information. Hence, regular ritualized practice of verbal learning and memory skills during the highly active mental state induced by hoasca may perhaps strengthen verbal learning in other contexts as well.

There were no differences between groups on the American version of the Nelson Adult Reading Test (AMNART) scores estimating pre-morbid intelligence suggesting that the groups were also equivalent with regard to overall cognitive ability prior to the UDV group's use of hoasca. Neither there were differences between the groups on the Stroop, Trail Making Test, Rey–Osterrieth Complex Figure and Connners Continuous Performance Test. These data differ dramatically from studies indicating that alcohol, cocaine, opiates, or amphetamines abusers, and benzodiazepine users, score worse on cognitive tests than controls. In addition, cognitive function worsens with the duration of these substances' use [58–60]. While it is difficult to assert that there is truly no effect of hoasca on neurocognitive functioning using inferential statistical analysis, the current findings of very small effect sizes in between groups analyses coupled with a lack of correlational findings between levels of hoasca use and cognitive functions strongly support the null hypothesis. That this is the fourth study [see References 4, 24, and 50] to report a lack of differences between hoasca users and control groups on tests of cognitive function serves as additional evidence that hoasca has no long term effects.

5. Conclusion

In this, the most comprehensive and rigorous evaluation of ritual hoasca users in North America to date, we controlled for the well-known association between participation in organized religion and mental health in choosing our control group. Compared to a carefully SES-and-church-attendance-matched group of normal controls, we found that UDV members demonstrated better scores on mood, personality, and quality of life variables. In addition, with one exception (better performance among UDV members on the interference list of the California Verbal Learning Test) there were no significant differences in cognitive performance between the two groups. It also appears that participation in the UDV facilitated cessation of use and abuse of alcohol and cannabis.

Limitations of this cross-sectional design make the study vulnerable to selection-bias. That is, we did not study those who left the UDV in their early stages of participation, and thus with minimal use of hoasca. Moreover, multiple comparisons increase the likelihood of type I error. Therefore, prospective mental health and neuropsychological assessments of new hoasca users are necessary in order to address this issue. Neuroimaging studies will also shed light on hoasca effects on brain structure and activity, and are currently underway.

Hoasca religions are increasingly popular and legally-sanctioned in North America and Europe, thus adding to these cultures' religious diversity. In addition, non-religious hoasca use is increasing around the world. This study provides evidence for reassuring safety of long-term hoasca use among UDV members, and indicates several intriguing beneficial effects.

Acknowledgment

We wish to thank the following persons and organizations for their contributions to the study. From the University of New Mexico, Albuquerque, NM: for data collection, Michael Hunter; for quality assurance and regulatory compliance, Erika Griffiths and Linda A. Schenkel. From Centro Espírita Beneficente União do Vegetal (UDV): Departamento Médico Científico (DEMEC) and the leadership and volunteers for supporting the study. From the Albuquerque religious communities which participated in the study: priests, ministers and volunteers for their support and time to undergo the evaluations.

References

[1] McKenna DJ, Towers GH, Abbott F. Monoamine oxidase inhibitors in South American hallucinogenic plants: tryptamine and beta-carboline constituents of ayahuasca. J Ethnopharmacol 1984;10(2):195-223.
[2] McKenna DJ. Clinical investigations of the therapeutic potential of ayahuasca: rationale and regulatory challenges. Pharmacol Ther 2004;102(2):111-29.
[3] Gaujac A, Navickiene S, Collins MI, Brandt SD, de Andrade JB. Analytical techniques for the determination of tryptamines and β-carbolines in plant matrices and in psychoactive beverages consumed during religious ceremonies and neo-shamanic urban practices. Drug Test Anal 2012;4(7–8):636-48.
[4] 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(2):86-94.
[5] Riba J, Rodríguez-Fornells A, Urbano G, Morte A, Antonijoan R, Montero M, et al. Subjective effects and tolerability of the South American psychoactive beverage ayahuasca in healthy volunteers. Psychopharmacology (Berl) 2001;154(1):85-95.
[6] Riba J, Barbanoj MJ. Bringing ayahuasca to the clinical research laboratory. J Psychoactive Drugs 2005;37(2):219-30.
[7] Barbosa PCR, Giglio JS, Dalgalarrondo P. Altered states of consciousness and short-term psychological after-effects induced by the first time ritual use of ayahuasca in an urban context in Brazil. J Psychoactive Drugs 2005;37(2):193-201.

[8] Callaway JC, McKenna DJ, Grob CS, Brito GS, Raymon LP, Poland RE, et al. Pharmacokinetics of hoasca alkaloids in healthy humans. J Ethnopharmacol 1999;65(3):243-56.
[9] Trichter S, Klimo J, Krippner S. Changes in spirituality among ayahuasca ceremony novice participants. J Psychoactive Drugs 2009;41(2):121-34.
[10] de Araujo DB, Ribeiro S, Cecchi GA, Carvalho FM, Sanchez TA, Pinto JP, et al. Seeing with the eyes shut: neural basis of enhanced imagery following ayahuasca ingestion. Hum Brain Mapp 2012;33(11):2550-60.
[11] Riba J, Romero S, Grasa E, Mena E, Carrió I, Barbanoj MJ. Increased frontal and paralimbic activation following ayahuasca, the pan-Amazonian inebriant. Psychopharmacology (Berl) 2006;186(1):93-8.
[12] Callaway JC, Raymon LP, Hearn WL, McKenna DJ, Grob CS, Brito GS, et al. Quantitation of N,N-dimethyltryptamine and harmala alkaloids in human plasma after oral dosing with ayahuasca. J Anal Toxicol 1996;20(6):492-7.
[13] Luna LE. Indigenous and mestizo use of ayahuasca. An overview. In: & Santos RG, editor. The ethnopharmacology of ayahuasca. Tivandrum: Transworld Research Network; 2011. p. 1-21. http://ejournal.narotama.ac.id/files/Indigenous%20and%20mestizo%20use%20of%20Ayahuasca.%20An%20overview.pdf [accessed 09.01.2016].
[14] Tupper KW. Ayahuasca healing beyond the Amazon: the globalization of a traditional indigenous entheogenic practice. Glob Netw 2009;9:117-36.
[15] UNCPS - United Nations United Nations Economic and Social Council. Convention on psychotropic substances, Vienna, Austria. https://treaties.un.org/doc/Publication/MTDSG/Volume%20I/Chapter%20VI/VI-16.en.pdf. 1971 [accessed 07.09.2016].
[16] de Rios MD, Rumrrill R. A hallucinogenic tea, laced with controversy: ayahuasca in the Amazon and the United States. Westport, CT: Praeger Publishers; 2008.
[17] CONAD - Conselho Nacional Antidrogas. Grupo Multidisciplinar de Trabalho - GMT. Ayahuasca: Relatório final. http://www.ayahuascabrasil.org/index.php?op=noticia010. 2012 [accessed 07.09.2016].
[18] CONFEN - Conselho Federal de Entorpecentes. 6th resolution. http://www.ayahuascabrasil.org/index.php?op=legis093. 1986 [accessed 07.09.2016].
[19] Labate BC, Feeney K. Ayahuasca and the process of regulation in Brazil and internationally: implications and challenges. Drug Policy 2012;23(2):154-61.
[20] Gonzales V. O Centro Espirita Beneficente União do Vegetal 2006; 546 U.S. 418, 126 S.Ct. 1211, 163. L. Ed. 2d 1017 U.S. LEXIS 1815 2006, 74 U.S.L.W. 4119.
[21] Bullis RK. The "vine of the soul" vs. the controlled substances act: implications of the hoasca case. J Psychoactive Drugs 2008;40(2):193-9.
[22] RFRA - Religious Freedom Restoration Act of 1993. 1993, 42 U.S.C. § 2000bb.
[23] Groisman A, de Rios MD. Ayahuasca, the U.S. Supreme Court, and the UDV-US government case: culture, religion and implications of a legal dispute. In: Winkelman MJ, & Roberts TB, editors. Psychedelic medicine: social, clinical and legal perspectives (Vol 1). Westport, CT: Praeger Publishers; 2007.
[24] Bouso JC, González D, Fondevila S, Cutchet M, Fernández X, Barbosa PCR, et al. Personality, psychopathology, life attitudes and neuropsychological performance among ritual users of ayahuasca: a longitudinal study. PLoS One 2012;7(8):e42421.
[25] Barbosa PCR, Mizumoto S, Bogenschutz MP, Strassman RJ. Health status of ayahuasca users. Drug Test Anal 2012;4(7–8):601-9.
[26] Fábregas JM, Gonzáles 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(3):257-61.
[27] Barbosa PCR, Cazorla IM, Giglio JS, Strassman R. A six-month prospective evaluation of personality traits, psychiatric symptoms and quality of life in ayahuasca-naïve subjects. J Psychoactive Drugs 2009;41:205-12.
[28] Halpern JH, Sherwood A, Passie T, Blackwel KC, Ruttember AJ. Evidence of health and safety in American members of a religion who use a hallucinogenic sacrament. Med Sci Monit 2008;14(8):SR15-22.
[29] Moreira-Almeida A, Neto FL, Koenig HG. Religiousness and mental health. Rev Bras Psiquiatr 2006;28(3):242-50.
[30] CEBUDV - Centro Espirita Beneficente União do Vegetal. Ayahuasca, Fundamentos e Objetivos. Brasília, DF; 1989.
[31] CASAA - Center on Alcoholism, Substance Abuse, and Addiction. Demographic interview. http://casaa.unm.edu/inst.html. 1997 [accessed 07.09.2016].
[32] Koenig HG, Büssing A. The Duke University Religion Index (DUREL): a five-item measure for use in epidemological studies. Religions 2010;1:78-85.
[33] Underwood LG, Teresi JA. The daily spiritual experience scale: development, theoretical description, reliability, exploratory factor analysis, and preliminary construct validity using health-related data. Ann Behav Med 2002;24(1):22-33.
[34] McHorney CA, Ware Jr JE, Raczek AE. The MOS 36-item short-form health survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31(3):247-63.
[35] McNair DM, Lorr M, Droppleman LF. EdITS manual for the profile of mood states. San Diego, CA: EdITS Educational and Industrial Testing Service; 1992.
[36] John OP, Srivastava S, John OP. The big five trait taxonomy: history, measurement, and theoretical perspectives. In: & Pervin LA, editor. Handbook of personality: theory and research. New York: Guilford Press; 1999. p. 102-38.
[37] Stanford MS, Mathias CW, Dougherty DM, Lake SL, Anderson NE, Patton JH. Fifty years of the Barratt impulsiveness scale: an update and review. Personal Individ Differ 2009;47:385-95.
[38] McLellan AT, Kushner H, Metzger D, Peters R, Smith I, Grissom G, et al. The fifth edition of the addiction severity index. J Subst Abuse Treat 1992;9:199-213.
[39] Grober E, Sliwinski M. Development and validation of a model for estimating premorbid verbal intelligence in the elderly. J Clin Exp Neuropsychol 1991;13(6):933-49.
[40] Reitan RM. Validity of the trail making test as an indicator of organic brain damage. Percept Mot Skills 1958;8:271-6.
[41] Bowie CR, Harvey PD. Administration and interpretation of the trail making test. Nat Protoc 2006;1:2277-81.
[42] Lansbergen MM, Kenemans JL. Stroop interference and attention-deficit/hyperactivity disorder: a review and meta-analysis. Neuropsychology 2007;21:251-62.
[43] Conners CK. Conners' continuous performance test II user's manual. Toronto, On: Multi-Health Systems; 2000.
[44] Norman MA, Evans JD, Miller WS, Heaton RK. Demographically corrected norms for the California Verbal Learning Test. J Clin Exp Neuropsychol 2000;22(1):80-94.
[45] Shin MS, Park SY, Park SR, Seol SH, Kwon JS. Clinical and empirical applications of the Rey–Osterrieth Complex Figure Test. Nat Protoc 2006;1(2):892-9.
[46] Laerd Statistics. Binomial logistic regression using SPSS statistics. Statistical tutorials and software guides. https://statistics.laerd.com. 2015 [accessed 07.09.2016].
[47] Kotov R, Gamez W, Schmidt F, Watson D. Linking "big" personality traits to anxiety, depressive, and substance use disorders: a meta-analysis. Psychol Bull 2010;136(5):768-821.
[48] Ruiz MA, Pincus AL, Schinka JA. Externalizing pathology and the five-factor model: a meta-analysis of personality traits associated with antisocial personality disorder, substance use disorder, and their co-occurrence. J Pers Disord 2008;22(4):365-88.
[49] Malouff JM, Thorsteinsson EB, Rooke SE, Schutte NS. Alcohol involvement and the five-factor model of personality: a meta-analysis. J Drug Educ 2007;37(3):277-94.

[50] Doering-Silveira E, Lopez E, Grob CS, de Rios M, Alonsi LK, Tacla C, et al. Ayahuasca in adolescence: a neuropsychological assessment. J Psychoactive Drugs 2005;37(2):123-8.
[51] Da Silveira DX, Grob CS, de Rios MD, Lopez E, Alonso LK, Tacla C, et al. Ayahuasca in adolescence: a preliminary psychiatric assessment. J Psychoactive Drugs 2005;37(2):129-33.
[52] MacLean KA, Johnson MW, Griffiths RR. Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. J Psychopharmacol 2011;25(11):1453-61.
[53] 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(3):289-99.
[54] Osório F de L, Sanches RF, Macedo LR, dos Santos RG, Maia-de-Oliveira JP, Wichert-Ana L, et al. Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report. Rev Bras Psiquiatr 2015;37(1):13-20.
[55] Oliveira-Lima AJ, Santos R, Hollais AW, Gerardi-Junior CA, Baldaia MA, Wuo-Silva R, et al. Effects of ayahuasca on the development of ethanol-induced behavioral sensitization and on a post-sensitization treatment in mice. Physiol Behav 2015;142:28-36.
[56] Pierce RC, Kumaresan V. The mesolimbic dopamine system: the final common pathway for the reinforcing effect of drugs of abuse? Neurosci Biobehav Rev 2006;30(2):215-38.
[57] Delis DC, Freeland J, Kramer JH, Kaplan E. Integrating clinical assessment with cognitive neuroscience: construct validation of the California Verbal Learning Test. J Consult Clin Psychol 1988;56(1):123-30.
[58] van Holst RJ, Schilt T. Drug-related decrease in neuropsychological functions of abstinent drug users. Curr Drug Abuse Rev 2011;4(1):42-56.
[59] Fernández-Serrano MJ, Pérez-García M, Schmidt Río-Valle J, Verdejo-García A. Neuropsychological consequences of alcohol and drug abuse on different components of executive functions. J Psychopharmacol 2010;24(9):1317-32.
[60] Barker MJ, Greenwood KM, Jackson M, Crowe SF. Cognitive effects of long-term benzodiazepine use: a meta-analysis. CNS Drugs 2004;18(1):37-48.