Available online at www.sciencedirect.com
ScienceDirect
Journal of Ethnopharmacology 112 (2007) 507–513
Journal of ETHNO-PHARMACOLOGY
www.elsevier.com/locate/jethpharm

Effects of ayahuasca on psychometric measures of anxiety, panic-like and hopelessness in Santo Daime members

R.G. Santos [a,*], J. Landeira-Fernandez [b], R.J. Strassman [c], V. Motta [a], A.P.M. Cruz [a]

[a] *Departamento de Processos Psicológicos Básicos, Instituto de Psicologia, Universidade de Brasília, Asa Norte, Brasília-DF 70910-900, Brazil*
[b] *Department of Psychiatry, University of New Mexico School of Medicine, Albuquerque, NM 87131, USA*
[c] *Departamento de Psicologia, Pontifícia Universidade Católica do Rio de Janeiro, PUC-RJ, Brazil*

Received 21 December 2006; received in revised form 16 April 2007; accepted 18 April 2007
Available online 25 April 2007

Abstract

The use of the hallucinogenic brew ayahuasca, obtained from infusing the shredded stalk of the malpighiaceous plant *Banisteriopsis caapi* with the leaves of other plants such as *Psychotria viridis*, is growing in urban centers of Europe, South and North America in the last several decades. Despite this diffusion, little is known about its effects on emotional states. The present study investigated the effects of ayahuasca on psychometric measures of anxiety, panic-like and hopelessness in members of the Santo Daime, an ayahuasca-using religion. Standard questionnaires were used to evaluate state-anxiety (STAI-state), trait-anxiety (STAI-trait), panic-like (ASI-R) and hopelessness (BHS) in participants that ingested ayahuasca for at least 10 consecutive years. The study was done in the Santo Daime church, where the questionnaires were administered 1 h after the ingestion of the brew, in a double-blind, placebo-controlled procedure. While under the acute effects of ayahuasca, participants scored lower on the scales for panic and hopelessness related states. Ayahuasca ingestion did not modify state- or trait-anxiety. The results are discussed in terms of the possible use of ayahuasca in alleviating signs of hopelessness and panic-like related symptoms.

Keywords: Ayahuasca; *Banisteriopsis caapi*; *Psychotria viridis*; Emotional states; BHS; ASI-R

1. Introduction

Ayahuasca is a Quechua term derived from the juxtaposition of the terms: *Aya*–"*soul*" "*dead spirit*"; *Waska*–"*rope*", "*vine*", and thus is loosely translatable "vine of the souls" or "vine of the dead". Ayahuasca refers to the vine used as the principle ingredient of a psychoactive beverage used by more than 70 different indigenous groups spread along Brazil, Colombia, Peru, Venezuela, Bolivia and Ecuador (Goulart, 2005; Luna, 2005). The word *ayahuasca* is used to describe the spiritual force in the beverage or the beverage itself, which is made with several species of the *Banisteriopsis* vine (e.g., *Banisteriopsis caapi*, *Banisteriopsis muricata*) (Malpighiaceae), usually in combination with other plants, such as *Psychotria viridis* or *Diplopterys cabrerana* (Ott, 1994). Ayahuasca also may refer to preparations containing only the vine, as made by the Maku Indians, for example (Davis, 1997).

Since the beginning of the 20th century ayahuasca has been used by syncretic religious cults created in the Amazonian Brazilian states of Acre and Rondônia. These groups, of which Santo Daime, Barquinha and União do Vegetal (UDV) are the main ones, use ayahuasca as a healing tool and as a vehicle to gain access to the divine realm. These churches are highly syncretic, containing influences from popular Catholicism, European esoteric and spiritual beliefs, African cosmologies, and indigenous botanical knowledge. Their use of ayahuasca as sacrament resembles that of the Christian Eucharist. In the Santo Daime and UDV rites, members drink ayahuasca usually twice a month, and in Barquinha it is not unusual to consume the brew four times per week (Araújo, 1999; Labate and Araújo, 2004).

Abbreviations: DMT, *N*,*N*-dimethyltryptamine; THH, tetrahydroharmine; 5-HT, 5-hydroxytryptamine; MAO, monoamine oxidase; SSRIs, selective serotonin reuptake inhibitors; SPECT, single photon emission computerized tomography; GC/MS, gas chromatography/mass spectrometry; STAI, state–trait-anxiety inventory; A-state, state-anxiety; A-trait, trait-anxiety; ASI-R, revised anxiety sensitivity index; BHS, Beck hopelessness scale; UDV, União do Vegetal

* Corresponding author. Current address: Centre d'Investigació de Medicaments, Institut de Recerca, Servei de Farmacologia Clínica, Hospital de la Santa Creu i Sant Pau (HSCSP), St. Antoni Maria Claret, 167, Barcelona 08025, Spain. Tel.: +34 93 2919019; fax: +34 93 2919286.
E-mail address: banisteria@gmail.com (R.G. Santos).

0378-8741/$ – see front matter © 2007 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.jep.2007.04.012

Several studies (e.g., McKenna and Towers, 1981; McKenna et al., 1984; Callaway, 1988; McKenna et al., 1990, 1998; Callaway et al., 1999) have indicated that the main components of ayahuasca, the *N*,*N*-dimethyltryptamine (DMT) and some beta-carbolines, are structurally similar to serotonin (5-hydroxytryptamine or 5-HT), a neurotransmitter present in the nervous system of most animal species. Correspondently, further observations found these ayahuasca components to display high affinity for serotonin receptors, especially the 5-HT_2 receptor subtype (Smith et al., 1998; Grella et al., 2003).

The beta-carbolines in ayahuasca include harmine, harmaline and tetrahydroharmine (THH). DMT is an ultra-short-acting hallucinogenic tryptamine (Callaway et al., 1999) present in several plants used as admixtures to the *Banisteriopsis caapi* vine in ayahuasca preparations. DMT also is present in tissues of mammals, marine animals and amphibians. In human beings it also is endogenous, being found in blood, urine and cerebrospinal fluid (Strassman, 2001). Despite being a potent psychoactive chemical, DMT is inactive following oral administration at doses up to 1000 mg, probably due to degradation by gastrointestinal and liver MAO (monoamine oxidase) (McKenna et al., 1984). However, when DMT is combined with inhibitors of the MAO enzymes, as are the beta-carbolines present in ayahuasca, it becomes able to reach the systemic circulation and the central nervous system, thus producing its effects (McKenna et al., 1984).

The beta-carbolines present in ayahuasca are potent natural, selective, reversible, competitive inhibitors of peripheral MAO, and are more active against MAO-A than MAO-B. They also have a relatively low affinity for liver MAO compared to brain MAO (McKenna et al., 1984, 1998). There is some evidence, however, that THH, the second most abundant beta-carboline in the beverage, acts as a selective inhibitor of serotonin reuptake as well as an MAO inhibitor (McKenna et al., 1998; Frecska et al., 2004). The inhibition of both systems – MAO and serotonin reuptake – by ayahuasca's beta-carbolines may result in elevated levels of brain serotonin (McKenna et al., 1998; Luna, 2005).

Despite the fact that the use of ayahuasca is a relatively widespread practice in countries like Brazil, Peru and Colombia, and that this practice is spreading to the United Sates, Europe and other parts of the world, there are few studies that have examined the brew with rigorous methodologies. One of these investigations is the biomedical study conducted by Grob et al. (1996), who investigated 15 long-term users of the brew regarding its acute and long-term psychological effects as well assessing peripheral serotonergic function (Callaway et al., 1994; Grob et al., 1996).

Grob et al.'s study reported that the ayahuasca-using members of the UDV church among whom the volunteers came were more reflective, confident, gregarious and optimistic compared to the control group, which had never used ayahuasca and was age-, gender-, education-, and socio-economically matched.

However, with respect to our research objectives, the most interesting findings were those that showed that before membership in the religion, 11 of the participants were diagnosed as having previously been afflicted with alcohol abuse disorders, 2 with major depressive disorders, 4 with drug abuse (cocaine and amphetamines), 11 with tobacco addiction, and 3 with phobic anxiety disorders. Five of the participants with a history of alcoholism also had histories of violent behavior associated with binge drinking. All of these psychiatric diagnoses remitted following entry into the religion. All participants reported that their use of ayahuasca within the religious context led to improved mental and physical health and significant improvements in interpersonal, work, and family interactions (Grob et al., 1996; McKenna et al., 1998).

Assessing serotonergic function the authors found a significant up-regulation in the density of the serotonin transporter in blood platelets of the ayahuasca drinkers compared to the control group (Callaway et al., 1994). Up- or down-regulation of peripheral platelet receptors is considered to reflect similar biochemical events occurring in the brain. None of the participants showed evidence of any neurological or psychiatric deficit.

Callaway hypothesized that the causative agent of this platelet effect was tetrahydroharmine (THH). In a self-experiment, he underwent single photon emission computerized tomography (SPECT) scans of his own brain 5-HT uptake receptors before and after a 6-week course of daily dosing with THH. He found that the density of central 5-HT receptors in the prefrontal cortex had increased. During recovery over the next several weeks their density gradually returned to previous levels.

According to McKenna et al. (1998) a deficit of serotonin reuptake sites in frontal cortex has been found to correlate with aggressive behavior in alcoholics. If THH were able to specifically reverse this deficit, it may have applications in the treatment of this behavior. As mentioned previously, the majority of the participants in the Grob et al. study had a previous history of alcoholism, some displaying violent behavior. Although the behavioral transformation could be due to the supportive social and psychological environment of a religious group, the finding of this long-term change in precisely the serotonin system that is deficient in violent alcoholics argues that biochemical factors also may play a role (McKenna et al., 1998).

It is well established that anxiety, panic and depressive-related symptoms are significantly attenuated by 5-HT agonists, such as tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs), as well as by MAO-A inhibitors that also exert an indirect agonist action on serotonergic neurotransmission (for recent reviews, see Wikinski, 2004; Nash and Nutt, 2005; Starcevic, 2006). The fact that ayahuasca preparations contain alkaloids that inhibit both the serotonin reuptake and MAO-A suggests that the brew might attenuate emotional states regulated by the serotoninergic system. The present study investigated this possibility by assessing anxiety, panic and depression psychometric items in a double-blind protocol in long-term members of the ayahuasca-using Santo Daime cult.

2. Methodology

2.1. Subjects

Nine healthy volunteers (6 males and 3 females; between 35 and 56 years of age) of the Santo Daime cult community

Céu do Planalto participated in the study. Eight volunteers had graduated high school, while one had finished college.

Eligibility criteria included: (1) voluntary participation as documented through the signing of written informed consent; (2) long-term use of the brew, as defined by a minimum of ten years use at a frequency of once every 2 weeks, within the context of the Santo Daime cult.

Exclusion criteria included: (1) prior history of hypertension, diabetes or cardiac pathology; (2) current treatment with any of the following drugs: antipsychotics, anxiolytics, antidepressants, mood stabilizers, or appetite suppressants related to amphetamine; (3) pregnant or breastfeeding women.

No alcoholic beverages or other drugs were consumed 24 h before the psychometric evaluation, but five of the volunteers had consumed ayahuasca before data collection, at 22, 20, 18, 16 and 6 h (data not treated differently). Volunteers refrained from tobacco and caffeine-rich beverages 1 h before the data collection.

The study was conducted in accordance with the Declarations of Helsinki and Tokyo concerning experimentation on humans, and was approved by the university's ethics committee at the University of Brasilia, Brazil (#059/2005).

2.2. Ayahuasca

We obtained a 2 l standard sample of the brew prepared by members of the Santo Daime community consisting of the stalks of *Banisteriopsis caapi* Spruce ex Grisebach (Malpighiaceae) combined with the washed leaves of *Psychotria viridis* Ruíz et Pavón (Rubiaceae), boiled and concentrated for several hours. All the ayahuasca used in the study was from this first sample.

To each liter of ayahuasca were added 70 g of artificial grape juice (®*Fresh*, Kraft Foods Brazil S.A.), 3 ml of cherry essence (®*Saborfort*, Mix Industry of Food Products LTDA., Brazil) and 3 ml of saccharin- and cyclamate-based artificial sweetener (®*Finn*, Boehringer Ingelheim Brazil). This procedure was designed to disguise the distinctive flavor, odor and color of ayahuasca in order to blind the volunteers regarding whether they received ayahuasca or vehicle-control.

The vehicle-control solution consisted of the same admixtures, while mineral water was used instead of ayahuasca. This solution was used only in the pre-treatment session.

In order to give the control solution the flavor of ayahuasca, to minimize the probability of solution identification by the participants of the study, 60 ml/l of ayahuasca were added to the vehicle-control solution used in the experimental sessions. As the doses used during the study were established in 50 ml, each individual dose of this ayahuasca-flavored solution contained approximately 3 ml of ayahuasca.

Solutions were administered in a double-blind manner.

2.3. Chemical analysis

A 500 ml sample of the ayahuasca used in the present study was assayed for the concentration of relevant alkaloids. This analysis was performed using gas chromatography/mass spectrometry (GC/MS) with the following instruments: chromatograph Agilent Technologies 6890N, mass selective detector (operating at 70 eV) Agilent Technologies 5973-Inert (500-40 *m/z*), automatic injector Agilent Technologies 7683B Series equipped with a DB-5ms column (0.2 mm × 25 m × 0.33 μm). Initial temperature was 200 °C, while the final was 300 °C. The ramp rate was 50 °C/min initiated 0 min after the injection of the sample. Injector temperature was 280 °C. About 0.2 μl of ayahuasca were injected.

2.4. Psychometric instruments

As opposed to the relative lack of physiological measures of motivation, psychometric research has developed several scales to evaluate the explicit motivational system. We used three scales to evaluate anxiety: one to evaluate state, or current, anxiety (anxiety-state), one to evaluate more persistent traits of anxiety (anxiety-trait), and one to evaluate panic.

State- and trait-anxiety were measured by the state–trait-anxiety inventory (STAI), previously translated and validated for a Brazilian sample. The STAI quantifies state-anxiety (A-state), which fluctuates in intensity throughout time. State-anxiety is to be distinguished from, trait-anxiety (A-trait), characterized by more persistent nature of one's reactivity to the environment.

In order to evaluate panic-like related states, the anxiety sensitivity index (ASI-R) was used, a Brazilian version that is still in the validation phase. The concept of anxiety sensitivity relates to the *fear* of feeling anxious; in other words, the belief that the somatic anxiety symptoms may have disastrous consequences. A person with high scores in anxiety sensitivity, for example, will more likely interpret somatic anxiety symptoms such as palpitations, dizziness, nausea and sweating as indicative of a highly pathological process, compared to a person that is less sensitive to these symptoms. Several studies have showed that this anxiety sensitivity index is closely related to the diagnosis of panic disorder.

In order to evaluate hopelessness related symptoms the Beck hopelessness scale (BHS) was used. This instrument is composed of statements regarding thoughts and beliefs about the future. These items measure three aspects of hopelessness: pessimism about the future, loss of motivation, and negative expectations. This hopelessness construct operates in many mental disorders and is highly correlated with measures of clinical depression and suicidal ideation.

2.5. Study design and experimental procedure

Initially, a general description of the study was made to the members of the Santo Daime cult, including information about the objectives of the research and methods to be used.

Volunteers were enrolled through the signing of a written informed consent. Baseline, pre-treatment, evaluations were then performed to assess state-anxiety, trait-anxiety, state panic, and depression, using a ritual developed exclusively for this study. During this 1 h ceremony the study participants remain seated chanting religious hymns, and the inactive vehicle-control solution is administered in a non-blind manner. We designed this procedure, which is essentially a Santo Daime ceremony

without active ayahuasca, in order that the participants could experience the taste, odor and color of the vehicle-control solution.

The inactive vehicle solution was administered to all participants at the beginning of the ritual. One hour after the consumption of this solution the questionnaires were distributed to each participant in a randomized fashion and participants were then instructed as how to fill out the rating scales. Since ayahuasca can produce effects in different times from person to person, this randomized method guarantees more veracity to the results when the participants are under the effects of ayahuasca in the experimental sessions, because each questionnaire will be answered in distinct moments. We chose this 1 h point after the consumption of the solution because the most intense effects of ayahuasca occur between 60 and 120 min (Riba et al., 2001).

The following week the first experimental session took place, using the same methodology and structure of the pre-treatment session. However, in this session, five participants took the full-ayahuasca solution and four took the ayahuasca-flavored solution in a double-blinded manner. Questionnaires were distributed similarly as in the pre-treatment session, and one of the authors briefly reminded subjects of the correct procedure to fill out the questionnaires.

A week later, the second experimental session took place in which those who had received the full-ayahuasca solution took the ayahuasca-flavored solution, and those who had consumed the ayahuasca-flavored solution took the full-ayahuasca solution.

The solutions were in opaque plastic cups in order to further disguise the appearance of each solution. Each volunteer was assigned a number by which he or she would know which cup to take from a table upon which the cups were placed.

2.6. Statistical analysis

The results were initially evaluated by a *t*-test to verify an order ingestion effect upon any of the outcome measures. Then, *t*-test was also employed to examine any treatment (vehicle × ayahuasca) effect. We required a significance level of $P < 0.05$ to be considered statistically significant.

3. Results

3.1. Chemical analysis

The analysis showed the presence of the beta-carbolines harmine, tetrahydroharmine (THH), harmaline, harmol, and *N*,*N*-dimethyltryptamine (DMT) (Fig. 1). These findings are consistent with the data from previous investigations that found harmine, tetrahydroharmine, harmaline, and *N*,*N*-dimethyltryptamine as the mains constituents of ayahuasca (McKenna et al., 1984; Callaway et al., 1999). Our identification of harmol confirms previous reports of the presence of trace concentrations of other beta-carbolines in ayahuasca (McKenna et al., 1998; Riba et al., 2003).

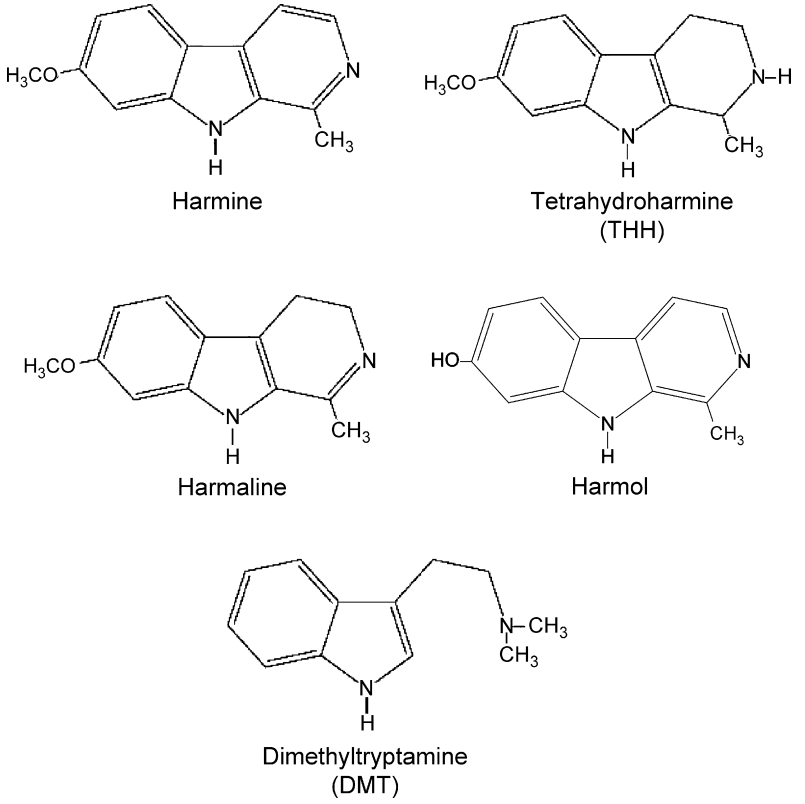

Fig. 1. Chemical analysis by gas chromatography/mass spectrometry (GC/MS) of the ayahuasca preparation used in this study.

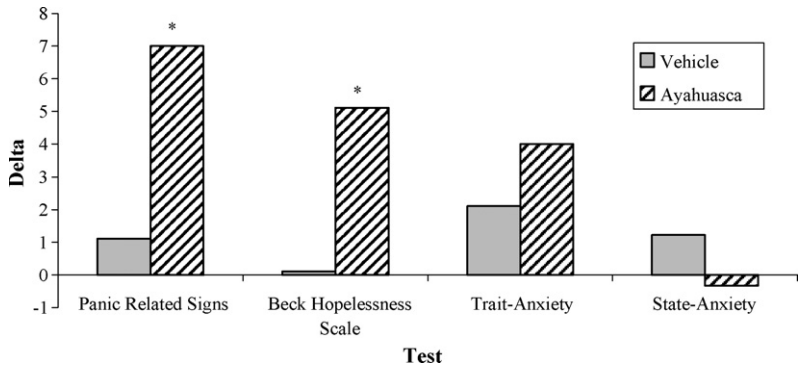

Fig. 2. Mean of changing scores from baseline to experimental sessions across the four different test. Participants ($n = 9$) ingested the vehicle-control solution (ayahuasca-flavored solution) or the full-ayahuasca solution. Asterisk (*) indicates a statistically difference between vehicle and ayahuasca treatments with a significance level of $P < 0.05$.

3.2. Psychometric measures

t-Test revealed that there was no significant effect of order of ingestion upon any outcome measures [panic-like related signs: vehicle ($t(7) = 0.24$; $P = 0.8$), ayahuasca ($t(7) = 0.46$; $P = 0.7$); Beck hopelessness scale: vehicle ($t(7) = 0.04$; $P = 0.9$), ayahuasca ($t(7) = 1.31$; $P = 0.1$); trait-anxiety: vehicle ($t(7) = 0.91$; $P = 0.3$), ayahuasca ($t(7) = 0.47$; $P = 0.7$); state-anxiety: vehicle ($t(7) = 1.24$; $P = 0.1$), ayahuasca ($t(7) = 0.98$; $P = 0.3$)]. Therefore data from the first and the second experimental sessions were pooled together. Moreover, statistical analyses were performed in change values, in which each score test from baseline was subtracted from those resulting from vehicle and from those resulting from ayahuasca and then compare these change scores to each other. A positive value indicates a reduction in the score whereas a negative value indicates an increase in the score from baseline to the experimental session.

Fig. 2 presents the mean change across the four measures. *t*-Test revealed a statistical significant change in panic-like related signs ($t(8) = 7.84$; $P < 0.001$) and Beck hopelessness scale: vehicle ($t(8) = 6.20$; $P < 0.001$), but no significant changes in trait-anxiety ($t(8) = 1.01$; $P = 0.2$) or state-anxiety vehicle ($t(8) = 0.64$; $P = 0.5$).

4. Discussion and conclusions

The present study investigated the effects of ayahuasca in anxiety, hopelessness and panic-like measures through a double-blind protocol in Santo Daime members. Acute ingestions of the brew significantly attenuated hopelessness and panic-like parameters as detected by BHS and ASI-R psychometric scales, respectively.

In accordance with previously reported studies (McKenna et al., 1984; Callaway et al., 1999), our sample of ayahuasca revealed the presence of the beta-carbolines harmine, THH and harmaline, and the tryptamine *N*,*N*-dimethyltryptamine (DMT). These chemical constituents are structurally similar to serotonin (McKenna et al., 1998; Callaway et al., 1999), exhibit great affinity for 5-$HT_{2A/2C}$ receptor subtypes (Smith et al., 1998; Grella et al., 2003) and exert an indirect agonist action in the serotonergic system. For example, THH selectively inhibits serotonin reuptake, while also inhibiting MAO-A (McKenna et al., 1998; Frecska et al., 2004). Harmine and harmaline reversibly inhibit the MAO-A and thus raise central levels of noradrenalin and serotonin. Also, it has been further indicated that these beta-carbolines preferentially inhibit MAO-A, the form of enzyme in which serotonin, and presumably other tryptamines, including DMT, are the preferred substrates in the brain (McKenna et al., 1984, 1998).

Taking into account this indirect agonist action of ayahusca at the monaminergic system, including the noradrenergic but preferentially the serotonergic system, we might speculate that the reduction of BHS and ASI-R psychometric parameters observed in the present study were mediated at least in part by this mechanism. This suggestion is supported by the fact that the majority of antidepressant/antipanic drugs also enhance noradrenergic and serotonergic functions, either inhibiting noradrenalin and serotonin reuptake, such as the tricycle antidepressants, or selectively inhibiting serotonin reuptake, such as the widely used selective serotonin reuptake inhibitors.

It also is possible that DMT, a 5-$HT_{2A/2C}$ agonist that exerts an effect similar of serotonin itself (Smith et al., 1998), could attenuate panic-like parameters since 5-HT_2 receptor activation in the dorsal periaqueductal grey has been associated to an alleviation of panic symptoms (Deakin and Graeff, 1991; Graeff et al., 1996). However, it is important to note that none of our volunteers had panic disorders or pathological depression, so clinical implication of these findings should be analyzed with caution.

In contrast to significant effect of ayahuasca in the BHS and ASI-R psychometric scales, the brew did not affect state- and trait-anxiety as assessed by STAI. To this respect, we must consider that our volunteers, all quite experienced in the use of ayahuasca, and all long-term members of the Santo Daime church, may have begun this study with low levels of anxiety. Thus, there was little room for change in a relatively low-anxiety group, and any putative anxiolytic effect of ayahuasca would not be apparent when pre-treatment levels were so low to begin with. Further studies might compare anxiolytic effects in ayahuasca-naïve volunteers. Besides, the complexity of ayahuasca's pharmacology, acting simultaneously upon other

different neurotransmitter systems, selectively affecting different subtypes of serotoninergic receptors, located throughout the brain, could also explain the absence of effects of ayahuasca on state- and trait-anxiety. Some receptors may have anxiogenic effects, while others could be anxiolytic, neutralizing the action of one against the others.

Considering that the volunteers, as members of the Santo Daime cult, believe that participation in the rituals, using ayahuasca, is helpful, the psychological changes observed in this study should be interpreted with caution. The acute psychological effects of ayahuasca can include euphoria, visions, new insights and even mystical experiences, all with potential beneficial effects, especially with people that have organized their live around the religious ceremonies with the brew.

Nevertheless, even if someone is not a member of a religious group that use ayahuasca, those profound psychological effects, mediated somehow by the pharmacology of ayahuasca, might by their own merit affect the psychological changes described. This line of reasoning, although considering the extrapharmacological variables, suggests that the brew, as solely a pharmacological agent, can produce beneficial effects on mood and anxiety.

Although this study investigated acute effects of the brew in those using it for at least 10 consecutive years, it is worth speculating that these positive effects may be applicable to the larger population. Many of the commonly prescribed and effective anxiolytic, anti-panic and antidepressant drugs have the same mechanisms of action as those of ayahuasca. In addition, the psychological effects of ayahuasca may have their own set of beneficial properties.

The possible therapeutic use of substances like ayahuasca also must take into account extra-pharmacological variables, usually referred to as *set* and *setting*. *Set* contains the motivation, expectation, and preparation of the individual, as well as his or her biology and personality. The *setting* is the environment, social and interpersonal, within which the person's experience takes place; it subsumes, as well, the personalities of the people administering the compound of interest. From a quality control and experimental consistency point of view, one also must consider the purity and consistency of the drug itself, and dose effects.

Careful consideration of these variables and their optimal management will be necessary to maximize the therapeutic potential and minimize adverse sequelae associated with hallucinogenic substances (Strassman, 1984; Grof, 2001).

Acknowledgements

This work was made possible by the support from Fernando de la Rocque Couto and other members of the Centro Eclético da Fluente Luz Universal Alfredo Gregório de Melo (CEFLAG), who provided the ayahuasca and participated in the study. We also wish to thank Vitor Augusto Motta Moreira for his help in the research project, Adriano Maldaner, who did the chemical analyses of our ayahuasca sample, and Jordi Riba for his critical comments on the manuscript. Research supported grants from the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, Brazil) to A.P.M. Cruz and J. Landeira-Fernandez. R.G. Santos was recipient of a master fellowship from CNPq.

References

Araújo, W.S., 1999. Navegando sobre as ondas do Daime: história, cosmologia e ritual da Barquinha. Ed. da Unicamp, São Paulo.

Callaway, J.C., 1988. A proposed mechanism for the visions of dream sleep. Medical Hypotheses 36, 119–124.

Callaway, J.C., Airaksinen, M.M., McKenna, D.J., Brito, G., Grob, C.S., 1994. Platelet serotonin uptake sites increased in drinkers of *ayahuasca*. Psychopharmacology 116, 385–387.

Callaway, J.C., McKenna, D.J., Grob, C.S., Brito, G.S., Raymon, L.P., Poland, R.E., Andrade, E.N., Andrade, E.O., Mash, D.C., 1999. Pharmacokinetics of Hoasca alkaloids in healthy humans. Journal of Ethnopharmacology 65, 243–256.

Davis, W., 1997. One River: Explorations and Discoveries in the Amazon Rain Forest. Simon and Schuster Inc., Touchstone, New York.

Deakin, J. F.W., Graeff, F.G., 1991. 5-HT and mechanisms of defense. Journal of Psychopharmacology 5, 305–315.

Frecska, E., White, K.D., Luna, L.E., 2004. Effects of ayahuasca on binocular rivalry with dichoptic stimulus alternation. Psychopharmacology 173, 79–87.

Goulart, S.L., 2005. Contrastes e continuidades em uma tradição religiosa amazônica: os casos do Santo Daime, da Barquinha e UDV. In: Labate, B.C., Goulart, S.L. (Orgs.), O uso ritual das plantas de poder. Mercado de Letras, Campinas, pp. 355–396.

Graeff, F.G., Guimarães, F.S., de Andrade, T.G., Deakin, J.F.W., 1996. Role of 5-HT in stress, anxiety and depression. Pharmacology Biochemistry and Behavior 54, 129–141.

Grella, B., Teitler, M., Smith, C., Herrick-Davis, K., Glennona, R.A., 2003. Binding of beta-carbolines at 5-HT_2 serotonin receptors. Bioorganic and Medicinal Chemistry Letters 13, 4421–4425.

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., Strassman, R.J., Boone, K.B., 1996. Human psychopharmacology of hoasca, a plant hallucinogen used in ritual context in Brasil. Journal of Nervous and Mental Disease 184, 86–94.

Grof, S., 2001. LSD psychotherapy. Multidisciplinary Association for Psychedelic Studies (MAPS). Sarasota, Florida.

Labate, B.C., Araújo, W.S. (Orgs.), 2004. O uso ritual da ayahuasca. Mercado de Letras, Campinas.

Luna, L.E., 2005. Narrativas da alteridade: a ayahuasca e o motivo de transformação em animal. In: Labate ,B.C., Goulart, S.L. (Orgs.), O uso ritual das plantas de poder. Mercado de Letras, Campinas, pp. 333–354.

McKenna, D.J., Towers, G.H.N., 1981. Ultra-violet mediated cytotoxic activity of beta-carboline alkaloids. Phytochemistry 20, 1001–1004.

McKenna, D.J., Towers, G.H.N., Abbott, F., 1984. Monoamine oxidase inhibitors in South American hallucinogenic plants: tryptamine and beta-carboline constituents of Ayahuasca. Journal of Ethnopharmacology 10, 195–223.

McKenna, D.J., Repke, D.B., Lo, L., Peroutka, S.J., 1990. Differential interactions of indolealkylamines with 5-hydroxytryptamine receptor subtypes. Neuropharmacology 29, 193–198.

McKenna, D.J., Callaway, J.C., Grob, C.S., 1998. The scientific investigation of Ayahuasca: a review of past and current research. The Heffter Review of Psychedelic Research 1, 65–77.

Nash, J.R., Nutt, D.J., 2005. Psychopharmacoterapy of Anxiety. Handbook of Experimental Pharmacology, Vol. 169, pp. 401–469.

Ott, J., 1994. Ayahuasca Analogues: Pangaean Entheogens. Natural Books Co., Kennewick, WA.

Riba, J., Rodrígues-Fornells, A., Urbano, G., Morte, A., Antonijoan, R., Monteiro, M., Callaway, J.C., Barbanoj, M.J., 2001. Subjective effects and tolerability of the South American psychoactive beverage *Ayahuasca* in healthy volunteers. Psychopharmacology (Berl) 154, 85–95.

Riba, J., Valle, M., Urbano, G., Yritia, M., Morte, A., Barbanoj, M.J., 2003. Human pharmacology of ayahuasca: subjective and cardiovascular effects,

monoamine metabolite excretion, and pharmacokinetics. Journal of Pharmacology and Experimental Therapeutics 306, 73–83.

Smith, R.L., Canton, H., Barret, R.J., Sanders-Bush, E., 1998. Agonist properties of *N*,*N*-dimethyltryptamine at 5-HT_{2A} and 5-HT_{2C} serotonin receptors. Pharmacology Biochemistry and Behavior 61, 323–330.

Starcevic, V., 2006. Anxiety states: a review of conceptual and treatment issues. Current Opinion in Psychiatry 19, 79–83.

Strassman, R.J., 1984. Adverse reactions to psychedelic drugs: a review of the literature. The Journal of Nervous and Mental Disease 172, 577–595.

Strassman, R.J., 2001. DMT: The Spirit Molecule. Park Street Press, Rochester, Vermont.

Wikinski, S., 2004. Depression and anxiety: from clinic to pharmacological treatment. Vertex 15, 208–212.