

Exploring the therapeutic potential of Ayahuasca: acute intake increases mindfulness-related capacities

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Abstract

Background Ayahuasca is a psychotropic plant tea used for ritual purposes by the indigenous populations of the Amazon. In the last two decades, its use has expanded worldwide. The tea contains the psychedelic 5-HT_{2A} receptor agonist *N,N*-dimethyltryptamine (DMT), plus β -carboline alkaloids with monoamine-oxidase-inhibiting properties. Acute administration induces an introspective dream-like experience characterized by visions and autobiographic and emotional memories. Studies of long-term users have suggested its therapeutic potential, reporting that its use has helped individuals abandon the consumption of addictive drugs. Furthermore, recent open-label studies in patients with treatment-resistant depression found that a single ayahuasca dose induced a rapid antidepressant effect that was maintained weeks after administration. Here, we conducted an exploratory study of the psychological mechanisms that could underlie the beneficial effects of ayahuasca.

Methods We assessed a group of 25 individuals before and 24 h after an ayahuasca session using two instruments designed to measure mindfulness capacities: The Five Facets Mindfulness Questionnaire (FFMQ) and the Experiences Questionnaire (EQ).

Results Ayahuasca intake led to significant increases in two facets of the FFMQ indicating a reduction in judgmental processing of experiences and in inner reactivity. It also led to a significant increase in decentering ability as measured by the EQ. These changes are classic goals of conventional mindfulness training, and the scores obtained are in the range of those observed after extensive mindfulness practice.

Conclusions The present findings support the claim that ayahuasca has therapeutic potential and suggest that this potential is due to an increase in mindfulness capacities.

Keywords Ayahuasca · Therapeutic potential · Mindfulness · Decentering · Human

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Introduction

Ayahuasca is a psychotropic beverage prepared by infusing in water the stalk of *Banisteriopsis caapi* together with the leaves of *Psychotria viridis* (Rubiaceae) or *Diplopterys cabrerana* (Malpighiaceae). This tea has been used for centuries in Amazonian traditions for ritual and medical purposes (Schultes 1980), and more recently, its use has extended to North American and European countries (Tupper 2008). *B. caapi* contains β -carboline alkaloids, mainly harmine, tetrahydroharmine (THH), and to a lesser extent, harmaline (Rivier and Lindgren 1972; McKenna et al. 1984). These alkaloids show monoamine-oxidase (MAO) inhibiting properties (Buckholtz and Boggan 1977a), while THH is also a serotonin reuptake inhibitor (Buckholtz and Boggan 1977b). The leaves of *P. viridis* and *D. cabrerana*, the most common admixtures used in ayahuasca preparation, contain the psychedelic indole *N,N*-dimethyltryptamine or DMT (Rivier and Lindgren 1972; Schultes 1980).

DMT is structurally related to the neurotransmitter serotonin (5-hydroxytryptamine; 5-HT) and shows agonist activity at the 5-HT_{2A} and 5-HT_{1A} receptors. More recently, it has been shown that DMT also interacts with the sigma-1 receptor (Fontanilla et al. 2009). DMT induces intense modifications of the ordinary state of awareness when administered parenterally, but it is devoid of psychoactivity when ingested (Riba et al. 2015) due to degradation by MAO (Suzuki et al. 1981) and cytochrome-dependent mechanisms (Riba et al. 2015). Ayahuasca is a remarkable ethnopharmacologic combination in which the presence of the MAO-inhibiting β -carbolines prevents the gastrointestinal degradation of DMT, allowing its access to systemic circulation and the CNS (Riba 2003).

Ayahuasca is receiving increased attention from the general public and biomedical researchers for its therapeutic potential (Frood 2015). Acute administration induces an introspective dream-like experience characterized by visions and autobiographic and emotional memories (Riba et al. 2001). Studies of long-term users have suggested that ayahuasca may have beneficial effects for individuals with substance use disorders. Reports of decreased consumption of alcohol, cocaine, and other addictive drugs are common in regular ayahuasca users (Fábregas et al. 2010; Thomas et al. 2013). Ayahuasca may also have potential to treat other psychiatric conditions. In a recent pilot study conducted in patients with treatment-resistant depression, the authors reported a rapid-onset antidepressant effect that was maintained weeks after administration of the single dose (Osório et al. 2015). These results have been replicated using a larger patient sample (Sanches et al. 2015).

Despite these initial reports of beneficial psychological effects and of amelioration of some forms of psychopathology, little is known with regard to the psychological mechanisms that may underlie these effects. Several aspects of the

ayahuasca-induced subjective experience are analogous to the experience of mindfulness practice as understood by contemporary Western psychological conceptualizations. Although mindfulness is a complex construct difficult to define (Grossman 2008, 2011), from a secular perspective, being “mindful” entails a particular quality of awareness, that is present-centered, non-reactive, characterized by openness, acceptance, and by a non-judgmental stance towards the experience (Kabat-Zinn 1990; Bishop et al. 2004; Baer et al. 2006). Another construct, closely related to mindfulness is the notion of “decentering”. Decentering or “defusion” is the ability to take a detached view of one’s own thoughts and emotions considering them as impermanent events of the mind (Fresco et al. 2007b). The analogy is based on the following: First, studies on the phenomenology of the ayahuasca experience emphasize the detached view of one’s own thoughts and emotions that the substance elicits (Shanon 2002). Increasing this capacity is the goal of mindfulness interventions (Brown and Ryan 2003; Shapiro et al. 2006; Holzel et al. 2011). The recollection of highly emotional events simultaneous with a detached view of these events, as induced by ayahuasca (Riba et al. 2001, 2006), may help the reprocessing of emotional experiences. Second, both ayahuasca and mindfulness practice seem to induce similar effects on other domains including increased awareness, changes in self-perspective, decreased hopelessness, and positive impact on general well-being (Santos et al. 2007).

Based on the common aspects of the ayahuasca experience and mindfulness practice, the present study aimed to further understand the psychological experience induced by ayahuasca and to explore if an enhancement of mindfulness-related capabilities could be achieved through ayahuasca use. To this end, we assessed the effects of the intake of a single dose of ayahuasca on several mindfulness-related measures.

Experimental procedures

Participants and study procedure

The investigators contacted circles of individuals involved in ayahuasca use and explained to them the goals and methods of the study. Contacts were asked to pass the information to their acquaintances and a sample of 25 individuals (14 females) was recruited. Exclusion criteria included current psychiatric disorder and alcohol or other substance use disorders and evidence of current significant medical illness. Their mean \pm SD age was 43.6 \pm 12 years, and were relatively well-educated, with an average 15 \pm 4 years of education. They all have an interest in psychoactive drugs for personal experimentation. Twenty-three had prior experience with ayahuasca, having taken it on average 79 times (range 1–500). The other two took it for the first time in the course of the study. All

participants had abstained from ayahuasca for at least 15 days before assessment and neither consumed alcohol, medications, or any other drugs in the day prior to ayahuasca intake nor in the 24 h thereafter.

Ayahuasca was taken in a non-religious setting, and participants were not affiliated to any ayahuasca religion. The main motivation of the participants was to use ayahuasca as a tool for self-knowledge and introspection. Ayahuasca was taken in a dimly lit room, with participants sitting or lying down on mattresses. Recorded music was played throughout the session, and participants could freely leave the room to go to the bathroom or to a room next door if they wished to stay on their own for some time. Experimenters were present before, during, and after the ayahuasca session and directly administered the questionnaires to the participants.

The study was conducted in accordance with the Declaration of Helsinki and subsequent amendments concerning research in humans and was approved by the Sant Pau Hospital Ethics Committee. All volunteers gave their written informed consent to participate.

Participants were requested to first respond to the questionnaires described below during the 24 h prior to the ayahuasca session they had planned to attend. They were instructed to respond to the pre-intake questions indicating how they normally felt and acted in the absence of any psychoactive substance. Following the ayahuasca session, they were again asked to respond to the questions indicating how they have felt and acted in the 24 h thereafter.

Participants recorded the total volume of ayahuasca ingested by each individual during the session and facilitated samples for analysis. Alkaloid concentrations were determined using a previously described method implementing liquid chromatography-electrospray ionization-tandem mass spectrometry (McIlhenny et al. 2009). Based on the analysis, participants ingested on average 43.6-mg DMT (range 28.82–69.81), a moderate dose as compared to the dosages used in a laboratory by our group (Riba et al. 2001).

Measures

Mindfulness facets were assessed using the following psychometric instruments:

The Five Facet Mindfulness Questionnaire (Baer et al. 2006; Cebolla et al. 2012). The FFMQ measures five different factors: (1) Observe: noticing external and internal experiences, e.g., body sensations, thoughts, or emotions; (2) Describe: putting words to, or labeling the internal experience; (3) Acting with awareness: focusing on the present activity instead of behaving mechanically; (4) Non-judging the inner experience: taking a non-evaluative stance towards the present experience, thoughts, or emotions; and (5) Non-reacting to the inner

experience: allowing thoughts and feelings to come, without getting caught up in, or carried away, by them. Sample items for each sub-scale include the following: Observe “When I take a shower or bath, I stay alert to the sensations of water on my body”; Describe “I’m good at finding words to describe my feelings”; Acting with awareness “I am easily distracted”; Non-judging “I tell myself I should not be feeling the way I am feeling”; and Non-reacting “I watch my feelings without getting lost in them”. Participants were asked to rate the degree of concordance with each statement on a 5-point Likert scale that ranges from 1 (never or very rarely, true) to 5 (very often or always, true). The FFMQ has shown adequate psychometric properties in both non-clinical and clinical samples. Cronbach’s α for the Spanish version of FFMQ range from 0.8 to 0.91 (Cebolla et al. 2012), and the internal consistency of the scale in our sample was of 0.83 and 0.86 (pre- and post-intake, respectively).

The Experiences Questionnaire or EQ (Fresco et al. 2007a; Soler et al. 2014b). This instrument comprises 11 items and measures “decentering”, defined as the capacity to observe one’s thoughts and emotions as temporary events of the mind. The EQ items are scored in a 5-point-Likert-type scale, ranging from *never* to *all the time*, with higher scores indicating more decentering. Sample items include the following: “I can observe unpleasant feelings without being drawn into them” or “I can separate myself from my thoughts and feelings”. The Spanish version of the EQ has demonstrated good psychometric properties, including internal consistency in clinical and non-clinical samples. Internal consistency in our sample was 0.88 at pre-intake and 0.94 at post-intake).

To explore if the changes induced by ayahuasca could be comparable to those induced by meditation practice, the MINDSENS Composite Index was also calculated (Soler et al. 2014a). This index includes those FFMQ and EQ items that have proven to be the most sensitive to meditation practice and to discriminate accurately between meditators and no-meditators (Soler et al. 2014a).

Data analysis

Scores on the composite MINDSENS index, the five FFMQ subscales, and the EQ questionnaire were analyzed using repeated-measures analyses of variance (ANOVAs) with ayahuasca session (before vs. after) as factor. Additionally, in view of the high variability in the degree of previous experience with ayahuasca (from 0 to 500 times), a second analysis was conducted introducing this value as a covariate in the repeated-measures ANOVA.

Given the exploratory nature of the present study, no formal correction for multiple comparisons was carried out. Results were considered significant for p values <0.05 .

Results

Figure 1 shows the scores obtained for the study variables before and 24 h after the ayahuasca session. The MINDSENS composite index showed a statistically significant increase following the ayahuasca session ($F(1,24)=6.78, p=0.016$).

The analysis of the individual questionnaires showed a significant effect of ayahuasca session on the EQ score ($F(1,24)=8.55, p=0.007$). Two of the five subscales of the FFMQ also showed significant increases in the 24 h following ayahuasca: Non-Judge ($F(1,24)=7.86, p=0.010$) and Non-React ($F(1,24)=5.06, p=0.034$).

The introduction of the prior experience with ayahuasca as a covariate in the analysis did not greatly modify the results for the MINDSENS composite index ($F(1,23)=5.26, p=0.031$). However, it decreased significance of changes on the EQ questionnaire score ($F(1,23)=6.45, p=0.018$) and increased significance of the pre- vs. post-comparison of scores on the FFMQ Non-Judge ($F(1,24)=8.39, p=0.008$) and Non-React ($F(1,24)=5.06, p=0.009$) subscales.

Despite the changes in F and p values, the overall pattern of results remained unchanged.

Discussion

By exploring the effects of ayahuasca intake on mindfulness capacities, the present study aimed to better understand the psychological mechanisms underlying the therapeutic

potential of ayahuasca. Our findings indicate that ayahuasca intake leads to a rapid increase in several mindfulness-related parameters. Two FFMQ facets changed after ayahuasca, suggesting a decrease in the judgmental processing of personal experiences, along with a reduction in inner reactivity. Additionally, decentering ability was also increased after ayahuasca intake. These combined modifications provide an explanatory mechanism that could contribute to the beneficial effects reported for ayahuasca in the treatment of addiction and depression (Thomas et al. 2013; Osório et al. 2015). It is worth mentioning that prior studies showing benefits associated with long-term ayahuasca use have the confounding factor of participants being members of a religious group (Fábregas et al. 2010; Bouso et al. 2012). The present results obtained in a lay setting support the notion that ayahuasca may have therapeutic potential per se in the absence of the religion confound.

The scores in some mindfulness capacities observed after ayahuasca are analogous to those of experienced meditators (Soler et al. 2014a). Thus, Soler and colleagues report the following average scores in their experienced meditator sample: “Non-react”, 24.84; “Non-judge”, 30.61; EQ, 41.07; and MINDSENS, 3.70. These values are very close and in some cases lower than those obtained here in the post-ayahuasca assessment: “Non-react”, 25.56; “Non-judge”, 33.16; EQ, 41.41; MINDSENS, 3.66. The similar values obtained in the MINDSENS are a relevant finding. The MINDSENS index was created with those FFMQ and EQ items that were more sensitive

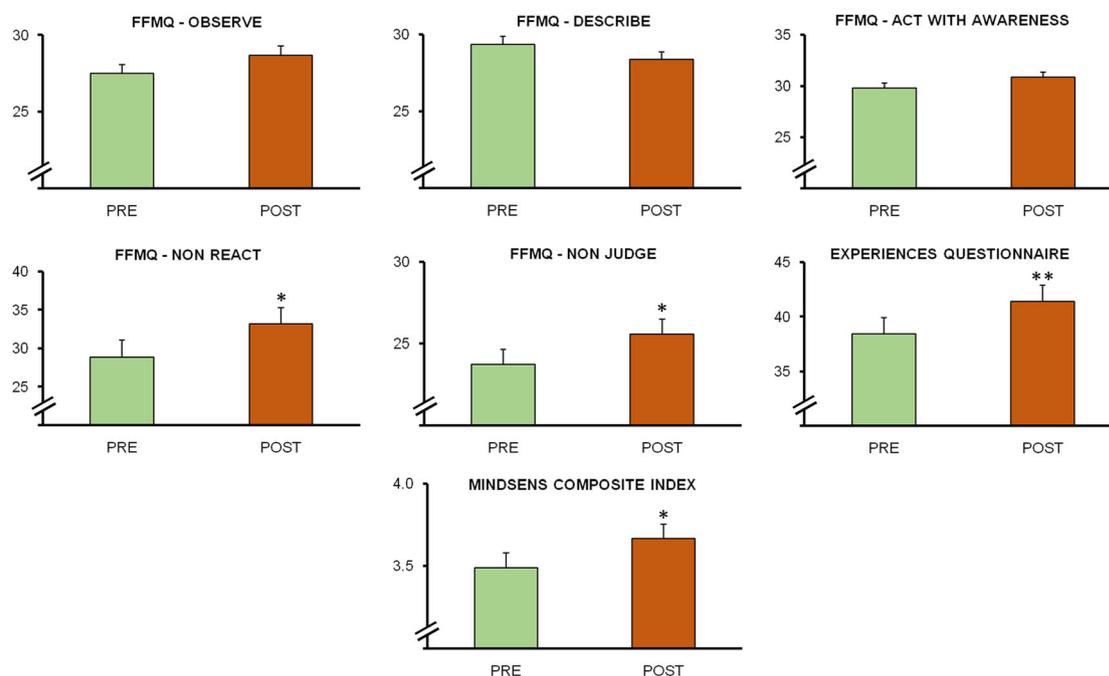


Fig. 1 Ayahuasca-induced changes in the FFMQ subscales, the Decentering score, and the MINDSENS composite score. The error bars denote 1 standard error of mean. * $p < 0.05$, ** $p < 0.01$

to meditation practice. This index is sensitive to several aspects of meditation practice, i.e., to the overall years of practice and to the frequency and length of meditative sessions (Soler et al. 2014a). Our study indicates that improvements in mindfulness capacities are not exclusive of mindfulness meditation practice, as they can also be obtained by a pharmacological intervention.

Our results showed that not all mindfulness facets are equally affected by ayahuasca. Analogously, previous studies comparing meditators vs. non-meditators suggested that not all mindfulness facets are equally modified by practice. For example, in a study comparing a large sample of meditators ($n=384$) to individuals without meditative experience ($n=286$), the first group scored significantly higher in all FFMQ facets and decentering. However, certain facets such as “Observe”, “Non-react”, and “Decentering” appear to be more sensitive than the others to formal meditation practice (Soler et al. 2014a, b). Increased ability to “Observe” has been pointed out as essential capacity of meditating individuals (Lilja et al. 2012). Out of the five facets of the FFMQ, significant changes were observed in the “Non-judge” and “Non-react” facets.

Mindfulness is considered a two-factor construct comprising both attentional and attitudinal elements (Bishop et al. 2004). The “Non-judge” and “Non-react” subscales are considered to measure acceptance (Baer et al. 2006). Thus, ayahuasca would particularly foster acceptance of the thoughts and feelings experienced by the individual. This increased self-acceptance could contribute to the therapeutic effects of ayahuasca, as suggested by Thomas (Thomas et al. 2013). Indeed, a state of increased self-acceptance would be clinically useful, since the attitudinal component of mindfulness, rather than the attentional, appears to be particularly impaired in patients with psychopathology (Coffey et al. 2010; Tejedor et al. 2014).

The ayahuasca experience may induce an introspective exposure to emotional memories (Riba et al. 2001, 2006), similar to that used in emotional reprocessing interventions (Foa et al. 1995). As intended in such interventions, the use of ayahuasca may promote a detached relationship with one’s own emotions. This detached manner of approaching the inner experience has been defined as “decentering” or “defusion”, understood as the metacognitive ability to take a detached view of one’s own thoughts and emotions. It allows patients to consider thoughts and emotions as objective temporary events of the mind, rather than statements that are necessarily true (Fresco et al. 2007a).

Deficits in decentering have been postulated as a transdiagnostic index of psychopathology. Compared to healthy controls, it is diminished in individuals with cocaine use disorders, eating disorders, major depression, and borderline personality disorder (Soler et al. 2014a). Increases in decentering have been observed after cognitive behavioral

therapy for depression and also after mindfulness-based interventions (Bliss and McCardle 2013; Hayes-skelton et al. 2014). Similar to a study in which increases in decentering were reported in a group of patients responding to antidepressant treatment (Fresco et al. 2007b), our data show that psychotropic substances, in our case ayahuasca, can also enhance this ability. Increases in this capacity would explain findings suggesting that ayahuasca has therapeutic effects in depression (Sanchez et al. 2015; Osório et al. 2015), a disorder in which the decentering capacity is impaired (Teasdale et al. 2002; Segal et al. 2006; Carmody et al. 2009).

Our results are in line with the recent research exploring the therapeutic potential of other psychedelic 5-HT_{2A} agonists, substances which in recent years are receiving renewed attention in psychiatry (Sessa and Johnson 2015). For instance, psilocybin was safely administered to advanced-stage cancer patients and proved effective in reducing anxiety and depressive symptoms related to illness (Grob et al. 2011). Promising results have also been reported for lysergic acid diethylamide (LSD), another classic psychedelic (Gasser et al. 2014). From a mechanistic perspective, these drugs show modulatory activity on the amygdala and the anterior cingulate cortex following acute administration (Vollenweider and Kometer 2010; Kraehenmann et al. 2014). These areas are key structures of the emotional brain and their function is deregulated in affective disorders (Pezawas et al. 2005). Regular use of psychedelics has also been associated with differences in brain structure relative to non-users. In a study assessing long-term ayahuasca users, the authors found thinning in the posterior cingulate cortex (PCC), a key hub of the default mode network (Raichle et al. 2001). Thinning in the PCC inversely correlated with prior use of ayahuasca and with scores on self-transcendence (Bouso et al. 2015). This personality trait, which comprises religiousness, spirituality, and transpersonal feelings, was higher in ayahuasca-using subjects. No differences were found with controls with regard to neuropsychological functioning or indicators of psychopathology. This finding suggested that regular ayahuasca use may lead to default mode network deactivation, which is overactive in depression (Sheline et al. 2010). Analogously, conventional mindfulness practice also has an impact on the default mode network (Taylor et al. 2013), indicating further commonalities between the ayahuasca experience and mindfulness training. Although to our knowledge, studies with other psychedelics have not specifically examined modifications in mindfulness capacities, it is possible that psilocybin and LSD also show these facilitating effects. Future studies with these substances should explore this possibility.

The current findings should be taken as preliminary, as the study was intended as exploratory and has some limitations

that need to be considered. First, the characteristics of the participant sample and its relatively limited size could be biasing our results. Prior exposure to ayahuasca may have led to a ceiling effect, as suggested by the increases in significance obtained in the repeated measures ANCOVA for “Non-Judge” and “Non-react” subscales. On the other hand, it can be argued that the fact that a single ayahuasca dose increases mindfulness capacities in experienced users who were already more “mindful” than the general population (as shown for instance by the EQ pre-administration values), underscores the power of ayahuasca to enhance these abilities even when the baseline level is high. Although participants manifested being free of any current psychiatric or medical condition, no rigorous criteria were applied to exclude subjects with past diagnoses of mental disorders. The absence of a control group also limits the generalization of the present findings. However, FFMQ facets and decentering appear to be stable over time (Veehof et al. 2011; Soler et al. 2014b). This makes it unlikely that our results are due to natural fluctuations of these variables, rather than the consequence of ayahuasca intake. Lastly, only one dose of ayahuasca was ingested, although the subjective effects of ayahuasca are dose-dependent (Riba et al. 2001). Future studies should explore the impact of different doses and be conducted using randomized controlled designs.

In summary, the present study provides evidence supporting the claim that ayahuasca has therapeutic potential. The present findings additionally suggest that this is due to increases in mindfulness-related capacities. Further research is warranted to corroborate these results, to test whether the benefits induced by ayahuasca on mindfulness capacities are maintained over time. Positive results would argue strongly in favor of conducting studies involving psychiatric populations.

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Conflict of interest The authors declare that they have no competing interests.

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