

*Bringing Ayahuasca
Clinical Research Labor*

Ayahuasca Scientific Information

La ayahuasca is a serotonergic-acting psychotropic brew of which one of the main uses in traditional cultures is as a medicine. This is the reason why in Western culture ayahuasca is popularly considered to have medicinal properties, even if it is used outside of its traditional context. But what are the evidences of efficacy as a therapeutic tool? Is ayahuasca safe? And what are its exact mechanisms of action?

Evidence of Efficacy

One of the main uses of ayahuasca in traditional cultures is as a medicine. This is the reason why in Western culture ayahuasca is popularly considered to have medicinal properties, even if it is used outside of its traditional context. However, the clinical evidence of the efficacy of ayahuasca to treat medical or psychological diseases is scarce. There are no clinical trials where efficacy of ayahuasca has been assayed, and there is only one follow-up study with patients (1). The evidence existing until now is anecdotal and based on very few subjects;

The classical work of Grob et al. (2), where a group of 15 regular ayahuasca users, all of them members of the Brazilian church Uniao do Vegetal, were interviewed, found that 11 out of the 15 participants had a history of moderate to severe alcohol use; 5 reported episodes of associated violent behavior and a diagnosis of alcohol abuse disorder prior to the involvement in the UDV; 4 subjects also reported previous use of other drugs of abuse, including cocaine and amphetamines; 8 of the 11 subjects who had a history of alcohol and other drug abuse were addicted to nicotine at the time of their first ayahuasca session; 2 subjects had past major depressive disorders; and 3 had past phobic anxiety disorders. The authors found that, at the time of the assessment, none of the UDV subjects had a current psychiatric diagnosis using the CIDI. According to the authors, all those problems were resolved as a consequence of their regular ritual use of ayahuasca.

A recent study (3) where 32 regular ayahuasca users belonging to the Igreja do Santo Daimé in Oregon (US) were assessed, also found that while most of them had shown some past psychiatric disorder or some drug or alcohol abuse disorder, at the time of the assessment only two of them reported an active psychiatric disorder. Again, the participation in the ayahuasca rituals is thought to be responsible of the reported benefits.

The only study (4) designed specifically to assess clinical efficacy of ayahuasca for medical disorder is an exploratory one, involving 3 female participants with a clinical diagnosis of recurring depressive disorder and current mild/severe

depressive episode without psychotic symptoms. Subjects received an oral dose of 3ml/kg of ayahuasca. After a single ayahuasca dose, depressive symptoms were significantly decreased from 40 minutes after intake until day 14, when symptoms began to reach baseline levels.

Ayahuasca has also the reputation to be an efficient tool in the treatment of drug abuse disorders but, again, despite the anecdotal evidence cited above, there are no clinical studies that sustain that claim. Although there are some clinics throughout the world where addiction treatment programs with ayahuasca are provided, no data regarding efficacy has been published until now.

The increasing personal accounts of Ayahuasca's role in therapeutic and personal growth practices emphasize the need for thorough clinical studies.

Mechanisms of Action

Ayahuasca is a serotonergic-acting psychotropic brew. The most common botanical sources of ayahuasca are *Banisteriopsis caapi* and *Psychotria viridis*. *B. caapi* contains beta-carboline alkaloids with MAOI (Monoamino Oxidase Inhibitor) action, mainly harmine, harmaline, and tetrahydroharmine (THH); whereas *P. viridis* contains the serotonergic receptor agonist N,N-Dimethyltryptamine (DMT). DMT is not active orally because it is destroyed by the action of the MAO enzymes in the gastrointestinal tract, but the combination with MAOI harmala alkaloids blocks its metabolic breakdown and renders it orally active (5).

It is generally accepted that the main neurobiology mechanism of action of hallucinogens is acting as agonists of the 5-HT_{2A} receptors located at the pyramidal glutamatergic neurons of the layer V of the prefrontal cortex (6). When 5-HT_{2A} receptors are activated, a release of the excitatory neurotransmitter glutamate occurs, increasing the neural firing all along the frontal cortex (6). One EEG study in humans has demonstrated the cognitive stimulant properties of ayahuasca, showing an increase in the relative power of the EEG beta band (7), an effect induced by ayahuasca but not by d-amphetamine.

In a recent study using the neuroimaging technique SPECT, where ayahuasca was administered to healthy volunteers (8), activation in frontal regions, specifically in the medial frontal and anterior cingulate cortices was found, areas implicated in somatic awareness, subjective feeling states, and emotional arousal. Parahippocampal areas, also involved in the processing of emotional arousal and memory, were also activated. This neurobiological mechanism of action may imply that ayahuasca allows subjects to "travel" throughout personal past experiences being aware of emotions, thoughts and memories that are usually difficult to access in ordinary states. Frontal areas are also involved in anticipatory and planning behavior, and in abstract reasoning, so the activation of those areas may be the basis to explain the complex and meaningful cognitive experiences that take place under the effects of ayahuasca. Another recent neuroimaging study confirmed that results and also show that imagining a picture under the effects of ayahuasca activate the same visual areas that are activated when one is seeing the real image (9).

Psychology

Two important books have thoughtfully described the phenomenological experience of ayahuasca in different contexts: shamanic, psychotherapeutic and religious (10) (11). The psychological effects profile of ayahuasca has also been assessed in controlled studies using both rating scales and Visual Analogue Scales (5).

The rating scales used to assess the psychological effects of ayahuasca were the HRS (Hallucinogen Rating Scale) and the ARCI (Addiction Research Center Inventory). The HRS is the main rating scale used to assess the effects of entheogens. It consists on six different clusters of the psychedelic-induced experience: Somaesthesia, reflecting somatic effects; Affect, sensitive to emotional and affective responses; Volition, indicating the volunteer's degree of incapacitation; Cognition, describing modifications in thought process or content; Perception, measuring visual, auditory, gustatory, and olfactory experiences; and, finally, Intensity, which reflects the strength of the overall experience.

Scores on the six sub-scales show that, at the administered doses, ayahuasca is able to induce distinct psychedelic effects. As would be expected from conventional drugs and somewhat in contrast to popular belief, the most interesting results from the cited studies were that when administered in a clinical setting and carefully controlled for expectancy (blind designs), ayahuasca is found to act in a dose-dependent manner. The ayahuasca experience is also scored by the voluntary subjects in the following VAS: "liking", "good effects", "visions", "stimulated" and "high".

Safety

Though no serious psychological adverse events have been reported in the clinical studies after the acute administration of ayahuasca, a note of caution should be made regarding ayahuasca's safety. The studies were mainly performed in healthy young volunteers who had extensive experience in psychedelic drug use, so the conclusions cannot be extrapolated to ayahuasca-naïve individuals. Although in the clinical studies there is only one subject reported that suffered an episode of disorientation (12), a case report describes a patient who presented a psychotic breakdown after acute ayahuasca intake who needed antipsychotic medication until his remission (13). Other few cases of psychiatric adverse reactions, including psychotic disorders, have been reported following acute ayahuasca ingestion (14). Although the prevalence of those adverse psychiatric reactions is statistically anecdotal and the psychological safety margin of ayahuasca is quite acceptable (15) (16), it is necessary to take them into account in order to get a complete picture of the possible negative psychiatric risks of ayahuasca use.

On the other hand, other studies have reported significant reductions of minor psychiatric symptoms and positive changes in behavior in the four days following the first ayahuasca experience (17). Another study found reductions in the scores of panic and hopelessness one hour after ayahuasca ingestion, as compared to baseline (18). One final study found improvements in several psychological measures in a six month follow-up study in subjects after their first ayahuasca experience, finding positive correlations between some of the psychological changes and the frequency of ayahuasca use, and negatively with the wash-out period (19).

There are some researches that focused on potential psychiatric and cognitive sequels in long term ayahuasca users both in adults (2) (3) and in adolescence population (20) (21). Neither psychopathological alterations nor neuro-cognitive deficits were found in the published studies. It should be noted however that the participants studied may have suffered a self-selection bias, since the participants may have been those who did not experience any negative neuropsychiatric consequences derived from their maintained ayahuasca use. Subjects experiencing adverse consequences might have given up ayahuasca use and therefore not accessible as participants. In that way, it would be desirable to include in future studies people who used ayahuasca regularly in the past but decided to discontinue its use.

Lastly, one recent study carried out in two different samples of a total of 112 long term ayahuasca users compared to 115 matched controls along one year of follow-up, found that ayahuasca users take less drugs of abuse than controls, including alcohol, and concluded that "the ritual use of ayahuasca (...) does not seem to be associated with the psychosocial problems that other drugs of abuse typically cause" (22). A recent paper where that same sample was studied has demonstrated that long term use of ayahuasca is not harmful for neuropsychological functions, does not cause psychopathology nor personality alterations. However, these results should be interpreted with caution since they may not be extrapolated to people that start ayahuasca use but discontinue because of potential adverse reactions. The most important issue of that paper is that, besides the difficult extrapolation in terms of psychopathology, the fact that long term users of ayahuasca do not show neuropsychological damage may indicate that ayahuasca is not neurotoxic (23)..

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