

Gut–Mind Interactions in Psychedelic Healing: A Case Study Assessing the Effects of Huachuma and Ayahuasca on the Mind and Microbiome

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ABSTRACT

Background: Psychedelic plant medicines such as Ayahuasca and Huachuma (San Pedro cactus) are gaining scientific attention for their potential to improve mental health. However, the interplay between these traditional medicines, the gut microbiome, and mental health outcomes remains underexplored.

Objective: The main objectives of this study are to investigate the effects of Ayahuasca and Huachuma ceremonies on the gut microbiome, depression, and subjective connectedness in a single patient and to generate hypotheses for future studies.

Case: A 35-year-old female with prior psychedelic experience participated in separate Ayahuasca and Huachuma ceremonies. Qualitative data were collected through patient interviews. Quantitative data included stool samples collected before and after each ceremony for microbiome analysis, as well as survey data using the Hamilton Depression Rating Scale (HAM-D) and Watts Connectedness Scale (WCS) administered pre- and post-ceremony.


Results: Both ceremonies resulted in substantial reductions in depression scores (HAM-D decreased: Ayahuasca from 18 to 6; Huachuma from 12 to 2) and connectedness scores (WCS increased: Ayahuasca from 62.3% to 95.37%; Huachuma from 58.32% to 84.65%). Although Ayahuasca and Huachuma induced different gut microbial composition shifts, reductions in pro-inflammatory taxa,

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normalization of inflammation-linked bacterial species, and increases in beneficial butyrate-producing bacterial species were observed for both. These microbial shifts aligned with improved subjective mental health and reduced inflammation. Qualitative interviews revealed distinct archetypal experiences with each medicine, informing personalized therapeutic approaches.

Conclusion: This hypothesis-generating case study illustrates a potential link between psychedelic-induced microbiome changes and improvements in mental health which may contribute to reduced inflammation and sustained antidepressant effects via the microbiota–gut–brain axis.

Keywords: Psychedelics; Ayahuasca; Huachuma; San Pedro; Microbiome; Depression; Connectedness

INTRODUCTION

Depression is a highly common and increasingly prevalent health condition, affecting more than 280 million people globally.¹ The contribution of social isolation and disconnection to the increase in depression was highlighted by the COVID-19 pandemic.² From a biological perspective, depression is influenced by multiple physiological mechanisms that modulate critical neurobiological pathways that include neurotransmission, neuroplasticity, neuro-metabolism, and neuroinflammation. Despite an improved understanding of the multiple drivers of depression, modern therapeutics have lagged behind in terms of efficacy and ability to target alterations in specific neurobiological pathways. Because conventional treatments for depression often show variable results, there has been a growing interest in psychedelics as an alternative, leading to a marked rise in their research and clinical use.³

Depression and other mental health disorders are increasingly understood to be impacted by the gut microbiome.⁴ The microbiome is a collection of microorganisms that include bacteria, viruses, and fungi that live on and in the body and greatly influence overall health.⁵ The microbiota–gut–brain axis is a well-established bidirectional connection between the gut microbiome and the central nervous system via immune, endocrine, and neural pathways including the vagus nerve.⁶ The gut microbiome responds to diet, environmental

stimuli, the gut immune system, and signals produced by gut cells. In turn, the microbiome produces a host of signals, including neurotransmitters and cytokines, that can influence the brain and psychological state. Thus, the microbiome plays a key role in mental health.⁷

Serotonin, a neurotransmitter involved in mental health, is made by gut microbes when humans eat tryptophan.⁶ Studies have identified that selective serotonin reuptake inhibitors, a conventional pharmacological approach to treating depression, change the composition of the gut, thereby impacting serotonin levels.^{6,8,9} Likewise, serotonergic psychedelics, akin to serotonergic antidepressant drugs, may interact with gut microbes to alter depression.⁶

Psychedelics are powerful psychoactive substances with hallucinogenic properties that alter perception, cognitive processes, and mood by binding to different receptors in the brain.^{10–12} These receptors are primarily serotonin receptors, including 5-HT_{2a} and 5-HT₁, as well as tropomyosin receptor kinase B (TrkB), which is involved with brain-derived neurotrophic factor. Interactions with dopamine receptors and trace amine-associated receptors also contribute to the complex neuropharmacology of psychedelics.^{13,14} The Controlled Substance Act of 1970 placed psychedelics under the most restrictive classification,

Schedule 1, which rendered their use illegal and effectively ended research on their safety and therapeutic value^{10,15,16} This classification also asserts an absence of recognized medical use cases and a high risk of abuse, which poses challenges for research.¹⁷

Ayahuasca, the “grandmother medicine,” is an ancient Amazonian brew commonly made from many plants, but typically includes two plants: (1) *Psychotria viridis* leaves, which contain dimethyltryptamine (DMT), the psychoactive molecule and (2) *Banisteriopsis caapi* vines, which contain β -carboline alkaloids, monoamine oxidase (MAO) inhibitors needed for the DMT to be orally bioavailable.^{18,19} Additionally, DMT interacts with sigma-1 receptors, which are involved in neuroprotection, neuroplasticity, and immune regulation.²⁰ β -Carboline alkaloids, including harmala, harmine, and harmaline, act as reversible MAO-A inhibitors, preventing the breakdown of DMT and enabling it to have bioactivity when taken orally.²¹ Additionally, β -carboline alkaloids interact with norepinephrine and dopamine systems by inhibiting neurotransmitter metabolism and reuptake, leading to increased neurotransmitter levels in the brain, which contribute to mood-enhancing effects.²¹

Ayahuasca is classified as a serotonergic psychedelic because DMT binds to the 5-HT_{2a} receptor.²² Tryptamine, the chemical class of DMT, is derived from tryptophan and contains an indole ring structure with an ethylamine side chain at the C3 position.²³ Tryptamines serve as the chemical backbone for serotonin and many classic psychedelics such as DMT and psilocybin; they primarily act on serotonin (5-HT) receptors, especially 5-HT_{2a}, producing pronounced effects on mood, perception, and cognition, which are typically hallucinogenic and psychoactive.^{24,25} Ayahuasca was used traditionally for altering perception, facilitating communication with ancestors, and healing. Currently, it holds therapeutic promise for its antidepressive and anti-inflammatory properties.^{26–28}

Huachuma, also known as San Pedro cactus (Latin name *Trichocereus/Echinopsis pachanoi* and the “grandfather medicine”), is native to the Andes of South America.²⁹ Similar to Ayahuasca, Huachuma is a sacred plant medicine that has been used for thousands of years in healing, rituals, and other spiritual contexts.^{30–32} Huachuma contains

mescaline, 3,4,5-trimethoxyphenethylamine, a psychedelic alkaloid that interacts with D1/2/3 dopamine receptors, as well as being a 5-HT_{2Aa/2c} receptor agonist and an α 1A/2A adrenergic receptor agonist.³³ Mescaline falls in the class of compounds of phenylethylamine (PEA), which are derivatives of phenylalanine and have a chemical structure consisting of a benzene ring with an attached ethylamine side chain, lacking the indole ring found in tryptamines. PEAs include neurotransmitters and psychoactive compounds such as dopamine, amphetamines, and some psychedelics including mescaline, primarily affecting dopamine and norepinephrine transmission with a broader stimulant profile.³⁴ They also enhance serotonin release and activate serotonin receptors such as 5-HT_{2a}, contributing to their psychoactive and mood-enhancing effects.³⁵ Mescaline, primarily found in cacti, has been used in many indigenous cultures to treat physical illnesses such as burns, wounds, fever, and rheumatism, in addition to spiritual purposes.³³ Although there is limited research, mescaline has been reported to improve mental health conditions, including post-traumatic stress disorder, schizophrenia, alcoholism, drug use disorders, and depression.^{33,36}

This case study describes a woman who participated in an ongoing observational research study of Ayahuasca (IRB # HZ4623). The patient reported that she was also going to be participating in a Huachuma ceremony and offered to share her data for this experience, which also included interviews. Ayahuasca (containing DMT) and Huachuma (containing mescaline) are classified as Schedule I controlled substances under the U.S. Controlled Substances Act. The protocol for the Huachuma study was reviewed and approved by the National University of Natural Medicine Institutional Review Board (IRB#: HZ82224). The patient consented via REDCap and provided verbal informed consent for publication of this case study and quotations. Data were collected using procedures to ensure confidentiality and informed consent, in accordance with federal ethical standards. Objective data collected in this study were obtained through participant self-collection of microbiome test kits, and interviews were conducted remotely via Microsoft Teams. Outcomes were assessed using gut microbiome sequencing, quantitative surveys, and qualitative

interviews. At no point did the research team administer, provide, recommend, or facilitate access to these substances; all use occurred independently of the research, at locations and times unknown to the researchers, and with no investigator presence or supervision. This project did not constitute an experiment or intervention, but rather an observation and documentation of patterns of use reported by the individual already engaging in these activities. No Drug Enforcement Administration registration or Food and Drug Administration Investigational New Drug approval was required. The dates of when the ceremonies took place have been removed to preserve anonymity.

CASE STUDY

A 35-year-old white female with an extensive history of psychedelic use that included psilocybin, lysergic acid diethylamide, Ayahuasca, 3,4-methylenedioxymethamphetamine, and ketamine shared microbiome data and her experience with taking Ayahuasca and Huachuma. She reported use of psychedelics for treatment of depression and mental health support and has experienced multi-month benefits to her mental health. The patient described having different relationships with each psychedelic and identified Ayahuasca as her “medicine.” To prepare for each ceremony with Ayahuasca and Huachuma, the patient made dietary modifications and set intentions (Table 1). The diet changes started 1–2 weeks before each medicine ceremony and included the elimination of red meat, salt, sugar, dairy, alcohol, and recreational drugs including cannabis. The patient fasted 4–8 hours before each ceremony.

PSYCHEDELIC SESSIONS

The set and setting of each ceremony occurred in distinct locations individually curated and facilitated by different ceremony leaders, as detailed in the following paragraphs.²¹ While these environments are not clinically controlled and there are other attendees present in the ceremonies, this serves as a benefit for the study, as it allows for the authentic capture of traditional practices and the preservation of cultural integrity surrounding

the use of these medicines. Both ceremonies were conducted by curanderos, or healers, who have permission to serve their respective medicines.

The Ayahuasca ceremony took place during an evening in May 2024 at a cabin located in the woods with an intentionally low light environment. The patient reported that the ceremony was conducted by an ayahuasquero, one who prepares and uses Ayahuasca in a ritualistic and healing context to facilitate physical, psychological, and spiritual healing and a sense of well-being. The ayahuasquero opened and maintained the ceremony by singing icaros, traditional songs or chants used to connect with the medicine, and called up each of the 13 attendees to sing to them individually.⁴¹ The patient described this as a very impactful experience and felt it helped the medicine work through them.

The Huachuma ceremony started at 8:30 AM in a gazebo located on a farm during an August day in 2024. A curated music playlist played lightly in the background, as the curandero called each participant forward to receive a personal icaro.⁴² The patient reported that this singing was especially meaningful, described as helpful to “open the medicine” within her. There were two facilitators, including a curandero and their assistant, and seven attendees in the ceremony.

METHODS

Stool samples were collected pre- and post-retreat using GI360 Microbiome Stool Kits (Doctor’s Data, St. Charles, IL). The GI360 platform employs genetic sequencing to assess bacterial, parasitic, and fungal populations within the gastrointestinal tract. This method has been utilized in prior publications to characterize microbial composition and identify associations with disease states, providing a validated framework for examining microbiome shifts in relation to therapeutic interventions.^{43–46} The kits included one test requisition form using a fake name provided by the study, one stool collection container, one yellow-capped vial containing 50 mL of a liquid preservative, one disposable glove, one ziplock bag with absorbent material, and one FedEx Clinical Pak with a billable stamp. The Ayahuasca

Table 1: Representation of themes from qualitative interviews in the patient's own words.

Theme	Ayahuasca (quote)	Huachuma (quote)	Interpretation
Motivations for engagement with psychedelic therapy	<p>"I wanted tools for working through the grief I knew was coming."</p> <p>"Sometimes connecting through psychedelics experiences can help tie loose ends."</p> <p>"I am always looking to better myself, to look deep within and see what can be observed and softened."</p> <p>[...] "how to call in healthier connections in the future"</p> <p>"I want to be able to move my body well into my aging process. I want the ability to keep strong, healthy bones, joints, and muscles. I've been so tired from overworking, that improving my physical health is important."</p>	<p>"It might be a nice thing to do some processing work around what's going on with my mom."</p>	<p>The patient described seeking Ayahuasca and Huachuma to support personal transformation in response to significant psychosocial stressors. Motivations included coping with anticipatory grief, addressing unresolved emotional and spiritual concerns, recovering from occupational burnout, and re-establishing physical vitality. Ayahuasca and Huachuma were viewed as therapeutic modalities facilitating introspection, insight, and holistic healing during periods of life transition.</p>
Ceremony intention	<p>"my intention was all about feeling more connected to people around me" [...] "to do the work I need to do to make sure I'm taking responsibility for my part and not attracting negative energy into my life."</p>	<p>"We're working on a group intention" [...] "I really do want us to start living in a space where people have personal medical autonomy."</p> <p>"guidance on how to be in these final years with my mom and what do I need to do to make sure that I make the most of these years."</p>	<p>Perhaps due to the extensive history of psychedelic use, the patient understood the importance in setting an intention. It has been reported to reduce challenging psychedelic experiences and improve perceptual effects during the psychedelic experience.^{37,38} The patient's intentions reflect an active participation in both personal and collective growth.</p>
Diet preparation impact	<p>"salt-free is very important for me. I've come to find that is what allows the medicine to launch." [...] "I also wanted to do it right and be respectful of the medicine. If that's how the medicine wants to be taken then I want to respect that."</p>	<p>"This ceremony was a bit different in that I was offered chips upon arrival because the food hadn't quite been prepared. From my experience with Aya, I tried to steer clear, but it felt less emphasized."</p>	<p>The patient prepared for both ceremonies with diet restrictions as described in the case study. One paper noted indigenous users of Ayahuasca consider breaking the diet as "extremely unwise".³⁹ Given the diet was broken for the Huachuma ceremony, perhaps that contributed to changes in HAM-D and WCS scores being less than Ayahuasca.</p>
Setting	<p>7:00 PM "a small cabin in the middle of nowhere, we gathered in a living room where all household items were removed to allow space for each attendee to get comfortable in their own sit spot. We were asked to stay in our own process and not engage with our neighbors. Windows were covered with blackout curtains and each individual was served their medicine before the lights were turned out for the remainder of the ceremony. We were asked to maintain the ceremony circle and only leave if needing to use the restroom."</p>	<p>8:30 AM "large like a 20 acre farm and we had a big like we had like this gazebo that everyone started under and then it was a big grass field like a huge grass field that we could all go lie in the sunshine or explore, within a reasonable distance. We needed to be within eyesight of the curandero the whole ceremony."</p>	<p>The Ayahuasca ceremony was at night, more enclosed and introspective. The darkness, limiting external stimuli, may have prioritized solitary inward focus with minimal engagement with other attendees. The Huachuma ceremony taking place during the daytime and in an open, communal area, seemed to support shared experience with movement and social proximity. Additionally, the sunlight and nature invite multi-sensory connection to the outdoors.</p>

Table 1: Continued

Theme	Ayahuasca (quote)	Huachuma (quote)	Interpretation
Energy of the medicine	<p>“she is grandmother medicine.” [...] “I know what I’m signing up for when I’m going to sit Aya and I know that I’m digging into my shadow. I welcome the shifts and changes that she challenges me with.” [...] “So much depth and so much wisdom. “you know, she’s a vine.” [...] “you take the medicine and she’s kind of acquainting herself with you, spiraling around you, getting a sense of who you are, ‘who is this being? While simultaneously asking how can I help?’ in a sense of taking this person to that next step or that next level of seeing/understanding. But she has to understand you before she can show you. She’s got some ***** wisdom.”</p> <p>“like she just ***** slams you and she’s there. She doesn’t feel bad about it at all. She’s just gonna hand it to you, and then it’s up to you to figure out what to do with it after that.” [...] “she shows you the vision whether it’s a metaphor or reality.” [...] “some of it was point-blank reality” [...] “others are metaphor, visual representations you can relate to in the way you can best integrate your own experience.”</p>	<p>“I struggled to connect initially [...] I was advised by my curandero to approach the grandfather and ask him directly for answers. I got less of a visual experience and more of an increased connection to the natural world around me and quick intuitive answers” [...] “It was more an inner sense of knowing. Trusting.”</p>	<p>The patient described Ayahuasca as an elder feminine spirit that facilitates deep self-exploration and transformation through a relational, symbolic, and often intense inner journey. In contrast, Huachuma was experienced as a more stoic, masculine presence offering intuitive clarity and internal knowing with minimal interpretation. The dynamic with Ayahuasca was described as reciprocal and guided with passive receptivity and emotional surrender, whereas with Huachuma, the patient held more agency in seeking insight and required more active inquiry to engage the medicine.</p>
Engagement/interaction with the medicine	<p>“you have to approach it, you can’t just wait for it to happen.”</p>	<p>The patient described Ayahuasca as a forceful presence, delivering insights with intensity; often confronting the individual with unfiltered truth or metaphor. In contrast, Huachuma was perceived as more subtle and responsive, requiring active engagement to access its guidance. This contrast suggests differing relational dynamics, with Ayahuasca eliciting a more passive reception of revelations, while Huachuma invites active engagement and personal agency in the process.</p>	<p>The patient described Ayahuasca as a forceful presence, delivering insights with intensity; often confronting the individual with unfiltered truth or metaphor. In contrast, Huachuma was perceived as more subtle and responsive, requiring active engagement to access its guidance. This contrast suggests differing relational dynamics, with Ayahuasca eliciting a more passive reception of revelations, while Huachuma invites active engagement and personal agency in the process.</p>
Integration	<p>“I do work to integrate” [...] “I have a couple of breathwork sessions I do twice a month” [...] “It’s an online community, so I usually utilize that just to stay in that space where my intentions have been” [...] “we always write intentions before we go into breathwork.” [...] “I really appreciate that and I try to journal most days.” [...] “I also work with a therapist who is comfortable with and well versed in entheogenic medicines, their encouragement and integration support are appreciated.”</p>	<p>Psychedelc integration is the process of incorporating insights and experiences from psychedelc sessions into daily life, which is especially important in Western contexts where traditional cultural frameworks may be absent.⁴⁹ Activities the patient reported incorporating, such as breath work, journaling, and connecting with community, are all ways to promote lasting personal transformation and well-being.</p>	<p>Psychedelc integration is the process of incorporating insights and experiences from psychedelc sessions into daily life, which is especially important in Western contexts where traditional cultural frameworks may be absent.⁴⁹ Activities the patient reported incorporating, such as breath work, journaling, and connecting with community, are all ways to promote lasting personal transformation and well-being.</p>

An interpretation was created to support providers and the public on how to best approach these medicines. HAM-D, Hamilton Depression Rating Scale; WCS, Watts Connectedness Scale.

retreat was 3 days long and consisted of three evenings of ceremony. The stool was collected within 24 hours prior to the first ceremony and within 48 hours after the third ceremony, making the stool collection dates 5 days apart. The Huachuma retreat was 3 days long and consisted of one ceremony. The stool was collected within 5 days prior to the ceremony and 4 days after the ceremony, making the stool collection dates 9 days apart. Figure 1 describes the timeline and data collection sequence for both ceremonies.

The data collected in pre-ceremony surveys via REDCap included the Hamilton Depression Rating Scale (HAM-D), Watts Connectedness Scale (WCS), and open-ended questions regarding past experience with psychedelics, intentions for the ceremony, and ways in which the patient intended to prepare for the ceremony. Post-survey via REDCap included the HAM-D, WCS, Mystical Experience Questionnaire (MEQ), the Challenging Experience Questionnaire (CEQ), and open-ended questions regarding the setting of the ceremony, facilitator, attendees, and experience with the medicine. These surveys were sent to the patient within 1 week before and after their ceremony. An interview was conducted before and after the Huachuma ceremony while also capturing information about their previous Ayahuasca experience and history of psychedelic use. Interviews were transcribed from Microsoft Teams recordings and read multiple times to familiarize with the content. Transcript segments were grouped by interview questions and reviewed

to identify recurring patterns. These patterns were then developed into key themes representing participants' experiences. This process follows thematic analysis principles, allowing for systematic interpretation of the qualitative data without software.

Stool samples were analyzed using a multiplex polymerase chain reaction (PCR), matrix assisted laser desorption ionization-time of flight (MALDI-TOF), and microscopy to assess pathogens, viruses, parasites, and bacteria in the gut. The patient's data results were compared to a highly defined normobiotic reference population ($n > 1100$).

The patient was interviewed twice (Table 1), after the Ayahuasca ceremonies before taking Huachuma, and again after the Huachuma ceremony. Four questionnaires were used to assess mental health and psychedelic experience: the HAM-D, which is a 17-item survey on a scale of 0–52 that assesses depression severity, and the WCS, which is scored on a percentage of 0–100% and measures one's feeling of connectedness to oneself, to others and the world. An average of the three categories was used to generate a general connectedness score which was used in all surveys. The MEQ is a 30-item survey on a scale of 0–150 that assesses the intensity and quality of mystical-type experiences during a psychedelic session, measuring areas such as feelings of unity, positive mood, transcendence of time and space, and ineffability. It is scored by participants rating the degree to which they experienced each phenomenon on a scale from

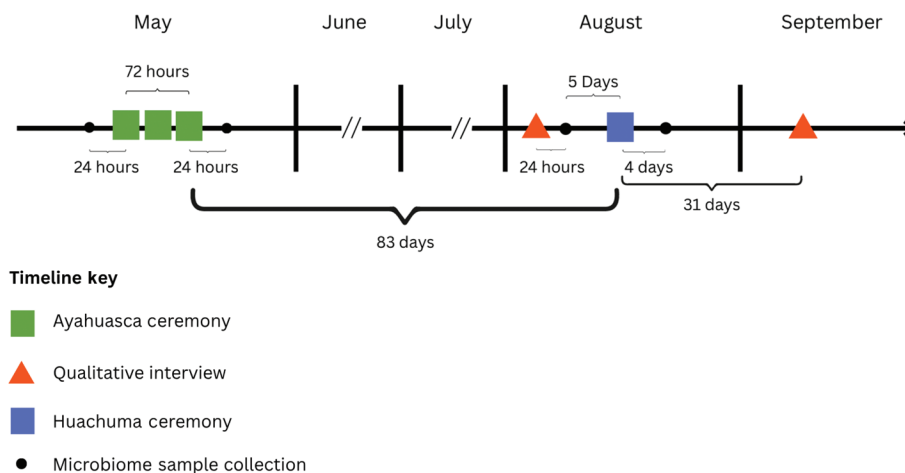


Figure 1: Timeline of ceremonies and data collection.

0 (none) to 5 (extreme); scores are then calculated as percentages across four subscales, with a “complete mystical experience” typically defined as scoring 60% or higher on all subscales, which correlates with more positive long-term psychological outcomes.⁴⁷ Finally, the CEQ assesses difficult or adverse aspects of the psychedelic experience through 26 self-reported items on a scale of 0–130, measuring seven dimensions: fear, grief, physical distress, insanity, isolation, death, and paranoia. It is used to quantify the intensity and breadth of challenging experiences during the psychedelic session.⁴⁸ In the post-ceremony surveys, the patient was asked about safety and offered an open-ended textbox to expand on safety improvement if applicable. The patient reported they felt safe at both ceremonies.

RESULTS

This case study presents findings from a single patient who participated in two separate ceremonial experiences involving two different traditional plant medicines. Notable changes were observed in both psychological well-being and gut microbiome composition across distinct time points and different psychedelic compounds. The following sections detail the quantifiable outcomes and self-reported intentions associated with each ceremonial intervention.

AYAHUASCA CEREMONY OUTCOMES

The patient initially presented with an HAM-D score of 18, consistent with moderate depression. One week following the Ayahuasca ceremony, the HAM-D score decreased to 6, indicating remission of depressive symptoms. Concurrently, the patient’s sense of connectedness, measured by WCS, improved from 62.3% at baseline to 95.37% post-ceremony, reflecting enhanced social and emotional connectedness. The MEQ yielded high scores for all four subscales: 23 out of 30 (77%) for transcendence, 30 out of 30 (100%) for positive mood, 15 out of 15 (100%) for ineffability, and 72 out of 75 (96%) for the mystical factor, resulting in a total score of 140 out of 150 (93%). On the CEQ, the

patient scored 21 out of 130. The patient’s stated intentions for the Ayahuasca ceremony included seeking ancestral wisdom, improving physical health, and strengthening interpersonal relationships, with the primary emotional goal of fostering greater connectedness with others (Table 1).

Dysbiosis, defined as an alteration in microbial community composition, has been associated with various neurological and psychiatric disorders.⁴⁹ A dysbiosis score, operationally defined as >2, indicates dysbiosis; this indicates a microbiota profile that differs from the defined normobiotic reference population. The higher the dysbiosis index, the more the sample deviates from the normobiotic profile. This dysbiosis score decreased from 3 to 2 on a 5-point scale, indicating partial normalization of the microbiome.

Microbiome diversity is defined as the variety and distribution of microbial species present in a given environment or sample.⁵⁰ A diversity score (Shannon Diversity Scale) was used to assess gut microbiome; alpha diversity remained unchanged, indicated by a score of 3 on a 5-point scale both before and after Ayahuasca.

With individual microbes, assessment was evaluated based on standard deviations from a normobiotic population. With the particular test provided by Doctor’s Data, a microbe value returning to zero is referenced as normalization or return to normal. As shown in Table 2, microbiome analysis revealed a reduction in *Alistipes* spp. from +2 to 0, which could indicate anti-inflammatory and anti-depressive effects although the research is mixed.^{52,78} We observed an increase in *Bacilli* spp. from 0 to +1 which could indicate anti-inflammatory effects.⁷⁹ *Bacteroides* spp. decreased from +1 to 0. Some studies suggest that *Bacteroides* spp. are anti-inflammatory, thus this decrease would be unexpected. *Prevotella* spp. also decreased from +1 to 0. Some studies suggest that *Prevotella* spp. have pro-inflammatory properties, and this would suggest a positive change. However, other studies suggest that *Prevotella* spp. can be antidepressants, and this decrease would be counterintuitive.^{58,60,80} We observed an increase in *Bacteroides zoogloefirmans* from 0 to +2. There is limited research on *B. zoogloefirmans* specifically, but *Bacteroides* spp. in general support anti-inflammatory properties.⁵⁸

Table 2: Representation of microbial shifts in the microbiome.

Microbe	Ayahuasca	Huachuma	Description
<i>Agathobacter rectalis</i>	No change	Decreased (from 0 to -1)	Decrease in <i>Agathobacter rectalis</i> : A butyrate producer; reduction could negatively impact gut–brain signaling but requires context. ⁵¹
<i>Alistipes</i> spp.	Decreased (+2 to 0)	Decreased (+2 to +1)	Produce short-chain fatty acids (SCFAs; e.g., butyrate, acetate, and propionate), modulate inflammation via sulfonolipids, and metabolize plant polysaccharides. Too high levels correlated with stress, depression, and fatigue. ⁵² Overgrowth is linked to depression and anxiety. ^{53,54} The patient had elevated levels in the pre-ceremony stool sample and a reduction in the post-ceremony sample, which aligns with improvements in dysbiosis and mental health and improved depression scores.
<i>Bacilli</i> class	Increased (from 0 to +1)	No change	Some <i>Bacilli</i> are known SCFA producers which can exert anti-inflammatory effects. ⁵⁵ Additionally, this class of microbes can influence neurotransmitter production, such as serotonin. Dopamine, noradrenaline, glutamate, and GABA, and immune signaling, both of which are involved with mood. ^{56,57}
<i>Bacteroides</i> spp.	No change	Increased (from 0 to +1)	Butyrate-producing microbes that are considered immunomodulatory and can exert both pro-inflammatory and anti-inflammatory effects depending on the strain and context. ⁵⁸ In abundance, this microbe can be linked to depressive behavior. ⁹ Bacteroides are capable of producing GABA, tyrosine, tyramine, dopamine, and norepinephrine. Additionally, some strains can impact tryptophan metabolism, a precursor of serotonin. ⁵⁹
<i>Bacteroides</i> spp. and <i>Prevotella</i> spp.	Decrease (from +1 to 0)	No change	<i>Bacteroides</i> spp. are described above.
<i>Bacteroides stercoris</i>	No change	Decreased (from +2 to +1)	<i>Prevotella</i> spp. have immunomodulatory effects that exhibit pro- and anti-inflammatory effects based on strain, context of the host, and genetic diversity among the genus. ^{60,61} Direct effects on depression have not been studied; however, strains that promote inflammation may worsen mood. ⁶⁰
<i>Bacteroides zoogloefirmitans</i>	Increased (from 0 to +2)	No change	A reduction in <i>Bacteroides stercoris</i> , a butyrate-producing microbe with immunomodulatory properties that are anti-inflammatory and pro-inflammatory, may demonstrate a return to a balanced normobiotic microbiome. <i>Bacteroides</i> spp., including <i>B. stercoris</i> , have been identified to influence host nervous and immune systems via neuroactive metabolites. ^{9,58}
<i>Dorea</i>	Decreased (from +1 to 0)	Increased (from 0 to +3)	A butyrate-producing microbe that digests complex carbohydrates, produces SCFAs (acetic, propionic, and succinic acids), and supports gut lining integrity. Low levels correlated with fatigue and impaired metabolic health. Specific <i>Bacteroides</i> species can modulate immune responses and reduce inflammation, potentially supporting mental health. ^{62–64}
<i>Escherichia</i> spp.	No change	Increased (from 0 to +1)	SCFA producer which has immunomodulatory effects such as promoting T-regulatory cells and has pro-inflammatory and anti-inflammatory effects depending on the surrounding microbes and host factors. ⁶⁵ High levels have been linked to inflammatory conditions. One study identified a connection between the gut–brain axis and <i>Dorea</i> , highlighting its role in maintaining gut barrier function, which may indirectly influence mood. ⁶⁶ Some <i>Escherichia</i> spp. strains can produce SCFA, and their metabolites can suppress expression of inflammatory cytokines (including IL-1 β , IL-6, IL-8, and TNF- α) and enhance production of regulatory cytokines like IL-10 in immune cells in laboratory settings. ^{67,68} An overgrowth of <i>Escherichia</i> spp. is associated with increased inflammation and is frequently observed in conditions like inflammatory bowel disease or depression, so effects are strain and context dependent. ⁶⁹ Healthy strains producing anti-inflammatory metabolites may help maintain gut–brain balance, regulate neurotransmitter availability, and support mental health. ⁷⁰

Table 2: Continued

Microbe	Ayahuasca	Huachuma	Description
<i>Medierraneibacter gnavus</i> (formerly known as <i>Ruminococcus gnavus</i>)	No change	Decreased (from +1 to 0)	<i>Medierraneibacter gnavus</i> , formerly known as <i>Ruminococcus gnavus</i> , tends to have predominantly pro-inflammatory effects, with some strain variation showing modest anti-inflammatory activity. Its inflammation-promoting role suggests possible contributions to depression via immune-inflammatory pathways, but direct anti-depressive or social behavior influences are not well documented. ^{71,72}
<i>Phascolarctobacterium</i> spp.	Decreased (from +3 to +1)	No change	Produce SCFAs including acetate and propionate, support gut barrier, and reduce inflammation. ^{73,74} Lower levels of <i>Phascolarctobacterium</i> spp. have been linked to depressive symptoms. ⁷⁵
<i>Veillonella</i> spp.	No change	Increased (from -1 to 0)	Studies reveal mixed results on the immunomodulatory properties of <i>Veillonella</i> spp., comprising anti-inflammatory and pro-inflammatory effects dependent on strain, local immune environment, and host context. ^{76,77} There are no studies that have directly assessed depressive symptoms and <i>Veillonella</i> spp.

The Doctor's Data laboratory (St. Charles, IL) based their normobiotic information on more than 1100 participant samples. The scale, ranging from -3 to +3, was based on deviations from normobiotic population reference ranges. This table provides information about changes from before and after the psychedelic ceremony and deviation from normobiotic populations. GABA, gamma-aminobutyric acid; IL, interleukin; TNF, tumor necrosis factor.

Dorea, which research identifies as having anti-inflammatory effects due to its ability to produce short-chain fatty acids, decreased from +1 to 0.⁸¹ This may indicate lower anti-inflammatory properties; however, the reduction does not fall below normobiotic levels. Finally, *Phascolarctobacterium* spp., which are short-chain fatty acid producers and have anti-inflammatory effects, decreased from +3 to +1.^{52,82} No clear microbiome pattern emerged that would drive the change in mental health observed in the patient following Ayahuasca.

HUACHUMA (SAN PEDRO) CEREMONY OUTCOMES

Prior to the Huachuma ceremony, the patient presented with a HAM-D score of 12, consistent with mild depression. Following the ceremony, this score decreased to 2, indicating remission of depressive symptoms. Correspondingly, the patient's WCS score improved from 58.32% pre-ceremony to 84.65% post-ceremony, reflecting enhanced feelings of connectedness. In the MEQ, the patient scored 14 out of 30 (47%) in transcendence, 16 out of 30 (53%) in positive mood, 5 out of 15 (33%) in ineffability, and 42 out of 75 (56%) in the mystical dimension, with a total score of 77 out of 150 (51%). On the CEQ, the patient scored 7 out of 130. The patient reported participating in a shared group intention during the ceremony, with personal goals centered on receiving guidance for navigating the final years of caregiving for a terminally ill parent and gaining clarity regarding an intimate partnership.

Similar to Ayahuasca, microbiome analysis after Huachuma revealed *Alistipes* spp. reduction from +2 to +1, which could indicate anti-inflammatory and anti-depressive effects.^{52,78} *Bacteroides* spp. increased from 0 to +1, which may contribute to an anti-inflammatory effect.^{58,83} *Bacteroides stercoris* reduced from +2 to +1, which may indicate lower anti-inflammatory properties; however, the reduction does not fall below normobiotic levels. *Dorea*, which has anti-inflammatory properties due to being a short-chain fatty acid producer, increased from 0 to +3, which indicates an increase in anti-inflammatory action.⁸¹ *Agathobacter rectalis*, which produces butyrate and therefore has possible anti-inflammatory effects, decreased from 0 to -1.⁵¹

Mediterraneibacter gnavus, which has been identified as more pro-inflammatory, decreased from +1 to 0, which broadly suggests an anti-inflammatory trend.⁷¹ *Veillonella* spp., which seem to vary in their inflammatory effects based on strain and context, increased from –1 to 0.^{76,84} *Escherichia* spp., which have primarily pro-inflammatory properties, increased from 0 to +1 (Table 2).⁸⁵

Following the Huachuma ceremony, the patient's dysbiosis score decreased from 3 to 2 on a 5-point scale, indicating potential partial normalization of the gut microbiome. This sample, collected 4 days post-ceremony, may reflect early microbial shifts influenced by the intervention. The alpha diversity, assessed via the Shannon Diversity Index, remained unchanged at 3 out of 5, consistent with observations reported in Ayahuasca studies. These findings suggest that while overall microbial diversity is maintained, specific compositional changes may contribute to the therapeutic effects observed.

SUBJECTIVE EXPERIENCE ANALYSIS

The patient's narrative revealed marked differences in both physical and spiritual experiences with Ayahuasca and Huachuma. Physically, Ayahuasca ceremonies were described as heavier and more intense, characterized by strong visual effects and a direct, forceful delivery of insights. In contrast, Huachuma was experienced as a gentle medicine, less visual and more intuitive, with subtler bodily effects that facilitated emotional awareness through an inner sense of knowing and connection rather than vivid imagery. Spiritually, these medicines were interpreted through gendered archetypes in which Ayahuasca embodied a fierce feminine energy, offering insights through emotion and metaphor and requiring an emotional surrender and passive reception of insight. Huachuma was viewed as a grandfather figure with masculine qualities, encouraging active inquiry and engagement during the experience. These energetic differences influenced how the patient received insights: Ayahuasca demanded openness and surrender, while Huachuma fostered introspection and dialogue with the medicine, reflecting distinct traditions of engagement and interaction (Table 1).

DISCUSSION

This hypothesis-generating case study highlighted an acute reduction of depressive symptoms from moderate and mild depression scores to no depression following two distinct psychedelic experiences. This trend suggests that although depressive symptoms may re-emerge over time, subsequent psychedelic experiences may potentially offer psychological benefits and support a dynamic process of mood regulation and integration.

There are studies that highlight a potential relationship between psychedelics and the microbiome; however, to date, no studies have assessed Ayahuasca- or Huachuma-induced microbiome shifts.^{6,86–88} This case study identifies a gap in the literature regarding additional potential mechanisms of how psychedelics may influence health.

While no single microbial pattern emerged, there were changes in some microbial species that could be consistent with reducing inflammation, increasing the production of specific neurotransmitters, or both. Moreover, shifts in microbial patterns could be related to neurotransmitters directly or indirectly modulated through short-chain fatty acids or cytokine production resulting in systemic inflammatory changes.^{56,89,90} Given the well-established role of inflammation in the pathophysiology of depression and many mental health disorders, it was anticipated that the observed improvements in WCS and HAM-D scores are associated with microbial shifts that increase short-chain fatty acid production and reduce systemic inflammation observed in this study.^{6,55,91} These findings align with the current understanding that reducing inflammation can alleviate depressive symptoms.⁵⁵

For instance, in this study, Ayahuasca administration was associated with a reduction in *Alistipes* spp., while Huachuma use corresponded with normalization of *Mediterraneibacter gnavus* levels (Table 1). Both microbial shifts have been implicated in inflammatory processes and depressive symptoms.^{52,71,78,91} Additionally, in the literature, both taxa have been previously linked to the production of pro-inflammatory cytokines interleukin-6 and tumor necrosis factor- α .⁹² Psychedelic shifts in microbes may lead to a normobiotic microbiome with reduced

inflammatory cytokines and, thus, may be a mechanism by which these psychedelics are improving depression and connectedness scores post-ceremony.

In this case, both Ayahuasca and Huachuma increased connectedness. In other studies, a reduction in *Dorea*, pro-inflammatory *Firmicutes*, which was seen with Ayahuasca, correlates with enhanced connectedness, as chronic inflammation is tied to social withdrawal and alienation.^{92–94} Similarly, when the patient used Huachuma, there was an increase in *Veillonella* spp., which are butyrate producers, thus reducing inflammation.⁷⁵

Multiple scientific studies suggest long-term psychological benefits from psychedelic compounds.^{91,95,96} However, it remains unknown how singular experiences can sustain long-term effects or how durable these effects are. It is possible that psychedelic compounds contribute to shifts in microbiome, neurotransmitters, and microbial metabolite byproducts that can affect mood changes.⁶

Although there is no established link between *Dorea* spp., *Bacteroides* spp., and *Alistipes* spp. having direct antidepressant action, these microbes produce short-chain fatty acids such as butyrate, acetate, and propionate.^{97,98} These short-chain fatty acids have anti-inflammatory properties through various mechanisms, with butyrate having the strongest effects.⁹⁸ Studies show a correlation between butyrate deficiency and depression. Thus, butyrate-producing microorganisms may contribute to an antidepressant effect.⁸⁶ Additionally, as inflammation is known to exacerbate depression, the microbes with anti-inflammatory properties may have an indirect effect on depression through a short-chain fatty acid production.⁹⁹

Ayahuasca ceremonies elicited much stronger mystical experiences than Huachuma, with a 93% total MEQ score versus 51% for Huachuma. Subscales like transcendence and positive mood were notably higher for Ayahuasca, alongside a threefold greater difficulty score, indicating a more intense but challenging experience. The trend of this study is consistent with a previous systematic review evaluating the effects of Ayahuasca on psychiatric disorders.¹⁰⁰

The Ayahuasca ceremonies elicited much stronger mystical experiences than Huachuma, with a 93% total MEQ score, classified as a complete mystical

experience, compared to 51% for Huachuma. Subscales such as transcendence and positive mood were notably higher for Ayahuasca, alongside a threefold greater CEQ score, indicating a more intense but challenging experience. These findings suggest that experiences characterized by greater mystical intensity and emotional difficulty may facilitate deeper psychological processing and integration, mechanisms which have been linked to greater improvement in depression severity following psychedelic use.¹⁰¹ This pattern aligns with evidence that the magnitude of mystical experience is a key predictor of positive therapeutic outcomes, even when accompanied by transient difficulty during the session. The trend of this study is consistent with a previous systematic review evaluating the effects of Ayahuasca on psychiatric disorders.¹⁰⁰

Both psychedelic experiences reported here incorporated aspects of dietary preparation, setting intentions, and ceremonial tradition led by a certified curandero.^{102–105} The psychedelic substance is only one part of a multifaceted process and may serve as a catalyst, rather than the single mechanism or sole solution for a journey of change. This case study highlights different experiences with Ayahuasca and Huachuma and potentially informs preparation for different plant medicines, including indications and personalized therapeutic approaches.

LIMITATIONS

These data are from a single patient and use tests (HAM-D, WCS) that are typically used to observe group change. While the data suggest the patient underwent change, the degree of change cannot be determined from a single patient. It is important to note that microbiome analysis in individuals is still in its infancy. Thus, the changes observed in different microbial species need to be interpreted within the context of each individual's microbial ecosystem. Given the high inter-individual variability in gut microbiome composition, similar microbial shifts may have differing functional outcomes depending on the unique ecological context of each individual's microbiome.¹⁰⁶ While changes in microbiome were observed for both psychedelics, to date there has not been robust research that defines

a microbial pattern that is “anti-inflammatory” or “anti-depressive.” Furthermore, because microbial ecosystems vary between individuals, there may never be a specific microbial pattern that indicates good mental health.¹⁰⁷ Instead, there may be a collection of microbial metabolites that, at certain levels, indicate influence on mental health. The patient had differing time windows between stool collections, and it is unknown whether this influenced her results. The ceremonies were conducted at different times of day and in non-controlled environments with other attendees as mentioned above, which may also influence microbial patterns. Further investigation is needed to understand the sustainability of the antidepressant effects that the patient experienced, as well as the roles of set, setting, and integration in long-term outcomes.

Moreover, the improvements observed in HAM-D and WCS scores across repeated assessments may partially reflect a “practice effect,” wherein familiarity with the scales and repeated administrations lead to reporting changes independent of true clinical improvement.¹⁰⁸ This phenomenon underscores the need for cautious interpretation, particularly in single-subject designs where alternate explanations for score changes cannot be excluded.

CONCLUSION

This case study suggests that psychedelic use improved depression and sense of connectedness in a single patient. Moreover, a potential link between psychedelic-induced changes in the gut microbiome and improvements in mental health may exist. If this relationship is accurate, mental health benefits may be mechanistically related to reduced inflammation and sustained antidepressant effects via the microbiota–gut–brain axis. These findings highlight the promise

of integrating microbiome research into personalized psychedelic therapies, paving the way for innovative, holistic approaches to mental health care.

Future research could build upon this case study by conducting randomized controlled trials and larger controlled cohort studies to rigorously evaluate the effects of Ayahuasca and Huachuma on depression severity, connectedness, and their mechanistic links with gut microbiome changes and mental health outcomes.

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