Psychedelics and Well-Being: An Experiment in Brazil

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Abstract

We partnered with an ayahuasca center in Brazil to study the well-being effects of a one-time ayahuasca treatment within a ritualized group setting. The center enrolled 429 first-time ayahuasca users to participate in the largest randomized controlled trial of psychedelics ever run. Relative to placebo, ayahuasca increases happiness and reduces psychological distress six months later by roughly 0.4 standard deviations. The field experimental setting allows investigation of aspects not explored in the large clinical literature. Positive effects are almost entirely driven by participants that were distressed at baseline. Improvements in well-being are strongly positively correlated with the mystical nature of trips. The mystical experience can also be induced by placebo with ritual, though less frequently, and when done so induces a similar magnitude of well-being improvement. Effects are larger for older people, consistent with the idea that psychedelics reopen a window of heightened malleability. We estimate the mental health benefits of participating in an ayahuasca ceremony to be roughly 200 times the cost of 24 USD.

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1 Introduction

Mental health disorders affect over one billion people worldwide, with particularly severe burdens in low- and middle-income countries (WHO 2025). These disorders impose substantial economic costs through lower financial empowerment (Baranov et al. 2020), reduced labor supply (Biasi et al. forthcoming), and decreased productivity (Lerner and Henke 2008). Yet existing treatments remain limited in reach and economic accessibility (Singla et al. 2017). Recent clinical trials have raised hopes of a new weapon to battle mental ill-health: psychedelics—substances that "reliably... induce states of altered perception, thought, and feeling that are not experienced otherwise except in dreams or at times of religious exaltation" (Jaffe 1990). Psychedelics have been shown to have large beneficial effects on depression and PTSD in clinical settings (Griffiths et al. 2016; Goodwin et al. 2022; Mitchell et al. 2023). Lawmakers and regulators in a number of US states have moved towards legalization or de-criminalization of such substances, with high profile individuals advocating for wider access based on personal experiences.[1] Yet such enthusiasm is tempered by a stark knowledge gap: we have little evidence of the effects of psychedelics outside rich-country clinical trials, or among individuals without pre-existing mental health disorders. Moreover, we still understand little about the way such substances work, or which individuals they help. Are psychedelics akin to potent pharmaceuticals to be administered only in extreme situations, or are they important tools to help otherwise healthy individuals live more fulfilling lives?

We partnered with an ayahuasca center to conduct the largest randomized controlled trial of psychedelics to date, enrolling 429 first-time users in group ceremonies in Brazil, where ayahuasca is legal for ritual use (Labate and Feeney 2012). Ayahuasca is a traditional Amazonian psychedelic tea containing N,N-Dimethyltryptamine (DMT) that has been used in indigenous ceremonies for centuries (Labate and Cavnar 2014), and produces hours-long alterations in perception, emotion, and cognition.

Our naturalistic setting offers key advantages over clinical trials. Ethics protocols typically require trials to bundle psychedelics with costly one-to-one psychotherapy, restricting enrollment to clinical populations with diagnosed conditions, and enforcing conservative screening criteria. This leads to costs in the thousands of dollars per enrolled subject, and tells us little about what these substances would do for non-selected samples. In contrast, the vast majority of psychedelic use worldwide occurs in traditional settings like ours, in countries such as Brazil, Peru, Bolivia, Uruguay, and the Netherlands, where psychedelics are available legally with minimal screening, consumed by millions, and often in the context of group rituals (Psychedelic Al-

[1] For a recent example see: https://www.psychologytoday.com/ca/blog/psychedelics-to-the-rescue/202302/celebrities-are-speaking-out-on-psychedelics?.

pha 2024). The scale of our study, and its open admission criteria, allow us to address the effects on populations without pre-existing conditions, to compare the effects on such populations with those more closely resembling the usual clinical subjects, and to explore heterogeneous treatment effects that speak to the most prominent theories of why psychedelics seem to work.

Our partner center randomly assigned participants to receive either ayahuasca or a placebo (jurema, a non-psychedelic tea). We surveyed participants three days, six weeks, and six months after the ayahuasca ceremony, exploring well-being outcomes (Kessler-10 scale of psychological distress, self-reported happiness, and flourishing). We examine three mechanisms underlying any observed effects: age heterogeneity consistent with psychedelics reopening critical periods of neural plasticity, the content of experiences during trips, and placebo effects. Using difference-in-differences estimation, we also estimate effects of the ceremony itself absent the psychedelic, comparing ceremony-attenders with participants that chose not to attend. Finally, we quantify the mental health benefits of ayahuasca relative to costs.

The group ceremony includes 32 to 60 people, with the center owners beginning by giving a brief lecture on what effects to expect, and on general life lessons. Participants are given up to two servings of tea (ayahuasca or placebo), and largely stay silent during a four-hour ceremony in which music is played. While the center did not intentionally select participants based on mental health, 58% are classified as moderately or severely psychologically distressed at baseline. Perhaps reflecting this, 62% say that they are trying ayahuasca because they are looking for healing, while the most common reason given for trying ayahuasca is to improve spirituality (82% of participants).

Consistent with (and in some ways exceeding) findings from the clinical literature, participants that took ayahuasca experience visual effects, profound emotions (both positive and negative), deep insights into the self, and feelings of peace, self-love, and forgiveness of others. Participants deem these ayahuasca experiences to be deeply meaningful. Three days after the ceremony, 36% report that the experience was the single most meaningful experience in their entire life, while a further 40% report the experience to be in their top five. These are not ephemeral feelings—we see similar numbers in our 6-week follow-up survey—and the high numbers do not reflect a lack of meaningful experiences at baseline. The most common "most meaningful experience" reported at baseline is the experience of parenthood (32% of responses). Even restricting to these participants that found the most meaning in parenthood, 42% reported their ayahuasca experience to be their new most meaningful experience.

Reports of placebo-taking participants are much more neutral. We estimate a roughly one standard deviation effect of ayahuasca, relative to placebo, on a range of "first stage" outcomes: (i) perceived meaningfulness of the experience, (ii) a mystical experience score which captures

feelings of ineffability, sacredness, and gain of insightful knowledge, (iii) an ego dissolution score which captures feelings of oneness with others and dissolution of the self, (iv) the number of words written when describing the experience, and (v) whether the participant had visions. On the other hand, ayahuasca also increases immediate negative side effects (e.g. vomiting and diarrhea), along with the frequency of reported challenging and bad trips. We explore the well-being effects of these difficult trips when considering adverse effects below.

Relative to participants assigned to the placebo, those assigned to ayahuasca experience reductions in self-reported psychological distress ($p < 0.01$) and increases in self-reported happiness ($p < 0.001$), though null effects on a flourishing scale ($p = 0.56$), which captures positive psychology aspects of relationships, meaning, and competence. The effects on distress and happiness persist to the six-month point, with instrumental variable (IV) effect sizes of roughly 0.4 standard deviations. Participants that give more socially desirable answers at baseline do not drive these positive effects, speaking against demand effects (Bursztyn et al. forthcoming).

Due to the large sample we can go beyond small-N clinical studies and examine heterogeneous effects by baseline characteristics. Our positive findings are entirely driven by the distressed. This finding supports the REBUS ("relaxed beliefs under psychedelics") theory from neuroscience (Carhart-Harris and Friston 2019), which predicts that psychedelics are effective for depression because they lift people out of rigid, ruminative patterns of thinking. Under this model, psychedelics are less transformative for those that are not stuck with rigid self-beliefs to begin with, which we confirm. For those entering with normal levels of distress, there are no long-term benefits of ayahuasca ingestion relative to placebo. Ayahuasca helps individuals get out of a rut, but appears to have only transient effects on subjects entering without distress.

Having established positive effects of ayahuasca on well-being, we explore three candidate mechanisms, drawing from theories in neuroscience and psychology. First, we test the neuroscientific idea that psychedelics re-open "critical periods"—finite periods of heightened plasticity, and openness to learning, that close as one ages. Consistent with this theory, we find that the well-being effects of ayahuasca are significantly larger for older participants. This age heterogeneity contrasts with meta-analytic evidence for psychotherapy, which is found to be more effective for younger adults than older adults (Cuijpers et al. 2020), and the common finding in economics and political science that people are more malleable when in their early, impressionable years (Malmendier and Nagel 2011; Ghitza et al. 2023; Giuliano and Spilimbergo 2023). Psychedelics appear to be effective because they *make* people impressionable, rather than through exploiting pre-existing plasticity.

Second, we test the debated theory that the subjective experience of trips—including so-called "mystical" experiences, perceived meaningfulness, and revealed insights about the self—

is central to driving beneficial effects (Yaden and Griffiths 2020). We find strong evidence for this hypothesis: among those that took ayahuasca, well-being improvements are larger for those that reported more mystical (or meaningful) experiences. Taking this a step further, we even find similar evidence among those that participated in the ritual (the ceremony), but only took the placebo. Some placebo-takers nevertheless report mystical-like experiences (perhaps through meditation and introspection), and these participants experience larger subsequent improvements in well-being. These findings suggest that deep, spiritual, experiences promote well-being, regardless of whether they are triggered by a psychedelic or through a non-psychedelic group ritual. The comparative effectiveness of psychedelics seems to be their ability to facilitate such experiences more reliably than a group ritual alone.

Third, given the importance of subjective experiences in generating benefits, it is possible that benefits are partly driven by placebo effects, with a subject's perceived treatment status mediating effects on well-being. As in previous psychedelic trials, our single-blind approach does not work in practice; most participants can correctly guess their actual treatment status after being treated. Given this, we use three suggestive approaches to test for placebo effects, and find only weak evidence for their role in driving effects.

Finally, we explore the effects of the group ceremony itself. Using a difference-in-differences design, we find suggestive evidence of positive well-being effects of attending the group ceremony without receiving the ayahuasca. Here, there is even some sign of positive effects on flourishing—an outcome unaffected on average by ayahuasca—suggesting complementary mechanisms of the psychedelic and the ceremony: the psychedelic pulls people out of a rut, while the ceremony elevates people towards more fulfilling lives.

Given the uncertainty that still surrounds the risks of psychedelic use, particularly in lightly regulated settings, we pay close attention to possible adverse effects. On the one hand, we find (i) null negative side effects six months later, (ii) null effects on repeat use, speaking against addiction, and (iii) no evidence of negative tail effects of ayahuasca, even when focusing on participants that reported having had challenging or bad trips. On the other hand, we see suggestive evidence of increased use of other drugs ($p = 0.09$), and we note the important caveat that we are not powered to detect rare negative effects—effects that, though rare, may be sufficiently negative as to deter the typical potential user.

Turning to policy, we quantify the benefits of ayahuasca by assigning a dollar value to the reductions in distress, following the approach of Open Philanthropy. We find the benefits to range from 200 to 500 times the cost. These benefit-cost ratios are notable given that clinical regimens, involving psychotherapy, are orders of magnitude more costly, without correspondingly

larger benefits (BrainFutures 2022; Marseille et al. 2023).[2]

We contribute to work by economists on low-cost mental health treatment in the Global South (Haushofer and Fehr 2014; Ridley et al. 2020). Recent work finds both short- and long-term mental health effects of cognitive behavioral therapy (Baranov et al. 2020; Barker et al. 2022; Bhat et al. 2022), positive mental health effects of pharmacotherapy combined with livelihoods assistance (Angelucci and Bennett 2024), and improved labour market outcomes due to mental health treatment (Lund et al. 2024). These papers study the effects of modern mental health treatments designed within the Western psychiatric tradition. We instead study and unpack the effects of an indigenous, ritual-based approach—one not explicitly designed to improve mental health. This leads to distinctive findings, including that psychedelics are more effective for the old than for the young, in contrast with cognitive behavioral therapy, and that a one-off treatment can deliver enduring mental health benefits—a finding with broad implications, given the roughly half a billion people affected by anxiety and depressive disorders worldwide (GBD 2022).

Second, we advance understanding of the production function for subjective well-being and revealed choices (Layard et al. 2008; Benjamin et al. 2012, 2014, 2024). We find that psychedelics dig distressed participants out of a rut, but do little to elevate non-distressed participants to more fulfilled lives; while the ceremony without the psychedelic shows more promise for creating fulfillment. These findings we show that the production function for distress is not the mirror of that for flourishing.

Third, we build on a nascent literature on the societal role of rituals (reviewed by Xygalatas (2022)). Ghosh et al. (2025) find that adding collective rituals—like singing and dancing in unison—to Hindu-Muslim youth camps leads to mental health benefits for Hindus. Butinda et al. (2023) show that traditional African ritual spells change the perceived risk of theft of entrepreneurs, increasing profits. In contrast, we study a profoundly mind-altering ritual, with potential implications for a broader set of religious and spiritual practices (Clingingsmith et al. 2009; Campante and Yanagizawa-Drott 2015), and for the myriad cultures that have used mind-altering substances as part of group rituals throughout history (Lissarrague 2014; Labate and Cavnar 2014; Ferrara 2016). Related, in spotlighting the deep meaning attributed to trips, we complement a small economics literature that considers the effort-motivating effects of meaning at work (Ariely et al. 2008; Cassar and Meier 2018; Khan 2025; Ashraf et al. 2025).

Finally, we fill an important gap in the psychedelics literature. A recent systematic review by Thomson and Thomacos (2025) examined 1,672 studies of psychedelics on healthy subjects,

[2]Reports of high costs of administering psychedelics are also common in non-clinical settings, see: https://www.theguardian.com/us-news/2025/dec/12/oregon-pyschedelic-mushrooms.

identifying only 19 with controlled or naturalistic experimental designs and follow-up beyond seven days. Of these, only four included control comparators. Previous randomized studies of psychedelics on non-clinical populations include Griffiths et al. (2008), who found positive effects on personality and well-being in spiritually-active middle-aged participants ($N = 36$), though in a non-naturalistic clinical setting; Mendes Rocha et al. (2021), who studied ayahuasca in Brazil ($N = 30$) but found inconclusive results on personality measures; Mason et al. (2019), who examined the effect of psilocybin (the psychoactive compound in "magic mushrooms") on creativity ($N = 60$); and Netzband et al. (2020), who studied ayahuasca's effects on personality ($N = 24$) using matched comparators without randomization. Our study is the largest RCT of psychedelics yet run, the first large-N placebo-controlled experiment on psychedelics without psychotherapy, and the first to unbundle a psychedelic ceremony into effects driven by the ritual versus the substance.

2 Background and experiment design

2.1 Background

Ayahuasca. Ayahuasca is a traditional Amazonian tea that contains the hallucinogen DMT. Like other psychedelics, individuals that take ayahuasca experience an hours-long "trip," typically experiencing altered visual perception, synesthesia (e.g. seeing colors when hearing sounds), one-ness with others and the world, strong emotions (both positive and negative), profound meaning, and insights into the self (Nichols 2016). Ingestion has some immediate ill-effects, most commonly nausea and vomiting (Dos Santos et al. 2016). However, ayahuasca is considered relatively safe in healthy individuals (Guimarães dos Santos 2013; Netzband et al. 2020), with extremely low incidence of serious mental health consequences (Dos Santos et al. 2017).[3] The use of ayahuasca for religious and ritualistic purposes is legal in Brazil, following a set of rules established in 2010 (Labate and Feeney 2012). Our partner center has the necessary legal authorization that allows them to administer ayahuasca.

Placebo. Following the suggestion of our partner center, we administer jurema (*Mimosa tenuiflora*) as our placebo condition. The key advantages of jurema as a placebo are that (i)

[3] Animal studies indicate that the median lethal dose of DMT in humans would amount to 20 times more than that used in ceremonial ayahuasca practice (Gable 2007), and neither acute ayahuasca administration nor long-term consumption seems to be toxic to humans (Guimarães dos Santos 2013). Use of the brew in religious ceremonies has a safety margin comparable to codeine, mescaline, or methadone (Gable 2007), with minimal risk of sustained psychological disturbance. Cardiovascular risk has been found to be low (Riba et al. 2003), as has the addiction potential of the brew (Fábregas et al. 2010).

like ayahuasca, jurema is served as a tea, and is similar in color, (ii) like ayahuasca, jurema contains DMT, and (iii) unlike ayahuasca, the DMT does not cause psychoactive effects (i.e. trips) when ingested, because the DMT is broken down by a stomach enzyme—a process that is inhibited in ayahuasca due to it containing monoamine oxidase (MOA-A) inhibitors (Ruffell et al. 2020). In principle, features (i) and (ii) should help preserve the blinding in our experiment—preventing participants from realizing what treatment they received. In practice, and as in most psychedelic experiments,[4] we see evidence of *functional* unblinding: the intense psychoactive effects only present with ayahuasca make it easy for most participants to guess their treatment assignment. The practical role of the placebo is then the same as in most experiments in economics: to hold constant certain aspects of the treatment (in this case, the ritual of undergoing the ceremony and drinking the tea), but not to hold constant perceived treatment status. For further details on jurema, see Appendix D.1.

Partner center and ceremony. Our partner center is in a large Brazilian city, and hosts roughly 1,400 ayahuasca participants per year. Unlike most ayahuasca centers in Brazil, the center holds universalist ceremonies, with no affiliation with the religions most associated with the use of ayahuasca as a sacrament (e.g. Santo Daime, União do Vegetal). The center is not a retreat oriented to foreigners (Londoño 2024), and reflecting this, all of our participants are adults living in Brazil.

Each experimental session is attended by the two center owners and two center employees, and follows the same structure as the center's regular sessions. The experimental session sizes range from 32 to 60 people. Despite the group setting, the treatment entails little actual social interaction with other participants—in fact, the center instructs participants to not talk to, or touch, other participants during the ceremony (see Appendix D.2 for the full set of instructions). The center owners begin by giving a brief explanation of the effects of ayahuasca to expect, followed by a short lecture on general life lessons (see lecture text in Appendix D.3), with no accompanying therapy otherwise. Participants are given one serving of tea (ayahuasca or jurema; blinded to the participant but not the center), and advised to be silent and to close their eyes throughout the ceremony, in which music is played. Each participant is later offered a second, optional, serving of the same substance.[5] Unlike clinical settings, there is no "integration"—in which guides help participants make sense of their experiences—at the end

[4] Exceptions include microdosing experiments, in which the dose is sufficiently small as to not have perceptible effects (Szigeti et al. 2021), and experiments in which psychedelics are administered under anesthesia (Lii et al. 2023).

[5] Eighty percent of the participants that received ayahuasca opted for the second serving, as did 86% of those that received the placebo.

of the ceremony. The full ceremony takes roughly four hours.

2.2 Experiment design details

Recruitment, screening, and ethics. The center recruited participants following its status quo protocols that include social media, walk-in registrations, and other forms of outreach. Those who had not taken ayahuasca before were given the option of participating in an experimental session, in which they would be randomly assigned to receive either ayahuasca or the placebo.

The center follows their status quo screening protocols: they reduce dosing for individuals taking the antidepressant fluoxetine,[6] and they fully exclude participants that self-declare having a history of schizophrenia. In addition, the center sends a set of instructions to sign-ups prior to the ceremony—telling them to check in with their doctor if they take certain medications, along with some guidance on what to bring and what to expect (see Appendix D.2). These inclusion criteria are less stringent than typical inclusion criteria in clinical trials. But since these criteria are applied in the status quo (i.e. in the absence of our experiment), we keep them in tact for the experiment.

Our study received ethics approval from UBC (certificate numbers H21-00789 and H24-01148). On the point of risk to participants, our study differs from typical clinical trials in that (i) our setting is one in which psychedelics are legally available, and (ii) our experimental participants are those that already planned to take ayahuasca at our partner's center. As a result, our experiment randomizes the participants "down" to the placebo, or to the status quo; clinical trials typically expose participants to psychedelics that they would not have been able to obtain legally otherwise.

Experiment design. Our experiment design is summarized in Figure 1. The center recruited 434 participants for the experimental sessions, and screened out five. The remaining 429 participants completed a baseline survey, and were assigned to the next available session date, with six experimental sessions in 2023 and 2024. The center used a random number generator to randomize the 429 participants 50:50 to ayahuasca or placebo, stratifying on session-by-gender. Since the study is single-blind, participants were not informed of their actual treatment status

[6] According to the center owners, they are concerned with a scientific literature providing evidence of an ayahuasca interaction with fluoxetine. The center cannot suspend the use of this medication, as it is prescribed by a doctor. The center's approach is then to allow such participants to go to the ceremony, but with them given a lower dose of ayahuasca.

until the end of the 6-week follow-up survey.[7]

Participants in the experimental sessions have their session cost waived, and receive 70 BRL (13 USD) for completing each of the first two follow-up surveys, and 100 BRL (18 USD) for completing the third follow-up survey.[8] Of the 429 participants, 144 did not attend their assigned ceremony. We still send follow-up surveys to these "no-shows," and we use their data for a difference-in-differences analysis of the effects of attending the ceremony. Thirty-three participants attended the sixth experimental session, but all were given ayahuasca due to error. We exclude these participants from our analysis of the effects of ayahuasca relative to the placebo, but use their data for other analyses.

Two-hundred and fifty-two participants attended one of the first five sessions—137 participants that were randomly assigned to ayahuasca, and 115 to the placebo. These numbers depart somewhat from 50:50 due to ayahuasca-assigned participants having a higher attendance rate than placebo-assigned participants. This difference in attendance is due to chance, given that participants did not know their treatment status in advance. Supporting this, baseline characteristics of the two groups of attenders are similar, and consistent with randomization, as we show in Section 3. Compliance with assigned treatment was imperfect, with 83% of the ayahuasca-assigned given ayahuasca and 90% of the placebo-assigned given the placebo. Given this, we estimate ITT effects, and IV effects, with assigned treatment as an instrument for actual treatment status. Follow-up response rates are high for those that attended their assigned ceremony, ranging from 88% to 100%, but lower for the no-shows, ranging from 67% to 75% (Figure 1).

Since ayahuasca is legally available in Brazil, one concern was that participants assigned to the placebo would nevertheless take ayahuasca elsewhere in subsequent weeks, making it impossible to characterize the long-term effects of ayahuasca. To mitigate this concern, at baseline we asked participants to pledge not to take ayahuasca after the ceremony date until they had completed the 6-week follow-up. We then asked participants detailed questions about ayahuasca and other psychedelic usage in the 6-week and 6-month follow-ups, telling participants that they should feel free to be honest (i.e. we won't mind if they broke their pledge). In practice, we show in Section 4.2 that relatively few participants took ayahuasca after their assigned ceremony dates, and we do not see a difference between those assigned ayahuasca and those assigned the placebo.

[7] Twelve participants entered the study twice. We keep only one set of surveys for each participants (see details in Appendix D.4). Our results are nearly identical if we instead include the full set of survey responses, with standard errors clustered at the participant-level.

[8] Anticipating higher expected attrition six months following the ceremony date we increased the incentive for the third follow-up survey.

Pre-registration. We pre-registered our experiment in the AEA RCT Registry (#10400), and detail deviations in Appendix D.5. We summarize two important points here. First, we initially pre-registered and ran experimental sessions with a low-dose ayahuasca group rather than a jurema placebo group. These sessions had a first-stage problem, in that low-dose ayahuasca takers still frequently experienced trips, often reporting that these were among their most meaningful experiences ever. We pivoted to the jurema-placebo design as a result and updated the pre-registration at that point. We only report results from the jurema design in this paper. Second, our pre-registration covers additional non-well-being-related outcomes. In this paper, we only explore effects on well-being outcomes—though we report those outcomes exhaustively. We plan to analyze the other outcomes when we are able to link our participants to administrative labor market data, but must wait for the administrative data to be released for the years that we study.

2.3 Survey questions

We give an overview of our survey measurement in this sub-section. For the full survey questions, see Appendix C.

Baseline. In the baseline survey, we measure basic background and demographic information (including race, gender, education, income, employment, religiosity, and drug use), and psychological well-being (described in detail below). We ask participants why they wanted to try ayahuasca, with one example answer category being "I was looking for healing," how much they expected their experience with ayahuasca to improve their well-being (from 1 to 10), and what their most meaningful experience in life has been so far (open-text).

Given our reliance on self-reported measures of well-being, we ask participants a subset of the Marlowe-Crowne social desirability scale (Crowne and Marlowe 1960; Dhar et al. 2022). In Section 4.2, we use this scale to show that our positive treatment effects are not driven by participants that give more socially desirable answers.

Trip reports. We elicit measures of the ceremony experience in the 3-day follow-up. Following Griffiths et al. (2006) and others, we ask how meaningful participants found the experience, with answers on an eight-point scale ranging from 0 = "No more than routine," to 6 = "Among the five most meaningful experiences of my life" and 7 = "The single most meaningful experience of my life." We interrogated specific aspects of the trip experience by administering seven items from the *Mystical experience questionnaire* (Pahnke 1963), covering a participant's feelings of loss of usual sense of time, sacredness, ineffability, and feelings of universal or infinite

love. Each dimension is scored from 0 = None to 5 = Extreme, yielding a summed mystical experience score ranging from 0 to 35. We measure reduced identification with ego through five items from the *Ego dissolution* questionnaire (Nour et al. 2016), with participants rating, for example, how much they experienced a dissolution of self, union with others, and how much they felt more special or important than others (reverse-coded). Each dimension is scored from 0 = No more than usually to 100 = Entirely or completely, yielding a summed ego dissolution score ranging from 0 to 500.

We ask participants to describe their experience in their own words, and to report what domains their trip covered, with 12 select-many categories, including family members, revived old memories, had visions, love or peace, sadness or pain, and insights about bad habits. To capture immediate adverse effects, we also ask participants to select which of the following happened to them: vomit, diarrhea, dizziness, bad trip, challenging trip, hypersalivation, or other. To characterize the success of the blinding, we ask participants to guess their treatment status—we discuss details in Section 5.3.

Psychological well-being. No bio-marker exists for psychological well-being, and as a result, we rely on self-report scales, as in related work by development economists (Baranov et al. 2020; Bhat et al. 2022), and as used widely by practitioners for screening.[9]

We exhaustively report the well-being outcomes that we pre-registered. We pre-registered three primary well-being outcomes, and measured these at baseline, as well as in all three follow-up surveys. We measure psychological distress using the Kessler-10 scale (Kessler et al. 2003; Barker et al. 2022), which asks participants how much they have felt ten symptoms over a recent time period, which varies depending on the exact survey (i.e. only three days for the 3-day follow-up, but two weeks for the 6-week follow-up, etc.). The ten symptoms include feeling tired out for no good reason, depressed, worthless, nervous, so restless you could not sit still, and that everything was an effort. Participants answer 0 = Never to 4 = All the time, yielding a summed Kessler-10 score that ranges from 0 to 40. We primarily use a binary variable for scoring 15 and above, an existing cutoff used to indicate moderate or severe psychological distress (Yiengprugsawan et al. 2022). The Kessler-10 items capture symptoms of both depression and anxiety, and are very similar to items used in the PHQ-9 and GAD-7 scales commonly used to screen for these conditions.[10]

[9]Clinician assessments can improve on self-reports. For example, clinicians can ask follow-up questions to patients to determine whether recent weight loss is a feature of depressive under-eating versus the effects of Ozempic. Clinician assessments were not possible in our outside-of-the-clinic setting, although encouragingly, meta-analytic evidence finds that effects of psychotherapy on self-reports tend to be smaller than those on clinician assessments (Miguel et al. 2025).

[10]For example, the PHQ-9 asks "Over the last two weeks, how often have you been bothered by any of the

We measure happiness with the question "In general, how happy would you say you are these days?" with answers from 0 = Not very happy to 6 = Very happy. We also ask a retrospective version of this question at baseline ("In the past month, how happy have you felt?") as well as a prospective question in the 3-day follow-up (pre-specified as secondary, "Please guess how happy you will be in six weeks").

Our third primary well-being outcome is the *Flourishing Scale* (Diener et al. 2010), which aims to capture the more positive dimensions of psychological health. Participants are asked whether they disagree or agree (0 = Strongly disagree to 4 = Strongly agree) with each of eight statements, including "I lead a purposeful and meaningful life," "People respect me," and "I actively contribute to the happiness and well-being of others." We sum the answers to give a score ranging from 0 to 32.

Other health and drug use. In the 6-month follow-up, we capture possible negative side effects by asking participants to report the presence of 11 negative symptoms, including visual disturbances, paranoid thoughts and behaviors, and increased heart rate. In all three follow-up surveys, we also ask participants to describe their general state of health from 0 = Very poor to 4 = Very good. Finally, we ask follow-up survey questions on the use of both ayahuasca and other drugs, which we explore when considering the addictive or gateway drug-potential of ayahuasca.

2.4 Summary statistics

Sixty-two percent of participants are female, 45% are non-white, and 45% practice a religion (Table A1); making this sample much less religious than the average Brazilian (91% of Brazilians practiced a religion in 2022, de Geografia e Estatística (2025)). Participants display the full range of psychological well-being at baseline, with 58% being classified as distressed. The median participant falls in an income bracket of BRL 2,001 to 3,000 (363 to 544 USD) per month, where BRL 3,000 is roughly the average monthly earnings in the country in 2023 (Instituto Brasileiro de Geografia e Estatística, 2023).

The most common reasons given for wanting to try ayahuasca are that participants want to improve their spirituality (82% of participants, Figure A1), understand why patterns are repeating in their life (67%), or understand why they are the way they are (64%). Sixty-two percent say that they were looking for healing, while only 11% say that they were taking ayahuasca out

following?" with categories including feeling down, depressed, or hopeless, and feeling tired or having little energy. The GAD-7 asks "Over the last two weeks, how often have you been bothered by the following problems?" with categories including feeling nervous, anxious or on edge, and being so restless that it is hard to sit still.

of curiosity.

3 Econometric specification and balance

Our main specification estimates ITT effects, by comparing ceremony participants assigned ayahuasca with those assigned to the placebo. The sample includes the participants that attended the five experimental sessions in which there was variation in actual treatment (i.e. we drop the sixth, in which due to an error all attendees were given ayahuasca). We estimate the following cross-section regression, separately for each timepoint t:

$$y_{it} = \gamma_s + \beta_{0t} y_{i0} + \beta_{1t} \text{Assigned Ayahuasca}_i + \varepsilon_{it} \tag{1}$$

where y_{it} is the well-being outcome for participant i at survey timepoint t, while γ_s are randomization strata (gender-by-session) fixed effects. With two genders and five sessions, these are ten dummy variables. For $t \in \{\text{3-day, 6-week, 6-month}\}$ we control for the outcome measured at baseline (y_{i0}). While we do not need to control for this variable for unbiased estimates of causal effects, we do so to increase precision. For happiness, we have an additional timepoint, since we also have a retrospective measure at baseline.

The key regressor is Assigned Ayahuasca$_i$, which is equal to one if the participant was randomly assigned to receive ayahuasca, and equal to zero if the participant was randomly assigned to receive the placebo. It follows that $\hat{\beta}_{1t}$ is our ITT estimate of the effects of ayahuasca relative to placebo by time t. We estimate robust standard errors.

Balance. Baseline characteristics are largely balanced between ceremony participants randomly assigned ayahuasca versus those assigned to the placebo, including when restricting only to the respondents to each follow-up (columns 1 to 4, Tables A2 to A5, with joint test p-values of 0.33, 0.21, 0.47, and 0.27). The one important exception is that baseline happiness is lower among those assigned ayahuasca ($p = 0.03$). This imbalance would bias us against finding positive effects of ayahuasca, though we anyway control for the baseline dependent variable in our regressions.

Balance looks similar when comparing groups based on *actual* assignment, rather than intended assignment (columns 5 to 8, Tables A2 to A5, with joint test p-values of 0.42, 0.52, 0.14, and 0.07). The center's deviations from randomization appear to be arbitrary, which fits with our anecdotal understanding that errors were driven by logistical difficulties (e.g. a participant arriving late) rather than the desire to ensure that certain participants receive ayahuasca. Given

this, we show below that our core results are similar when comparing groups based on actual assignment.

As might be expected, the no-shows are selected, being less educated, less likely to be employed, less happy, and more distressed, than those that attended and took the placebo (column 9, Table A2, joint $p < 0.01$).

4 Results

4.1 Ceremony experiences

Meaning. Participants that take ayahuasca report remarkable experiences in the first follow-up survey three days later: 36% report that the experience was the single most meaningful experience they have ever had, while a further 40% report it to be among their top five most meaningful experiences. These large numbers do not reflect a fleeting warm-glow effect: we ask the same question in the 6-week follow-up, and rates are similar (at 36% and 38%, respectively), and highly correlated with the 3-day responses ($\hat{\beta} = 0.78$, $p < 0.0001$). These rates are higher than those reported in seminal clinical trials of psilocybin (Griffiths et al. 2006, 2016), which may partly be an effect of the ritualized ceremony setting here as compared with the clinical setting.

To help contextualize these reports of meaningful experiences, we can look at how the same set of participants answered our baseline question "What was the most meaningful experience of your life so far?" The modal response is the experience of parenthood—mentioned in 32% of responses (nearly three-quarters of those that actually have children), while 13% describe a romantic relationship (including break-ups), 10% describe a spiritual or religious experience, and 8% describe a professional experience (e.g. becoming a lawyer). The only other categories with at least 5% of respondents are schooling, travel, and bereavement-related experiences.[11] Even participants that reported parenthood as their most meaningful experience found taking ayahuasca to be deeply meaningful: 42% reported their ayahuasca experience to be their (new) single most meaningful life experience.

Reports of meaningful experiences are also reflected in the rich descriptions participants give in response to our open-text question, including:

> With the force of the Ayahuasca, I was able to face my traumas, fears, and anxiety.

[11] While economists often model utility as a function of consumption, we see little evidence of consumption producing meaning—only three of 126 responses describe consumption experiences, all three involving renting or buying a house. One additional participant reported going bankrupt as their most meaningful experience.

> Not only did I face them, but I was able to understand all of it – that I can avoid being affected. Ayahuasca embraced me, and I felt like I was in the lap of God.
>
> I felt like I was living through other lives, with everything happening in extreme slow motion – time felt surreal. Most of the time I smiled and cried easily, as if I were in the grace of the divine. I saw myself as a child.
>
> I experienced a healing sensation across many aspects of my life – for example, forgiving my adoptive mother, my biological mother, biological father, adoptive father, adoptive sister, and ex-boyfriend.
>
> It was without a doubt the greatest experience of my life. I heard in my mind myself guiding and orienting me throughout the entire session. I saw people from my childhood... I forgave everyone who had hurt me and asked for forgiveness from everyone I had somehow offended, harmed, or caused damage to. I saw many geometric figures with bright colors I had never seen in my life...

First stage effects. Using treatment assignment as an IV for actually receiving ayahuasca, we find that ayahuasca substantially increases reports of meaningfulness, mystical experiences, and ego dissolution, relative to the placebo condition (Table 1).[12] These first stage effects are roughly the size of one standard deviation in the placebo group. For meaningfulness, the average placebo group participant reports that the experience was similar to meaningful experiences that occur once every few years (i.e. still quite meaningful). Ayahuasca causes participants to score 2.4 points higher on the meaningfulness scale—roughly to the point of reporting the experience as in their top five ever. Ayahuasca also causes participants to have trips that touch on more areas of life, to have more visions, and to write 59% more in the open-text question asking them to describe their experience (columns 4 to 6, Table 1).

On the negative side, ayahuasca causes more vomiting (5% vs. 67%, using IV estimates, Table 2), diarrhea (4% vs. 15%), and dizziness (9% vs. 36%). These are well-known immediate side effects of ayahuasca, and often considered a positive and necessary element of an ayahuasca ceremony, given a perception of purging as cleansing (Bouso et al. 2022; Lustig Vijay et al.

[12]The average mystical experience scores for placebo-takers are low, and with a mass at zero (Figure A2), consistent with participants not experiencing psychedelic trips through taking jurema. For example, the average score of 12/35 on the seven-item Mystical Experience Questionnaire is consistent with participants answering "So slight I cannot decide" or "Slight" to questions like "Please rate the degree to which you experienced... Feelings of universal or infinite love." In contrast, the average score of 24/35 (69%) for participants that took ayahuasca is comparable to the 64% average, though on the 30-item Mystical Experience Questionnaire, for high psilocybin dose participants in a seminal clinical trial for patients with life-threatening cancer (Griffiths et al. 2016).

2024). Ayahuasca also increases self-reports of "bad" (3% vs. 13%) and "challenging" trips (5% vs. 24%). We show below that bad and challenging trips are not followed by negative effects on well-being.

4.2 Effects on well-being

Recipients randomly assigned to ayahuasca experience significant and durable reductions in distress, and improvements in happiness, relative to placebo (Figure 2A). Pooling the three follow-up surveys, we estimate statistically significant beneficial effects on distress ($p < 0.01$) and happiness ($p < 0.001$), though we estimate null effects on flourishing ($p = 0.56$). The effects are relatively stable over time, and the IV effects of ayahuasca on distress and happiness are roughly 0.4 standard deviations (Cohen's d) at the 6-month follow-up.[13]

For all three well-being outcomes, there is also a large pre-post improvement for the participants randomly assigned to the placebo. This improvement reflects three forces: (i) some participants in this group actually received ayahuasca (due to imperfect compliance), leading to well-being benefits, (ii) mean reversion given low well-being at baseline (which is also a common feature of clinical trials that select participants based on poor baseline mental health), and (iii) well-being effects of the ceremony and ritual, absent the ayahuasca. We unpack these forces in Section 6.

The well-being effects of ayahuasca relative to placebo are similar, though more precise, if we instead compare groups based on *actual* treatment—for which we also see balance on observables—as opposed to assigned treatment. In addition, the 6-month standardized IV effects are smaller, at roughly 0.3 (Figure A5).

Clinical trials of psychedelics restrict to participants that suffer from mental or physical ill-health. A feature of our setting is that we can also estimate effects for healthy participants—relevant for policy-makers considering legalization of psychedelics beyond strictly medical use (Smith and Appelbaum 2021). We split the sample and estimate effects separately for those distressed at baseline (Kessler-10 score ≥ 15, 53% of participants) and those not. The effects of ayahuasca on well-being are entirely driven by distressed participants; for whom the 6-month effect on distress and happiness is roughly 0.9 standard deviations (Figure 2B).[14] In contrast, the only statistically significant effect we find for non-distressed individuals is a positive, but

[13] Effects on distress are similar if we use the continuous Kessler-10 score (from 0 to 40) or Kessler-6 score (0 to 24, Kessler et al. (2002)) instead of the binary cutoff (Figure A3). As for our pre-registered secondary health-related outcomes, we see immediate positive effects on optimism about future well-being, and if anything, positive (though statistically insignificant) effects on health in general (Figure A4). A natural interpretation of the latter would be that ayahuasca improves mental, but not physical, health.

[14] We see a similar pattern of results if we instead split by the median of baseline happiness (Figure A6).

fleeting, effect on happiness (Figure 2C).

This finding supports the interpretation of psychedelics' being effective for lifting participants out of a rut, but less so for elevating happy participants to more fulfilling lives. This finding is consistent with the theorized REBUS ("relaxed beliefs under psychedelics") model from neuroscience (Carhart-Harris and Friston 2019), the basic premise being that (i) the brain relies on strong priors (e.g. beliefs about the self and others) to interpret the world, (ii) this can be maladaptive when these priors become too rigid (e.g. leading to ruminative thinking), and (iii) psychedelics relax these priors, leading maladaptive beliefs to update. The REBUS theory predicts heterogeneous effects by baseline well-being (or maladaptive beliefs), consistent with our findings.

The positive effects for distressed participants are comparable to the effects of single-dose psilocybin relative to placebo in clinical trials with depressed participants (Goodwin et al. 2022; Raison et al. 2023; von Rotz et al. 2023). These clinical trials always combine psychotherapy with psychedelics; our experiment shows that similar effects on mental health can be achieved in the absence of costly therapy. A Cohen's d of 0.9 is also comparable to the effects of cognitive behavioral therapy (Cuijpers et al. 2016), though the question remains as to whether the effects of ayahuasca are as enduring—Baranov et al. (2020) find the mental health effects of psychotherapy in Pakistan to persist seven years later, while Bhat et al. (2022) find five-year persistence of a psychotherapy intervention in India. We plan to track and re-survey our participants to allow comparison.

Experimenter demand effects. Given that our well-being measures are self-reported, one concern might be that our effects are inflated by experimenter demand—in which participants over-report their well-being when treated, and vice versa when in control, in order to help the experimenter. Such demand effects are typically small (de Quidt et al. 2018), and by having participants take surveys remotely using Qualtrics links, we minimize forces that might distort reporting, like in-person surveyor pressure (Reisinger 2022; Bursztyn et al. forthcoming). Nevertheless, we explore this concern by testing for whether the positive effects on well-being are driven by participants that give more socially desirable answers at baseline (Crowne and Marlowe 1960; Dhar et al. 2022). We do not see evidence of this (Table A6), suggesting that experimenter demand effects are unlikely to be biasing our findings. In addition, certain patterns of results seem more consistent with theorized mechanisms for the effects of psychedelics than with experimenter demand effects. For example, we might expect demand effects to also lead to positive (average) effects on flourishing, and positive effects on well-being for non-distressed participants, but we do not see this. Furthermore, in Section 5 we show additional treatment ef-

fect heterogeneity consistent with extant mechanistic theories—heterogeneity that again would not naturally be explained by demand effects. Finally, the partial masking of treatment status through the placebo-controlled design—absent in typical experiments in economics—helps to limit demand effects, even if many participants were able to determine their actual treatment status.

Adverse effects. The clinical consensus is that psychedelics are non-addictive, and generally safe (Nichols 2016), though there are concerns of rare adverse events, including hallucinogen persisting perception disorder and psychosis (Barber et al. 2022), particularly for those with a family history of mental health issues (Schlag et al. 2022). In exploring adverse effects in our setting, we note two points. First, the center uses much less conservative screening criteria than modern clinical trials, and abuse potential is higher in Brazil given that ayahuasca is legally available for people to continue to access. Our setting then permits us to explore adverse effects in a less-regulated environment than that of US-based clinical trials. Second, an important caveat is that our relatively small samples give us limited statistical power to detect rare negative effects.

We do not detect any negative side effects after six months (Table A7). The only statistically significant effect is a self-reported *reduction* in blood pressure (column 2), and we estimate a null effect on the total number of negative symptoms reported (column 12).

We also find no evidence of ayahuasca being addictive: the fraction that report having taken ayahuasca in the six months following the ceremony is only 25%, and not significantly different between those assigned ayahuasca versus jurema ($p = 0.91$, Figure A7).[15] On the other hand, there is some suggestive evidence of ayahuasca increasing other drug use, though with no p-values below 0.09 (Figure A7). We might then be concerned that ayahuasca operates as a gateway drug.

While we showed large positive effects on average well-being in Figure 2, one concern is that psychedelics may cause negative tail events, obscured by a focus on the first moment and not the second. To explore this, we plot the full distributions of pre-post changes in distress and happiness, separately for those that actually took ayahuasca and those that took the placebo (Figure A8). This figure replicates the previous finding, that the mean improvement in distress

[15]The rarity of repeat use prompts two questions. First, if the well-being effects of ayahuasca are large, why don't more treated participants keep taking it? Second, once the placebo group learn that they received the placebo, why don't more of them return to take the real thing? The first point likely reflects the fact that, while ayahuasca experiences are meaningful, they are intense and effortful, taking up a whole night, and often with challenging elements. A participant may then reasonably delay a repeat experience until they reach a point where they again feel like they need "healing." We suspect a similar motivation explains the low revisit rate of the placebo group. This group also experiences large pre-post improvements in well-being, reducing the need to return to take ayahuasca.

and happiness is statistically significant for the ayahuasca group, at all follow-up timepoints. More importantly, we see little evidence of more negative tail events (i.e. large pre-post increases in distress or decreases in happiness) in the ayahuasca group.[16]

An alternative hypothesis is that negative well-being effects are caused by particular types of trips. We explore this by considering the participants that reported having had bad or challenging trips. Participants that report having had bad trips are more likely to have had negative side effects (diarrhea, dizziness, hypersalivation), and they are more likely to have faced sadness and pain, and confused and disordered thoughts, as part of their trip experiences (left panel, Figure A9). Nevertheless, they report a higher likelihood of having had visions and insights about bad habits. The differences between challenging and non-challenging trips are somewhat similar (right panel, Figure A9), though most trip domains are more likely to be reported by those that had challenging trips.

Participants that report having had challenging ayahuasca trips experience greater mean improvements in well-being than placebo participants (Figure A10), consistent with the view of the center owners that a trip is challenging when a participant is truly working through their problems. Bad trips and the placebo deliver similar mean changes in well-being (Figure A11)—so bad trips are ineffective, but not harmful. In addition, we do not see a greater prevalence of negative tail events following bad or challenging trips relative to the placebo. This null finding is strengthened by the fact that the 6-week follow-up response rate for those that had bad or challenging trips is 100%—our findings are then not masking participants that reported having difficult trips and later stopped responding.

5 Mechanisms

5.1 Reopening critical periods

A key mechanistic hypothesis for the enduring therapeutic effects of psychedelics is that such drugs re-open "critical periods": finite windows of time in which our brains are especially impressionable, and open to learning (Hensch 2005; Nardou et al. 2019; Lepow et al. 2021). The most prominent evidence for this channel comes from Nardou et al. (2023), published in *Nature* (for an accessible summary, see Nuwer (2023)). That paper shows that young mice are more impressionable than old mice when it comes to "social reward learning": when exploring

[16]The one exception is a treated participant that experienced an increase of 18 points on the Kessler-10 scale between baseline and the 3-day follow-up—a larger increase than any other participant. Encouragingly, this was a transitory increase: this participant's Kessler-10 score fell by nine points by the 6-week follow-up, and fully returned to the baseline score by the 6-month follow-up.

a cage with two sections, young mice prefer to spend time in the section where they previously spent time with other mice. Old mice are indifferent between the two sections. When given psychedelics—including ketamine, psilocybin, LSD, and igobaine—the old mice start acting like the young mice. Or as summarized in the title of the paper: psychedelics reopen the social reward learning critical period.

These results suggest that the enduring effects of psychedelics in humans may be due to the reopening of a critical period, and the subsequent learning that a participant experiences while in an impressionable state—a state that lasts far beyond the psychedelic trip. This mechanism has a simple testable implication: we should expect effects to be larger for older participants than for younger participants. This implication contrasts with a common intuition in the social sciences, that attitude-shaping interventions should be more effective on the young, as the young remain in their "impressionable years" (Krosnick and Alwin 1989; Malmendier 2021; Ghitza et al. 2023; Giuliano and Spilimbergo 2023). If the core mechanism for the effects of psychedelics is that of *making* participants impressionable, we have the polar opposite prediction: psychedelics should work better for those that are the least impressionable ex ante.

To maximize power to detect age heterogeneity, we split our sample at the median age of 32, giving us 127 participants at or below median age (aged 18 to 32, roughly the "impressionable years"), and 124 participants above median age (aged 33 to 66). At baseline, these old and young participants have similar levels of distress, happiness, and flourishing (Figure 3), meaning that any heterogeneous treatment effects by age are not merely reflecting the heterogeneous effects by baseline well-being emphasized in Figures 2B and 2C.

Ayahuasca has little effect on the well-being of below-median age participants (Figure 3A). The only statistically significant effect is in the opposite direction: a negative effect on flourishing at the 6-month endpoint ($p = 0.07$). In contrast, the effects for above-median age participants are positive and enduring on all three outcomes (Figure 3B), including the flourishing scale, for which we do not see effects on average (the average null reflects offsetting coefficients for the young and the old). Pooling all the post-periods, we can reject the null that the effects on happiness and flourishing for the young and old are equal ($p = 0.03$ and $p < 0.01$), though we cannot reject that null for distress ($p = 0.50$). The non-rejection reflects our limited power, since the point estimates are meaningfully larger for older participants (e.g. 0.54σ versus 0.17σ for the 6-month IV effect size).

The age heterogeneity we find for psychedelics contrasts with meta-analytic evidence for psychotherapy. Cuijpers et al. (2020) meta-analyze randomized trials comparing psychotherapy for depression with control conditions, finding a mean standardized effect size of 0.98 (95% CI: 0.79-1.16) for adults aged 18 to 24, 0.77 (95% CI: 0.67-0.87) for adults aged 24 to 55, and

0.66 (95% CI: 0.51-0.82) for adults aged 55 to 75. For adults, the effects of psychotherapy fall in age, while those of ayahuasca increase in age, consistent with a critical period re-opening mechanism.

5.2 Subjective experience

A second hypothesized mechanism is that of subjective experience: participants that ingest psychedelics frequently experience deeply intense trips, attributing to them great meaning, and leaving with insights that they then apply in their lives. These subjective experiences may then be necessary for therapeutic benefits (Yaden and Griffiths 2020). However, this point is debated, with mixed evidence in the clinical literature (Olson 2020; Yaden et al. 2024). Resolving this question is of importance to the pharmaceutical industry, given the interest of some companies in developing drugs that work without trips (Whelan 2023; Drug Discovery & Development 2022; Jarow 2023); it is also important for determining the disciplines required for the study of psychedelics. To the extent that subjective experience drives effects, more social science research is needed on the meaning-making and behavioral change that follows meaningful experiences.

We explore this question by correlating participants' reports of mystical experiences with well-being changes from baseline to follow-up, following and improving on the approaches of Griffiths et al. (2016) and Ross et al. (2016). We measure mystical experience using the 0 to 35 mystical experience score, reflecting a participant's experience of loss of sense of time, ineffability, gain of insightful knowledge, etc. While the mystical-ness of experiences was not randomly assigned, the intensity of the mystical experience reported is not statistically significantly correlated with baseline distress, happiness, or flourishing (first column, Figure 4). Nevertheless, when correlating mystical experience with well-being changes, we control for the baseline measure of the well-being outcome.[17] We estimate the following regression, keeping only participants that actually received ayahuasca, which this time includes participants across all six experimental sessions:

$$\Delta y_{it} = \psi_s + \phi_0 y_{i0} + \phi_1 \text{ Mystical Experience Score}_i + u_{it} \tag{2}$$

where Δy_{it} is the change in the well-being measure from baseline to follow-up survey t, ψ_s are session-by-gender fixed effects, and y_{i0} is the well-being measure at baseline. The key regressor is Mystical Experience Score$_i$ (0 to 35). We estimate robust standard errors.[18]

[17] In doing so, we also shut down the baseline-distress channel for heterogeneous effects, emphasized in Section 4.2.

[18] Note that this approach follows the logic of a difference-in-differences design—in that we test for whether the

In each panel of Figure 4 we report the slope (i.e. $\hat{\phi}_1$), and a p-value that tests the null hypothesis that the slope is equal to zero. We also show the binscatter based on the same specification (i.e. still controlling for strata fixed effects and the baseline-measured well-being outcome), with seven bins throughout. In the first column of Figure 4, the left-hand-side variable is instead the baseline measure, y_{i0}, and accordingly, these regressions do not include the baseline measure as a control variable.

More mystical experiences are associated with greater improvements in well-being. At the 3-day follow-up, more mystical experiences predict a larger reduction in distress ($p < 0.01$), a larger increase in happiness ($p < 0.0001$), and even a larger increase in flourishing ($p < 0.001$)—suggesting that our overall null effect on flourishing masks positive effects for those with the most intense subjective experiences (second column, Figure 4). These correlations are similar at the 6-week and 6-month follow-ups (third and fourth columns), although they attenuate over time, and two of three are no longer statistically significant after six months (with $p = 0.15, 0.09$, and 0.21).[19] These findings of strong associations between well-being improvements and acute subjective experiences are similar if we use alternative measures of subjective experience, although the correlations at the 6-month point become even less robust (Table A8). These patterns are not just picking up the age heterogeneity mentioned above—the below- and above-median-aged ayahuasca-takers have similar mystical experience scores ($p = 0.96$ for the difference, using the specification with strata fixed effects).

Our evidence here corroborates the hypothesis that subjective experience is a key channel for the effects of psychedelics. But we can also consider a more general hypothesis: could it be that these mystical and meaningful experiences per se lead to improvements in well-being, regardless of whether they are psychedelic? This question is motivated by a psychological literature on "quantum change," going back to William James' *Varieties of Religious Experience* (James 1902), which claims that mystical and insightful experiences can cause personal transformation, regardless of their source (Miller and C'de Baca 2001; Miller 2004; Griffiths et al. 2018). Under this worldview, the power of psychedelics is that they reliably create mystical experiences; but such experiences need not be psychedelic to be effective.

We explore this hypothesis using the participants that attended the ceremony and took the placebo. As expected, placebo-takers score much lower than ayahuasca-takers on the mystical experience questionnaire, with a large mass at zero (Figure A2). But there is still variation,

change in well-being from baseline to follow-up is larger for those with higher versus lower mystical experience scores, though while also controlling for baseline well-being. The effects can then be interpreted as causal given the usual parallel trends assumption.

[19] Taken literally, this pattern may imply that subjective experiences are a stronger mediating channel for short-run than for long-run effects, with alternative channels, like the re-opening of critical periods, mediating the latter.

with some placebo-takers reporting having had mystical experiences, despite not experiencing psychedelic trips. A natural interpretation of these experiences is that some placebo-takers meditated and introspected during the ceremony, leading to a similar "loss of your usual sense of time," and "gain of insightful knowledge." Consistent with this, placebo-takers that reported at baseline that they practice meditation report 0.38σ higher mystical experience scores than those that did not ($p = 0.08$).

To explore the role of mystical experiences in the placebo group, we replicate Figure 4, but keeping only the placebo-taking participants. Among these participants, baseline well-being again tends to be orthogonal to the mystical experience score, with the exception of a marginally significant positive relationship with baseline distress ($p = 0.06$, first column, Figure 5). Controlling for baseline well-being, mystical experience scores again consistently predict well-being improvements, at each endline timepoint (columns two to four, Figure 5). Remarkably, the slopes are very similar to those in Figure 4, suggesting that mystical experiences provide a unifying explanation for the well-being effects of both psychedelics and non-psychedelic rituals.

5.3 Placebo effects

If response to treatment depends positively on a participant's expectation, we say that that the treatment has placebo effects (Malani 2006). Clinical trials often shut down this channel by using placebo-controlled designs, which fix beliefs about perceived treatment status across treatment arms. Such blinding does not work well in psychedelic trials, and as a result, scholars debate the role of placebo effects, with mixed evidence (Carhart-Harris et al. 2018; Szigeti et al. 2024).

To shed light on perceived treatment status in our setting, in the 3-day follow-up we asked participants to guess which treatment they had actually received. We asked whether they thought they had received a "regular" ayahuasca dose, referring to treatment, or a "less concentrated" ayahuasca dose. The latter option was an unintentional miswording on our part—the intended option was "jurema" (see full details in Appendix C). Since all participants had already been informed that the placebo for the experiment was jurema, which was explained as a medicine with DMT but no psychedelic effects, it would seem likely that they interpreted "less concentrated" as referring to the placebo. Noting this limitation, we proceed under the interpretation that those who answered "regular" dose are more likely to believe they received ayahuasca than those who answered "less concentrated" dose. Using these answers, we see a clear indication of functional unblinding: 75% of those that received ayahuasca guess that they were given the regular concentration, compared with only 9% of those that received the placebo. This unblinding

opens the possibility of placebo effects contributing to our positive effects on well-being.

We use three suggestive approaches to explore the possibility of placebo effects. First, we run specifications 1 and 2 defined above, adding an extra control variable: a dummy variable equal to one if the participant guessed that their actual treatment was regular concentration ayahuasca. The effects of ayahuasca relative to placebo, and the effects of more versus less mystical trips are similar after adding this control (Figures A12 and A13), though the estimates are less precise in the former case. The results of this first approach speak against a large role for placebo effects.

The second approach takes advantage of the fact that we reveal each participant's actual treatment status at the end of the 6-week follow-up survey (with the correct wording). For the sake of this exercise, we assume that participants that guessed they received the low-concentration ayahuasca actually believed that they received the placebo, jurema—i.e. we assume that they remembered what the true treatment options were. For some participants, the revelation of the actual treatment received at the 6-week point is a shock to their beliefs—some thought previously that they were treated, but now learn that they were not, and vice versa. For other participants there is no shock to their beliefs—their guess is revealed to have been correct. These two types of participants allow us to run a variant of a difference-in-differences specification—effectively comparing whether participants that learn that they were actually treated (control) have larger (smaller) improvements in well-being from the second to the third follow-up survey than those that were correct about their treatment all along. The specification is:

$$y_{it} = \alpha_i + \alpha_{st} + \gamma \,\text{Believe Took Ayahuasca}_{it} + e_{it}, \tag{3}$$

where we keep only participants that attended their assigned ceremony, and only their answers to the 6-week and 6-month follow-up surveys. y_{it} is as defined above, while α_i are participant fixed effects, and α_{st} are randomization strata fully interacted with indicators for each follow-up survey. Believe Took Ayahuasca$_{it}$ is a dummy variable equal to one if participant i believes at the start of follow-up survey t that they were given ayahuasca during the ceremony they attended. For $t =$ 6-week this belief is based on the participant's guess during the 3-day follow-up survey, while for $t =$ 6-month the belief is set to the truth, given that treatment status is revealed at the end of the 6-week follow-up survey. As a test for parallel pre-trends, we run the same specification, but keeping only survey answers to the 3-day and 6-week follow-up surveys, and replacing the key regressor with Believe Took Ayahuasca$_{i,t+1}$. This tests for whether participants that would later learn that they were treated (control) were already trending towards improved (worsened) well-being than participants that would learn that they guessed correctly.

Using this approach, we see some suggestive evidence that participants who learn at the 6-week follow-up that they received ayahuasca have greater improvements in well-being six months later than those who learned that they did not (columns 1 to 3, Table A9, though only one of three effects is statistically significant, with $p = 0.08$), and these effects are not driven by pre-existing trends (columns 4 to 6).

Our third approach is to estimate heterogeneous treatment effects of ayahuasca by baseline-reported expectancy—the 1 to 10 answer given to "At this moment, how much do you expect your experience with ayahuasca... to be useful in improving your well-being?" Expectancy is not predictive of treatment effects (Table A10).

In summary, we see only weak evidence that placebo effects contribute to the positive effects on well-being.

6 Ritual effects and cost-benefit analysis

Having unpacked the effects of ayahuasca relative to the placebo, we now make use of the follow-up data for no-shows—those participants that did not attend their assigned ceremony. With this data, we can shed light on the well-being effects of the ceremony (and placebo), in the absence of the psychedelic.

6.1 Ritual effects

Here we take a difference-in-differences approach: we test for whether the *improvement* in well-being from baseline to each follow-up is larger for those that attended the ceremony than for those that did not attend. Our core difference-in-differences specification is:

$$y_{it} = \alpha_i + \alpha_{st} + \theta_1(\text{Attended}_i \times \text{3-day Follow-up}_t) + \theta_2(\text{Attended}_i \times \text{6-week Follow-up}_t) + \theta_3(\text{Attended}_i \times \text{6-month Follow-up}_t) + e_{it}, \quad (4)$$

where there are now up to four observations per participant (for t = baseline, 3-day, 6-week, and 6-month), and y_{it} is defined above. α_i are participant fixed effects, while α_{st} are randomization strata fully interacted with follow-up survey fixed effects. Attended_i is equal to one if participant i attended their assigned ceremony, and equal to zero otherwise (i.e. for no-shows). 3-day Follow-up_t is equal to one if $t = 3$ days, and similarly for 6-week and 6-month. For the happiness outcome, we run a specification that also includes an interaction between Attended_i

and Retrospective Report at Baseline$_t$, where the latter is a dummy variable equal to one for a participant's retrospective report of happiness over the past month, answered in the baseline survey. This is what permits a suggestive test of parallel pre-trends (unfortunately we lack pre-baseline data). We keep only the participants that completed the baseline and answered at least one follow-up survey, and we cluster standard errors at the participant-level.

In Figure 6 we plot the point estimates and 95% confidence intervals for θ_1, θ_2, and θ_3. These are our difference-in-differences-estimated effects of attending the ceremony on well-being at each timepoint. To get at the effects of attending and taking the placebo, we run the regression keeping only those that didn't attend or attended and took the placebo. To get at the full effects of attending the ceremony and taking ayahuasca, we keep only those that didn't attend or attended and took ayahuasca.

Encouragingly, we do not find evidence for differential pre-trends using the retrospective happiness question (central column, Figure 6). We have shown that no-shows differ from placebo-takers in levels at baseline—they are less educated, less likely to be employed, less happy, and more distressed (column 9, Table A2). But given mean reversion, their lower well-being at baseline actually biases us away from finding positive effects of the ceremony (indeed, we show below that our results become stronger after allowing for trends to depend on baseline well-being). This all said, participants that decide to go to an ayahuasca ceremony may be those that would attempt to improve their mental health even in the absence of the ceremony, causing the parallel trends assumption to fail. The following results come with this caveat.

We find suggestive evidence of positive well-being effects of attending the ceremony and taking the placebo (Figure 6A). This finding reduces the likelihood that our positive ITT effects of ayahuasca are due to disappointment lowering well-being in the placebo group. It also suggests that the ritual bundle itself—including a social gathering, a self-improvement lecture, the ingestion of jurema, and several hours of meditation and introspection—might deliver improvements in well-being. Notably, the ritual bundle improves average flourishing more than the psychedelic, suggesting complementary mechanisms of action of the ritual and the drug. As for the overall effect of the ceremony, including taking the psychedelic, we find large positive and enduring effects on all three measures of well-being, though the effect on flourishing is statistically insignificant at the 6-month point (Figure 6B).

Given the baseline differences in well-being between no-shows and placebo-takers, we also re-estimate our difference-in-differences regressions after adding interaction terms between baseline well-being and each of the follow-up survey indicators. When we do so, the effects of ceremony attendance are somewhat more positive, reflecting the mean reversion that leads low-well-being types to tend to improve following the baseline (Figure A14). The mean reversion

can be seen directly in Figure A15, where we plot the well-being levels for both the placebo-takers and the no-shows—all three well-being outcomes improve from baseline to follow-up even for the no-shows.

6.2 Cost-benefit analysis

We carry out two cost-benefit analyses: the first comparing the distress-reduction benefits of attending a ceremony and taking ayahuasca (relative to not attending) with the per-person price of the ceremony set by the center (24 USD). The second compares the distress-reduction benefits of receiving ayahuasca (relative to the placebo) with the per-person procurement cost of the ayahuasca itself.

Ceremony versus no-show. To estimate the benefits, we use the three difference-in-differences coefficients in the far-left panel of Figure 6B, and calculate the area between the grey dashed line at zero and the blue dashed line. This area gives the number of distressed years averted due to the ceremony under the assumptions that (i) the difference-in-differences estimates are unbiased estimates of causal effects, (ii) after six months there is no treatment effect of the ceremony (a conservative assumption), and (iii) treatment effects grow or fall linearly in between each of the four timepoints (baseline, 3-day, 6-week, 6-month).

Using equation 4 above, we estimate the number of distressed years averted X to be:

$$X = ((3/365) \times \hat{\theta}_1 \times 0.5) + ((42-3)/365) \times (\hat{\theta}_1 + \hat{\theta}_2) \times 0.5) + ((182.5 - 42/365) \times (\hat{\theta}_2 + \hat{\theta}_3) \times 0.5)$$

which is the sum of the area of one triangle (capturing the effects in the first three days) and two trapezoids. We find that $X = 0.12$ distressed years.

In the next step, we have to value the number of distressed years averted in dollars. We first convert a single distressed year averted to its disability-adjusted life year (DALY) equivalent, by applying the disability weight of 0.396 used by the Global Burden of Disease 2021 for moderate major depressive disorder.[20] Here we are taking moderate or severe distress according to the Kessler-10 scale (a score of 15 or above) to be approximately equivalent to a moderate major depressive disorder (the Global Burden of Disease does not have a disability weight for psychological distress itself). Finally, we value a DALY at 100,000 USD, following Open Philanthropy.[21] The benefits then amount to $0.396 \times 100,000 \times 12 = 4,608$ USD, or 192 times

[20] See https://ghdx.healthdata.org/record/ihme-data/gbd-2021-disability-weights.

[21] See https://www.openphilanthropy.org/research/technical-updates-to-our-global-health-and-wellbeing-

the 24 USD price of a ceremony.[22] Allowing for differential trends by baseline well-being, as in Figure A14, increases the benefits by roughly one-third.

Ayahuasca versus placebo. Our approach to valuing the distress-reduction benefits of ayahuasca relative to placebo follows similar steps. The key difference is that we use IV estimates of the causal effects of ayahuasca to estimate the number of years of distress averted, as opposed to difference-in-differences estimates.[23] These estimates of the benefits are then more credible, given that they do not rely on a parallel trends assumption.

To calculate the cost of the average participant's ayahuasca, we use the fact that the ayahuasca costs the center 400 BRL/liter, and the average dose in our experimental sample is 78.2 ml. The cost per person is then 31.3 BRL, or 5.59 USD. If we apply the same logic for the effects of ayahuasca relative to placebo (Figure 2), we estimate the benefits of ayahuasca to be 2,703 USD, or 484 times the 5.59 USD cost of the average ayahuasca dose.

7 Conclusion

Tens, and perhaps hundreds, of millions of people have ingested psychedelic substances and experienced their hallucinogenic effects (Krebs and Johansen 2013). Psychedelics are available legally in the Bahamas, Bolivia, Brazil, Jamaica, the Netherlands, Peru, and Uruguay, while there is a move toward deregulation in many other polities (Psychedelic Alpha 2024). Our findings give some initial evidence that the positive findings of tightly-controlled clinical trials generalize to the more naturalistic use of psychedelics, without accompanying psychotherapy, in the context of group ayahuasca ceremonies in Brazil. Furthermore, we show additional benefits of the ritual per se, in the absence of the psychedelic.

Our findings pose questions for future research, including some that are the focus of our ongoing partnership with the center in Brazil. First, beyond mental health benefits, do psychedelic rituals lead to changes in economic behaviors? While mental health treatment in low- and middle-income countries tends to increase labor market activity (Lund et al. 2024), we might instead predict that psychedelics lead to a shift away from economic priorities, toward relational goals, consistent with the famous counterculture-era call to "turn on, tune in, drop out." Alternatively, we might predict increases in bold major life decisions in general, including job

[22] We verified that our approach to valuation closely follows that of Open Philanthropy through personal correspondence with an Open Philanthropy research fellow on the Global Health and Well-Being cause prioritization team.

[23] Specifically, we use the IV version of equation 1, in which we use Assigned Ayahuasca as an instrumental variable for Took Ayahuasca.

transitions and relationship changes (Levitt 2021). Second, beyond six months, how long do the mental health benefits persist, and is persistence mediated by repeat participation in ayahuasca ceremonies? Third, how do the shared experiences of group ceremonies affect social outcomes, like group cohesion and ingroup bias (Depetris-Chauvin et al. 2020)? Work on these questions will reveal whether these profound experiences also lead to profound behavioral change.

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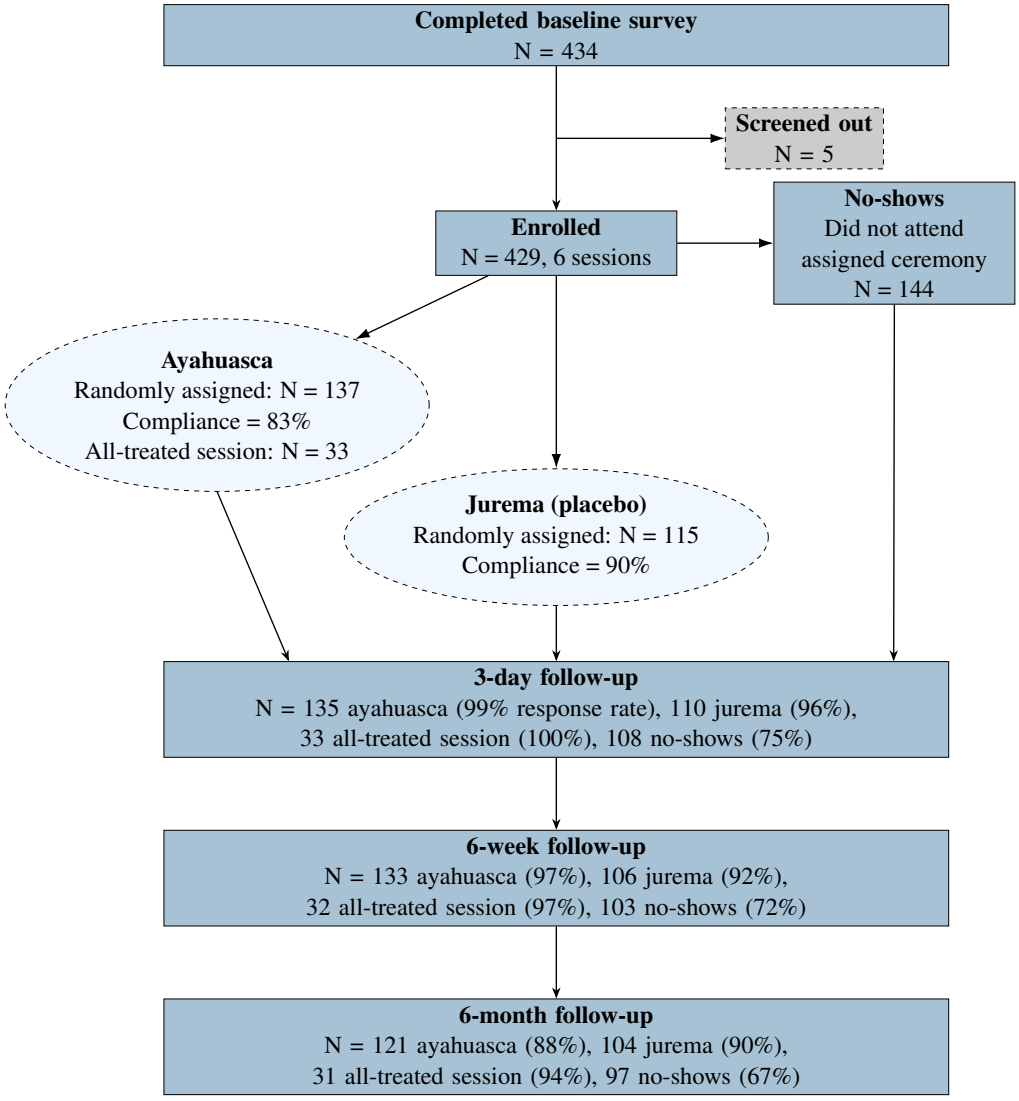
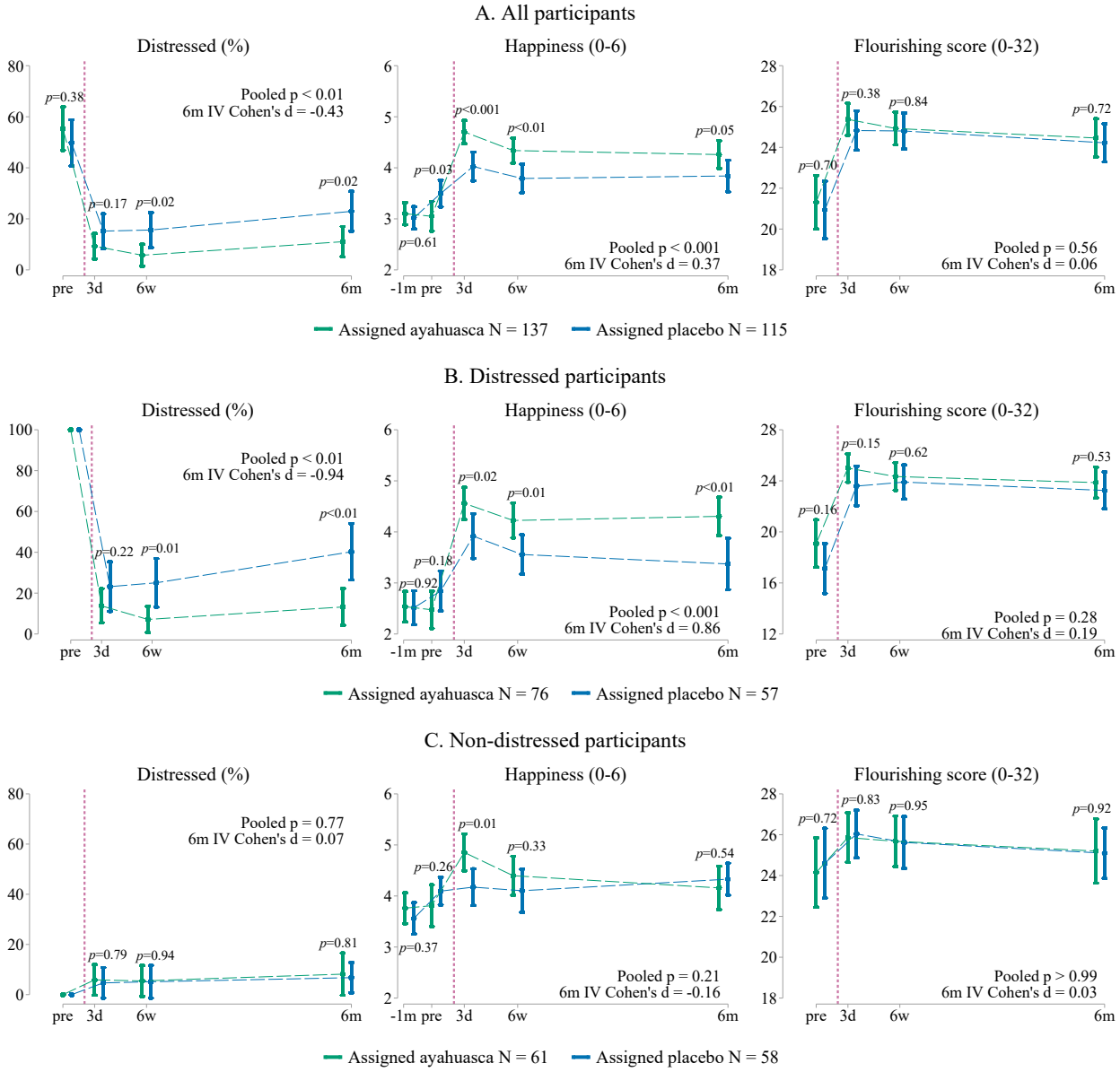
Figure 1: Enrollment, randomization, and follow-up details



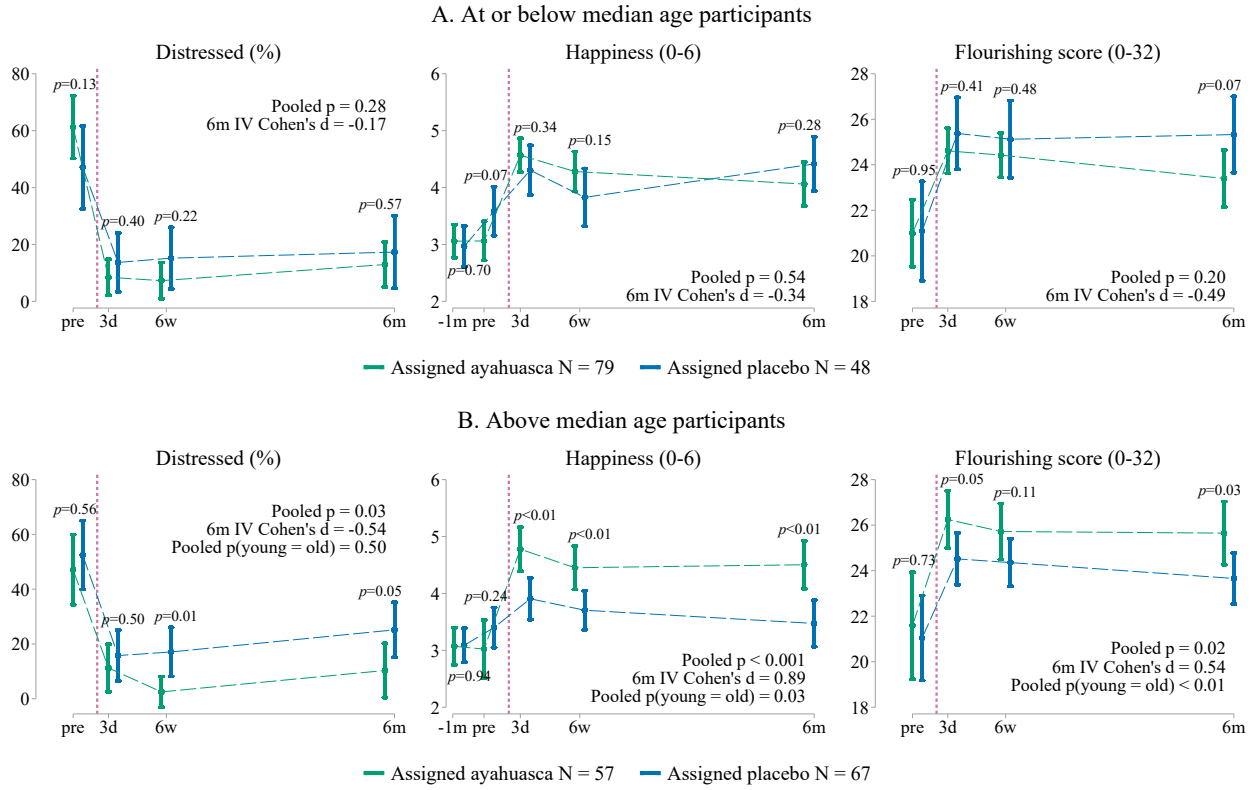
Note: The center screened out five participants with higher risks of psychosis identified through their personal and family medical history reported in the baseline survey. The center performed the randomization into ayahuasca or jurema before each session. *Compliance* refers to the percentage of participants who were actually given their randomly assigned treatment. In the last of the six sessions (All-treated session), by mistake, all 33 participants were given ayahuasca. Response rates to each follow-up survey are reported separately for four groups: those randomly assigned ayahuasca or jurema for the first five sessions, those in the all-treated session, and participants that did not attend their assigned session.

Figure 2: Ayahuasca durably improves well-being relative to placebo



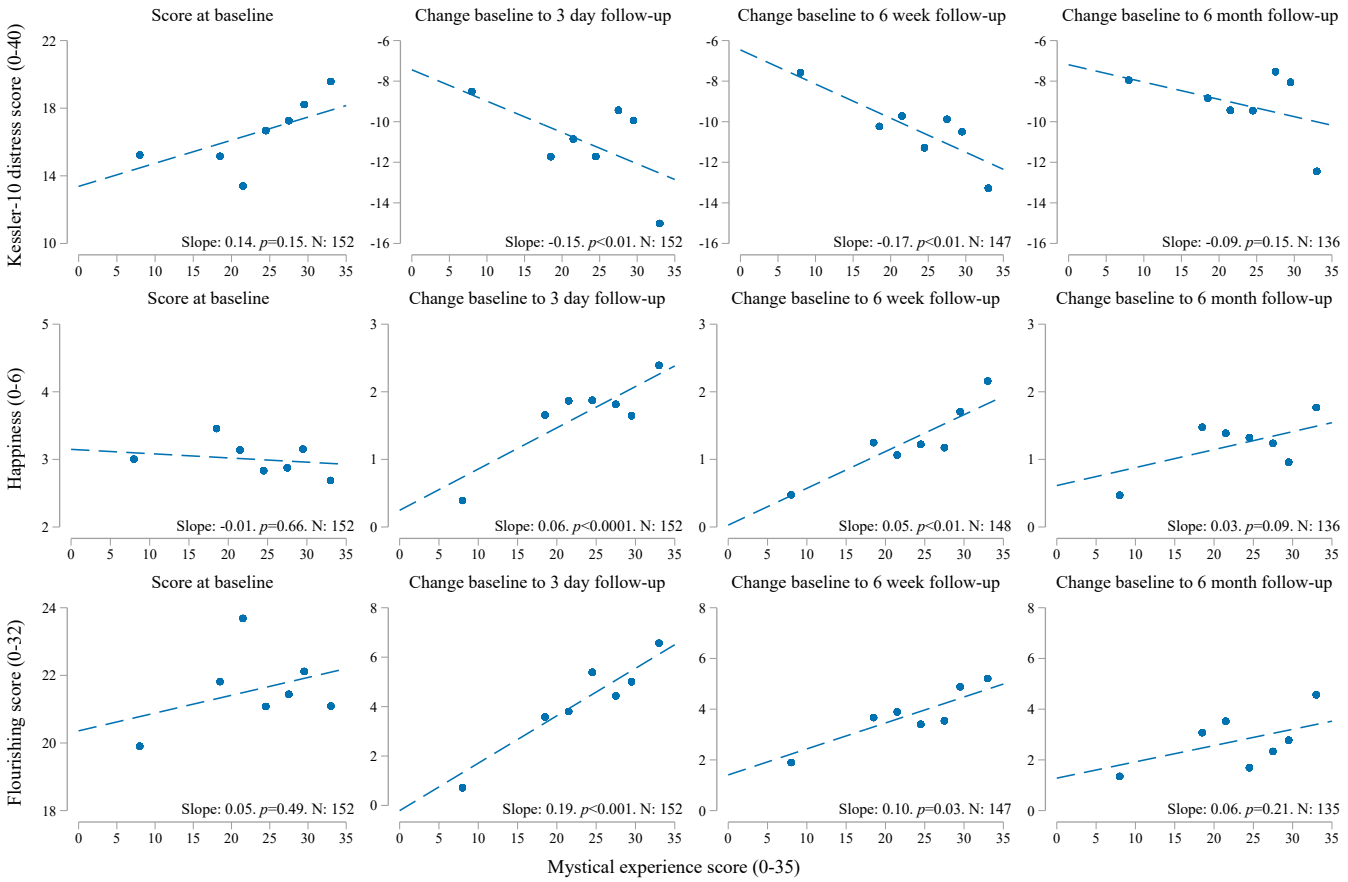
Note: Figure shows intent to treat effects. Baseline measures are denoted by pre, -1m denotes a retrospective measure for the past month. Distressed (%) is the percentage of participants that score 15 or above on the Kessler-10 Psychological Distress Scale. Happiness is the answer to *In general, how happy would you say you are these days?* on a scale from *Not very happy (0)* to *Very happy (6)*. Flourishing is the score from 0 to 32 from summing answers to eight statements like *I lead a purposeful and meaningful life (0 = Strongly disagree to 4 = Strongly agree)*. 95% confidence intervals are shown. *p*-values are from a regression that controls for the outcome at baseline (except for the baseline and retrospective comparisons) and session-by-gender fixed effects, with robust standard errors. The pooled *p*-value is obtained from a regression pooling data from the three follow-up surveys. 6m IV Cohen's *d* is the standardized effect of ayahuasca at six months, when using treatment assigned as an instrumental variable for treatment received. (**A**) presents results for the full sample of participants who attended one of the first five sessions (i.e. excluding those that attended the all-treated session), (**B**) restricts to distressed participants at baseline, while (**C**) restricts to non-distressed participants.

Figure 3: Well-being effects are larger for older participants, consistent with psychedelics re-opening critical periods



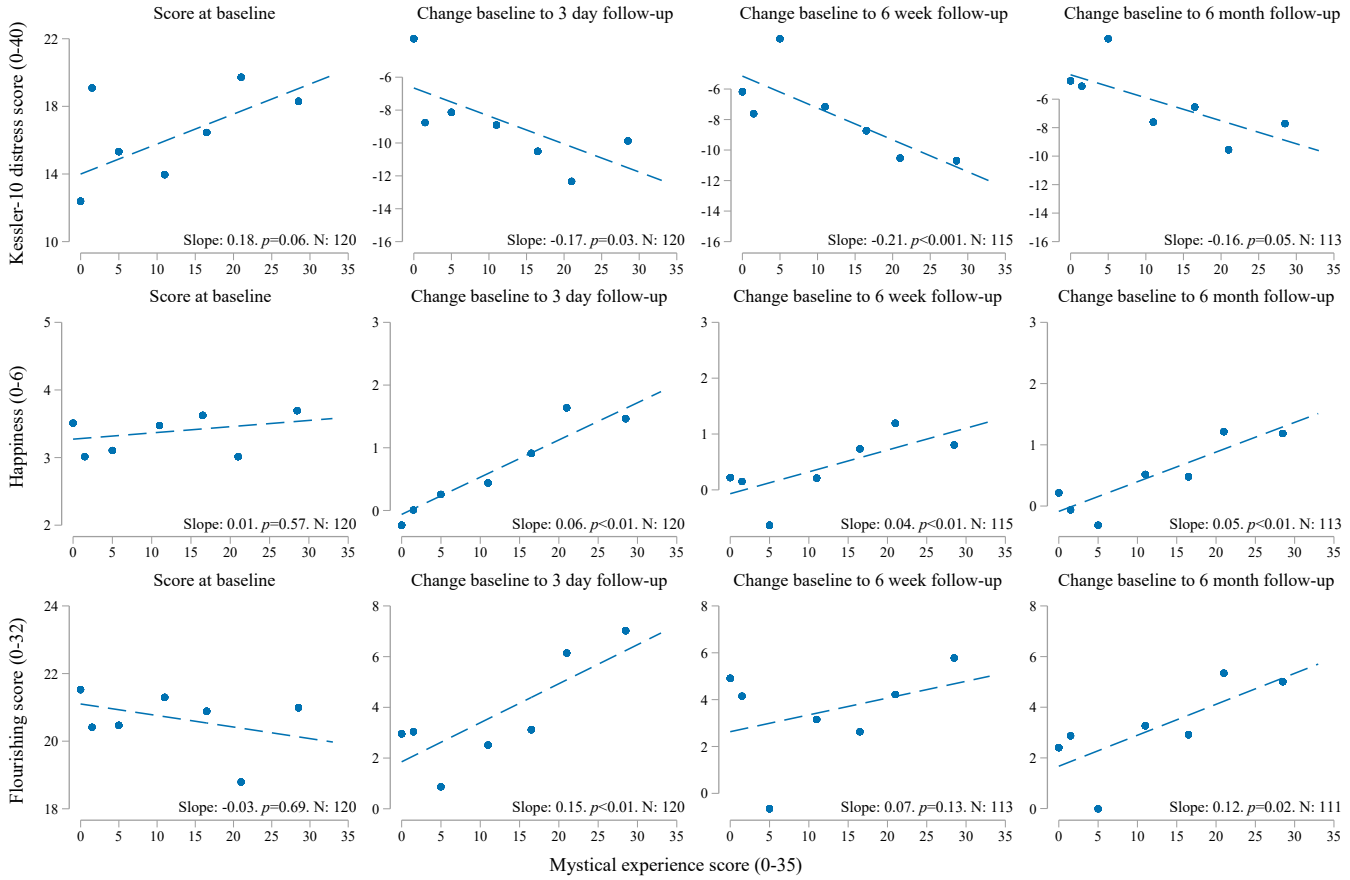
Note: This figure parallels Figure 2, but shows effects separately for above-median ($N = 124$) versus at-or-below-median age ($N = 127$) participants. One participant is excluded due to having missing age data at baseline.

Figure 4: More mystical trips predict greater improvements in well-being



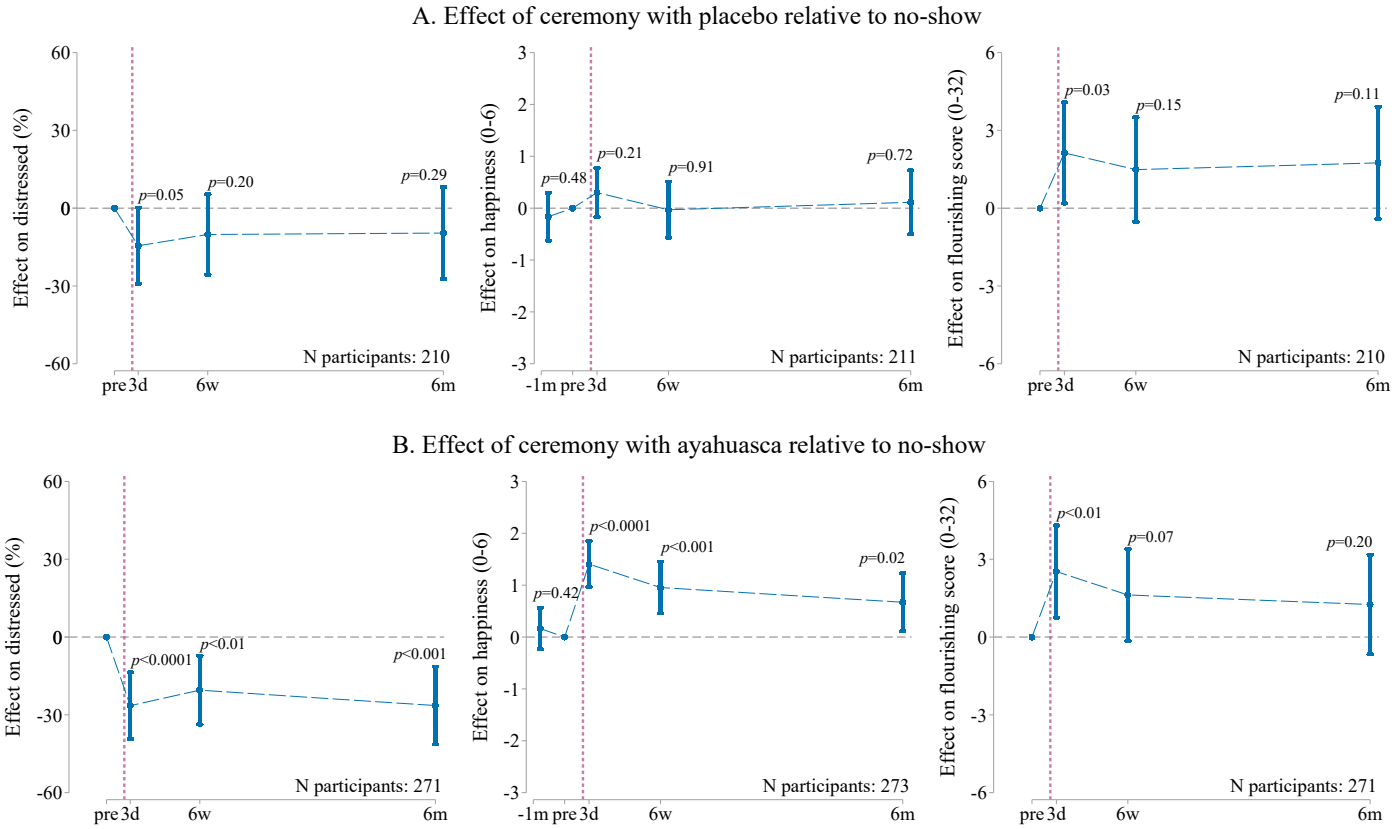
Note: Each panel shows a binscatter plot correlating the mystical experience score (measured at the 3-day follow-up) of participants that took ayahuasca with baseline measures of well-being (first column), and changes in well-being from baseline to each of the follow-up surveys (second to fourth columns). We use the raw Kessler-10 score rather than the indicator for a score of 15 or above to avoid floor effects (very few ayahuasca-takers are above this cutoff at the 3-day follow-up). Each panel controls for session-by-gender fixed effects, and with the exception of the first column, the well-being outcome measured at baseline. Standard errors are robust.

Figure 5: More mystical experiences in the placebo group also predict greater improvements in well-being



Note: The figure parallels Figure 4, but this time including only the participants that attended the ceremony and took the placebo, jurema.

Figure 6: Ceremonies durably improve well-being when combined with ayahuasca



Note: Figure shows difference-in-differences effects of (**A**) attending the ceremony and taking the placebo relative to no-shows, and (**B**) attending the ceremony and taking ayahuasca relative to no-shows. As an example, the first coefficient in the top-left panel shows that the fall in percentage distressed from baseline to the 3-day follow-up was almost 15 percentage points larger among those that attended and took the placebo than among those that did not attend the ceremony. 95% confidence intervals are shown, with standard errors clustered at participant-level.

Table 1: Ayahuasca causes more meaningful experiences than the placebo

	Meaningful score (1)	Mystical experience (2)	Ego dissolution (3)	Word count (4)	N trip domains (5)	Had visions (6)
Received ayahuasca	2.36***	11.81***	51.37***	37.50**	3.14***	0.53***
	(0.36)	(1.58)	(10.85)	(14.94)	(0.46)	(0.07)
Placebo group outcome mean	3.4	12.0	245.4	63.6	3.5	0.1
Placebo group outcome SD	2.5	9.8	58.0	66.8	2.4	0.3
Observations	241	240	240	240	241	241
Session-by-gender fixed effects	Yes	Yes	Yes	Yes	Yes	Yes

Notes: Table shows regression results from an IV specification, where treatment assigned serves as an instrument for actual treatment received. Sample includes participants that attended their assigned session, but excludes the session in which all participants were erroneously given ayahuasca. Placebo group refers to the participants that received the placebo. All outcomes are measured in the three-day follow-up survey. Meaningful score corresponds to the question *How personally meaningful was the experience?* on a scale from 0 to 7. Mystical experience corresponds to the 0-35 score on the mystical experience questionnaire, where participants rate seven items on a scale from 0 to 5 according to the degree to which they experience phenomena like *Sense of awe or awesomeness*. Ego dissolution corresponds to the 0-500 score after summing responses on a scale from 0 to 100 to five statements such as *I felt a sense of union with others*. Word count is the total number of words in the participant's open response to the question *Describe in detail your experience with the Ayahuasca in the box below. Please be specific about what you saw, heard, and felt.* N Trip Domains is the total number of domains, such as *Revived old memories* and *Love or Peace*, that the participant "tripped on." Had visions indicates whether the participant reported having visions during the ceremony. For further detail on outcome variable definitions, see Appendix C. The first stage coefficient is 0.73 (i.e. being randomly assigned ayahuasca increases the probability of actually receiving ayahuasca by 73 percentage points). *** p<0.01, ** p<0.05, * p<0.1.

Table 2: Ayahuasca causes more immediate adverse experiences than the placebo

	Vomit (1)	Diarrhea (2)	Dizziness (3)	Bad (4)	Challenging (5)	Hyper-salivation (6)	Other (7)	N neg effects (8)
Received ayahuasca	0.62***	0.11**	0.27***	0.10**	0.19***	0.04	0.02	1.35***
	(0.06)	(0.05)	(0.07)	(0.05)	(0.06)	(0.04)	(0.07)	(0.18)
Placebo group outcome mean	0.05	0.04	0.09	0.03	0.05	0.05	0.21	0.52
Placebo group outcome SD	0.22	0.20	0.29	0.16	0.22	0.22	0.41	0.77
Observations	240	240	240	240	240	240	240	240
Session-by-gender fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Notes: Table shows regression results from an IV specification, where treatment assigned serves as an instrument for actual treatment received. Sample includes participants that attended their assigned session, but excludes the session in which all participants were erroneously given ayahuasca. Placebo group refers to the participants that received the placebo. All outcomes are measured in the three-day follow-up survey. Outcomes in columns (1)-(7) correspond to checkboxes selected for the question *We know that some people can have negative effects during an ayahuasca session. Did any of the following happen during your trip? Please select all that apply.* N neg effects is the sum of negative effects selected, from 0 to 7. For further detail on outcome variable definitions, see Appendix C. The first stage coefficient is 0.73 (i.e. being randomly assigned ayahuasca increases the probability of actually receiving ayahuasca by 73 percentage points). *** p<0.01, ** p<0.05, * p<0.1.

Online Appendix

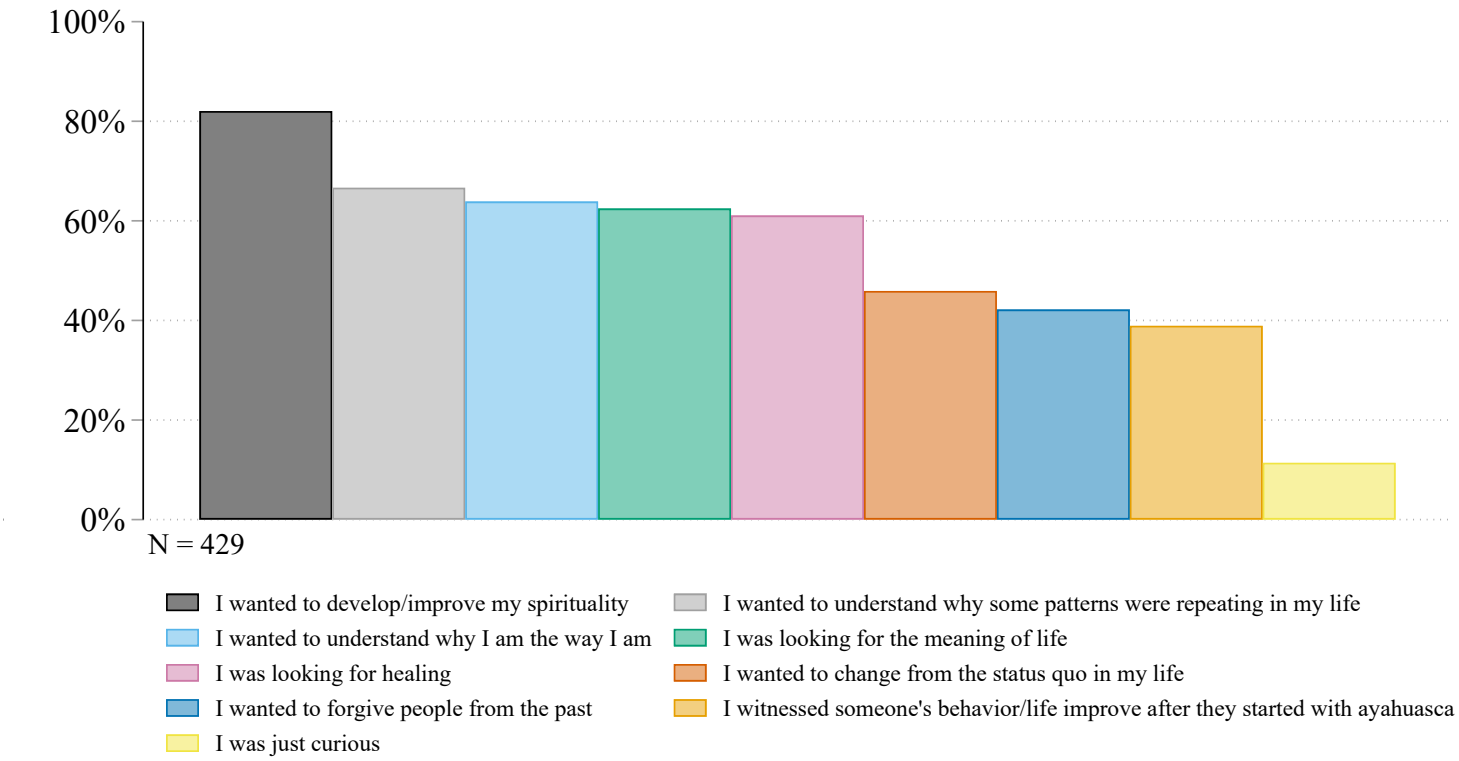
"Psychedelics, Rituals, and Well-Being: An Experiment in Brazil"

Patrick Francois*
Matt Lowe*
Ieda Matavelli+

**University of British Columbia*
+*University of New South Wales*

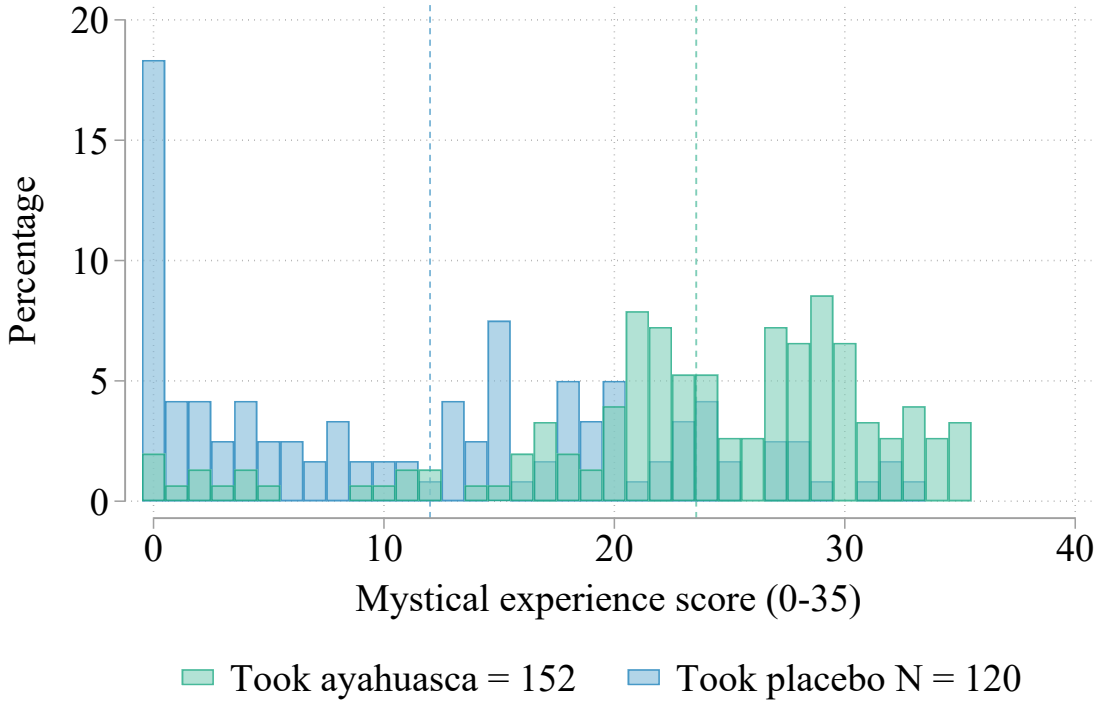
A Appendix figures

Figure A1: Reasons for trying ayahuasca



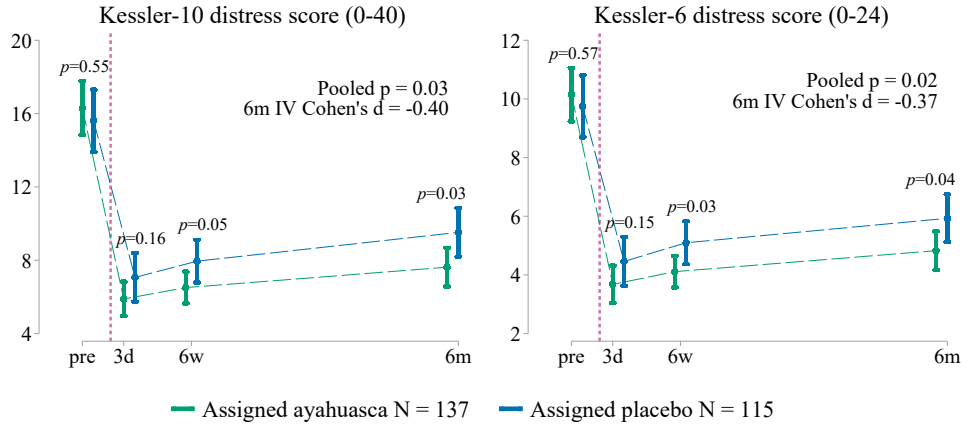
Note: The figure plots the percentage of participants that selected each reason in response to the baseline question: *What reason(s) best describes why you want or wanted to try ayahuasca in the first place? Select all options that apply.* The option to select *Other* was also available. Participants could select more than one reason.

Figure A2: Mystical experience scores by treatment group



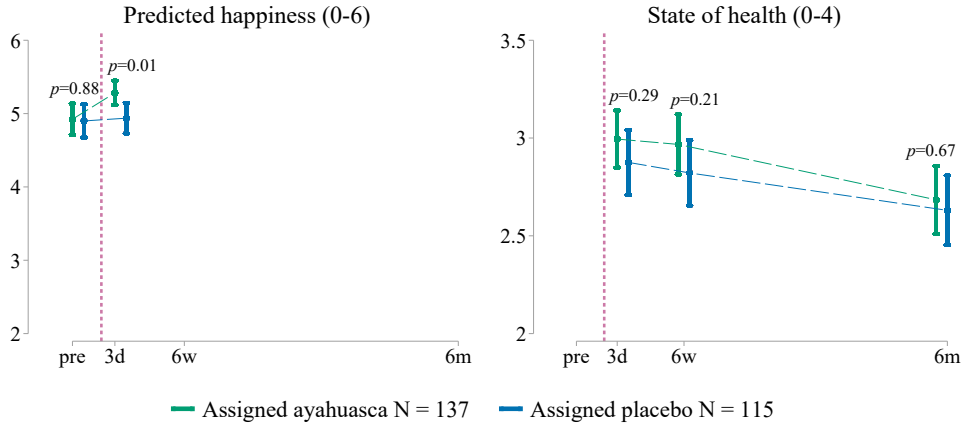
Note: Figure shows the histogram of mystical experience scores separately for those that took ayahuasca and those that took the placebo during the six experimental sessions.

Figure A3: Effects on psychological distress: robustness



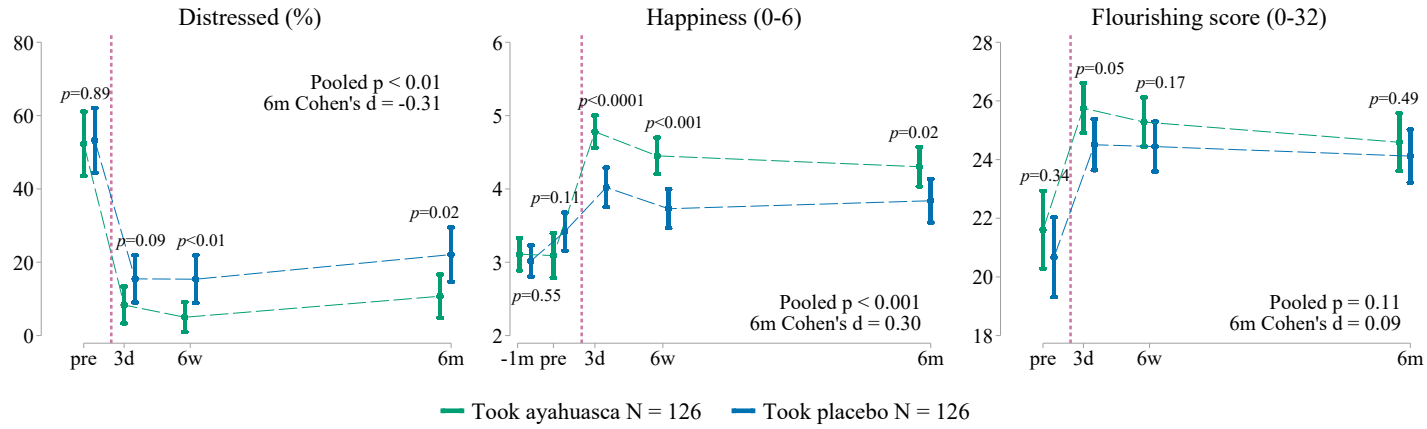
Note: Figure shows intent to treat effects. Baseline measures are denoted by pre, d/w/m denote days/weeks/months. Kessler-10 distress score is the 0 to 40 score on the Kessler-10 scale, while the Kessler-6 score is the score from the six-item version. 95% confidence intervals are shown. *p*-values are from a regression that controls for the outcome at baseline (except for the baseline and retrospective tests), and session-by-gender fixed effects, with robust standard errors. The pooled *p*-value is obtained from a regression pooling data from the three follow-up surveys. 6m IV Cohen's *d* is the standardized effect of ayahuasca at six months, when using treatment assigned as an instrumental variable for treatment received.

Figure A4: Effects of ayahuasca on predicted happiness and general health



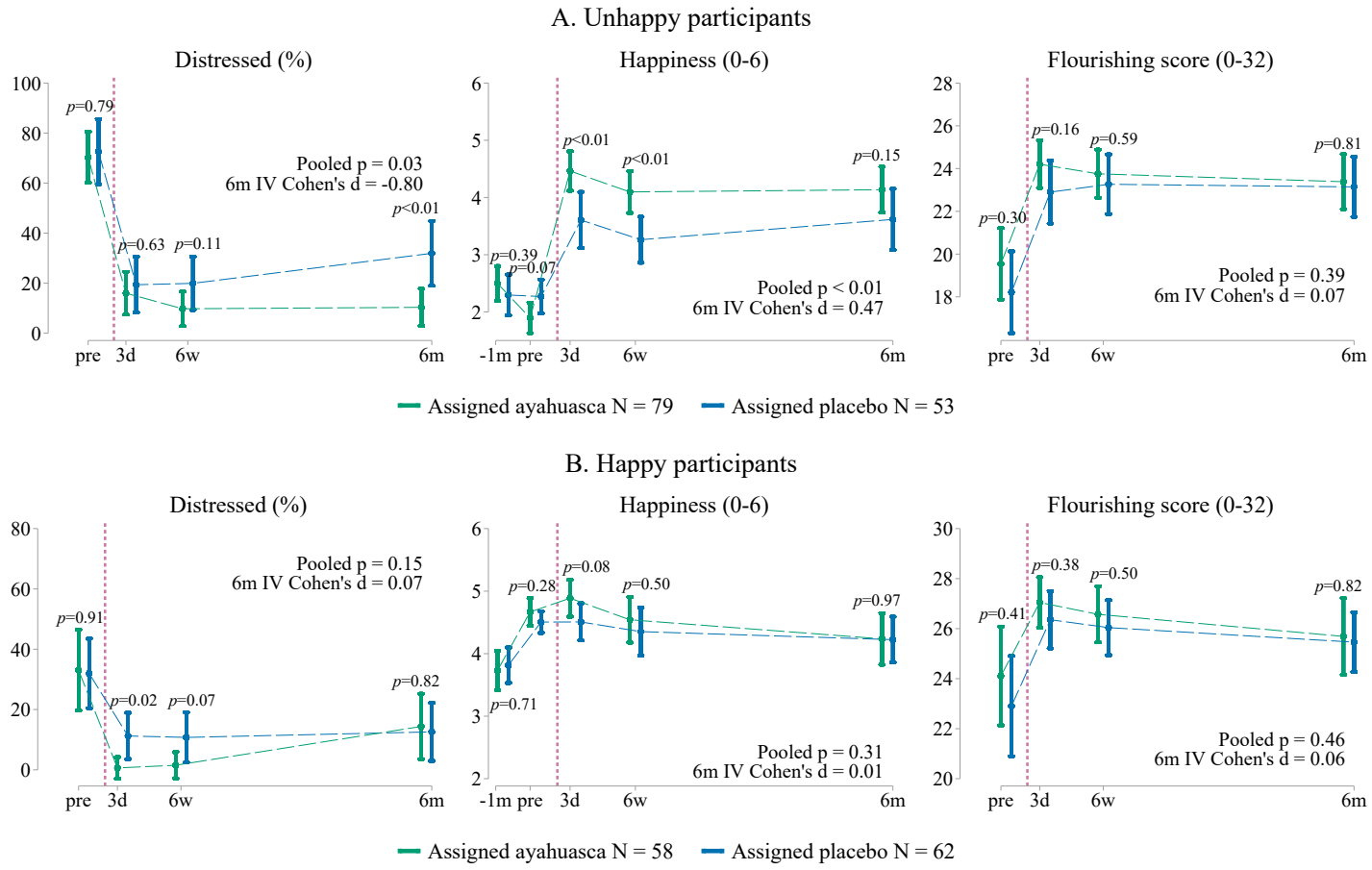
Note: Figure shows intent to treat effects. Baseline measures are denoted by pre and d/w/m denote days/weeks/months. First panel's outcome is the answer to the question *Now please predict how happy you will be in six weeks* on a scale from *Not very happy (0)* to *Very happy (6)*. Second panel's outcome is the answer to *All in all, how would you describe your state of health these days?* and choices go from *Very Poor (0)* to *Very Good (4)*. 95% confidence intervals are shown. *p*-values are from a regression that controls for the outcome at baseline where available (except for the baseline test), and session-by-gender fixed effects, with robust standard errors.

Figure A5: Well-being effects using treatment actually received



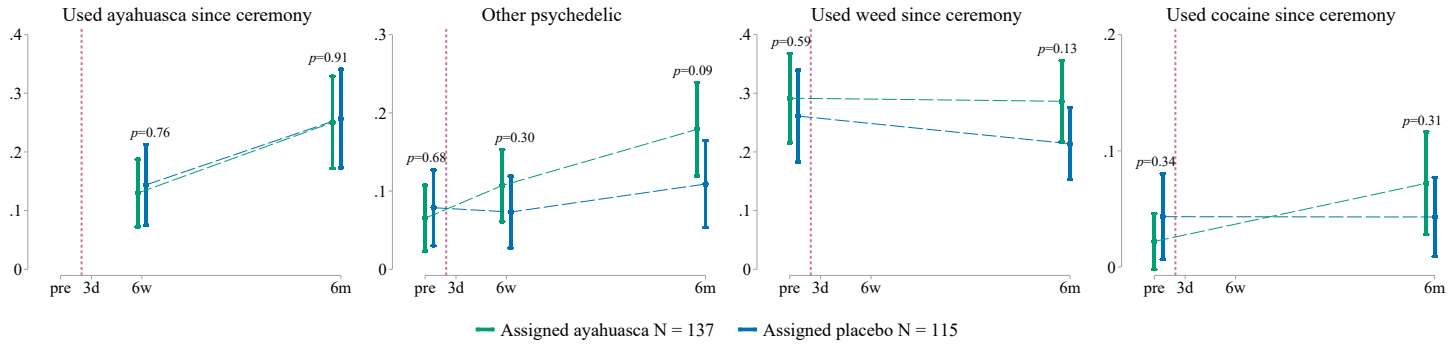
Note: Figure shows means by treatment actually received (as opposed to intent-to-treat estimates based on treatment assigned). Baseline measures are denoted by pre, -1m denotes a retrospective measure for the past month, d/w/m denote days/weeks/months. Distress (%) is the percentage of participants that score 15 or above on the Kessler psychological distress scale. Happiness is the answer to *In general, how happy would you say you are these days?* on a scale from *Not very happy (0)* to *Very happy (6)*. Flourishing is the score from 0 to 32 from summing answers to eight statements like *I lead a purposeful and meaningful life (0 = Strongly disagree to 4 = Strongly agree)*. 95% confidence intervals are shown. *p*-values are from a regression that controls for the outcome at baseline (except for the baseline and retrospective tests) and session-by-gender fixed effects, with robust standard errors. The pooled *p*-value is obtained from a regression pooling data from the three follow-up surveys. 6m Cohen's *d* is the standardized effect of ayahuasca at six months.

Figure A6: Well-being effects are driven by unhappy participants



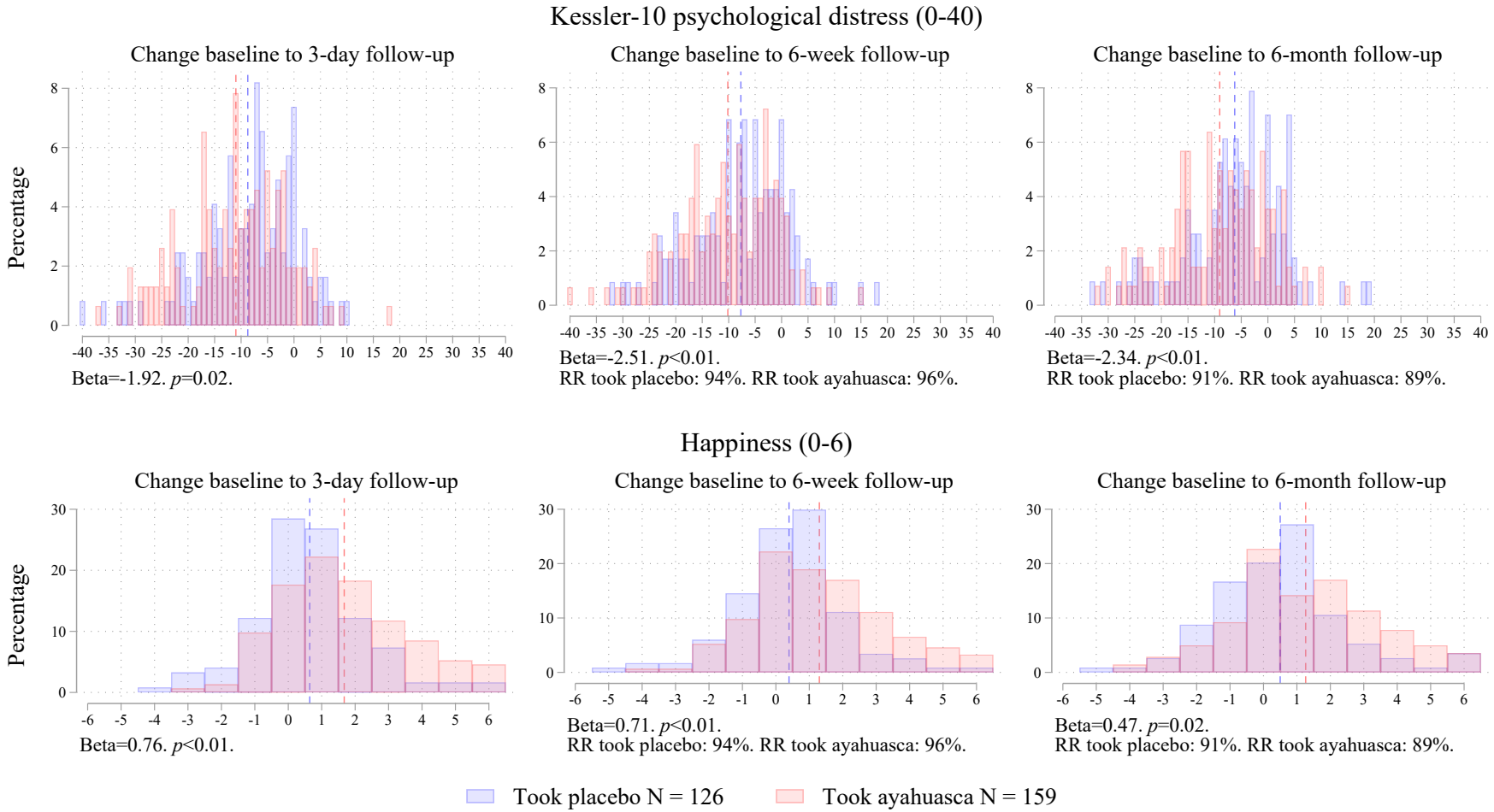
Note: Figure shows intent to treat effects. Baseline measures are denoted by pre, -1m denotes a retrospective measure for the past month. Distressed (%) is the percentage of participants that score 15 or above on the Kessler-10 Psychological Distress Scale. Happiness is the answer to *In general, how happy would you say you are these days?* on a scale from *Not very happy (0)* to *Very happy (6)*. Flourishing is the score from 0 to 32 from summing answers to eight statements like *I lead a purposeful and meaningful life (0 = Strongly disagree to 4 = Strongly agree)*. 95% confidence intervals are shown. *p*-values are from a regression that controls for the outcome at baseline (except for the baseline and retrospective comparisons) and session-by-gender fixed effects, with robust standard errors. The pooled *p*-value is obtained from a regression pooling data from the three follow-up surveys. 6m IV Cohen's *d* is the standardized effect of ayahuasca at six months, when using treatment assigned as an instrumental variable for treatment received. (**A**) presents results for the participants with below-median happiness at baseline ($0-3$), while (**B**) restricts to participants with above-median happiness at baseline ($4-6$).

Figure A7: Effects on subsequent drug use



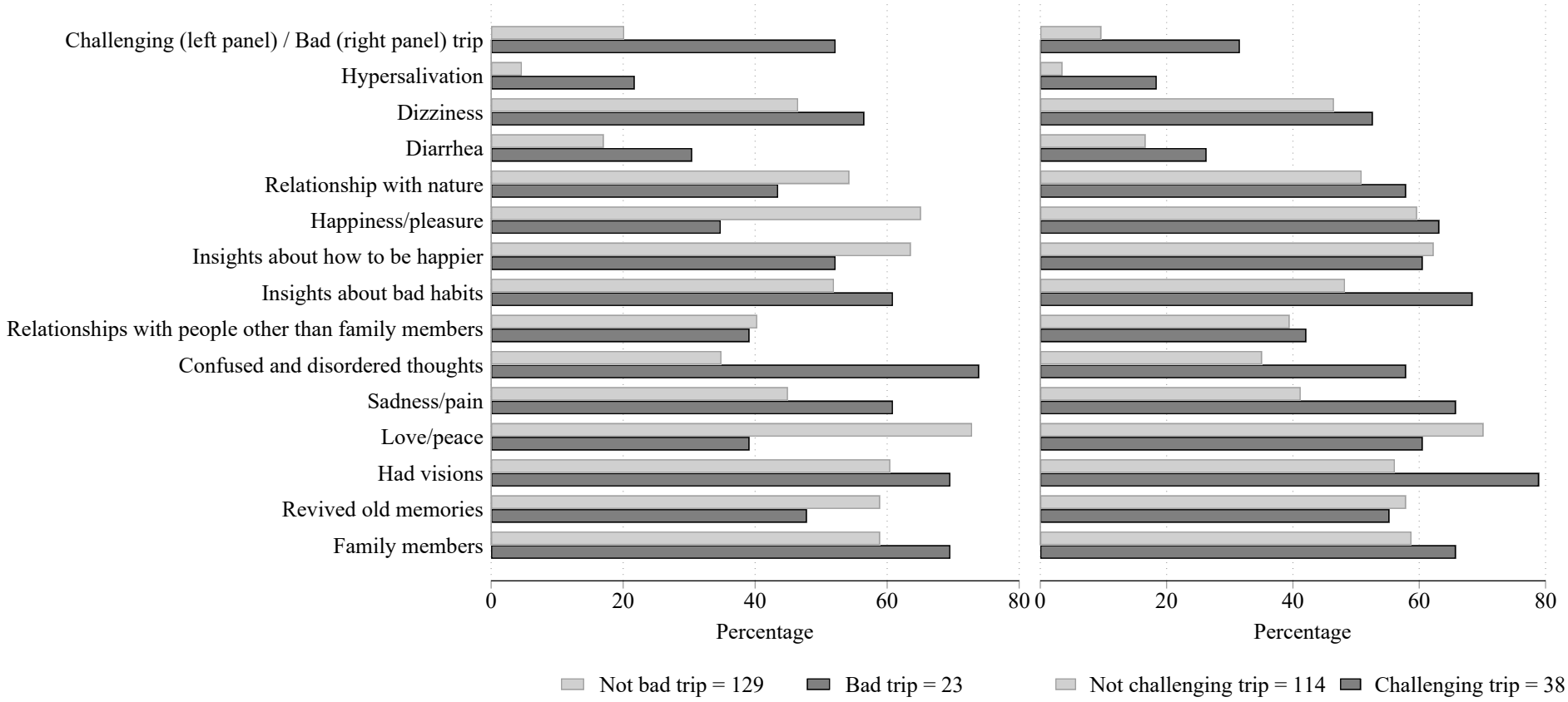
Note: Figure shows intent to treat effects. Baseline measures are denoted by pre, d/w/m denote days/weeks/months. Each panel shows effects of ayahuasca on binary outcomes: (i) whether the participant reports having taken ayahuasca since the ceremony, (ii) whether the participant reports taking psilocybin, LSD, or MDMA, (iii) whether the participant reports taking marijuana, and (iv) whether the participant reports taking cocaine. 95% confidence intervals are shown. *p*-values are from a regression that controls for the outcome at baseline when available (except for the baseline test) and session-by-gender fixed effects, with robust standard errors.

Figure A8: No evidence of negative tail events due to ayahuasca



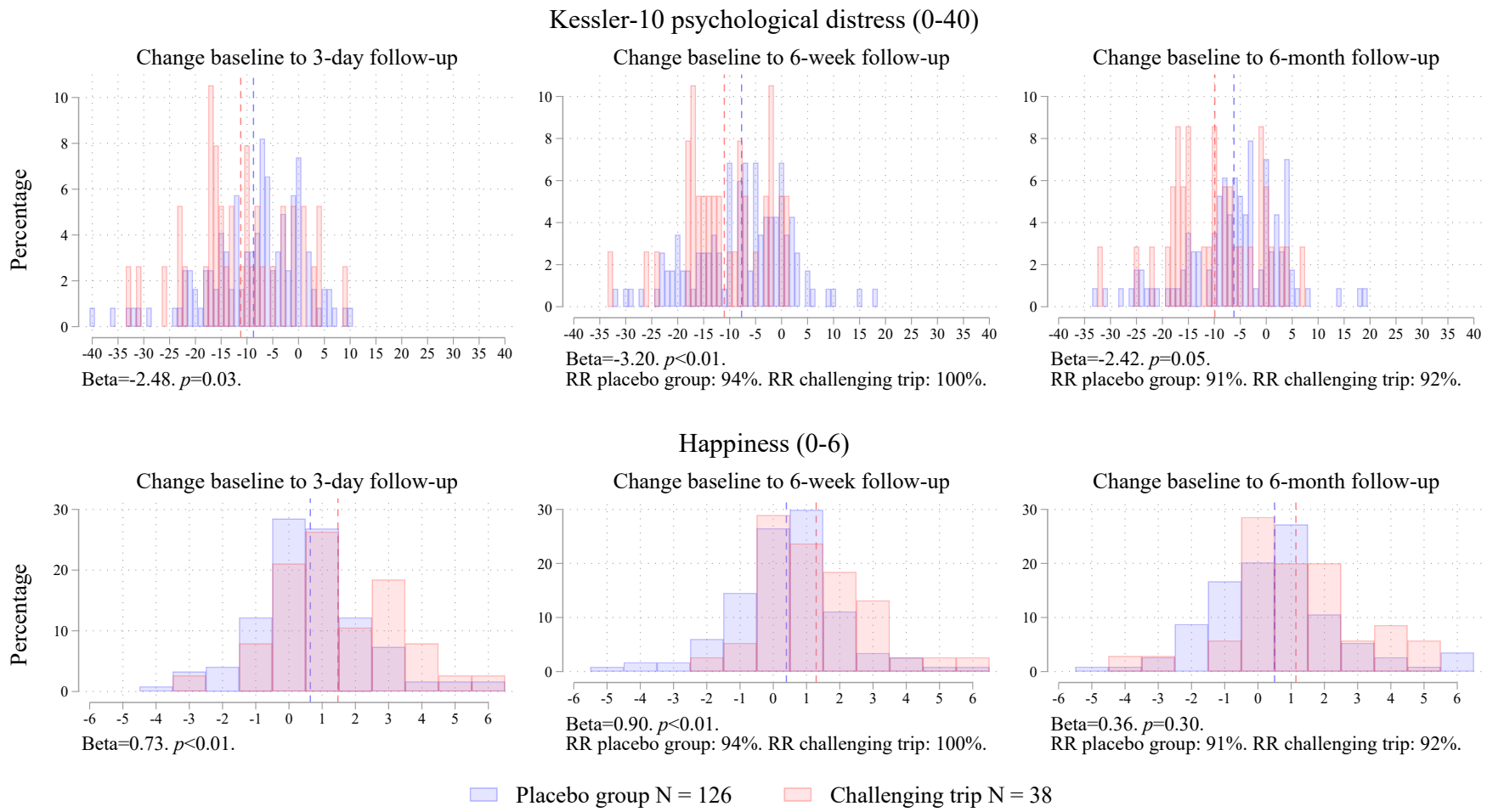
Note: The figure plots histograms of well-being changes for (i) participants that actually received ayahuasca, including in the all-treated session, and (ii) participants that received the placebo. RR refers to response rate. The high response rates in the ayahuasca group limit the possibility of negative effects obscured by non-response. Vertical dashed lines denote the mean well-being change for each group. The betas and *p*-values are obtained from a regression of the outcome on an indicator for taking ayahuasca (the omitted group comprises participants that received the placebo), controlling for the outcome at baseline, and session-by-gender fixed effects, with robust standard errors.

Figure A9: How do bad and challenging trips differ from other trips?



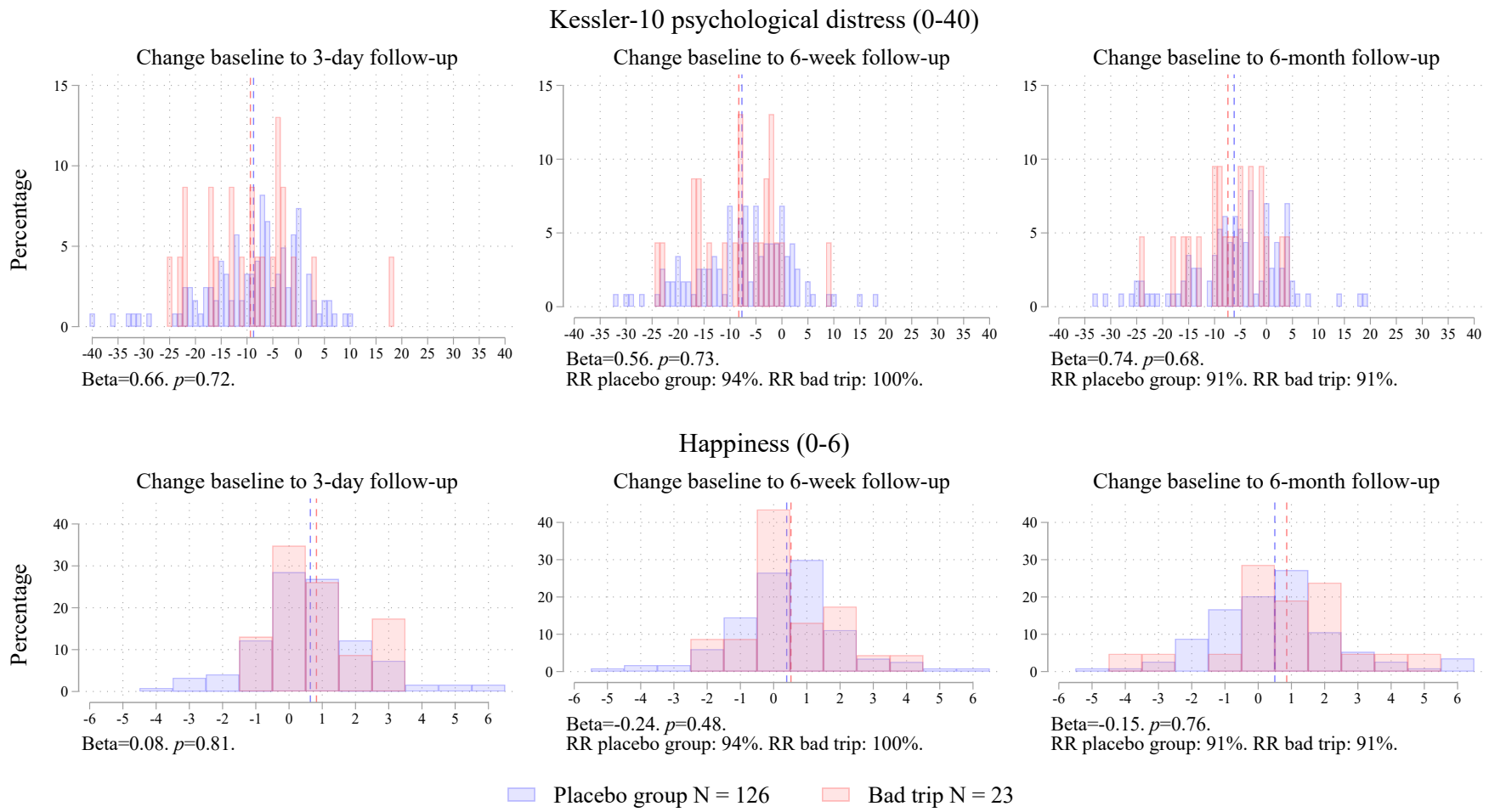
Note: Graph shows percentage of participants in each group that experienced each negative experience (bar pairs 1-4), or tripped on each broad domain (bar pairs 5-15) during the ceremony, as reported on the 3-day follow-up survey. Sample includes all participants that received ayahuasca.

Figure A10: Challenging trips improve well-being more than placebo



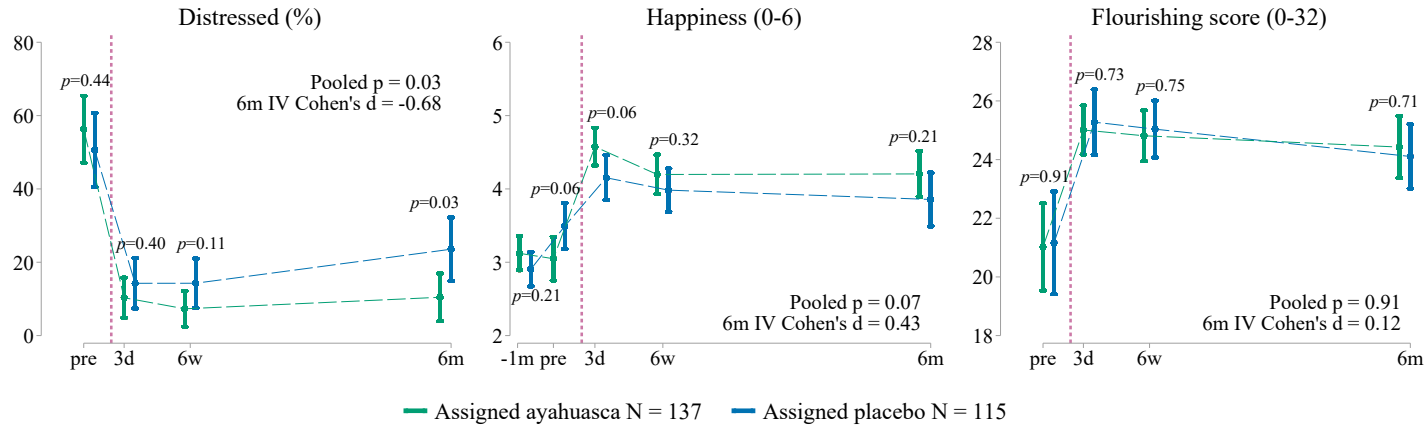
Note: The figure plots histograms of well-being changes for (i) participants that received ayahuasca and reported having a challenging trip, and (ii) participants that received the placebo. RR refers to response rate. Challenging trip participants have high response rates, limiting the possibility of negative effects obscured by non-response. Vertical dashed lines denote the mean well-being change for each group. The betas and *p*-values are obtained from a regression of the outcome on an indicator for having had a challenging ayahuasca trip (the omitted group comprises participants that received the placebo), controlling for the outcome at baseline, and session-by-gender fixed effects, with robust standard errors.

Figure A11: Bad trips and placebo deliver similar changes in well-being



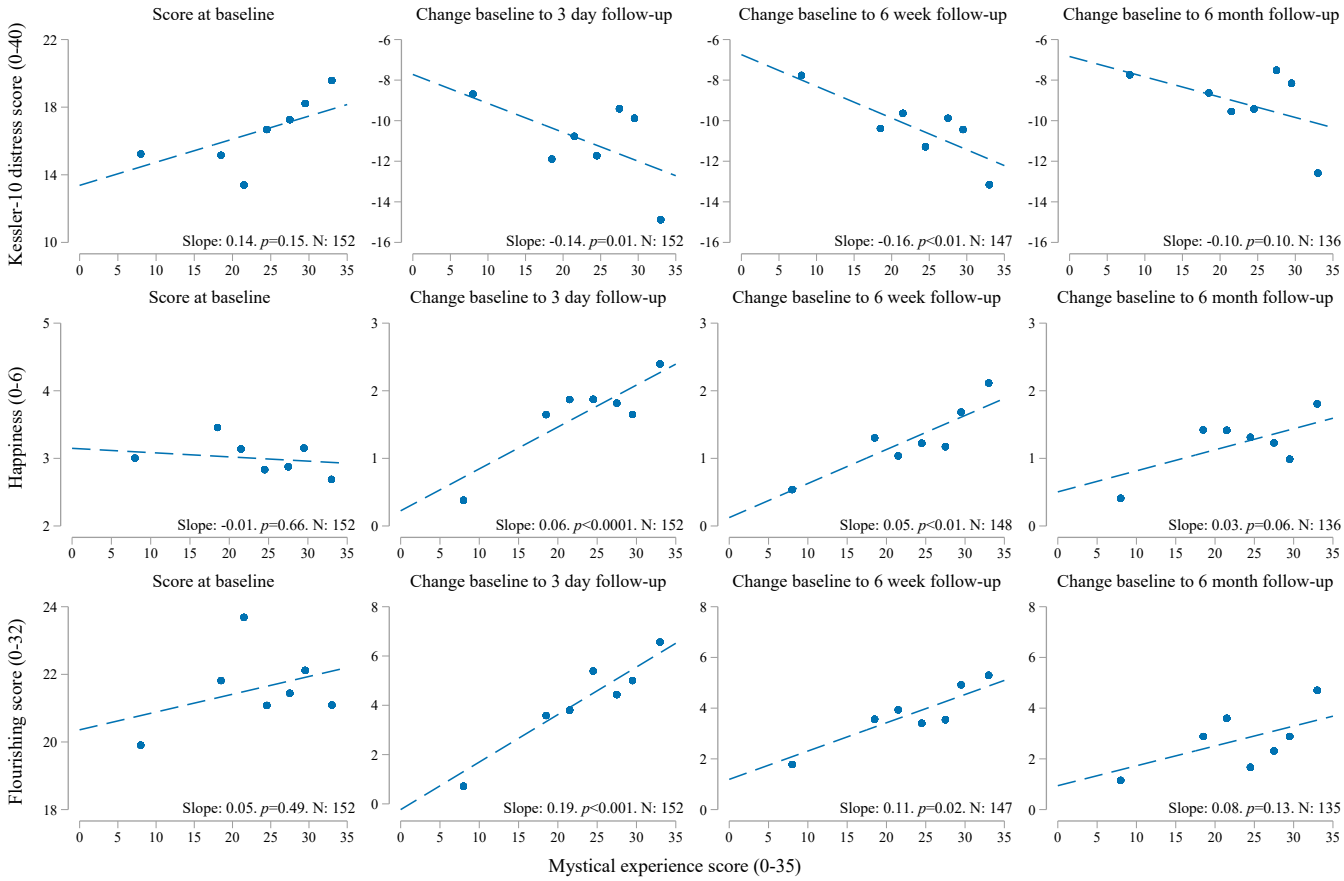
Note: The figure plots histograms of well-being changes for (i) participants that received ayahuasca and reported having a bad trip, and (ii) participants that received the placebo. RR refers to response rate. Bad trip participants have high response rates, limiting the possibility of negative effects obscured by non-response. Vertical dashed lines denote the mean well-being change for each group. The betas and *p*-values are obtained from a regression of the outcome on an indicator for having had a bad ayahuasca trip (the omitted group comprises participants that received the placebo), controlling for the outcome at baseline, and session-by-gender fixed effects, with robust standard errors.

Figure A12: Well-being effects controlling for guessed treatment



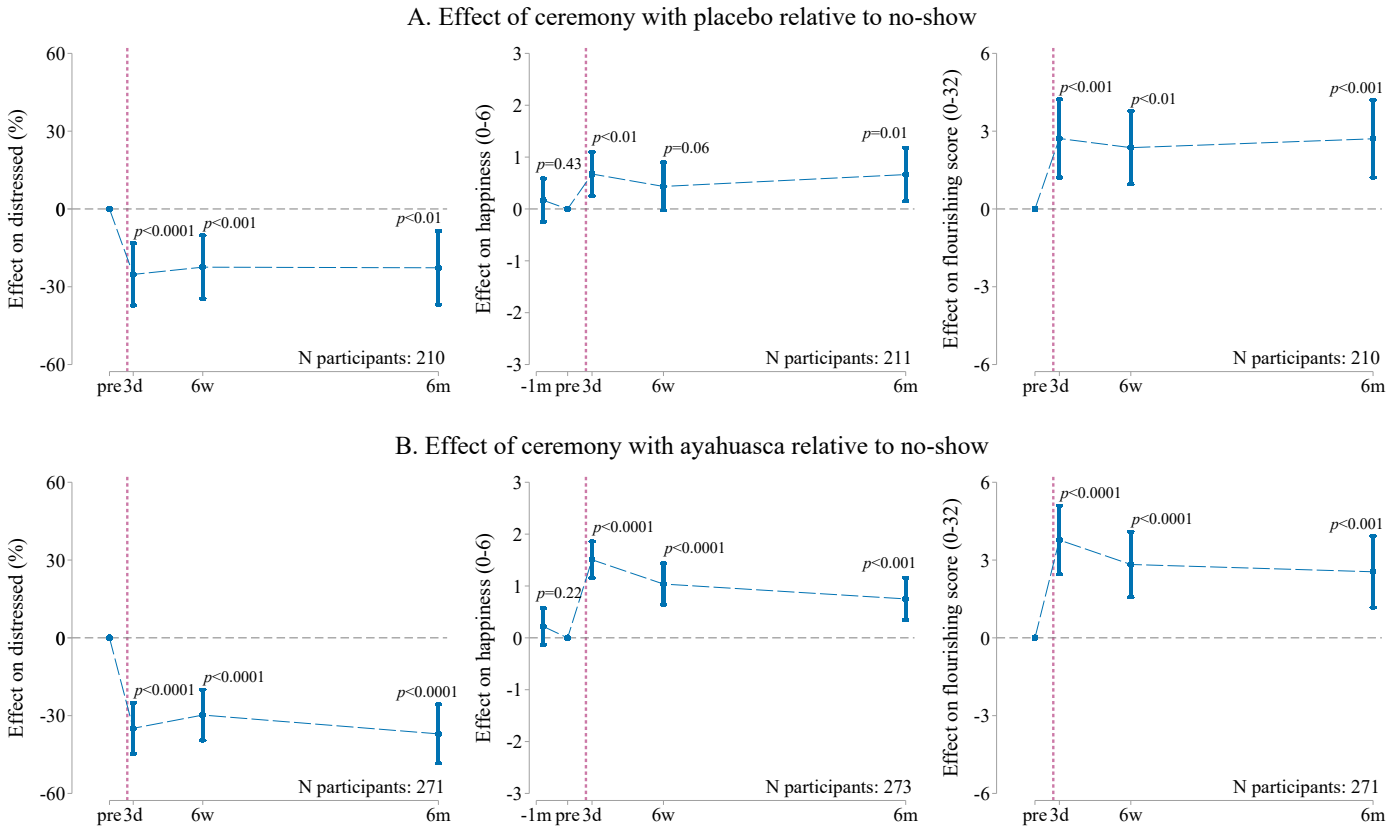
Note: Figure shows intent to treat effects. Baseline measures are denoted by pre, -1m denotes a retrospective measure for the past month, d/w/m denote days/weeks/months. Distress (%) is the percentage of participants that score 15 or above on the Kessler Psychological Distress Scale. Happiness is the answer to *In general, how happy would you say you are these days?* on a scale from *Not very happy (0)* to *Very happy (6)*. Flourishing is the score from 0 to 32 from summing answers to eight statements like *I lead a purposeful and meaningful life (0 = Strongly disagree to 4 = Strongly agree)*. 95% confidence intervals are shown. *p*-values are from a regression that controls for the outcome at baseline (except for the baseline and retrospective tests), a dummy variable equal to one if the participant guessed that they received regular-concentration ayahuasca, and session-by-gender fixed effects, with robust standard errors. The pooled *p*-value is obtained from a regression pooling data from the three follow-up surveys. 6m IV Cohen's *d* is the standardized effect of ayahuasca at six months, when using treatment assigned as an instrumental variable for treatment received.

Figure A13: More mystical trips predict greater improvements in well-being with guess control



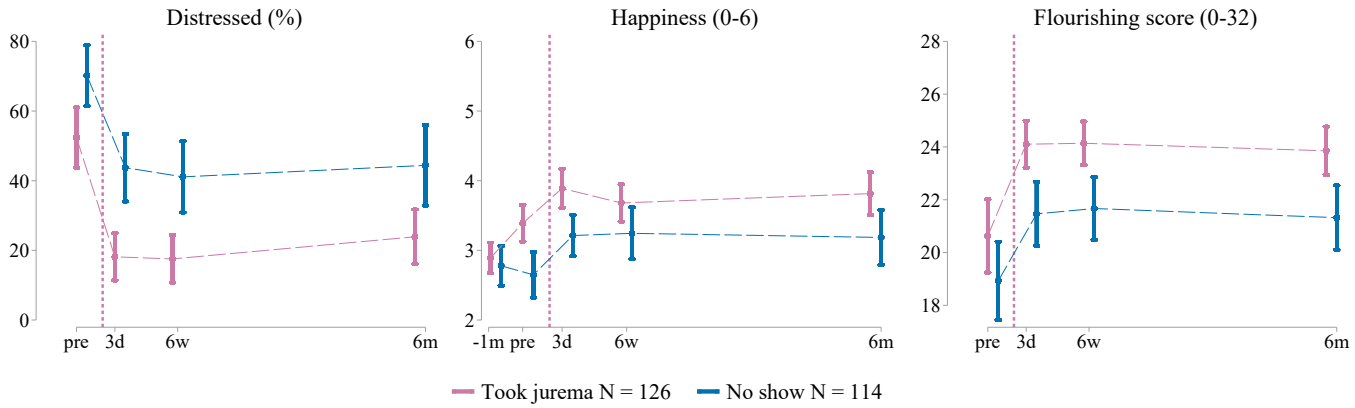
Note: Each panel shows a binscatter plot correlating the mystical experience score (measured at the 3-day follow-up) with baseline measures of well-being (first column), and changes in well-being from baseline to each of the follow-up surveys (second to fourth columns). Each panel controls for session-by-gender fixed effects, a dummy variable equal to one if the participant guessed that they received regular-concentration ayahuasca, and with the exception of column 1, the well-being outcome measured at baseline. Standard errors are robust.

Figure A14: Effects of ceremony controlling for baseline well-being-specific time trends



Note: Figure shows difference-in-differences effects of (**A**) attending the ceremony and taking the placebo relative to no-shows, and (**B**) attending the ceremony and taking ayahuasca relative to no-shows. The one difference from Figure 6 is that each regression includes the baseline well-being measure interacted with dummy variables for each follow-up survey. 95% confidence intervals are shown, with standard errors clustered at participant-level.

Figure A15: Well-being levels for placebo-takers and no-shows



Note: Comparison of those that took the placebo and those that didn't show up for their session (includes the 5 experimental sessions with variation in treatment).

B Appendix tables

Table A1: Characteristics of experimental participants

Variable:	N	Mean	St. dev	Min.	Pctl. 25	Median	Pctl. 75	Max.
(1) Age	426	34.72	9.92	18	27	33	42	66
(2) Female (0/1)	429	0.62	0.49	0	0	1	1	1
(3) Not white (0/1)	429	0.45	0.50	0	0	0	1	1
(4) Education (0-10)	429	5.70	1.68	1	4	6	7	9
(5) Married (0/1)	429	0.22	0.41	0	0	0	0	1
(6) Income (0-8)	429	2.77	1.48	0	2	3	4	7
(7) Has children (0/1)	429	0.49	0.50	0	0	0	1	1
(8) Employed (0/1)	429	0.81	0.39	0	1	1	1	1
(9) Employed in the formal sector (0/1)	429	0.42	0.49	0	0	0	1	1
(10) Drinks alcohol (0/1)	429	0.65	0.48	0	0	1	1	1
(11) Uses drugs (0/1)	429	0.31	0.46	0	0	0	1	1
(12) Practices a religion (0/1)	429	0.45	0.50	0	0	0	1	1
(13) Family history of alcoholism (0/1)	429	0.37	0.48	0	0	0	1	1
(14) Family history of depression (0/1)	429	0.44	0.50	0	0	0	1	1
(15) Family history of schizophrenia (0/1)	429	0.07	0.26	0	0	0	0	1
(16) Happiness (0-6)	429	3.03	1.67	0	2	3	4	6
(17) Predicted happiness (0-6)	429	4.79	1.44	0	4	5	6	6
(18) Depression last month (0-6)	429	2.69	1.99	0	1	3	4	6
(19) Happiness last month (0-6)	429	2.89	1.67	0	2	3	4	6
(20) K10 scale score (0-40)	429	17.24	9.30	0	10	17	25	40
(21) Meets moderate or severe psychological distress	429	0.58	0.49	0	0	1	1	1
(22) Flourishing score (0-32)	429	20.58	7.64	0	16	22	26	32
(23) Social desirability score (0-4)	429	2.10	0.82	0	2	2	3	4
(24) Work satisfaction (0-4)	349	2.32	1.07	0	1	3	3	4
(25) Cares what others think (0-4)	429	2.36	1.34	0	1	3	3	4

Notes: Table shows summary statistics from the baseline survey taken by the full set of 429 participants. For the outcome variable definitions that are not obvious, see Appendix C. Work satisfaction is only asked to participants that are employed.

Table A2: Balance on baseline characteristics: all participants

	Treatment assigned				Treatment received				Took the placebo (vs no-show)			
	Coef	SE	Control mean	N	Coef	SE	Control mean	N	Coef	SE	Control mean	N
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Age	-1.91	(1.20)	35.05	251	-3.12**	(1.20)	35.64	251	0.71	(1.39)	34.97	238
Not white (0/1)	-0.02	(0.06)	0.47	252	0.00	(0.06)	0.46	252	-0.00	(0.07)	0.46	240
Education (0-10)	-0.00	(0.21)	5.79	252	-0.15	(0.20)	5.87	252	0.47**	(0.21)	5.44	240
Married (0/1)	-0.06	(0.05)	0.25	252	0.02	(0.05)	0.21	252	0.01	(0.05)	0.19	240
Income (0-8)	-0.01	(0.18)	2.81	252	0.01	(0.18)	2.81	252	0.23	(0.20)	2.61	240
Has children (0/1)	-0.04	(0.06)	0.49	252	-0.06	(0.06)	0.50	252	-0.02	(0.07)	0.52	240
Employed (0/1)	0.02	(0.05)	0.83	252	-0.01	(0.05)	0.85	252	0.10*	(0.05)	0.75	240
Employed in the formal sector (0/1)	0.00	(0.06)	0.42	252	-0.00	(0.06)	0.42	252	0.02	(0.07)	0.42	240
Drinks alcohol (0/1)	0.01	(0.06)	0.65	252	0.00	(0.06)	0.65	252	0.07	(0.06)	0.57	240
Uses drugs (0/1)	0.02	(0.06)	0.29	252	0.00	(0.06)	0.29	252	-0.07	(0.06)	0.38	240
Practices a religion (0/1)	0.00	(0.06)	0.41	252	-0.02	(0.06)	0.42	252	-0.06	(0.06)	0.48	240
Family history of alcoholism (0/1)	0.09	(0.06)	0.35	252	0.00	(0.06)	0.39	252	0.04	(0.06)	0.35	240
Family history of depression (0/1)	0.03	(0.06)	0.46	252	-0.02	(0.06)	0.48	252	0.13**	(0.06)	0.37	240
Family history of schizophrenia (0/1)	0.02	(0.03)	0.06	252	-0.04	(0.03)	0.09	252	0.02	(0.03)	0.06	240
Happiness (0-6)	-0.45**	(0.20)	3.50	252	-0.33	(0.20)	3.40	252	0.74***	(0.21)	2.63	240
Predicted happiness (0-6)	0.02	(0.16)	4.90	252	0.04	(0.16)	4.90	252	0.36*	(0.20)	4.45	240
Depression last month (0-6)	-0.11	(0.24)	2.57	252	-0.08	(0.24)	2.55	252	-0.48*	(0.27)	3.05	240
Happiness last month (0-6)	-0.17	(0.19)	3.16	252	-0.09	(0.19)	3.11	252	0.54**	(0.22)	2.54	240
K10 scale score (0-40)	0.69	(1.14)	15.57	252	-0.15	(1.14)	16.05	252	-3.69***	(1.18)	19.68	240
Meets moderate or severe psychological distress	0.06	(0.06)	0.50	252	-0.01	(0.06)	0.53	252	-0.18**	(0.06)	0.69	240
Flourishing score (0-32)	0.38	(0.98)	20.94	252	0.93	(0.96)	20.69	252	1.70	(1.02)	18.86	240
Social desirability score (0-4)	-0.07	(0.10)	2.12	252	0.11	(0.10)	2.03	252	-0.05	(0.11)	2.08	240
Work satisfaction (0-4)	-0.03	(0.15)	2.40	213	0.02	(0.15)	2.37	213	0.07	(0.16)	2.29	192
Cares what others think (0-4)	0.31*	(0.17)	2.26	252	0.06	(0.17)	2.40	252	0.14	(0.19)	2.24	240
Pooled F-test p-value			0.33				0.42				<0.01	

Notes: The table excludes participants assigned to the all-treated session. Treatment assigned columns compare participants who attended their session and were randomly assigned to receive ayahausca versus the placebo (control mean is for the placebo group). Treatment received columns compare participants who attended their session and actually received ayahuasca with those that attended and actually received the placebo. Took the placebo vs no-show columns compare participants who attended their session and actually received the placebo to those that did not attend their session. Each coefficient and standard error is obtained from a regression of the covariate (listed in the far-left column) on a dummy for the comparison of interest, controlling for session-by-gender (randomization strata) fixed effects. Standard errors are robust. The pooled F-test p-value corresponds to the p-value from a test of joint significance for all the covariates in the table. *** p<0.01, ** p<0.05, * p<0.1.

Table A3: Balance on baseline characteristics: responded to 3-day follow-up

	Treatment assigned				Treatment received				Took the placebo (vs no-show)			
	Coef	SE	Control mean	N	Coef	SE	Control mean	N	Coef	SE	Control mean	N
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Age	-1.87	(1.21)	35.00	244	-3.08**	(1.22)	35.58	244	0.86	(1.53)	34.54	204
Not white (0/1)	-0.01	(0.07)	0.47	245	-0.00	(0.06)	0.46	245	0.01	(0.07)	0.45	206
Education (0-10)	-0.02	(0.21)	5.83	245	-0.16	(0.21)	5.89	245	0.51**	(0.23)	5.40	206
Married (0/1)	-0.06	(0.05)	0.25	245	0.01	(0.05)	0.22	245	-0.04	(0.06)	0.23	206
Income (0-8)	-0.00	(0.19)	2.81	245	0.03	(0.18)	2.80	245	0.22	(0.22)	2.61	206
Has children (0/1)	-0.02	(0.06)	0.48	245	-0.07	(0.06)	0.50	245	-0.05	(0.07)	0.54	206
Employed (0/1)	0.01	(0.05)	0.85	245	-0.01	(0.05)	0.85	245	0.12**	(0.06)	0.73	206
Employed in the formal sector (0/1)	0.00	(0.06)	0.42	245	-0.01	(0.06)	0.42	245	0.01	(0.07)	0.42	206
Drinks alcohol (0/1)	0.02	(0.06)	0.64	245	-0.00	(0.06)	0.64	245	0.06	(0.07)	0.58	206
Uses drugs (0/1)	0.01	(0.06)	0.29	245	-0.03	(0.06)	0.30	245	-0.09	(0.07)	0.40	206
Practices a religion (0/1)	0.01	(0.06)	0.41	245	0.00	(0.06)	0.41	245	-0.11	(0.07)	0.49	206
Family history of alcoholism (0/1)	0.08	(0.06)	0.35	245	0.01	(0.06)	0.39	245	0.05	(0.07)	0.35	206
Family history of depression (0/1)	0.03	(0.06)	0.46	245	-0.02	(0.06)	0.49	245	0.13*	(0.07)	0.37	206
Family history of schizophrenia (0/1)	0.01	(0.03)	0.06	245	-0.04	(0.03)	0.09	245	0.03	(0.04)	0.06	206
Happiness (0-6)	-0.45**	(0.20)	3.53	245	-0.28	(0.20)	3.41	245	0.72***	(0.24)	2.67	206
Predicted happiness (0-6)	0.08	(0.16)	4.87	245	0.08	(0.16)	4.87	245	0.29	(0.23)	4.48	206
Depression last month (0-6)	-0.17	(0.25)	2.63	245	-0.08	(0.24)	2.58	245	-0.59*	(0.30)	3.17	206
Happiness last month (0-6)	-0.11	(0.19)	3.12	245	-0.08	(0.19)	3.10	245	0.56**	(0.24)	2.53	206
K10 scale score (0-40)	0.65	(1.16)	15.72	245	-0.11	(1.15)	16.18	245	-3.37**	(1.35)	19.61	206
Meets moderate or severe psychological distress	0.06	(0.06)	0.50	245	-0.00	(0.06)	0.54	245	-0.14*	(0.07)	0.66	206
Flourishing score (0-32)	0.62	(0.99)	20.75	245	1.09	(0.97)	20.55	245	0.95	(1.15)	19.36	206
Social desirability score (0-4)	-0.06	(0.11)	2.12	245	0.10	(0.11)	2.04	245	-0.14	(0.13)	2.16	206
Work satisfaction (0-4)	-0.04	(0.16)	2.41	208	-0.01	(0.15)	2.39	208	0.00	(0.17)	2.34	166
Cares what others think (0-4)	0.26	(0.17)	2.31	245	0.04	(0.17)	2.43	245	0.25	(0.21)	2.18	206
Pooled F-test p-value		0.21				0.52				<0.01		

Notes: The table is identical to the first baseline balance table, with the exception that it restricts to participants that responded to the three-day follow-up survey.

Table A4: Balance on baseline characteristics: responded to 6-week follow-up

	Treatment assigned				Treatment received				Took the placebo (vs no-show)			
	Coef	SE	Control mean	N	Coef	SE	Control mean	N	Coef	SE	Control mean	N
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Age	-1.77	(1.23)	35.08	238	-2.85**	(1.23)	35.59	238	1.31	(1.59)	34.27	195
Not white (0/1)	-0.01	(0.07)	0.47	239	-0.01	(0.07)	0.47	239	0.04	(0.07)	0.42	197
Education (0-10)	-0.08	(0.21)	5.90	239	-0.20	(0.21)	5.96	239	0.55**	(0.23)	5.44	197
Married (0/1)	-0.06	(0.06)	0.25	239	0.02	(0.05)	0.21	239	-0.06	(0.06)	0.25	197
Income (0-8)	-0.07	(0.18)	2.84	239	0.05	(0.18)	2.79	239	0.35	(0.22)	2.49	197
Has children (0/1)	-0.02	(0.07)	0.48	239	-0.04	(0.07)	0.49	239	-0.01	(0.07)	0.49	197
Employed (0/1)	0.00	(0.05)	0.85	239	-0.01	(0.05)	0.86	239	0.13**	(0.06)	0.73	197
Employed in the formal sector (0/1)	-0.03	(0.06)	0.43	239	-0.01	(0.06)	0.42	239	0.03	(0.07)	0.41	197
Drinks alcohol (0/1)	-0.00	(0.06)	0.65	239	0.01	(0.06)	0.64	239	0.11	(0.07)	0.53	197
Uses drugs (0/1)	0.02	(0.06)	0.27	239	-0.03	(0.06)	0.30	239	-0.05	(0.07)	0.37	197
Practices a religion (0/1)	0.01	(0.06)	0.41	239	-0.01	(0.06)	0.42	239	-0.10	(0.07)	0.49	197
Family history of alcoholism (0/1)	0.06	(0.06)	0.36	239	-0.01	(0.06)	0.39	239	0.02	(0.07)	0.38	197
Family history of depression (0/1)	0.02	(0.07)	0.45	239	-0.04	(0.06)	0.48	239	0.10	(0.07)	0.39	197
Family history of schizophrenia (0/1)	0.00	(0.03)	0.07	239	-0.05*	(0.03)	0.09	239	0.01	(0.04)	0.08	197
Happiness (0-6)	-0.43**	(0.20)	3.46	239	-0.34*	(0.20)	3.38	239	0.72***	(0.23)	2.66	197
Predicted happiness (0-6)	0.06	(0.16)	4.87	239	0.10	(0.16)	4.85	239	0.30	(0.22)	4.43	197
Depression last month (0-6)	-0.20	(0.25)	2.64	239	-0.18	(0.25)	2.63	239	-0.63**	(0.30)	3.25	197
Happiness last month (0-6)	-0.08	(0.19)	3.08	239	0.01	(0.19)	3.03	239	0.56**	(0.23)	2.46	197
K10 scale score (0-40)	0.53	(1.18)	15.71	239	-0.21	(1.16)	16.14	239	-3.50**	(1.36)	19.70	197
Meets moderate or severe psychological distress	0.06	(0.07)	0.49	239	-0.02	(0.07)	0.53	239	-0.15**	(0.07)	0.67	197
Flourishing score (0-32)	0.15	(0.99)	20.98	239	0.57	(0.98)	20.81	239	1.49	(1.15)	19.20	197
Social desirability score (0-4)	-0.07	(0.11)	2.10	239	0.12	(0.11)	2.01	239	-0.21*	(0.12)	2.20	197
Work satisfaction (0-4)	-0.06	(0.15)	2.43	203	-0.07	(0.15)	2.44	203	0.06	(0.16)	2.34	159
Cares what others think (0-4)	0.26	(0.17)	2.34	239	0.05	(0.17)	2.46	239	0.16	(0.21)	2.28	197
Pooled F-test p-value		0.47				0.14				<0.01		

Notes: The table is identical to the first baseline balance table, with the exception that it restricts to participants that responded to the six-week follow-up survey.

Table A5: Balance on baseline characteristics: responded to 6-month follow-up

	Treatment assigned				Treatment received				Took the placebo (vs no-show)			
	Coef	SE	Control mean	N	Coef	SE	Control mean	N	Coef	SE	Control mean	N
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Age	-2.03	(1.30)	35.32	224	-3.13**	(1.31)	35.83	224	0.77	(1.57)	35.00	190
Not white (0/1)	-0.02	(0.07)	0.47	225	0.00	(0.07)	0.46	225	-0.00	(0.08)	0.46	191
Education (0-10)	-0.05	(0.22)	5.86	225	-0.17	(0.22)	5.91	225	0.50**	(0.24)	5.42	191
Married (0/1)	-0.05	(0.06)	0.26	225	0.05	(0.06)	0.21	225	-0.06	(0.06)	0.25	191
Income (0-8)	0.02	(0.19)	2.85	225	0.07	(0.19)	2.83	225	0.32	(0.23)	2.53	191
Has children (0/1)	-0.03	(0.07)	0.48	225	-0.04	(0.07)	0.49	225	-0.04	(0.08)	0.53	191
Employed (0/1)	0.01	(0.05)	0.86	225	-0.04	(0.05)	0.88	225	0.16**	(0.06)	0.72	191
Employed in the formal sector (0/1)	0.02	(0.07)	0.42	225	-0.01	(0.07)	0.43	225	0.05	(0.07)	0.41	191
Drinks alcohol (0/1)	0.01	(0.06)	0.65	225	0.04	(0.06)	0.63	225	0.08	(0.07)	0.55	191
Uses drugs (0/1)	-0.03	(0.06)	0.30	225	-0.03	(0.06)	0.30	225	-0.04	(0.07)	0.34	191
Practices a religion (0/1)	-0.01	(0.07)	0.43	225	-0.02	(0.07)	0.43	225	-0.11	(0.07)	0.53	191
Family history of alcoholism (0/1)	0.05	(0.07)	0.37	225	-0.00	(0.07)	0.39	225	0.04	(0.07)	0.37	191
Family history of depression (0/1)	0.00	(0.07)	0.48	225	-0.04	(0.07)	0.50	225	0.12	(0.07)	0.41	191
Family history of schizophrenia (0/1)	0.01	(0.04)	0.07	225	-0.05	(0.03)	0.10	225	0.04	(0.04)	0.05	191
Happiness (0-6)	-0.48**	(0.20)	3.46	225	-0.40*	(0.21)	3.37	225	0.68**	(0.25)	2.63	191
Predicted happiness (0-6)	0.07	(0.16)	4.85	225	0.08	(0.17)	4.83	225	0.20	(0.23)	4.54	191
Depression last month (0-6)	-0.15	(0.26)	2.56	225	-0.17	(0.25)	2.57	225	-0.56*	(0.31)	3.17	191
Happiness last month (0-6)	-0.07	(0.20)	3.16	225	-0.02	(0.20)	3.13	225	0.55**	(0.25)	2.51	191
K10 scale score (0-40)	0.73	(1.20)	15.59	225	0.30	(1.19)	15.91	225	-3.87**	(1.40)	20.07	191
Meets moderate or severe psychological distress	0.06	(0.07)	0.49	225	0.01	(0.07)	0.52	225	-0.17**	(0.07)	0.68	191
Flourishing score (0-32)	0.61	(1.00)	20.88	225	0.57	(1.01)	20.93	225	1.35	(1.18)	19.25	191
Social desirability score (0-4)	-0.09	(0.11)	2.13	225	0.11	(0.11)	2.03	225	-0.10	(0.13)	2.09	191
Work satisfaction (0-4)	-0.04	(0.16)	2.38	193	-0.10	(0.16)	2.40	193	-0.00	(0.17)	2.35	156
Cares what others think (0-4)	0.28	(0.18)	2.30	225	0.08	(0.18)	2.41	225	0.15	(0.22)	2.24	191
Pooled F-test p-value		0.27				0.07				<0.01		

Notes: The table is identical to the first baseline balance table, with the exception that it restricts to participants that responded to the six-month follow-up survey.

Table A6: Well-being effects are not driven by participants that give socially desirable answers at baseline

	Distressed			Happiness			Flourishing score		
	3d	6w	6m	3d	6w	6m	3d	6w	6m
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Assigned ayahuasca × Social desirability ≤ Median	-0.06	-0.11**	-0.11*	0.71***	0.69***	0.47*	0.82	0.81	0.13
	(0.05)	(0.05)	(0.06)	(0.22)	(0.21)	(0.25)	(0.72)	(0.70)	(0.86)
Assigned ayahuasca × Social desirability > Median	-0.04	-0.05	-0.15	0.57*	0.15	0.29	-0.20	-1.75	0.52
	(0.07)	(0.08)	(0.09)	(0.34)	(0.38)	(0.41)	(1.27)	(1.12)	(1.10)
p-value for the difference	0.80	0.51	0.71	0.74	0.23	0.72	0.48	0.05	0.79
Outcome mean	0.12	0.10	0.17	4.40	4.10	4.07	25.13	24.87	24.35
Observations	243	237	224	244	238	224	243	235	221
Session-by-gender fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Notes: 3d, 6w, and 6m refer to the outcome being measured in the 3-day, 6-week, and 6-month follow-up surveys. Sample includes participants that attended their assigned session, except the all-treated session. Social desirability score is a measure of a participant's tendency to give socially desirable answers, measured with true/false answers to statements like, *No matter who I'm talking to, I'm always a good listener*. For this statement, an answer of true is considered to be the socially desirable (and likely false) answer. For more details, see Appendix C. The table shows intent-to-treat effects of ayahuasca, separately for those that have a social desirability score above or weakly below the median. All specifications control for the outcome measure at baseline and an indicator for social desirability score below median. Robust standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1.

Table A7: Little evidence of negative side effects of ayahuasca

	Increased heart rate	Increased blood pressure	Chest pain or tightness	Agitation	Dizziness	Confusion	Headaches	Visual disturbances	Paranoid thoughts and behaviors	Mood disturbances	Other	Total symptoms
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Assigned ayahuasca	2.70	-6.66*	5.82	5.44	-2.16	0.25	-5.63	4.04	-2.40	1.37	5.31	0.08
	(2.72)	(3.42)	(4.27)	(5.92)	(3.81)	(4.11)	(6.23)	(3.30)	(4.18)	(6.33)	(4.78)	(0.23)
Placebo group outcome mean	2.9	10.7	8.7	22.3	9.7	9.7	35.9	4.9	11.7	32.0	13.6	1.6
Observations	223	223	223	223	223	223	223	223	223	223	223	223
Session-by-gender fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Notes: Table shows intent-to-treat effects from a regression of each health symptom on an indicator equal to one for participants assigned ayahausca, and zero for those assigned the placebo (jurema). At six-month follow-up, participants were asked *Do you experience any of the following? Check all that apply* with checkboxes for each of the symptoms above. *Total Symptoms* is the sum of symptoms checked (0-11). Sample includes participants that came to their session, and excludes the all-treated session. Robust standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1.

Table A8: Trip intensity predicts well-being changes

	Baseline			Change baseline to 3-day			Change baseline to 6-week			Change baseline to 6-month		
	MN	ME	ED	MN	ME	ED	MN	ME	ED	MN	ME	ED
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Outcome: K10	1.92	1.38	0.62	-2.14**	-1.57**	-1.43***	-2.23*	-1.70***	-1.18**	-0.23	-0.86	-0.67
	(1.74)	(.96)	(.78)	(.91)	(.56)	(.45)	(1.32)	(.57)	(.44)	(1.11)	(.59)	(.49)
Outcome mean	16.5	16.6	16.6	-11.0	-11.1	-11.1	-10.3	-10.4	-10.4	-9.1	-9.2	-9.2
N	153	152	152	153	152	152	148	147	147	137	136	136
Session-by-gender fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Outcome: Happiness	-0.14	-0.06	-0.06	0.92***	0.62***	0.37***	0.55*	0.55***	0.23*	-0.02	0.27*	0.13
	(.3)	(.15)	(.15)	(.25)	(.12)	(.13)	(.29)	(.17)	(.13)	(.23)	(.16)	(.13)
Outcome mean	3.0	3.0	3.0	1.7	1.7	1.7	1.3	1.3	1.3	1.2	1.2	1.2
N	153	152	152	153	152	152	149	148	148	137	136	136
Session-by-gender fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Outcome: Flourishing score	0.51	0.53	0.44	2.63**	1.94***	1.34***	2.17***	1.04**	0.72*	-0.46	0.65	0.72
	(1.09)	(.77)	(.56)	(1.18)	(.51)	(.39)	(.71)	(.48)	(.37)	(.94)	(.52)	(.46)
Outcome mean	21.7	21.6	21.6	4.3	4.3	4.3	3.8	3.8	3.8	2.8	2.8	2.8
N	153	152	152	153	152	152	148	147	147	136	135	135
Session-by-gender fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Notes: Sample includes all participants that received ayahuasca. MN is Meaningfulness, ED is Ego dissolution, and ME is Mystical experience. Table shows the results of regressing the well-being measure (either baseline or change from baseline to follow-up) on either MN, ED, or ME (each of these variables is standardized), controlling for session-by-gender fixed effects, and in the case of columns 4 to 12, controlling also for the well-being measure at baseline. K10 corresponds to the score, from 0 to 40, on the Kessler-10 distress scale, where participants rate how often they have felt things such as *tired out for no good reason* over the past 3 days. Happiness corresponds to the answer to *In general, how happy would you say you are these days?* on a scale from *Not very happy (0)* to *Very happy (6)*. Flourishing is the score from 0 to 32 from summing answers to eight statements like *I lead a purposeful and meaningful life (0 = Strongly disagree to 4 = Strongly agree)*. Meaningful score corresponds to answer to question *How personally meaningful was the experience?* on a scale from 0 to 7. Mystical experience corresponds to the score (from 0 to 35) on the mystical experience questionnaire, where participants rate on a scale from 0 to 5 the degree to which they experienced phenomena like *Sense of awe or awesomeness* during the ceremony. Ego dissolution corresponds to the score (from 0 to 500) obtained from adding the participant's responses to 5 statements where they rate (on a scale from 0 to 100) the extent to which they experienced things such as *I felt a sense of union with others* during the ceremony. All these outcomes were measured on the three-day follow-up. For detailed outcome variable definitions, see Appendix C. Robust standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1.

Table A9: Difference-in-differences effects of believing you received ayahuasca

	Distressed (1)	Happiness (2)	Flourishing (3)	Distressed (4)	Happiness (5)	Flourishing (6)
Believe took ayahuasca	-9.57	0.52*	-0.10			
	(6.12)	(0.30)	(0.70)			
Believe took ayahuasca (t+1)				0.08	-0.12	0.67
				(5.75)	(0.25)	(0.63)
Observations	486	488	478	524	526	520
Participants	243	244	239	262	263	260
Outcome mean	13.4	4.0	24.7	11.3	4.2	25.1
Participant fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
Session-by-gender-by-follow-up fixed effects	Yes	Yes	Yes	Yes	Yes	Yes

Notes: The unit of observation is the participant-by-follow-up survey. Regressions include all participants that attended their assigned ceremony. Distressed is equal to 100 if the participant scores 15 or more on the Kessler-10 psychological distress index, and zero otherwise. Happiness ranges from 0 (Not very happy) to 6 (Very happy). Flourishing is the score on the Flourishing scale from 0 to 32. Columns 1 to 3 keep only the six-week and six-month follow-up surveys. Columns 4 to 6 keep only the three-day and six-week follow-up surveys. Believe took ayahuasca is a dummy variable equal to one if the participant believes they were given ayahuasca in their assigned ceremony. For the six-week follow-up, this belief variable is determined by the participant's guess of their treatment in the three-day follow-up. Since treatment is revealed at the end of the six-week follow-up survey, the belief variable is set to the truth for the six-month follow-up. Believe took ayahuasca (t+1) is the lead (as opposed to the lag) of the believe took ayahuasca variable. It follows that columns 4 to 6 serve as a placebo, or parallel pre-trends, check. Standard errors are clustered at the participant-level. *** p<0.01, ** p<0.05, * p<0.1.

Table A10: Heterogeneous treatment effects by baseline expectation

	Distressed			Happiness			Flourishing		
	3-day	6-week	6-month	3-day	6-week	6-month	3-day	6-week	6-month
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Assigned Ayahuasca * Expectation	0.04	0.01	0.03	0.10	0.07	0.16	-0.14	-0.41	-0.87
	(.06)	(.05)	(.05)	(.22)	(.19)	(.2)	(.98)	(.69)	(.75)
Outcome mean	0.1	0.1	0.2	4.4	4.1	4.1	25.1	24.9	24.4
N	243	237	224	244	238	224	243	235	221
Session-by-gender fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Notes: Sample includes all participants that participated in a session with variation in treatment. Each outcome is regressed on an indicator for treatment assigned, the continuous measure of how useful the participant thinks ayahausca will be (measured at baseline), and the interaction between the two, controlling for session-by-gender fixed effects and the outcome at baseline. Expectation Usefulness is answer to "At this moment, how much do you expect your experience with ayahuasca in [partner center name redacted] to be useful in improving your well-being?" on a scale from 1 to 10. Robust standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1.

C Full survey questions

Baseline demographics and other variables. We ask the following questions in the baseline survey.

Race. "What is your race?" [White / Black / Yellow / Indigenous] (note that these are standard categories for race when asked in surveys in Brazil). We code participants as *Not White* if they do not select "White."

Education. "What is your highest level of education?" [0 = Less Than Middle School / 1 = Middle School (Incomplete) / 2 = Middle School (Complete) / 3 = High School (Incomplete) / 4 = High School (Complete) / 5 = Technical Degree / 6 = University (Incomplete) / 7 = University (Complete) / 8 = Other Post Graduate / 9 = Masters / 10 = PhD].

Income. "In the last 12 months, what was your average gross monthly income? Please, consider the average of all your income, including salary, rent, fees, and others." [0 = 0 to BRL500 / 1 = BRL501 to BRL1,000 / 2 =BRL1,001 to BRL2,000 / 3 = BRL2,001 to BRL3,000 / 4 = BRL3,001 to BRL5,000 / 5 = BRL5,001 to BRL10,000 / 6 = BRL10,001 to BRL20,000) / 7 = BRL20,001 to BRL100,000 / 8 = BRL100,001+].

Employment. "What is your current employment status?" [I am employed in the formal sector (that is, with a contract) / I am employed in the informal sector / I am an independent worker / I am unemployed / I'm retired]. We then code participants as *Employed* if they select one of the the first three options, and as *Employed in Formal Sector* if they select the first option.

Religion. "Do you practice any religion?" [Yes/No].

Work satisfaction. "How satisfied are you with your current job?" [0 = Very unsatisfied / 1 = Unsatisfied / 2 = Indifferent / 3 = Satisfied / 4 = Very satisfied]. This question is asked to those that report being employed.

Family history. "Are any of the symptoms below present in your family? Select all the applicable options." [Schizophrenia / Depression / Alcoholism / None]. For each option, we create a variable equal to 1 (and 0 otherwise) if the participants selects the option.

Cares what others think. "Please indicate below how much do you agree with the following sentence: I care a lot about what other people think of me." [0 = Strongly disagree / 1 = Disagree / 2 = Neither agree nor disagree / 3 = Agree a little / 4 = Strongly agree].

Depression last month. "In the past month, how depressed did you feel?" [answer from 0 = Not very depressed to 7 = Very depressed]. Unlike our analysis of effects on happiness, we do not use this variable as a retrospective measure of distress as this question is not comparable with our other measures of distress (which use the Kessler-10 Scale).

Reason for trying ayahuasca. "What reason(s) best describes why you want or wanted to try ayahuasca in the first place? Select all options that apply." [I wanted to develop/improve my spirituality / I wanted to understand why I am the way I am / I was looking for healing / I wanted to forgive people from the past / I was just curious / I wanted to understand why some patterns were repeating in my life / I was looking for the meaning of life / I wanted to change from the status quo in my life / I witnessed someone's behavior/life improve after they started with ayahuasca / Other (specify)].

Expectancy. "At this moment, how much do you expect your experience with ayahuasca in [partner center name redacted] to be useful in improving your well-being?" [1 to 10].

Most meaningful experience so far. "What was the most meaningful experience of your life so far?" [open-text].

Social desirability bias. To measure a tendency to give socially desirable answers, we ask participants a subset of the Marlowe-Crowne social desirability scale (Crowne and Marlowe 1960) in the baseline survey. In particular, we ask each participant to answer whether each of the following four statements is true or false for them: No matter who I'm talking to, I'm always a good listener / There have been occasions when I took advantage of someone / I sometimes try to get even, rather than forgive and forget / I am always willing to admit when I make a mistake.

Subjective experiences. We ask the following questions in the first follow-up (3-day) to measure the acute subjective experiences of the participants that attended the ceremony (with some receiving ayahuasca, others receiving the placebo).

Meaningfulness. "How personally meaningful was the experience?" [0 = No more than routine, everyday experiences, 1 = Similar to meaningful experiences that occur on average once or more a week, 2 = Similar to meaningful experiences that occur on average once a month, 3 = Similar to meaningful experiences that occur on average once a year, 4 = Similar to meaningful experiences that occur on average once every 5 years, 5 = Among the 10 most meaningful experiences of my life, 6 = Among the 5 most meaningful experiences of my life, 7 = The single most meaningful experience of my life.] (We also asked this question in the 6-week follow-up survey.)

Mystical experience questionnaire (7-item, Pahnke (1963)). "Please rate the degree to which at any time during your Ayahuasca session, you experienced each of the following phenomena." [Loss of feelings of difference between yourself and objects or persons in your surroundings / Loss of your usual sense of time / Feeling that you could not do justice to your experience by describing it in words / Feeling that you experienced something profoundly sacred and holy / Sense of awe or awesomeness / Gain of insightful knowledge experienced at an intuitive level / Feelings of universal or infinite love] [0 = None, 1 = So slight I cannot decide, 2 = Slight, 3 = Moderate, 4 = Strong, 5 = Extreme. Summed to give a score from 0 to 35.]

Ego dissolution (5-item). "Please rate the extent to which you have experienced any of the following statements during your Ayahuasca session. Please, slide the bar to indicate your answer, where 0 is 'No more than usually' and 100 is 'Entirely or Completely."' [I experienced a dissolution of my "self" or ego / I felt a sense of union with others / I felt far less absorbed by my own issues and concerns / I felt more special or important than others (reverse-coded) / I felt especially sure-of-myself (reverse-coded). Summed to give a score from 0 to 500.]

Open-text description of experience. "Describe in detail your experience with the Ayahuasca in the box below. Please be specific about what you saw, heard, and felt." [We use the total word count as another measure of the intensity of the experience.]

Trip domains. "If you had to describe a broad domain that you tripped on, what would that be? Select all that apply." [Family members / Revived old memories / Had visions / Love or peace / Sadness or pain / Confused and disordered thoughts / Relationships with people other than family members / Insights about bad habits / Insights about how to be happier / Happiness or pleasure / Relationship with nature / Other (Specify)] [We use the number of categories selected, and whether "Had visions" was selected, as additional measures of the intensity of the experience.]

Adverse effects. "We know that some people can have negative effects during an ayahuasca session. Did any of the following happen during your trip? Please select all that apply." [Vomit / Diarrhea / Dizziness / Bad trip / Challenging trip / Hypersalivation / Other (Specify) / None of the above]

Perceived treatment status. In your Ayahuasca session, you could take either a regular Ayahuasca dose or a less concentrated Ayahuasca dose. If you had to guess, which one would you say you took? We are going to tell which Ayahuasca dose you took by the end of the next survey, which we will send in 6 weeks. [Answer options: Ayahuasca with regular concentration / Ayahuasca with lower concentration (i.e. weaker)] (Note that we made an error in the wording: we meant the second option to be jurema/the placebo.)

Well-being measures. We ask the following questions in the baseline survey and all three follow-up surveys.

Kessler-10 Distress (Kessler et al. 2003). "Over the last [two weeks for baseline, three days for 3-day follow-up, two weeks for 6-week follow-up, four weeks for 6-month follow-up], about how often have you felt..." [tired out for no good reason / so depressed that nothing could cheer you up / depressed / worthless / nervous / so nervous that nothing could calm you down / hopeless / restless or fidgety / so restless you could not sit still / that everything was an effort] [0 = Never, 1 = A little of the time, 2 = Some of the time, 3 = Most of the time, 4 = All the time. Summed to give a score from 0 to 40. Score of 15+ indicates moderate or severe psychological

distress (Yiengprugsawan et al. 2022).]

Happiness. "In general, how happy would you say you are these days? Please use the scale below to indicate." [0 = Not very happy to 6 = Very happy.] At baseline we also ask the retrospective question, "In the past month, how happy have you felt?", and the prospective question, "Please guess how happy you will be in 6 weeks", with the same answer options.

Flourishing Scale (Diener et al. 2010). "Below are eight statements with which you may agree or disagree. Please indicate your agreement with each item." [I lead a purposeful and meaningful life / My social relationships are supportive and rewarding / I am engaged and interested in my daily activities / I actively contribute to the happiness and well-being of others / I am competent and capable in the activities that are important to me / I am a good person and live a good life / I am optimistic about my future / People respect me] [0 = Strongly disagree, 1 = Disagree a little, 2 = Neither agree nor disagree, 3 = Agree a little, 4 = Strongly agree.]

Broader health and side effects. As secondary outcomes, we ask in all three follow-up surveys "All in all, how would you describe your state of health these days?" [0 = Very Poor / 1 = Poor / 2 = Fair / 3 = Good / 4 = Very Good], and in the 6-month follow-up survey we ask "Do you experience any of the following? Check all that apply." [Increased heart rate / Increased blood pressure / Chest pain or tightness / Agitation / Dizziness / Confusion / Headaches / Visual disturbances / Paranoid thoughts and behaviors / Mood disturbances / Other negative health issue (Specify) / None].

Drug use. We measure self-reported use of ayahuasca, other psychedelics, marijuana, and cocaine. See Figure A7 for further details.

D Additional experiment details

D.1 Jurema and ayahuasca

Jurema, or *mimosa teniuflora*, is a shrub native to northeastern Brazil. The lack of MAO-A inhibitors, such as beta carbolines, ensures that the DMT in the jurema brew administered to our control subjects is rendered inactive (Ott 1999; Ruffell et al. 2020). It is broken down in the gut wall and liver and cannot reach the brain to cause 5-HT2A agonist activity. Consequently, placebo participants do not experience psychedelic trips, as confirmed in their responses to our 3-day follow-up questions about the ceremony experience.

Jurema has shown no toxicity in cancer and normal cells, and has antioxidant and antimicrobial actions (Silva et al. 2020). Proven medicinal uses of jurema concern outcomes that are far removed from psychological well-being—for example, topical ointments made from jurema extract have been found to effectively treat venous leg ulcers (Rivera-Arce et al. 2007; Lammoglia-Ordiales et al. 2012). For further information, and a review of the traditional use of jurema among indigenous groups, see Souza et al. (2008).

A serving of ayahuasca contains 9mg of DMT per 50ml, with 50ml given to men, and 40ml given to women.

D.2 Ceremony instructions

Prior to the ceremony, the center provides the following instructions (in Portuguese) to those that signed up (whether for one of our experimental sessions, or for one of the regular sessions outside of the experiment):

RECOMMENDATIONS FOR THE RITUAL WITH AYAHUASCA

For the Ritual:

- *Take a blanket or blanket and cushion to stay comfortable during the session, these items are very important for your comfort and well-being.*
- *Bring a 500 ml bottle of water to keep by your side.*
- *We serve a delicious soup at the end of work.*
- *Bring a plate of sweet or savory (vegetarian), juice or even fruit to share at the end of the ritual.*
- *The participant is not allowed to wear shorts, short skirts or low-cut clothing, remember that you are coming for a rite and we ask your clothes to be discreet and comfortable.*
- *Avoid black clothes, try to wear light colored clothes.*
- *Carrying any type of weapon is prohibited.*

- *It is not permitted to record, film or photograph during the session.*
- *Avoid sexual intercourse two days before the Ritual.*
- *Try to be with yourself and focus on what you are looking for from the experience.*
- *Do not drink alcoholic beverages or use drugs (including psychiatric drugs) two days before the session. During the session, the use of any type of drug is prohibited. We ask that if you use cannabis (marijuana), you do not use it 2 days beforehand.*
- *In the two days before the ritual, please take care of your diet, by not eating red meat, avoiding sexual intercourse, as well as preserving your body and spirit from fights and confusion.*
- *Try to eat up to a maximum of 2 hours before the start. The last meal should be light, preferably without any type of meat, fatty foods, fried foods, spicy, highly seasoned and sweet foods. Give preference to cereals, vegetables and fruits.*

During the ritual:

- *Try to stay connected to your breathing (soft, deep, calm), without unnecessary tension, with your eyes closed and your mind focused on the heart – home of the Natural Being – trying to stick to the guidance, music and calls.*
- *Leave cell phones and any electronic sound devices turned off.*
- *Smokers are not discriminated against, but they are asked not to smoke during the ceremony.*
- *It is not allowed to talk or touch other participants, except the facilitators. It is also important to try to remain seated and calm, avoiding sudden movements that could disrupt the concentration of others.*
- *If you need help and/or notice that someone needs help, call the designated facilitators and Guardians, avoiding any type of personal intervention with other participants, unless requested by a facilitator.*
- *After the Ritual, you may feel sensitive and therefore it is recommended to avoid tense emotional states, arguments, etc. Try, again, to be in peaceful and pleasant environments, if possible, take the next day off and look for a place with plenty of greenery to rest or meditate. The day after the session, avoid alcohol and drugs.*

Restrictions for drinking Ayahuasca:

- *Minors can only participate with written authorization with a notarized signature from their parents or guardians. [Note: this instruction regarding minors applied only to the non-experimental sessions]*

- *People who use antidepressants such as selective serotonin reuptake inhibitors or monoamine oxidation inhibitors (MAOIs) such as fluoxetine, citalopram, paroxetine, sertraline or tranylcypromine should consult their doctors, seeking appropriate authorization, avoiding risks to their health. In this case, they may consider stopping the medication for two days or changing the antidepressant, etc. by a medication from another category.*
- *People with a history of a psychotic break, previous psychiatric hospitalization or who are taking other medications, such as anorexics (weight loss medication) should first contact us for clarification.*
- *People who have consumed alcoholic beverages or heavy drugs two days before the session are prohibited from participating in the session.*

Gratitude!

D.3 Ceremony lecture

Below are excerpts from an English translation of the lecture given for an experimental session in October 2023, on the topic of happiness.

"I ask everyone to go to their mat, because we are going to start the work now, I will also give you some instructions on what this experience will be like... Ayahuasca is a medicine considered one of the oldest in the world, there are records from 100 years ago, 1930. This tea was brought by Raimundo Irineu Serra, from the Atlantic Forest to modern civilization, our Brazilian society knows this medicine from 1930 and Ayahuasca began to be increasingly used. The last census carried out in February 2022, showed that around 576 thousand people practiced this medicine, it is a relatively large number but when we look at a population of around 210 million inhabitants, it represents a little 0.25% of the population. The experience you will have tonight is still a taboo for Brazilian society. It is an experience used for millennia, with the purpose of healing people. Healing can be understood in different ways, Ayahuasca brings us more clarity about our lives, situations, and ourselves. Ayahuasca is used to get to know ourselves. A large part of the population, if you ask, says they know each other, but in reality, we know very little about each other. It's as if we were a machine with enormous potential and we don't know how to use it, as if we were a Ferrari, but we don't know how to drive it. What's the point of having a Ferrari if we don't know how to exploit its potential? We are a Ferrari and we can know how to use it, if we understand our instruction manual, and understand how we work.

Have you ever heard of the term consciousness expansion? It is a mechanism in which Ayahuasca can bring this to you. Defining expansion of consciousness is not easy, many of us hear about it but don't know exactly what it is. I would like to invite you to a very didactic definition. Imagine that each of you is this room that we are in here and all these objects are characteristics of you, things that are part of you. Now imagine that I turn off the lights, cover all the windows, seal all the cracks in the doors, so that there is total darkness inside this room. Are you still you? It's still you with all your characteristics but you can't see anything because

it's dark and you end up bumping into things and you can't find the tools that can help you. Now imagine that I go to the window and make a hole in the window and that through this beam of light you can see a small part of the room. This little light inside the room is called consciousness, it's what [CENTER OWNER'S NAME REDACTED] knows about [CENTER OWNER'S NAME REDACTED] and it's what you know about him and that's why 99% of people when they say they know who they are, they are correct, because they don't they know the whole room, but only that small area. Some people don't understand what happens in their life because they only know what happens in that small area. The expansion of consciousness allows me to go to that window, open it and that beam of light will allow me, for the first time in my life, to illuminate an area of the room that I had never seen before.

Will drinking this tea clear my vision? No! I've been drinking this tea for 15 years and every time it lightens a little more, it lightens little by little, we can access areas, characteristics, and situations that I had never seen before. I always tripped over this chair every day, now I see this chair. A few hours after taking Ayahuasca, the beam of light returns to the size it had before and it's not that it doesn't do anything, because the Ayahuasca process is 100% conscious, everything done today you will remember tomorrow. You may not be seeing the chair but you will remember that you saw the chair. Ayahuasca is not a miracle tool because in the 15 years I have been using it, it has never removed the chair for me, I am the one who has to remove the chair, it just shows me. It clearly shows situations in your life that can be modified so that you can perform better in life. What do I call performance? It depends on each person, what you are looking for in life. The fact is that many people in life believe that performing well in life means having a more satisfying life, being able to fulfill more of their desires, earning more money, this concept changes after this experience, as we begin to have access to things that are outside the clear area, what is inside the clear area were things that we were often taught from an early age, a certain path to personal fulfillment: the path to success, the path to making money in what you do, which are valid and which are really good for us, but the room is not just that and that night you will be able to gain access.

In this culture, we learn a mold that human beings must fit into, mold themselves into to be socially accepted. The problem is that a lot of the time, being socially accepted in this way is not making you complete, happy. You wake up, spend energy, try hard, do your best, but you feel like you're not complete. There's something missing for all of us, I'm nothing different from you because I've been drinking tea for 15 years, but I have many different things from [CENTER OWNER'S NAME REDACTED] 15 years ago. Ayahuasca brings much more clarity to issues in my life, things that I waste less time on, for example things that are bad for me. Today, I banish it from my life or I don't allow it to harm me, as I did in the past, like negative emotions, negative thoughts.

One of the most wrong things, in my opinion, that they teach children, to everyone, every day, is that pleasure and happiness are very similar things. Pleasure and happiness are extremely different things. If we stop to think about this moment, there are some people in this city who are feeling a lot of pleasure right now, they are living in a wonderful neighborhood in [PLACE REDACTED] called Cracolândia. I assure you that they are feeling a lot of pleasure, but are they happy? Certainly not. Part of us learns that we will only be happy if we manage to do everything we want: 'I'll be happy the day I no longer have problems, the day my life is all right, the day I no longer have a headache with nothing,' forget it, this is a childish fantasy, this

won't happen, a problem is something that people will always have. And amazingly, problems are good for our growth. Happy people are not people who don't have problems, they are people who learn to manage their problems. Do you realize that it has nothing to do with doing everything I want to do? The unhappiest people I know are the people who do whatever they want to do. Often, happiness lies more in the renunciation of desires than in their fulfillment. I'm not referring to all desires, I'm not saying that pleasure is bad. I am inviting you to analyze your life to understand that many of your sufferings, the problems you have today are associated with the search for this pleasure.

...There's a phrase like this: Don't poke the jaguar with a short stick. I say: don't poke the jaguar with a long stick or any stick, stay away from the jaguar. When we identify something in our lives that is dangerous to our happiness, to our growth, the best thing you can do is stay away from that danger. A strong human being is not one who has no weaknesses, but one who knows the weaknesses he has. When you know yourself, you know your weaknesses, you can prevent yourself from falling into a hole. I stayed away from the jaguar, because the jaguar and I already had something that only hurt me, that only hurt me and I don't want to fall into that again. Each person must identify their temptation. The problems I had were different from what I have today when I arrived in this house 15 years ago, I continue to have problems and challenges not to fall into the hole. Some things we learn from pain, other things you don't need to suffer to learn. Ayahuasca taught me many things about love, when I arrived I had hit my head a lot. Ayahuasca was my last resort, I tried many things to improve my living conditions. I didn't suspect that she would change my life as much as she did. The reference we have for this medicine is not because it is our work, everyone who works with this medicine has had a very beautiful life transformation. She saved our lives and I'm sure she can do that in your life too...

...It has two important active ingredients: the main active ingredient that expands consciousness, which is called dimethyltryptamine or DMT, which is a chemical molecule very similar to a substance we have inside us called serotonin. Serotonin is a neurotransmitter that exists within me, within you, within every living being, which is important for a series of metabolic processes to occur, mainly for the functioning of our central sector, thought, cognition, all of this depends on serotonin. Our brain activity works through serotonin, there are also other substances, but it is the main one. This dimethyltryptamine or DMT is so similar to serotonin that it activates the same serotonin receptors throughout your body and with this, we get the effects of serotonin but with one difference, the quantity. It's as if you've taken a flood of serotonin into your body. But serotonin is modeled in our body, we produce it and it remains at a very high rate, then another substance comes to reduce this rate, Monoamine oxidase (MAO), which destroys excess serotonin, so there is no point in increasing the rate if I do not inhibit this enzyme that destroys serotonin.

In Ayahuasca, along with DMT, there is a substance called harmaline that temporarily deactivates this enzyme (MAO). Basically, Ayahuasca fills your body with serotonin and doesn't let it out for at least two hours, this is how long it takes for this enzyme to be inhibited. The photosensitive scanner that is placed on top of the human being's head measures brain activity, if it is placed on Talita's head, I will notice that 10% of the areas of her brain are illuminated, this is her activity level. Now, if I put it in an hour or so, after the effects of the ayahuasca, I will be able to see 70% of the activity, an activity 7 times greater, a brain activity that you have

never had before and you will see that it is completely different.

...You will notice a lot of things, not just defects, problems, errors. Ayahuasca reveals potential that you are unaware of, talents that you are unaware of and are not exploring. That's what it's for, on the one hand, it minimizes the things that get in the way of your life. On the other hand, it shows that we expect others and blame our frustrations. Sometimes what someone else does to me is no worse than what we do to ourselves. Thinking, hurting yourself, cultivating that energy. Ayahuasca works with character, improving us. Character is something that everyone says they have, the 'guy' could be in prison for 50 years and he'll say he has character. We justify many of our defects. The greatest compass for us to know how our character is, it is based on the things we need to do in secret, pay attention to this, the number of things we need to do in secret, shows that we are out of alignment with our truth. Character seems to be something good to be socially accepted. Character is good for one thing, so you don't suffer. When we have character, our life has quality, we move towards one thing. The freedom not to hide anything from anyone, not to be in public what you are hidden. And the freedom for me, [CENTER OWNER'S NAME REDACTED], to give my cell phone to my wife, that is freedom. For me, this is a positive thing. When we start to behave more honestly, more decently, we gain quality of life. I talk a lot to boys, I work with men: 'Men, imagine that you have a serious relationship, when you are on the street with your wife, and a very attractive girl passes by on the other side, who attracts attention, if you have any sense, will you look? Of course not! And if she says the clothes are short, you still agree. Now, what if you are alone? If you don't do it in front of her, why do you do it hidden? This is about being honest, not with your wife, but with yourself.

I don't want to be the man who needs to hide in front of others. Not to brag, I have a lot to change. But for me, change comes when we move towards not wearing a mask, being a single person, a transparent person and not hiding anything from ourselves. It is not with [CENTER OWNER'S NAME REDACTED], my wife, but with my own conscience. Every day I ask myself, if I die today, with what face, will I return home, to the spiritual plane. I won't go back with shame because 15 years ago, I had the courage to live a different life than the one I lived before, to be a better person. Not for my mother to be proud of me, but for me to be proud of myself and live well. It's not about showing off to others, but about cultivating a more satisfying, fuller, healthier life. Much of what I'm talking about may sound subjective, puritanical, trippy, but in 4 hours you'll understand what I wanted to say. Ayahuasca proves itself over time."

D.4 Dealing with repeat participants

Twelve participants entered the study twice—either both times as a no-show (i.e. they were scheduled to a ceremony, did not show up, then later they were scheduled to a second ceremony, and did not show up again), or one time as a no-show and one time as a ceremony attender. These participants were sent the follow-up surveys twice—once relative to the timeline of their first scheduled ceremony, and again relative to the timeline of their second scheduled ceremony. In the analysis, we keep only one set of surveys for each of these participants—i.e. we make it so that they only enter the study once. For the participants that were twice a no-show, we

keep only the surveys they answered associated with their first scheduled ceremony. For the participants that were once a no-show and once showed up, we keep only the surveys they answered associated with the ceremony in which they showed up—we keep the latter, rather than the former, to maximize our statistical power for our more central test of the effect of ayahuasca relative to placebo. Since only a handful of participants entered the study twice, our results are nearly identical if we instead include the full set of survey responses, with standard errors clustered at the participant-level.

D.5 Relation to pre-registration

We pre-registered the experiment in the AEA RCT Registry, with ID #10400, at https://www.socialscienceregistry.org/trials/10400. There are two key differences between the pre-registration and the current paper. First, in the pre-registration we describe two experiments: one in which the center assigned participants to a high or low dose of ayahuasca (diluted-dosage experiment), and a second in which the center assigned participants to a high dose of ayahuasca or a placebo, jurema. In this paper, we report the findings of the latter experiment. As we explain in the pre-registration, the purpose of the diluted-dosage experiment was to isolate the effects of ayahuasca, but there was a first stage problem: even those with the low dose often had meaningful trips. For example, 26% of the low-dose participants reported that their trip was the single most meaningful of their entire lives, and 38% reported having had visions. We successfully addressed this issue by moving to an experiment design with a non-ayahuasca placebo (jurema) group.

Second, we pre-registered both outcome measures related to well-being and a broader set related to decision-making and economic outcomes (e.g. employment status, savings, prosociality, etc.). In the current paper, we consider only the well-being outcomes,though we report these outcomes exhaustively. We are writing a separate paper on the effects on decision-making and economic outcomes. In addition, while we mention that the topic of the lecture alternated between "happiness" and "taming the mind," we do not report the effects of the lecture variation on trips and treatment effects in this paper.

Otherwise, we had aimed to reach "ten or so sessions" with the jurema experiment design; but we ran out of funding after completing six sessions. Related, our goal was to reach 150-300 people in each of the two treatment arms: ayahuasca versus jurema. We came close to this target, with 126 receiving jurema and 159 receiving ayahuasca (or 126 receiving ayahuasca if we exclude the sixth session in which, by mistake, all participants were given ayahuasca).