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ORIGINAL INVESTIGATION

Ayahuasca's 'afterglow': improved mindfulness and cognitive flexibility in ayahuasca drinkers

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Abstract

Rationale There is a growing body of evidence demonstrating the therapeutic potential of ayahuasca for treating depression and anxiety. However, the mechanisms of action involved in ayahuasca's therapeutic effects are unclear. Mindfulness and cognitive flexibility may be two possible psychological mechanisms. Like other classic psychedelics, ayahuasca also leads to an 'afterglow' effect of improved subjective well-being that persists after the acute effects have subsided. This period may offer a window of increased therapeutic potential.

Objective To explore changes in mindfulness and cognitive flexibility before and within 24 h after ayahuasca use.

Methods Forty-eight participants (54% female) were assessed on measures of mindfulness (Five Facets Mindfulness Questionnaire (FFMQ)), decentering (Experiences Questionnaire (EQ)), and cognitive flexibility (Cognitive Flexibility Scale (CFS)), and completed the Stroop and Wisconsin Picture Card Sorting Task (WPCST) before drinking ayahuasca, and again within 24 h.

Results Mindfulness (FFMQ total scores and four of the five mindfulness facets: observe, describe, act with awareness, and non-reactivity) and decentering (EQ) significantly increased in the 24 h after ayahuasca use. Cognitive flexibility (CFS and WPCST) significantly improved in the 24 h after ayahuasca use. Changes in both mindfulness and cognitive flexibility were not influenced by prior ayahuasca use.

Conclusions The present study supports ayahuasca's ability to enhance mindfulness and further reports changes in cognitive flexibility in the 'afterglow' period occur, suggesting both could be possible psychological mechanisms concerning the psychotherapeutic effects of ayahuasca. Given psychological gains occurred regardless of prior ayahuasca use suggests potentially therapeutic effects for both naïve and experienced ayahuasca drinkers.

Keywords Ayahuasca · Psychedelics · Mindfulness · Cognitive flexibility · Psychological flexibility · Psychological mechanisms

Introduction

Renewed interest in the effects of classical psychedelics is providing evidence for their potential efficacy in treating a range of psychiatric illnesses and specifically, in improving outcomes for treatment-resistant patients (Bouso and Riba 2014; Griffiths et al. 2016; Grob et al. 2011; Moreno et al. 2006). Given the high failure rates in current treatments, the search for alternative treatment strategies is crucial (Vollenweider and Kometer 2010). Ayahuasca is one such classic psychedelic with potential therapeutic effects, shown to be beneficial in treating depression (Griffiths et al. 2016), anxiety (Grob et al. 2011), and substance abuse disorders (Bouso and Riba 2014).

Ayahuasca is a dimethyltryptamine (DMT) containing psychoactive plant tea most commonly combining two plants with water: the vine of *Banisteriopsis caapi* (*B. caapi*) and the leaves of *Psychotria viridis* (*P. viridis*) (Dominguez-Clavé et al. 2016). The combination of these plants renders the DMT in *P. viridis* orally active by inhibiting its degradation in the body and allowing uptake into the central nervous system, producing an altered state of consciousness that lasts between 4 and 6 h, with peak effects between 1 and 2 h after ingestion (Prickett and Liester 2002).

Like other classical psychedelics, ayahuasca's primary neural mechanism of action is as a 5HT agonist (Sampedro et al. 2017). Secondary effects as a 5HT2a agonist are thought to underlie the increased positive mood experienced in

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ayahuasca users for up to 2 months after use, commonly referred to as the 'afterglow' period (Sampedro et al. 2017). However, given the complexity and high comorbidity of the mental health problems that ayahuasca has been shown to effect, there are likely to also be psychological mechanisms that contribute to the increased psychological well-being observed in ayahuasca users in this afterglow period and longer term (Soler et al. 2016). Mindfulness and cognitive flexibility have recently been suggested as two such possible mechanisms which may be associated with ayahuasca's therapeutic effects (Kuypers et al. 2016; Carhart-Harris et al. 2014).

Mindfulness is a multi-faceted construct which is broadly defined as 'paying attention in a particular way: on purpose, in the present moment, and non-judgmentally' (Kabat-Zinn 2003). It is considered to have five distinct facets which can be measured using the Five Facets Mindfulness Questionnaire (FFMQ; Baer et al. 2006) including (1) observing, (2) describing, (3) acting with awareness, (4) non-judging of inner experience, and (5) non-reactivity to inner experience (Baer et al. 2006). Mindfulness-based interventions have proven clinical efficacy in treating numerous psychiatric disorders, including depression, anxiety, and addictions (Goldberg et al. 2018). Decentering is a closely related psychological construct, which is the ability to take a detached view of one's own thoughts and emotions, considering them as temporary events of the mind (Fresco et al. 2007). It is considered to mediate positive behavioural and psychological changes following mindfulness training (Hayes-Skelton and Graham 2013). Both decentering and mindfulness have been shown to increase following a single dose of ayahuasca. Soler et al. (2016) found levels of mindfulness (as measured by the FFMQ) and decentering (as measured by the Experiences Questionnaire; Fresco et al. 2007) significantly increased in the 24 h after ingestion in 25 ayahuasca users (23 had prior experience with ayahuasca, using on average 79 times (range 1–500)). They found that ayahuasca affected the mindfulness facets differently, with only non-judging and non-reactivity to inner experience significantly increasing following use. Uthaug et al. (2018) have since found three of the five mindfulness facets (non-judging, acting with awareness, and observing) increased the day after ayahuasca use in a large ($N = 57$) sample of ayahuasca users with a range of experience, which significantly correlated with a reduction in depression scores. Sampedro et al. (2017) replicated Soler et al.'s (2016) findings in 16 experienced ayahuasca users (previous use of an average of 62 ± 99 times), and further assessed the neural correlates 24 h after use and again 2 months later. They found that increased connectivity between the anterior cingulate cortex (ACC), a structure involved in emotional processing and cognitive control, and the posterior cingulate cortex (PCC), a key hub of the default mode network (DMN) involved in the sense of 'self', predicted increases in mindfulness 24 h after using ayahuasca, and sustained elevations in the non-judge facet of mindfulness 2 months after use. Ayahuasca may therefore lead to mid-term increases in mindfulness which suggests a therapeutic window of opportunity lasts beyond the acute effects of ayahuasca. Another recent study showed two ayahuasca sessions led to increases in the non-judging subscale of the FFMQ which are comparable with gains made in an 8-week Mindfulness-based Stress Reduction course (Soler et al. 2018). Improving this capacity is therapeutically significant as it promotes a person's ability to tolerate potentially distressing thoughts, emotions, and life situations by taking a less judgemental and more impersonal stance towards them (Soler et al. 2018). Taken together these findings support the assertion of Dominguez-Clave et al. (Dominguez-Clavé et al. 2016) that the mindfulness enhancing properties of ayahuasca could be used therapeutically to promote emotional reprocessing in patients with depression, addiction, and personality disorders.

A second possible psychological mechanism that could account for the psychotherapeutic benefits seen with ayahuasca is cognitive flexibility. Broadly defined, cognitive flexibility is the ability to shift perspective or approach in order to adapt to change in the environment (Johnco et al. 2014) and involves executive function abilities of problem solving and response inhibition (Johnco et al. 2014). Neuro-anatomically, cognitive flexibility is associated with the ACC and medial pre-frontal cortex (Bissonette et al. 2013; Kim et al. 2011). More recently its definition has expanded to a broader concept of 'mental flexibility' which also involves psychological and behavioural processes (Martin and Rubin 1995, p. 623). Higher cognitive flexibility has been associated with increased psychological well-being (Hayes et al. 2006), whereas cognitive inflexibility or rigidity is associated with psychopathology (Hayes et al. 2006). Low cognitive flexibility can also be a barrier to achieving therapeutic outcomes in treatment, and therapeutic approaches which help to increase cognitive flexibility have shown efficacy (Johnco et al. 2014). A growing body of neuropsychological evidence points to the potential of cognitive flexibility as a psychological mechanism which is involved in ayahuasca's therapeutic effects. Ayahuasca has been shown to acutely affect three key brain networks which are implicated in cognitive flexibility: DMN (in which the medial pre-frontal cortex (mPFC) and PCC is a key hub), central executive network (CEN), and the salience network (SN) (in which the ACC is involved). Ayahuasca temporarily disrupts the neural hierarchies of these networks by exciting posterior regions whilst loosening the 'cognitive grip' exerted by frontal regions responsible for executive control (Alonso et al. 2015). Palhano-Fontes et al. (2015) also found decreased functional connectivity in parts of the DMN acutely under the effects of ayahuasca, consistent with other classical psychedelics (Hermle et al. 1992; Vollenweider et al. 1997; Gouzoulis-Mayfrank et al. 1999; Riba et al. 2006).

Ayahuasca has also been associated with better neuropsychological performance in experienced users relative to controls and less experienced users in aspects of cognitive flexibility. Bouso et al. (2012) found experienced ayahuasca users ($n = 127$) performed better than closely matched controls both at baseline and 1 year later, on two measures of cognitive flexibility: Stroop and the Wisconsin Picture Card Sorting Task (WPCST) suggesting repeated ayahuasca use may be associated with sustained improvements in cognitive flexibility. Neuroanatomically, Stroop and the WPCST are associated with activation in the mPFC and ACC. The mPFC is part of the DMN, affected acutely after ayahuasca ingestion. The ACC is an area of the brain shown to be thicker in experienced ayahuasca users than in controls (Bouso et al. 2015). Interestingly, studies of executive function in people with severe depression found they performed worse than healthy controls on the WPCST (Leinonen, T. I. K.-M., Leinonen 2000). Given evidence of long-term structural brain changes to the PCC and ACC in experienced ayahuasca users (Bouso et al. 2015), it is possible that ayahuasca use leads to structural brain changes that account for positive changes in cognitive flexibility (Bouso et al. 2012). As well as explaining neuropsychological differences (Bouso et al. 2013), this could also potentially account for the increased significance in changes to mindfulness scores found by Soler et al. (2016) after controlling for previous ayahuasca use as a secondary analysis in their study. However, not all studies have shown acute or long-term differences in cognitive flexibility between experienced ayahuasca users and psychedelic-naïve controls or inexperienced users (Barbosa et al. 2016; Doering-Silveira et al. 2005), nor is it clear if changes in cognitive flexibility occur during both the acute and subacute phases of ayahuasca ingestion. For example, Kuypers et al. (2016) found improvements in more flexible divergent thinking acutely under the effects of ayahuasca, whereas Uthaug et al. (2018) found divergent thinking was not improved the day after ayahuasca use, but less flexible convergent thinking was significantly increased 4 weeks later. Given these inconsistencies across the literature with regard to changes in cognitive flexibility, further research is needed.

In summary, previous research has found increases in mindfulness in the 'afterglow' period (24 h) following ayahuasca use, as well as an association between the acute effects of ayahuasca and changes in cognitive flexibility and associated neural networks. Long-term changes in cognitive flexibility in experienced ayahuasca users may also be linked to structural brain changes associated with ayahuasca exposure (Bouso et al. 2012, 2015), but whether changes in cognitive flexibility occur specifically in the afterglow period needs further exploration. To further explore whether mindfulness and cognitive flexibility are potential psychological mechanisms associated with ayahuasca's therapeutic effects, the current study aimed to assess changes in mindfulness, decentering, and cognitive flexibility both at baseline (pre-ayahuasca) and within 24 h following ayahuasca use (post-ayahuasca). Previous research has distinguished between experienced and inexperienced users (i.e. based on the amount of prior use), yet we are still unclear on the role of prior use in relation to these specific psychological mechanisms; therefore, depending on the range of prior use reported, it may be necessary to control for prior ayahuasca experience. Given the previous literature demonstrating an association between ayahuasca use and mindfulness gains in this 24-h afterglow period, we expect to see a significant increase in participants' total mindfulness and decentering scores in the 24 h following ayahuasca use relative to baseline, and to determine whether there are any changes in cognitive flexibility in this same period.

Method

Participants

Participants were a self-selected sample, recruited through advertisements emailed to the mailing lists of groups with an interest in psychedelics. Participants were eligible to take part in the study if they were over 18, had used ayahuasca in the past, or had considered using it in the future. Participants were excluded if they self-reported current or prior drug dependency (including alcohol), current psychiatric or medical diagnoses, and use of prescribed psychiatric medication; were receiving any form of psychological treatment; and had a history of brain damage, head injury, or epilepsy. Participants were required to abstain from using any drugs or alcohol (except nicotine) for at least 24 h prior to assessment. The study was granted ethical approval by the University of East London Ethics Committee.

A total of 54 participants were initially recruited as meeting the inclusion criteria. Forty-eight completed both assessment points (with 6 failing to attend time point 2 assessment point). Twenty-six (54%) were female. Mean age was 38.48 (SD = 7.21) years. Participants were predominantly white (67%, $n = 32$), highly educated (83%, $n = 40$; educated to degree level or above), and with English as their first language (75%, $n = 36$). The previous number of times participants had used ayahuasca ranged from 0 to 130 times. Six (12.5%) were psychedelic-naïve participants, 10 reported previous use between 1 and 5 times (20.8%), 14 had used 6–10 times (29.2%), and 18 had used > 10 times (37.5%). Total years of use ranged from 0 to 9 years. One participant (2.1%) had last used ayahuasca 2 weeks before testing, and the remaining (97.9%) had not used ayahuasca for 1 month or more. There were no ayahuasca-dependent participants (as measured by the Severity of Dependence Scale; Gossop 1995).

Setting

Participants were members of an ayahuasca-using group who attended one of two secular ayahuasca ceremonies in a naturalistic setting between 2017 and 2018. Both ceremonies were conducted in a group format with the same proceedings. The researcher met with participants prior to the ceremony and again in the 24 h afterwards to conduct questionnaire and neuropsychological task assessments.

Measures

Following informed consent, participants completed the following measures in the order presented below. They were completed at time point 1 (baseline) and again approximately 24 h after using ayahuasca (time point 2). Each assessment session lasted approximately 30 min.

Personal history questionnaire This questionnaire captures basic demographic information including: gender, age, ethnicity, first language and highest level of education. Drug use history questionnaire was designed specifically for this study and addressed participants' self-reported drug use (including alcohol and tobacco and other classic psychedelics) and details on patterns of ayahuasca use, e.g. date first taken, date last taken, estimated lifetime use, and use in the last 12 months.

Severity of Dependence Scale (Gossop 1995) The Severity of Dependence Scale (SDS) is a brief 5-item questionnaire adapted to assess participants' levels of psychological dependence on ayahuasca. Items are scored on a 4-point scale ranging from 0 to 3. Higher total scores indicate higher levels of dependence. The scale has demonstrated excellent psychometric properties and validity for use with a diverse range of drug users (Gossop 1995).

Five Facets Mindfulness Questionnaire-Short Form (Baer et al. 2006) The FFMQ-Short Form is a 24-item validated self-report questionnaire which measures five mindfulness facets: (1) observe: noticing internal and external experiences, e.g. body sensations, thoughts, emotions, sounds: (2) describe: putting words to or labelling the internal experience; (3) act with awareness: focusing on activities in the present moment rather than responding habitually; (4) non-judge: taking a non-evaluative view of internal and external experiences in the present moment; and (5) non-react: maintaining equanimity with the flow of thoughts and feelings as they arise without getting caught up in or carried away by them (Bohlmeijer et al. 2011). Items are scored on a 5-point Likert scale: from 1 (never or very rarely true) to 5 (very often or always true). Example items include 'I tell myself I shouldn't be feeling the way I'm feeling' and 'I pay attention to physical experiences such as the wind in my hair or the sun on my face'. Higher scores indicate higher levels of mindfulness, with a total score and five subscale scores. The FFMQ has demonstrated good internal reliability and adequate psychometric properties in both clinical and non-clinical samples (Baer et al. 2008) (Cronbach's alpha = 0.85 in the current sample).

Experiences Questionnaire (Fresco et al. 2007) The Experiences Questionnaire (EQ) is a validated 11-item measure of decentering, for example 'I can slow my thinking at times of stress' and 'I can observe unpleasant feelings without being drawn into them'. Higher total and mean scores represent higher levels of decentering. EQ items are scored on a 5-point Likert scale ranging from never (1) to all the time (5). The EQ has demonstrated good construct validity and internal consistency, for use in meditating and non-meditating samples (Soler et al. 2014) (Cronbach's alpha = 0.84 in the current sample).

Cognitive Flexibility Scale (Martin and Rubin 1995) The Cognitive Flexibility Scale (CFS) is a validated measure of cognitive flexibility, measuring the ability to switch between thoughts and actions, based on the willingness to be flexible, a belief in self efficacy and awareness of alternative ways of responding to situations and experiences (Martin and Rubin 1995), and has proved effective in predicting symptoms in depression, anxiety, and substance abuse disorders as well as psychological well-being in non-clinical samples (Lee and Orsillo 2014). Consisting of 12 items, each is scored on a 6-point Likert scale ranging from (1) strongly disagree to (6) strongly agree. An example item is 'I have many possible ways of behaving in a given situation'. Higher total scores indicate higher cognitive flexibility (Cronbach's alpha = 0.81 in the current sample).

Stroop colour and word task (Stroop; Stroop 1935) A computerised version of the Stroop test was used, measuring aspects of cognitive flexibility including selective attention, conflict monitoring, and resistance to interference. Thirty-eight colour words were displayed in turn, on screen ('red', 'green', 'blue') in congruent and incongruent colours. Participants had to use a key on the keyboard that corresponded to a colour word (Z = red, X = blue, N = green, M = yellow) to select the written colour word whilst ignoring the colour it is written in. Performance was measured by number of errors and reaction time in the congruent and incongruent conditions. Better performance was reflected as lower mean reaction times and lower number of mean errors. A parallel version with different trial orders was used at each time point.

Wisconsin Picture Card Sorting Task (Berg 1948) The WPCST is the most widely used test of cognitive flexibility (Heaton 1981) consisting of 'set-shifting', measuring cognitive flexibility by requiring participants to creatively problem solve to

work out the picture card sorting rule and adapting to changing rules whilst inhibiting impulsive responding (Berg 1948). A simplified, computerised version of the WPCST was used whereby participants had to match 36 test cards to stimulus cards presented on screen, without knowing the rule by which the test card matched the stimulus cards. Cards were displayed in 3 separate trial blocks, one for colour, shape, and number. The sorting rule changed for each trial block (with no warning). In each trial, 4 stimulus cards appear at the top of the computer screen. These cards vary in colour, type of shape, and number of shapes on the cards. A test card is then displayed at the bottom of the screen. Participants were instructed to match the test card with one of the 4 stimulus cards by clicking on the stimulus card they thought it matched. Feedback is displayed on screen after a selection indicating whether the card had been matched correctly or not. Better performance was indicated by a higher percentage of correct answers, indicating a participant had worked the sorting rule out more quickly and continued to sort cards correctly throughout the remainder of the trial bock. Mean reaction times of correct answers was also calculated, faster reaction times indicating better performance. A parallel version of this task was used at each time point (pre- and post-ayahuasca), with different orders of the trials and sorting rules.

Data analysis

Total and mean scores were calculated for all questionnaire measures. Stroop task mean scores were calculated for reaction time and number of errors by congruency conditions. WPCST mean scores were calculated for reaction time and mean percentage of the number of correct answers. Of the 48 participants who completed both time points, there were no incomplete datasets. Data was analysed using SPSS 23. Given the wide range of prior ayahuasca use in the sample (from 0 to 130 times), repeated measures ANCOVAs were conducted on all outcome measures: the FFMQ, EQ, CFS, and WPSCT between the two time points (baseline pre-ayahuasca and 24-h post-ayahuasca), and prior ayahuasca use (lifetime) as the covariate. A 2 × 2 repeated measures ANCOVA was conducted on the Stroop reaction times based on congruency (congruent and incongruent) and time (baseline and post-ayahuasca) to establish the interference effect over time, with previous ayahuasca use (lifetime) as the covariate. A significance cutoff of $p = 0.05$ was used for all statistical analyses.

Results

Means (and SD) for all questionnaires at both time points are shown in Table 1. Mean scores showed increases on all questionnaire measures of mindfulness and cognitive flexibility and all five subscales of the FFMQ between the two time points. Significant increases were found for the FFMQ total ($F(1,46) = -8.21$, $\eta^2 = 0.15$), CFS ($F(1,46) = 8.25$, $\eta^2 = 0.15$), and EQ ($F(1,46) = 4.15$, $\eta^2 = 0.08$). Of the five FFMQ subscales, significant differences were found for observe ($F(1,46) = 13.38$, $\eta^2 = 0.24$), describe ($F(1,46) = 3.76$, $\eta^2 = 0.08$), act with awareness ($F(1,46) = 7.08$, $\eta^2 = 0.13$), and non-react ($F(1,46) = 0.02$, $\eta^2 = 0.10$) (see Table 1 for further details). In all cases, there was no significant covariate interaction between time and previous ayahuasca use (all p's > 0.05).

Neuropsychological task performance

For WPCST, means (and SD) for the WPCST outcome measures at both time points are reported in Table 1. There was no significant effect of time on reaction times on the WPSCT ($F(1,46) = 2.30$, $\eta^2 = 0.05$). Participants made significantly more correct responses 24 h after ayahuasca relative to before ($F(1,46) = 2.30$, $\eta^2 = 0.05$). In all cases, there were no significant covariate interactions between time and previous ayahuasca use (all p's > 0.05). For Stroop, Figs. 1 and 2 show the mean reaction times (ms) and number of errors for the Stroop by congruency and over the two time points. There was a significant main effect of condition on reaction time ($F(1,46) = 58.28$, $\eta^2 = 0.56$) and number of errors ($F(1,46) = 20.42$, $\eta^2 = 0.31$). There was no significant main effect of time on reaction time ($F(1,46) = 1.65$, $\eta^2 = 0.04$) or number of errors ($F(1,46) = 1.64$, $\eta^2 = 0.03$). There was a significant interaction between time and condition on number of errors ($F(1,46) = 4.11$), but not for reaction time ($F(1,46) = 0.02$, $\eta^2 = 0.001$) (see Fig. 1). In all cases, there was no significant covariate interaction between time and previous ayahuasca use (all p's > 0.05).

Discussion

The current study aimed to assess changes in mindfulness, decentering, and cognitive flexibility over two time points: baseline (pre-ayahuasca) and within 24 h following ayahuasca use (post-ayahuasca), whilst controlling for prior ayahuasca use. We found mindfulness (as measured by the FFMQ) and decentering (measured by the EQ) significantly increased in the 24 h after use. Cognitive flexibility (as measured by the CFS and the WPCST) was also significantly improved in the 24 h after ayahuasca use compared with that in baseline. Changes in both mindfulness and cognitive flexibility were not influenced by prior ayahuasca use. This is in-keeping with previous research looking at mindfulness and cognitive flexibility in the afterglow period which have found no differences in changes associated with previous use (e.g. Uthaug et al. 2018; Sampedro et al. 2017). Collectively, therefore, evidence

Table 1 Mean (SD) and significant and observed power for all measures of mindfulness and cognitive flexibility at time point 1 (baseline) and time point 2 (post-ayahuasca)

	Baseline	Post-ayahuasca	*p*	Observed power
FFMQ (total)	3.58 (0.46)	3.75 (0.62)	0.003*	0.80
FFMQ subscales				
1. Observe	3.99 (0.76)	4.23 (0.79)	< 0.001**	0.95
2. Describe	4.76 (0.89)	5.00 (0.95)	0.03*	0.48
3. Act with awareness	3.55 (0.67)	3.74 (0.79)	0.005*	0.74
4. Non-judge	3.23 (0.78)	3.33 (0.92)	0.06	0.33
5. Non-react	3.36 (0.76)	3.55 (0.81)	0.015*	0.61
EQ	40.60 (5.48)	41.75 (7.29)	0.025*	0.51
CFS	57.38 (7.11)	59.35 (7.87)	0.006*	0.80
WPCST				
Reaction time (ms)	3572.38 (2615.94)	4195.61(4617.67)	0.14	0.32
% of correct responses	63 (15)	71 (14)	0.005*	0.82

FFMQ Five Facets Mindfulness Questionnaire, *EQ* Experiences Questionnaire, *CFS* Cognitive Flexibility Scale, *WPCST* Wisconsin Picture Card Sorting Task, *ms* milliseconds. *$p < 0.05$, **$p \leq 0.001$

suggests even naïve users can potentially benefit from these mindfulness and cognitive flexibility gains; however, this may be only in the short term (up to 4 weeks) which contradicts evidence indicating long-term changes in cognitive flexibility (Bouso et al. 2012). Thus, to clearly elucidate the role of prior use on such psychological mechanisms both in the short and in the long terms, more controlled studies are needed.

Self-reported levels of mindfulness and decentering were found to be increased in the 24 h after drinking ayahuasca, with increases seen in four of the five subscales of the FFMQ (observing, describing, acting with awareness, and non-reactivity to inner experience) indicating that both attentional and emotional acceptance facets of mindfulness were affected by ayahuasca use. These findings are consistent with previous studies (Uthaug et al. 2018; Soler et al. 2016; Sampedro et al. 2017) insofar as they demonstrate overall mindfulness (assessed by total scores on the FFMQ) and decentering increased in the 24 h after drinking ayahuasca. However, differences between studies reside in the findings on individual subscales. Two of these previous studies found changes on only two of the five subscales (non-reactivity and non-judging of inner experience), both of which represent facets of emotional acceptance, whereas in line with Uthaug et al. (2018), we have further demonstrated effects of ayahuasca on two of the same attentional facets—observing and acting with awareness—and our study has additionally found the describing subscale to be significantly increased following ayahuasca use. Together these findings suggest that both attentional and emotional acceptance facets are affected by ayahuasca use. Inconsistencies in the findings for the facet subscales could be explained by the differences in samples (e.g. sample size, range of ayahuasca use) and measures. For example, all previous studies (Soler et al. 2016; Sampedro et al. 2017) have used the full length 39-item version of the FFMQ. Equally

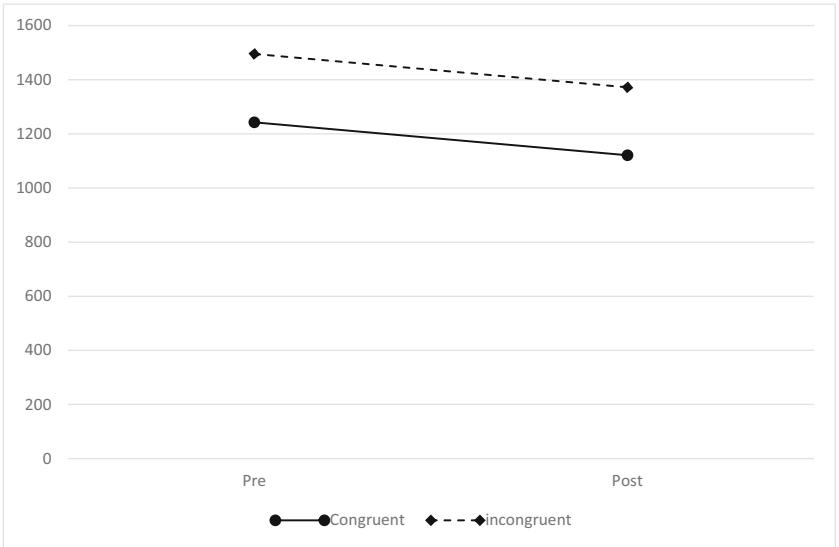

Fig. 1 Mean Stroop reaction times (ms) by congruency and time (pre- and post-ayahuasca use)

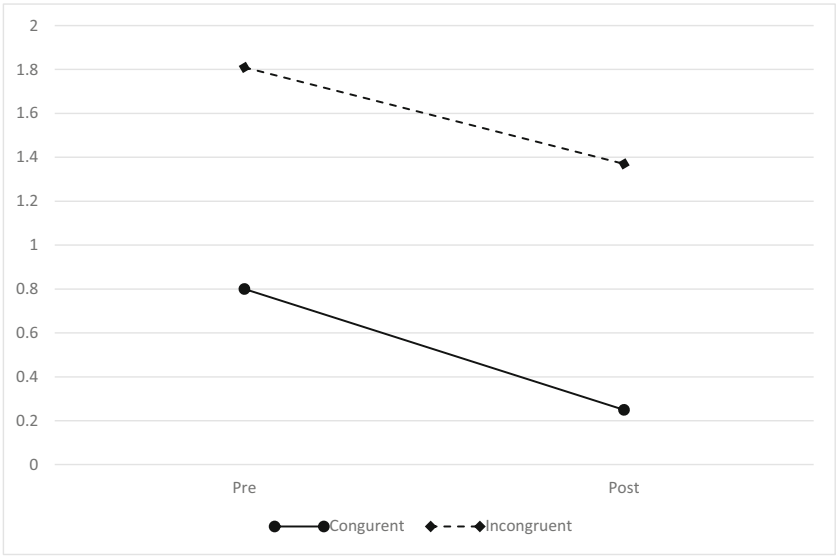

Fig. 2 Mean Stroop errors (*n*) by congruency and time (pre- and post-ayahuasca use)

studies looking at mindfulness gains following meditation training also report inconsistencies in facet-level changes and suggest different amounts of previous meditation experience may account for these inconsistencies (Pang and Ruch 2018). As neither this nor previous studies have controlled for previous meditation experience within the samples, this could account for such inconsistencies, and future research should control for this. However, given that an improvement in decentering abilities (measured by the EQ) was found in addition to one of the emotional acceptance facets in the current study following ayahuasca use, further supports the notion that ayahuasca has the capacity to affect both attentional and emotional acceptance components of mindfulness in the afterglow period.

This is because decentering to some extent involves a non-evaluative (or non-judgemental) perception of present moment experience in order for a person to take a more detached stance from their experiences as they arise into awareness. Given that changes in mindfulness following ayahuasca use remained significant regardless of previous ayahuasca use in the current study, supports previous findings (e.g. Soler et al. 2016) that ayahuasca can affect mindfulness abilities in experienced ayahuasca users as well as in less experienced users, even in psychedelic-naïve users. Clinically this is particularly beneficial since it suggests even those who are naïve to ayahuasca may benefit from mindfulness gains following a single ayahuasca session. The current findings suggest mindfulness warrants further investigation as a possible psychological mechanism of ayahuasca associated with its therapeutic potential. Further research exploring how mindfulness is affected beyond the 24-h 'afterglow' period, would offer further insight into the therapeutic window of such mindfulness gains and whether there are any longer term gains made by experienced users in mindfulness or cognitive flexibility.

The current study reports significant differences in cognitive flexibility 24 h after ayahuasca ingestion relative to baseline, regardless of prior ayahuasca use. Evidences for changes in flexible thinking in this study come from both a subjective self-report questionnaire measure (e.g. significantly higher mean scores on the CFS 24 h after ayahuasca use) and a more objective measure of cognitive flexibility, the WPCST. The mean number of correct answers on the WPSCT was significantly increased after ayahuasca use, with reaction times maintained, suggesting accuracy was improved without a significant slowing of response time. This is contrary to the findings of Uthaug et al. (2018) who assessed cognitive flexibility the day after ayahuasca and 4 weeks later with the Picture Concept Task. They found no significant differences for more flexible divergent thinking at either time point compared with baseline, and convergent thinking was significantly increased only at the 4-week point. The difference in findings could be a result of the different tasks used which may tap into a number of different aspects of cognitive flexibility, or indeed could perhaps be measuring two distinct but overlapping constructs (e.g. creativity (PCT) and cognitive flexibility (WPCST)). The improvements shown in cognitive flexibility in the current study are consistent with recent neurobiological research into ayahuasca, reporting changes to neural networks associated with cognitive flexibility, both acutely and in the afterglow period (and up to 2 months after use) (Sampedro et al. 2017). Changes to neural network functioning in this period may also alter neuropsychological functioning which could help to account for the changes in cognitive flexibility shown in this study. Whilst the Stroop findings failed to show an effect of ayahuasca on Stroop interference (arguably cognitive flexibility), there was some indication ayahuasca had an effect on general Stroop task performance, since errors in the incongruent condition were significantly reduced post-ayahuasca, indicating performance improvements specifically on

interference trials of the Stroop and such improvements warrant further investigation. Such changes in cognitive flexibility could be therapeutically significant because a loosening of 'cognitive grip' may be helpful for example in depressed patients who suffer from ruminative thinking and are 'stuck' in certain patterns of thoughts and behaviours. Supporting patients to consider alternative behavioural strategies and broaden perspectives is a key therapeutic goal of cognitive behavioural therapy (Kuypers et al. 2016). Given the current study reports changes in cognitive flexibility in both subjective and more objective task-based measures, therefore lends support to the assertion that cognitive flexibility is another potential psychological mechanism of action involved in the therapeutic effects of ayahuasca.

Whilst this study shows both improved cognitive flexibility and mindfulness gains in the afterglow period, it is not without its limitations. Firstly, it needs acknowledging that the WCST and the Stroop are very prone to learning and practice effects. Whilst parallel versions of the tasks were used for different time periods (pre and post) with different trial orders and sorting rules (in the case of the WCST) applied in an attempt to reduce these effects, learning and practice effects cannot be ruled out. Secondly, drug use data is self-reported and not biologically verified. In addition, the dose of ayahuasca taken by participants was unknown to the researchers and not recorded. The a priori hypothesis was to assess any changes within the 'afterglow period'; as such, we did not capture any data on the acute effects, and therefore are unable to assess any influence of such pre-post-acute effects on these changes. The absence of a control group also limits the generalisation of findings. Whilst the current study employed a good sample size of healthy users, they were a self-selected sample and largely experienced with ayahuasca, limiting the generalisability of the findings to psychedelic-naïve and clinical samples. However, relative to previous studies investigating mindfulness and neuropsychological functioning of ayahuasca users, the current sample was considerably less experienced overall in terms of previous ayahuasca use which is a strength.

In conclusion, the present study provides further evidence of ayahuasca's ability to enhance mindfulness and highlights it as a potential psychological mechanism of the psychotherapeutic effects of ayahuasca. In addition, it is the first to report that ayahuasca improves cognitive flexibility in the 'afterglow' period and suggests this is another possible psychological mechanism worthy of further exploration. Given that prior ayahuasca exposure had no significant effect on gains made to mindfulness and cognitive flexibility in the afterglow period highlights the potential beneficial effects of this psychedelic to both naïve and experienced users. The 'afterglow' effect of ayahuasca is significant therapeutically, and understanding the psychological mechanisms which occur during this period will be essential in developing effective ayahuasca-assisted treatments.

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Compliance with ethical standards

The study was granted ethical approval by the School of Psychology, University of East London's Ethics Committee.

Conflict of interest The authors declare that they have no conflict of interest.

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