

Supplemental Information

DMT, Madness, and Healing: Psychosis Model, Therapy Model, and Their Relations to Mystical Experiences and Positive Emotionality

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Supplemental Methods

Psychedelic Experiences

Intensity was measured on a visual analogue scale (VAS) from 0 (no effect) to 100 (extremely intense effect).

The 5D-ASC measures altered states of consciousness by 94 items on a VAS from 0 (no, not more than usual) to 100 (yes, much more than usual). The original German questionnaire comprises a total score and five larger dimensions Oceanic Boundlessness, Dread of Ego Dissolution, Visionary Restructuralization, Auditory Alterations, and Vigilance Reduction [1]. The Brazilian version (6D-ASC) comprises the same dimensions – composed of different items – and an additional dimension, Joyfulness [2]. We previously reported the results of the original dimensions [3] and reanalysed here the Brazilian dimensions published in the meantime. Furthermore, for both original and Brazilian version, the first three dimensions compose the 11-ASC, including a total score and the eleven factors Experience of Unity, Spiritual Experience, Blissful State, Insightfulness, Disembodiment (dimension Oceanic Boundlessness), Impaired Control and Cognition, Anxiety (dimension Dread of Ego Dissolution), Complex Imagery, Elementary Imagery, Audio-Visual Synaesthesia, and Changed Meaning of Percepts (dimension Visionary Restructuralization) [2,4].

The HRS assesses psychedelic experiences using 100 items rated mainly on a 5-point Likert scale from 0 (not at all) to 4 (extremely) [5]. The original, unvalidated factor structure comprises Intensity, Somaesthesia, Affect, Perception, Cognition, and Volition [5]. Although translated into Brazilian Portuguese, this version has not been validated [6]. We previously reported both the original structure and the only validated Spanish version [3], validated in 158 ayahuasca users and comprising Sensitive Distortion, Cognitive Distortion, Agitation, Security/Control, Visual Distortion, Quality of the Experience [7]. Recently, an updated eight-factor structure was derived from a pooled multi-study sample of 599 participants across 13 psychoactive substances [8]. We therefore reanalysed the HRS using these factors Vision, Meaningfulness, Dysphoria, Euphoria, Somesthesia, Auditory and Minor Senses, Liking, and Volition.

The MEQ measures mystical experiences by 30 items on a 6-point Likert scale from 0 (no, not at all) to 5 (extreme, more than ever before in my life). The items compose a total score, four factors, and four subfactors (Mystical, including Internal Unity, External Unity, Noetic Quality, and Sacredness; Positive Mood; Transcendence of Time and Space; Ineffability) [9].

Aberrant Salience

The five factors of the Aberrant Salience Inventory (ASI) are interpreted as following: Increased Significance – attributing exaggerated importance to trivial events; Senses Sharpening – refined sensory perception; Impending Understanding – feeling close to an important revelation; Heightened Emotionality – anxious or overwhelming emotional experiences; and Heightened Cognition – feeling part of something important [10].

For our previous LSD study [11], the ASI was translated into Brazilian Portuguese and adapted as a state measure by converting items from present tense (“do you ever feel”) to the past tense (“did you feel”) to assess acute effects. Validation of this Brazilian state version confirmed the five-factor structure, although with slightly different item compositions [12].

Moreover, our validation work proposed an alternative four-factor structure in which the single-item factor Impending Understanding (consisting only in the item #6) loaded onto Heightened Cognition [12]. To explore whether this slightly changed factor composition of Heightened Cognition would change the results, this factor was additionally analysed.

All items and their factor loadings in the original English trait scale and in the adapted Brazilian state scale with five and four factors, respectively, are listed in **table S1**.

Table S1. Item composition for the factors of the Brazilian state version of the Aberrant Saliency Inventory (ASI).

Item no.	Item	Original Factor	Brazilian 5 Factors	Brazilian 4 Factors
1	Certas coisas triviais de repente pareceram especialmente importantes ou significativas para você?	Sign	Sign	Sign
2	Você sentiu que estava à beira de algo realmente grande, mas não teve certeza do que era?	Unde	Cog	Cog
3	Seus sentidos pareceram aguçados?	Shar	Shar	Shar
4	Você sentiu que estava se aproximando rapidamente ao auge de seus poderes intelectuais?	Cog	Cog	Cog
5	Você notou pequenos detalhes que não havia percebido antes e que pareceram importantes?	Sign	Sign	Sign
6	Você sentiu que era importante para você descobrir algo, mas não tinha certeza do que era?	Unde	Unde	Cog
7	Você se sentiu especialmente religioso(a) ou místico(a)?	Cog	Cog	Cog
8	Você teve dificuldade de identificar se estava empolgado(a), assustado(a), aflito(a) ou ansioso(a)?	Emo	Emo	Emo
9	Você sentiu sua percepção mais aguçada?	Shar	Shar	Shar
10	Você sentiu necessidade de dar sentido a situações ou ocorrências aparentemente aleatórias?	Sign	Sign	Sign
11	Você sentiu que estava encontrando a peça que estava faltando em um quebra-cabeça?	Unde	Cog	Cog
12	Você sentiu que podia ouvir com uma clareza maior?	Shar	Shar	Shar
13	Você sentiu que era uma pessoa especialmente evoluída espiritualmente?	Cog	Cog	Cog
14	Observações normalmente insignificantes assumiram um significado ameaçador?	Emo	Emo	Emo
15	Você sentiu que as músicas pareceram ter um significado importante para sua vida?	Sign	-	-
16	Você atribuiu importância a objetos que normalmente não atribuiria?	Sign	Sign	Sign
17	Você sentiu que estava prestes a descobrir algo realmente grande ou importante, mas não teve certeza do que era?	Unde	Cog	Cog
18	Seu paladar lhe pareceu mais aguçado?	Shar	Shar	Shar
19	Você sentiu que os mistérios do universo estavam se revelando para você?	Cog	Cog	Cog
20	Você se sentiu superestimulado(a) por coisas ou experiências que normalmente são administráveis?	Emo	-	-
21	Você ficou fascinado(a) pelas pequenas coisas ao seu redor?	Sign	Sign	Sign
22	Seus sentidos pareceram pareciam extremamente fortes ou claros?	Shar	Shar	Shar
23	Você sentiu como se um mundo inteiro estivesse se abrindo para você?	Cog	Cog	Cog
24	Você sentiu que as fronteiras entre as suas sensações internas e externas foram removidas?	Emo	Cog	Cog
25	Você sentiu que o mundo estava mudando e que você estava buscando uma explicação?	Cog	Cog	Cog
26	Você teve um sentimento de urgência indizível sem ter certeza do que fazer?	Emo	Emo	Emo
27	Você ficou interessado(a) por pessoas, eventos, lugares ou ideias que normalmente não causariam uma impressão em você?	Sign	Sign	Sign
28	Seus pensamentos e percepções vinham mais rápido do que poderiam ser assimilados?	Emo	Emo	Emo

29	Você percebeu coisas que não havia percebido antes e que passaram a ter um significado especial?	Unde	Sign	Sign
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Abbreviations: Sign, Increased Significance; Unde, Impending Understanding; Shar, Senses Sharpening; Cogn, Heightened Cognition; Emo, Heightened Emotionality.

Suggestibility

For the Creative Imagination Scale (CIS), participants are instructed to sit comfortably with closed eyes and imagine as vividly as possible the suggestions read by the investigator following a standardized protocol. Afterwards, participants rate their imagined experience as compared to a real experience.

The sensory modalities comprised the following items: Weight (suggestions of arm heaviness and hand levitation), Sensation (finger anaesthesia; hot hand), Taste (drinking water; eating orange), External Ambience (hearing music; age regression), and Internal Ambience (time dilatation; relaxation).

Regarding the mystical item, we first translated the original protocol [13] into Brazilian Portuguese and then divided it into two parallel versions by roughly alternating the assignment of sentences between them. Moreover, we slightly adapted the beginning and end of each item version to overall fit the structure and length of the other CIS items. The two split versions of the mystical item are reproduced verbatim below.

In order to test whether the split versions were parallel, the scores of both versions (A and B) were analysed independently of drug and order in a Repeated Measures General Linear Model for each item, with the within-subjects factor version (A, B) and the between-subjects factor version order (AB, BA). There a main effect for Weight ($F(1,23)=32.2$, $p<0.001$, $\eta_p^2=0.58$, $\text{mean}_{\text{version A}}\pm\text{SD}=2.64\pm 1.09$, $\text{mean}_{\text{version B}}\pm\text{SD}=1.21\pm 1.18$), indicating more facility to imagine arm heaviness (version A) than hand levitation (version B). In a less pronounced way, there was a main effect of Internal Ambience ($F(1,15)=5.09$, $p=0.039$, $\eta_p^2=0.25$, $\text{mean}_{\text{version A}}\pm\text{SD}=2.42\pm 1.24$, $\text{mean}_{\text{version B}}\pm\text{SD}=1.57\pm 1.27$), indicating more facility to imagine time distortion (version A) than relaxation (version B). No other main effect emerged, indicating comparable parallel versions for all other modalities.

Mystical item, version A:

Keep your eyes closed. Using your imagination, you can experience a mystical, spiritual, metaphysical, or transcendental experience.

[Begin timing.]

You can summon all of your senses, be in tune with all of your senses, to become more and more aware of the world within and the world without, that is, the world beyond your ordinarily limited experience of yourself, going beyond your usual self-limitations to encounter a deep connection with all that is around you, a connection that extends to plants, and animals, and all things... your gaining a deep sense of awareness of yourself and your connection with all living and nonliving things that share this world with you, this universe with you.

You can connect with experience on a more intuitive level, a level of greater understanding and depth, a sense of how special and sacred it is to be alive, reaching a sense of greater understanding, feeling awe in the face of a higher reality that binds all things together in a more meaningful whole – just like each part of a tapestry or beautiful painting creates a new whole, larger than any one part; a sense of yourself as part of an eternal landscape of wondrous experience of the universe, beyond any one time, any one place; a sense of timelessness, a connection with eternity, the ever-lasting presence of an enveloping universe, knowing that there is a greater reality beyond what we experience at any given

moment... and you are a part of this ultimate reality, which you can experience on a higher order, a grander order, reaching new heights of appreciation for all that you can see and all that you cannot see, taste, touch, hear, and smell, and as you take on this new level of understanding, of comprehension, perhaps you can feel a sense of peace and tranquility that can extend to joy, joyful experience, of ecstasy that accompanies a sense of wonder and awe for all creation, you can feel that if you let all this happen.

[15 second pause]

[End of timing: about 3 minutes]

Now, tell yourself that the experience is ending and you are bringing time back to its normal rhythm and returning to the present time and space. Open your eyes.

Mystical item, version B:

Keep your eyes closed. Using your imagination, you can experience a mystical, spiritual, metaphysical, or transcendental experience.

[Begin timing.]

Get in touch with yourself, deeply in touch with yourself, and fully become aware of yourself in relation to your inner world, deeply in touch with your inner world and accepting of all that you experience, recognizing that you can learn to have an enhanced sense of yourself, an expanded sense of yourself . . . just let this happen.

You can get a sense of the boundaries getting smaller and smaller between yourself and the wonderful creations of all that exist in this world, this universe, consisting of stars, planets, comets, satellites, with unknown possibilities for awareness of so much beyond yourself.

Feel yourself part of a larger whole, a way of enriching your sense of being, your sense of awareness, your sense of connection, your sense of meaning in the beauty of the moment, the beauty of a sunset, the beauty of a moonrise, the rhythm of the waves, of the tides, the rhythm of your breath, the rhythm of the world spinning on its axis and moving around the sun, every day, every month, every year, time moving from the past to the present to the future, seamlessly into eternity, and you are a part of it all, a part of something so special, so mysterious, so awesome, so amazing... and you are increasingly aware of just how amazing and special your life is, each moment of your life... and you gain a special sense of merging in a safe way with a larger whole, a greater sense of being, a greater capacity to love and feel empathy for all living things that are a part of this amazing world, a sense of all this that goes beyond words and may be difficult to even describe, you can experience this if you let this all happen.

[15 second pause]

[End of timing: about 3 minutes]

Now, tell yourself that the experience is ending and you are returning to the present time and space. Open your eyes.

Supplemental Results

Participants

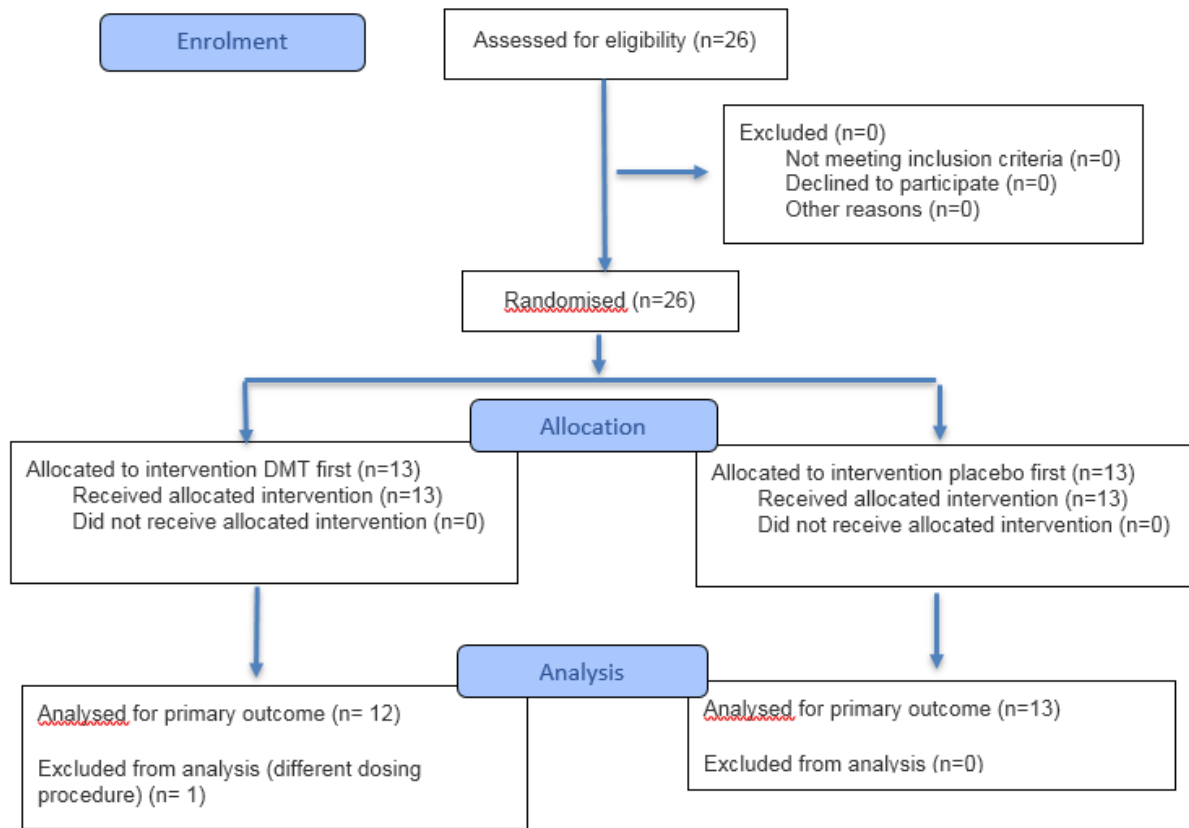


Figure S1. CONSORT 2025 Flow Diagram. Flow diagram of the progress through the phases of a randomised trial of two groups (that is, enrolment, intervention allocation, and data analysis)

Aberrant Salience

Table S2. Drug effects on the original factors and alternative Brazilian four factors of the Aberrant Salience Inventory (ASI).

Measurement	GLM values	Estimated marginal means \pm SD
ASI original		
Increased Significance	$F(1,23)=18.2, p=0.002, \eta_p^2=0.44$	DMT: 0.25 \pm 0.25, Placebo: 0.04 \pm 0.12
Senses Sharpening	$F(1,23)=54.4, p<0.001, \eta_p^2=0.70$	DMT: 0.60 \pm 0.33, Placebo: 0.08 \pm 0.21
Impending Understanding	$F(1,23)=21.6, p=0.001, \eta_p^2=0.49$	DMT: 0.34 \pm 0.37, Placebo: 0.02 \pm 0.08
Heightened Emotionality	$F(1,23)=38.4, p<0.001, \eta_p^2=0.63$	DMT: 0.32 \pm 0.23, Placebo: 0.03 \pm 0.08
Heightened Cognition	$F(1,23)=16.8, p=0.003, \eta_p^2=0.42$	DMT: 0.22 \pm 0.24, Placebo: 0.04 \pm 0.12
ASI Brazilian four factors		
Heightened Cognition	$F(1,23)=25.9, p<0.001, \eta_p^2=0.53$	DMT: 0.30 \pm 0.28, Placebo: 0.03 \pm 0.10

Note. Displayed are the values of the Repeated Measures General Linear Mixed Models (GLM), estimated marginal means, and standard deviations (SD). ASI factors were analysed according to the originally proposed factor structure [10] and the alternative Brazilian state structure with four factors [12]. Notably, since the three factors Increased Significance, Senses Sharpening, and Heightened Emotionality are identical in the four- and five-factor composition of the Brazilian version, only the differing factor Heightened Cognition was reanalysed. Significant effects are marked in **bold**. Results were Bonferroni-corrected by $n=5$ (original) and $n=4$ (Brazilian four-factor version). DMT, dimethyltryptamine.

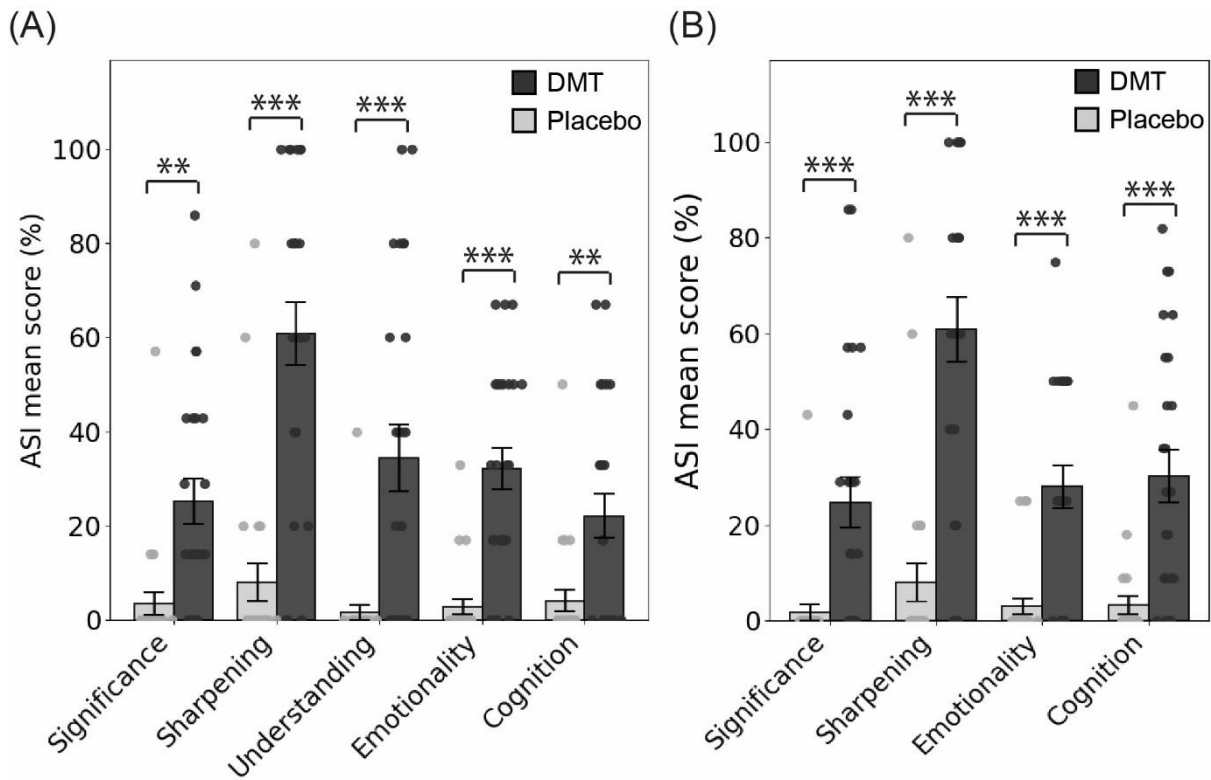


Figure S2. DMT, compared to placebo, increased all ASI factors based on the (A) original factor composition of the English trait scale [10] and (B) alternative four factor composition of the Brazilian state scale [12]. Displayed are means (bars) \pm SEM (error bars), and individual subject data (dots) in $n=25$ subjects. *** $p \leq 0.001$, ** $p \leq 0.01$ (Bonferroni-corrected).

ASI, Aberrant Salience Inventory: Significance, Increased Significance; Sharpening, Senses Sharpening; Understanding, Impending Understanding; Emotionality, Heightened Emotionality; Cognition, Heightened Cognition.

Suggestibility

The following subjects fell asleep depending on item and drug:

- Item #4 External Ambience: $n=1$ in DMT (subject #19) and $n=3$ in placebo (subject #5, 8, 22), resulting in a total loss of $n=4$ subjects for this item
- Item #5 Internal Ambience: $n=5$ in DMT (subject #8, 12, 19, 22, 24) and $n=6$ in placebo (subject #4, 6, 8, 19, 20, 22), resulting in a total loss of $n=8$ subjects for this item
- Item #6 Mystical: $n=5$ in DMT (subject #8, 12, 19, 22, 24) and $n=6$ in placebo (subject #6, 8, 13, 19, 20, 22), resulting in a total loss of $n=8$ subjects for this item

Altogether, we therefore lost a total of $n=10$ subjects (#4, 5, 6, 8, 12, 13, 19, 20, 22, 24) over all items and drug conditions.

When corrected for multiple comparisons ($n=7$), there were significant increases for DMT, compared to placebo, in total suggestibility ($p=0.003$) and the modality Internal Ambience ($p=0.016$).

Correlations

Table S3. Significant relationships of DMT-induced aberrant salience (Δ ASI) and suggestibility (Δ CIS) with alternative factor structures of psychedelic experience scales (Δ 5D-ASC from Dittrich et al. (2010), Δ HRS factors from Bouso et al.(2016), and Δ HRS factors from Strassman et al. (1994)).

	Aberrant Salience (Δ ASI)				Suggestibility (Δ CIS)
	Total	Sharpening	Understanding	Emotion	Mystical
Δ 5D-ASC					
Oceanic Boundlessness	0.70***		0.57*		0.70***
Dread of Ego Dissolution	0.58*	0.56*		0.56*	0.59*
Δ HRS factors Bouso et al. [7]					
Cognitive Distortion	0.67***	0.60**			0.53*
Agitation					-0.73**
Security/Control	0.57*				0.58*
Δ HRS factors Strassman et al. [5]					
Affect	0.69***				0.70***
Perception		0.59*			
Cognition	0.60**	0.70***			0.57*

Note. Displayed are Spearman's rank correlation coefficients for the total and factor scores in n=25 (ASI) and n=17 subjects (CIS Mystical). For presentation purposes, only significant coefficients are shown.

*** $p \leq 0.001$, ** $p \leq 0.01$, * $p \leq 0.05$ (Bonferroni-corrected by the number of factors plus total score, i.e. n=6 for Δ ASI and Δ CIS).

Δ , difference between DMT and placebo. DMT, dimethyltryptamine. ASI, Aberrant Salience Inventory: Sharpening, Senses Sharpening; Understanding, Impending Understanding; Emotion, Heightened Emotionality; Cognition, Heightened Cognition. CIS, Creative Imagination Scale. 5D-ASC, Five Dimensions of Altered States of Consciousness Questionnaire. HRS, Hallucinogen Rating Scale.

Table S4. Significant relationships of DMT-induced aberrant salience (Δ ASI), as measured by the originally proposed factor structure [10], with suggestibility (Δ CIS) and psychedelic experience scales (Δ Int, Δ 6D-ASC, Δ 5D-ASC [1], Δ 11-ASC, Δ HRS factors from Calder et al. [8], Δ HRS factors from Bouso et al. [7], Δ HRS factors from Strassman et al. [5], Δ MEQ).

	Δ ASI (English original)				Δ ASI (Bra 4-f)
	Significance	Sharpening	Understanding	Emotion	Cognition
Δ 6D-ASC					
Total		0.60**			0.62**
Oceanic Boundlessness			0.67**		0.71***
Dread of Ego Dissolution				0.60**	0.75***
Joyfulness		0.52*			0.66**
Δ 5D-ASC					
Oceanic Boundlessness			0.70***		0.69***
Dread of Ego Dissolution		0.56*		0.71***	0.50*
Visionary Restructuralization	0.58*				
Δ 11-ASC					
Total	0.53*	0.56*	0.56*		0.64**
Experience of Unity			0.67**		0.69***
Spiritual Experience			0.76***		0.64**
Blissful State	0.52*		0.61**		0.57*
Insightfulness			0.54*		0.55*
Disembodiment				0.62**	0.58*
Impaired Control & Cognition		0.53*		0.59*	0.53*
Changed Meaning of Percepts			0.59*		0.55*
Δ HRS [8]					
Vision		0.60**			
Meaningfulness			0.66**		0.54*
Euphoria	0.54*		0.70***		0.56*
Auditory and Minor Senses		0.55*			0.61**

Δ HRS [7]						
Cognitive Distortion		0.60**				
Security/Control			0.63**		0.58*	0.61**
Δ HRS [5]						
Affect			0.66**		0.68***	0.69***
Perception		0.59*				
Cognition		0.70***				0.51*
Δ MEQ						
Total	0.59*	0.61**	0.73***		0.81***	0.83***
Mystical	0.56*	0.54*	0.77***		0.81***	0.83***
Positive Mood	0.59*	0.59*	0.54*		0.62**	0.64**
Transcend. of Time & Space		0.55*	0.67***		0.78***	0.81***
Ineffability		0.52*				
Internal Unity	0.55*		0.80***		0.81***	0.85***
External Unity	0.56*	0.54*	0.63**	0.52*	0.79***	0.78***
Noetic Quality	0.57*		0.88***		0.83***	0.86***
Sacredness	0.62**	0.60**	0.80***		0.78***	0.80***

Note. Displayed are Spearman's rank correlation coefficients for $n=25$ subjects for the total and factor scores of the English original scale [10] and the alternative Brazilian four factors (Bra 4-f). Notably, since only the factor Heightened Cognition is different from the Brazilian five-factor composition, only this factor was analysed [12]. For presentation purposes, only significant coefficients are shown. *** $p \leq 0.001$, ** $p \leq 0.01$, * $p \leq 0.05$ (Bonferroni-corrected by $n=6$ [original] and $n=4$ [Brazilian four factors] for comparability with the other correlations in **table 3** and **table S2**).

Δ , difference between DMT and placebo. DMT, dimethyltryptamine. ASI, Aberrant Salience Inventory: Significance, Increased Significance; Sharpening, Senses Sharpening; Understanding, Impending Understanding; Emotion, Heightened Emotionality; Cognition, Heightened Cognition. 6D-ASC, Six Dimensions of Altered States of Consciousness Questionnaire. 5D-ASC, Five Dimensions of Altered States of Consciousness Questionnaire. 11-ASC, Eleven Factors of Altered States of Consciousness Questionnaire. HRS, Hallucinogen Rating Scale. MEQ, Mystical Experiences Questionnaire: Transcend. of Time & Space, Transcendence of Time and Space.

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