**Supplemental Content**

**Chemical Analysis of the Ayahuasca Sample**

*Ayahuasca sample extraction*

The extraction was performed according to the procedure described by Pires et al.2 First, 50 *µ*L of sample solution was diluted with deionised water (1:100). Borate buffer 0,25 M pH 9.0 (3 mL) was added into 500 *µ*L of the diluted solution and the internal standard diphenhydramine (100 *μ*L of a solution of 10 *µ*g/mL) was loaded onto a C18 cartridge previously conditioned (methanol 2.0 mL, deionised water 1.0 mL and borate buffer 2.0 mL). The loaded cartridge was further washed with deionised water (1.0 mL) and acetonitrile 10% (1.0 mL). After drying the cartridges for 7 min, the analytes were eluted with methanol (2.0 mL). Of this solution, 2 *μ*L was injected in the GC-NPD system.

*Reagents and chemicals*

Hydrogen borate, methanol and acetonitrile were purchased from Merck (Darmstadt, Germany). Classic Sep-Pack® C18 cartridges (360 mg) were purchased from Waters Co. (Bellefonte, PA, USA). Dimethyltryptamine, harmine and harmaline were purchased from Sigma Co. (St Louis, MO, USA). THH was synthetised according to the procedure described by Callaway et al.3

*GC-NPD analyses*

Analyses for dimethyltryptamine, harmine, harmaline and tetrahydroharmine were performed using an Agilent gas chromatograph model 6890 equipped with a nitrogen–phosphorous detector and 7683 series automatic injector (Little Falls, DE, USA). Chromatographic separation was achieved on an HP Ultra-2 fused-silica capillary column (25 m × 0.2mm× 0.33 μm film thickness) using ultra-pure-grade nitrogen as carrier gas at 1.0 mL/min in a constant flow rate mode. Injections (2 *μ*L) were made in splitless mode. The injector port and detector temperature was 280°C. The oven temperature was maintained at 70°C for 1 min; programmed at 30°C/min to 120°C, and 20°C/min to 300°C with a hold at 300°C for 4 min. The analytes were identified by comparing their retention times to those of authentic standards. Quantification was based upon the ratio of the integrated peak area to the internal standard. The final result was multiplied by 100 in order to compensate dilution.

**References**

1 - Marchioni C, de Souza ID, Grecco CF, et al. A column switching ultrahigh-performance liquid chromatography-tandem mass spectrometry method to determine anandamide and 2-arachidonoylglycerol in plasma samples. Anal Bioanal Chem 2017;409:3587–3596.

2 - Pires AP, de Oliveira CD, Moura S, et al. Gas chromatographic analysis of dimethyltryptamine and *β*-carboline alkaloids in ayahuasca, an Amazonian psychoactive plant beverage. Phytochem Anal 2009;20:149–153.

3 - Callaway JC, Raymon LP, Hearn WL, et al. Quantitation of *N,N*-dimethyltryptamine and harmala alkaloids in human plasma after oral dosing with ayahuasca. J Anal Toxicol 1996;20:492–497.

**Assessment of Ayahuasca Subjective and Somatic Effects**

Subjective states were evaluated with the Portuguese version of the *Visual Analogue Mood Scale* – VAMS.1 In this scale, the subject is told to mark a point that identifies his/her present subjective state on a 100-mm straight line placed between two words that describe opposite mood states. The Portuguese version of the VAMS contains 16 items that were grouped into four factors and then renamed.2,3 The factors are: (1) *anxiety*, comprising the items *calm–**excited*, *relaxed–tense*, and *tranquil–troubled*; (2) *sedation* (formerly *mental sedation*), including the items *alert–drowsy*, and *attentive–dreamy*; (3) *cognitive impairment* (formerly *physical sedation*), including *quick-witted–mentally slow*, *proficient–incompetent*, *energetic–lethargic*, *clear-headed–muzzy*, *gregarious–**withdrawn*, *well-coordinated–clumsy*, and *strong–feeble*; and (4) *discomfort* (formerly *other feelings and attitudes*), made up of the items *interested–bored*, *happy–sad*, *contented–discontented*, and *amicable–antagonistic*.

The Portuguese version of the *Beck Anxiety Inventory* (BAI),4 composed of 21 items rated on a Likert scale from 0 to 5, was used to assess general anxiety symptoms.

The *Bodily Symptoms Scale* (BSS)2 was used to detect physical symptoms such as fatigue, weakness, lethargy, headache, muscular tension, tremor, hanger, thirst, sweating, dyspnea, agitation, strong urge or difficulty to urinate/defecate, nausea, dry mouth, blurred vision, dizziness, tickling and chest pain. It is organized into 21 items, and the intensity of each symptom is rated on a Likert scale from 0 to 5.

**References**

1 - Zuardi AW, Karniol IG. Transcultural evaluation of a self-evaluation scale of subjective states. J Brasileiro Psiquiatr 1981;131:403–406.

2 - Zuardi AW, Cosme RA, Graeff FG, et al. Effects of ipsapirone and cannabidiol on human experimental anxiety. J Psychopharmacol 1993;7:82–88.

3 - Parente ACBV, Garcia-Leal C, Del-Ben C, et al. Subjective and neurovegetative changes in health volunteers and panic patients performing simulated public speaking. Eur Neuropsychopharmacol 2005;15:663–671.

4 - Cunha JA. Manual da versão em português das Escalas Beck. São Paulo:

Casa do Psicólogo, 2001.

**Analytical Method for Quantification of Endocannabinoids in Plasma**

To quantify anandamide (AEA) and 2-arachidonoylglicerol (2-AG) in plasma samples, aliquots (250 *µ*L) from samples were spiked with 40 *µ*L of the internal standards solution (AEA-d4 and 2-AG-d5) and subjected to acetonitrile precipitation of protein. The supernatants were collected and their volumes reduced under a Concentrator plus (Eppendorf®, Hamburg, Germany) and reconstituted in 150 *µ*L water:acetonitrile (90:10, v/v). The reconstituted solution (100 *μ*L) was injected into the multidimensional system. This system uses a column containing restricted access material (RP-8 ADS, 25 mm x 4 mm x 25 *μ*m) in the first dimension and a Kinetex C18 core-shell column (100 mm x 2.1 mm x 1.7 *μ*m) in the second dimension, followed by detection in a triple quadrupole mass spectrometer (multiple reaction monitoring mode), in the positive mode, as described previously.1 RP-8 ADS was used for enrichment with traces of endocannabinoids and macromolecular matrix size exclusion; the core-shell column was used for the chromatographic separation.

**References**

1 - Marchioni C, de Souza ID, Grecco CF, et al. A column switching ultrahigh-performance liquid chromatography-tandem mass spectrometry method to determine anandamide and 2-arachidonoylglycerol in plasma samples. Anal Bioanal Chem 2017;409:3587–96.