A Sacred Journey

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3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for post-traumatic stress disorder in military veterans, firefighters, and police officers: a randomised, double-blind, dose-response, phase 2 clinical trial

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Summary

Background Post-traumatic stress disorder (PTSD) is prevalent in military personnel and first responders, many of whom do not respond to currently available treatments. This study aimed to assess the efficacy and safety of 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for treating chronic PTSD in this population.

Methods We did a randomised, double-blind, dose-response, phase 2 trial at an outpatient psychiatric clinic in the USA. We included service personnel who were 18 years or older, with chronic PTSD duration of 6 months or more, and who had a Clinician-Administered PTSD Scale (CAPS-IV) total score of 50 or greater. Using a web-based randomisation system, we randomly assigned participants (1:1:2) to three different dose groups of MDMA plus psychotherapy: 30 mg (active control), 75 mg, or 125 mg. We masked investigators, independent outcome raters, and participants until after the primary endpoint. MDMA was administered orally in two 8-h sessions with concomitant manualised psychotherapy. The primary outcome was mean change in CAPS-IV total score from baseline to 1 month after the second experimental session. Participants in the 30 mg and 75 mg groups subsequently underwent three 100–125 mg MDMA-assisted psychotherapy sessions in an open-label crossover, and all participants were assessed 12 months after the last MDMA session. Safety was monitored through adverse events, spontaneously reported expected reactions, vital signs, and suicidal ideation and behaviour. This study is registered with ClinicalTrials.gov, number NCT01211405.

Findings Between Nov 10, 2010, and Jan 29, 2015, 26 veterans and first responders met eligibility criteria and were randomly assigned to receive 30 mg (n=7), 75 mg (n=7), or 125 mg (n=12) of MDMA plus psychotherapy. At the primary endpoint, the 75 mg and 125 mg groups had significantly greater decreases in PTSD symptom severity (mean change CAPS-IV total scores of −58·3 [SD 9·8] and −44·3 [28·7]; p=0·001) than the 30 mg group (−11·4 [12·7]). Compared with the 30 mg group, Cohen's *d* effect sizes were large: 2·8 (95% CI 1·19–4·39) for the 75 mg group and 1·1 (0·04–2·08) for the 125 mg group. In the open-label crossover with full-dose MDMA (100–125 mg), PTSD symptom severity significantly decreased in the group that had previously received 30 mg (p=0·01), whereas no further significant decreases were observed in the group that previously achieved a large response after 75 mg doses in the blinded segment (p=0·81). PTSD symptoms were significantly reduced at the 12-month follow-up compared with baseline after all groups had full-dose MDMA (mean CAPS-IV total score of 38·8 [SD 28·1] *vs* 87·1 [16·1]; p<0·0001). 85 adverse events were reported by 20 participants. Of these adverse events, four (5%) were serious: three were deemed unrelated and one possibly related to study drug treatment.

Interpretation Active doses (75 mg and 125 mg) of MDMA with adjunctive psychotherapy in a controlled setting were effective and well tolerated in reducing PTSD symptoms in veterans and first responders.

Funding Multidisciplinary Association for Psychedelic Studies.

Introduction

Post-traumatic stress disorder (PTSD) is a major public health problem, particularly among military veterans. Prevalence of PTSD in military personnel and veterans (17·1%)[1] and first responders (10–32%)[2] is much higher than the lifetime occurrence in the general population (8%). In addition to the severe psychological burden, chronic PTSD is associated with increased medical morbidity, occupational and relationship problems, decreased quality of life,[3] overall decreased life satisfaction and happiness, and increased risk of suicide.[4]

Treatment options for PTSD include pharmacotherapy and psychotherapies. The two medications approved by the US Food and Drug Administration (FDA) for PTSD, sertraline and paroxetine, reduce symptom severity with limited effectiveness,[5] especially in veterans. Off-label prescription of drugs, including antidepressants,


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Sacred Ceremony: Ayahuasca

Ayahuasca has been used for several thousand years by the indigenous people of the Amazon jungle for healing, learning, and divination

(Grob, 1998; Grof, 1998; Walsh, 2001).

The Indigenous People of the Amazon call Ayahuasca:

"*vine of the soul*" and "*vine of the spirits*"

Ayahuasca is believed to free the soul for flight into other realms.

People that attend these retreats are seeking:

- spiritual development
- emotional healing
- self-awareness

(Shanon, 2002; Winkelman, 2005).

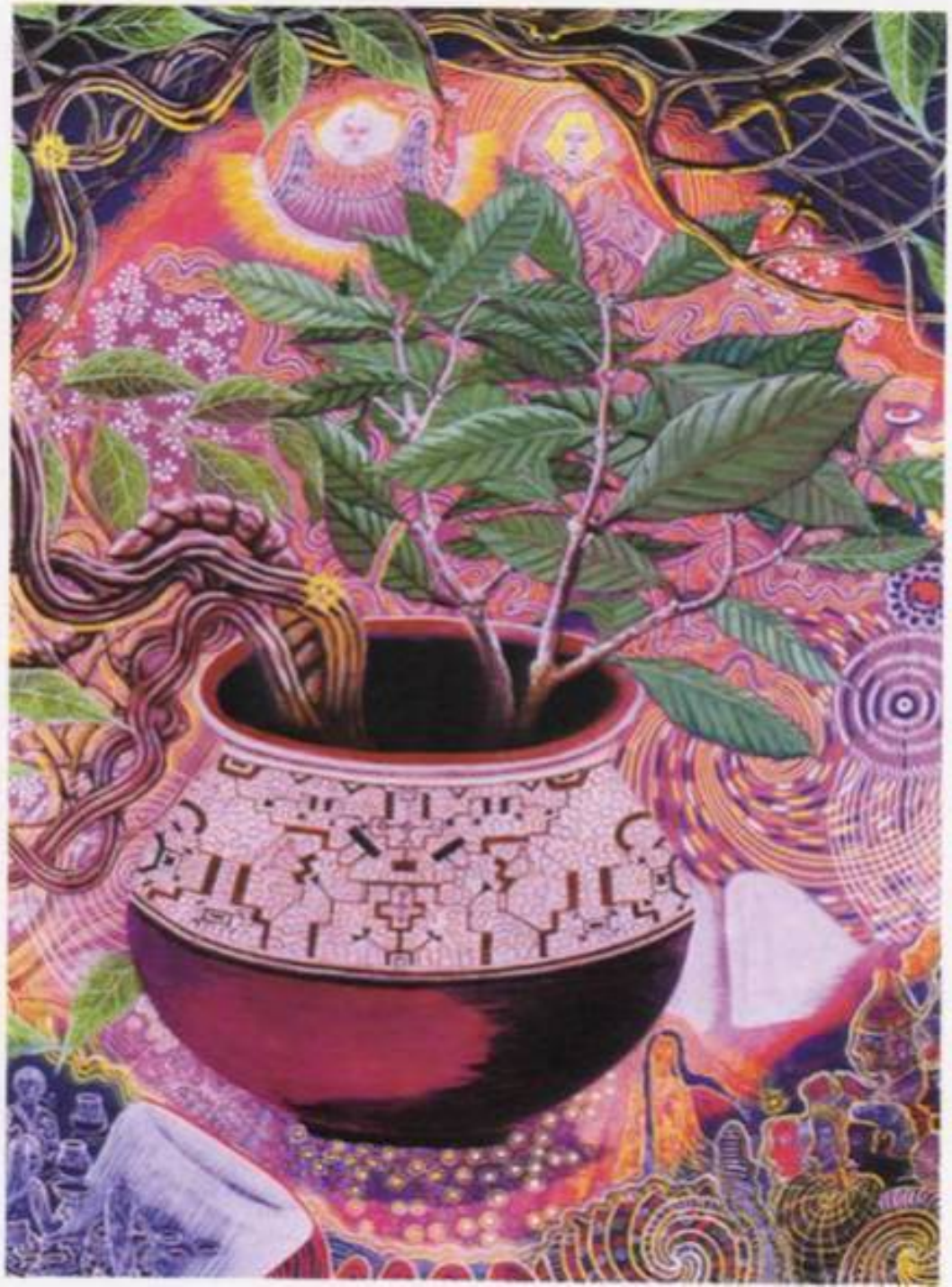
Studies indicate that Westerners who participate in traditional and/or neo-shamanic ayahuasca sessions can have a positive experience that promotes psychospiritual growth and development

.(Barbosa, Giglio, & Dalgalarrondo, 2005; Dobkin de Rios, & Grob, 2005; Grim, 2002; Grob, McKenna, Callaway, Brito, Oberlaender, Saide, Labigalini, Miranda, Strassman, & Boone, 1996; McKenna, Callaway, & Grob, 1998; Metzner, 1999; Riba & Barbanoj, 2005; Schultes & Hofmann, 1992; Stuckey, Lawson, & Luna, 2005; Walsh & Grob, 2005; Winkelman, 2002, 2005)

Pablo Amaringo

Banisteriopsis caapi

Psychotria viridis



Preparation of *Ayahuasca*

- There is synergism between the two plants

- Dimethyltryptamine (DMT) from *Psychotria viridis* causes visions but is active orally only if taken with a MAO inhibitor

- The B-carbolines (harmine, harmaline, and tetrahydroharmaline) from the *Banisteriopsis caapi* are monoamine oxidase (MAO) inhibitors that block the breakdown of DMT, serotonin, dopamine and other monoamines

- This mechanism allows oral DMT to become active.

- The MAO inhibitors act as anti-depressants that produce a sustained effect for several days. This is an important property that may facilitate integration of the experience.

- The nausea, vomiting and diarrhea that are so common with ayahuasca use may be a result of serotonin receptor stimulation by DMT in the brain and digestive tract.

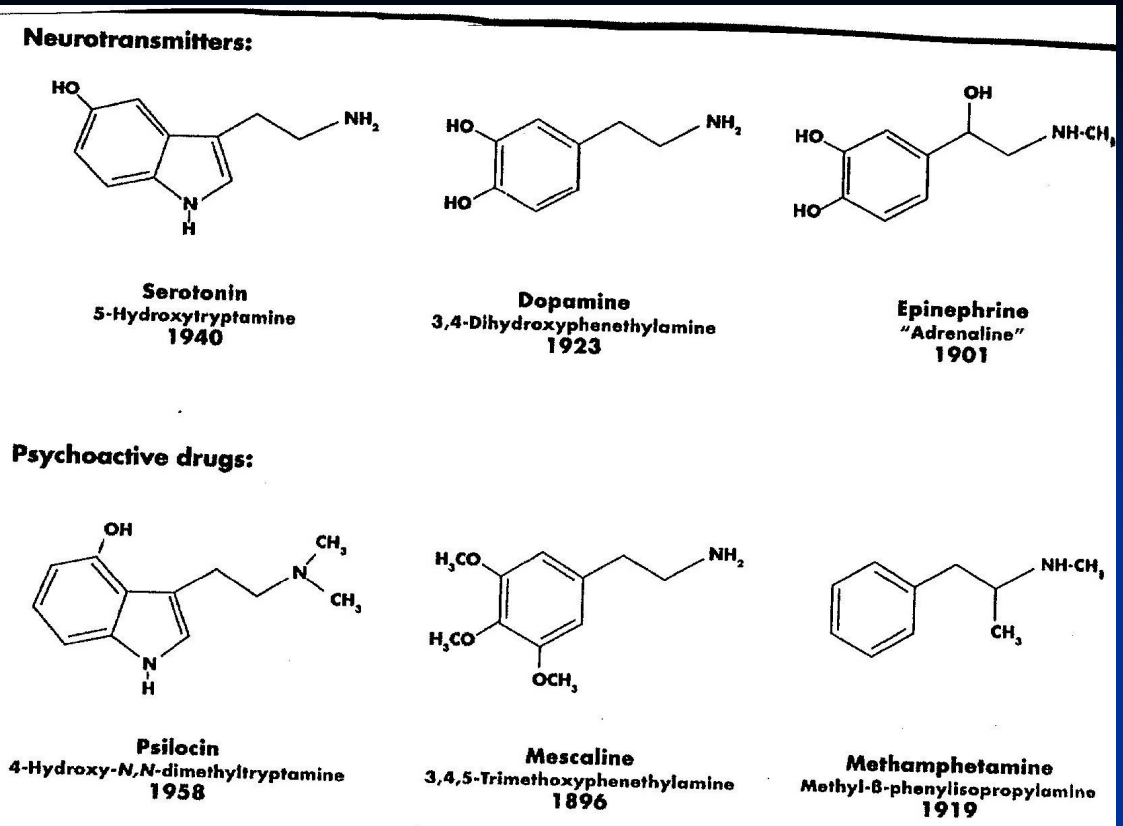


Figure 1. Molecular structures of the neurotransmitters serotonin, dopamine, and epinephrine, compared with the structures of psilocin, mescaline and methamphetamine. Also provided are the dates when these chemicals began to surface in the scientific literature, as a consequence of their unique properties on the human central nervous system.

Metzner, R. (Ed.). (1999). *Ayahuasca: Human consciousness and the spirits of nature*. New York: Thunder's Mouth Press. P. 257

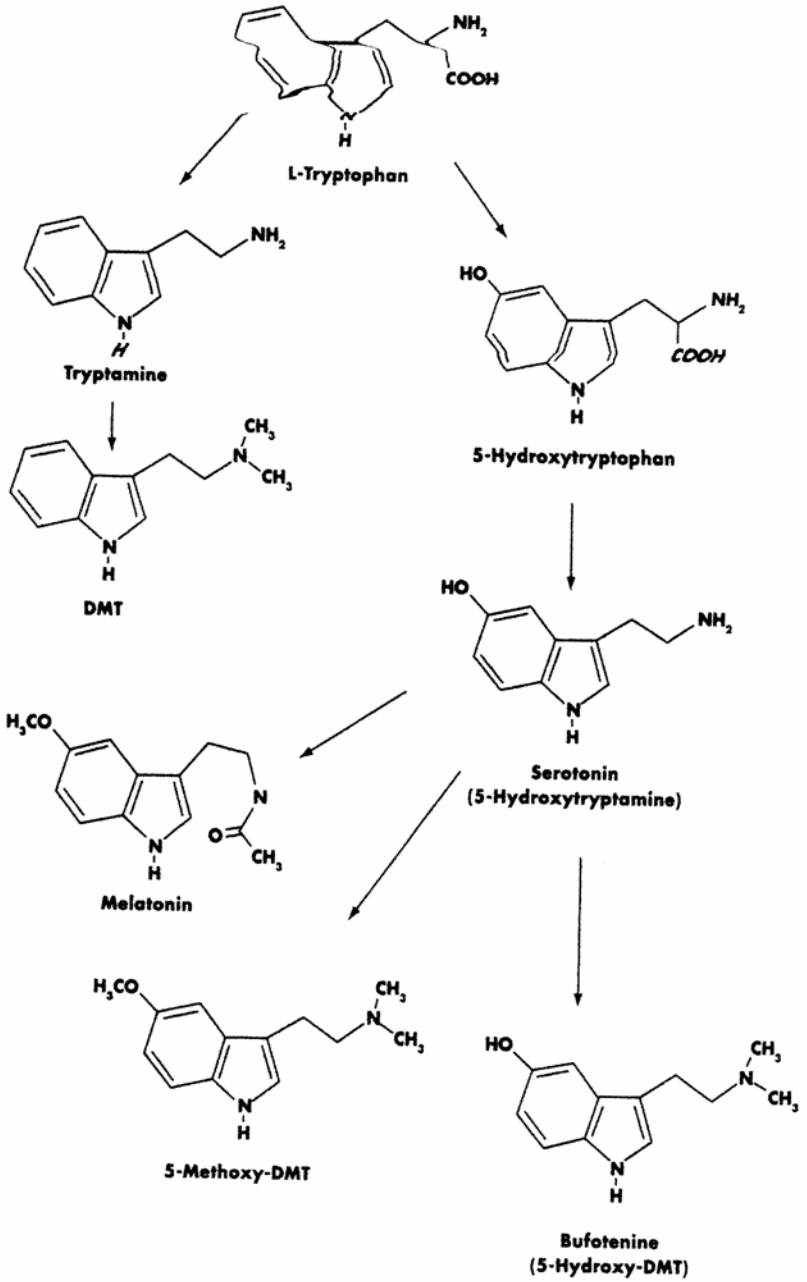


Figure 3. Metabolic pathways for the production of several endogenous indoles from dietary tryptophan.

Metzner, R. (Ed.). (1999). *Ayahuasca: Human consciousness and the spirits of nature*. New York: Thunder's Mouth Press. P. 257

Preparation for Ceremony

Pilgrimage

Special Diet and Purification

Sexual Abstinence

Setting of Intention

"Set and Setting"

Music and Sound

Harpers, August 2009

The Elements of Healing

- Empowerment
- Transformation
- Creative Expression
- The Quest for Meaning and Transcendence
- Unconditional Love

Qualities of a Healer

- Loving Kindness
- Joyfulness
- Skillful Means
- Reverence
- Humility