



Ayahuasca visions

THE SPIRITS OR MOTHER OF THE PLANTS

Defining "Psychedelics"

- - Humphrey Osmond 1956
- **Empathogen-entactogen**
 - "generating a state of empathy"
 - "touching within"
 - 1983-1984 Ralph Metzner and David Nichols



- **Entheogen**
 - "generating the divine within"
 - 1979 - Group of Enthobotanists including R. Gordon Wasson



MDMA vs "Psychedelics"

- **Entheogens**
 - DMT, Psilocybin, Mescaline, LSD
 - Prominent Hallucinations, slowing the DMN, mystical experi
- **Entactogens**
 - Substituted methylenedioxy- phenethylamines
 - 3,4-Methylenedioxy-N-methylamphetamine
 - Stimulant, empathy, openness, no real hallucinations



Psychedelics in Western Culture



1938 - Albert Hoffman synthesizes LSD from Ergot when looking for a drug for heart failure
 1943 - on 4/16 and 4/19 Hoffman takes LSD - Bicycle Day.
 1957 - R. Gordon Wasson reports on Mushrooms creating visions in Mexico

Lysergic Acid (LSD): Albert Hofmann



- Albert Hofmann, LSD, Bicycle day-April 19th, 1943

Psychedelics in Western Culture

Stanislav Grof, MD, PhD

- 1956 - Begins studying LSD as a Medical Student
- 1959 - Essay: "Serotonin and its significance for Psychiatry"
- 1960- Prague's Psychiatric Research Institute
 Conducts clinical research on patients with myriad conditions
- 1967 - Invited to John's Hopkins as Assistant Professor
- 1967-1973 - Chief of Psychiatric Research - Maryland Psychiatric Research Center



Stan Grof Cont.



- Used LSD to treat depression, anxiety, trauma, bipolar disorder, some psychosis
- Studied over 3000 patients

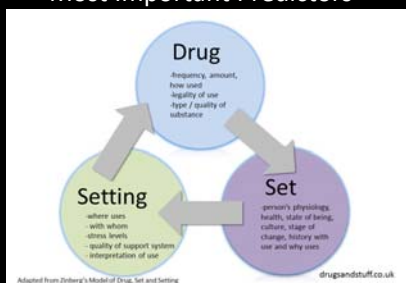
- Dangers:

- Hypertension
- Use of Anti-depressant (Serotonin drug)
- History of serious mental illness more difficult
 - Bipolar, schizophrenia, personality disorders

One rare lasting side effect: Hallucinogen persisting Perception Disorder (HPPD)
Continual presence of sensory disturbances
Anywhere from 0.5 – 4.5%

- Getting "stuck"
 - May necessitate a second trip

Most Important Predictors



Set



Setting



The Psychedelic Experience

- Visual changes: Geometric patterns and colors in 2D and 3D. With the eyes open or closed. Dose related. Synesthesia (Visual changes synchronize with music)
- Personal growth. Enhances empathy, love, insight and understanding of the self. A sense of interconnectedness. Creativity, Ability to relate ideas.
- Mystical experiences: Enhanced spirituality. Perceptions of alternative realities. Different perception of time and space. Ego death.



Psychedelic rock concert poster, art by Victor Moscosso

But What is Going On?

- Mystical Experiences Questionnaire
- Internal Unity
 - Disconnection from yourself
 - External Unity
 - Everything is one
 - Transcendence of Time and Space
 - Loss of sense of time
 - Ineffability and Paradoxically
 - Unable to explain, "Died, but never felt more alive"
 - Sense of Sacredness
 - Holiness, Profound
 - Noetic Quality
 - More real than real life - answers
 - Deeply Felt Positive Mood

Can psychedelics cause mental illness?

- Other Hallucinogen Use Disorder
- Other Hallucinogen Intoxication
- Hallucinogen Persisting Perception Disorder
- Hallucinogen animal models of psychosis
- Case reports of psychosis in humans. Higher risk in people with family history



Syd Barrett, Pink Floyd

Psychedelics: Mechanism of Action

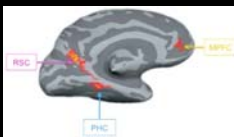
- Non selective serotonin agonism
- Other possible mechanisms
 - Glutamate, NMDA, AMPA
 - Other neurotransmitters
 - Second messengers
 - Anti-inflammatory
 - Neurotrophic factors
 - Reset



Greyed Rainbow, Action painting, Jackson Pollock

Mechanism of Action

Non selective serotonin agonist (5HT2)



Research Cut Short



Comprehensive Drug Abuse Prevention and Control Act 1970

War on Drugs based on Propaganda

"You want to know what this was really all about? The Nixon campaign in 1968, and the Nixon White House after that, had two enemies: the antiwar left and black people. You understand what I'm saying? We knew we couldn't make it illegal to be either against the war or black, but by getting the public to associate the hippies with marijuana and blacks with heroin, and then criminalizing both heavily, we could disrupt those communities. We could arrest their leaders, raid their homes, break up their meetings, and vilify them night after night on the evening news. Did we know we were lying about the drugs? Of course we did."



- John Ehrlichman, Nixon's former domestic policy advisor

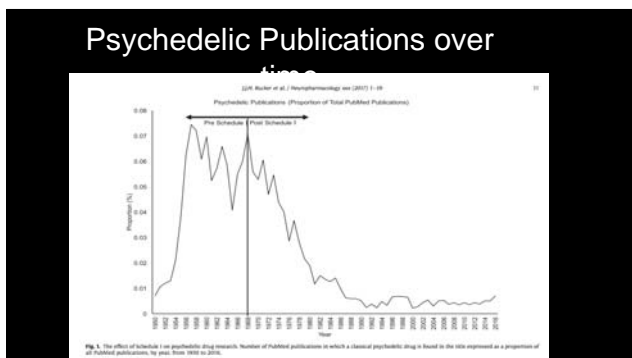
- https://www.youtube.com/watch?v=UjAMocYXQw&has_verified=1
blob:https://www.youtube.com/d03fa37f-232e-4cf4-9604-b58ee846ae1f



Controlled Substance Act

- October 27th, 1970 it was made official
- V Schedules
- Formation of DEA and FDA
- Regulates the manufacture and distribution of controlled substances such as hallucinogens, narcotics, depressants and stimulants

The image shows the cover of LIFE magazine. The central focus is a hand holding several colorful, translucent papers or cards. The text on the cover includes "THE EXPLOSIVE BEHIND ALL THE MADNESS OF THE 1960S" and "LSD".



Drug classifications

- Schedule I
no currently accepted medical use, high potential for abuse and lack of safety.
Examples: Heroin, LSD, cannabis, mescaline , MDMA (ecstasy), psilocybin

Schedule II/IIN Controlled substance

- Have high potential for abuse leading to severe psychological or physical dependence
- Have a valid medical application
- Examples of II narcotics include : Dilaudid, mathadone, Demerol, Oxycodone, fentanyl, morphine, opium, codeine, cocaine
- Examples of IIN stimulants include: amphetamine (Dexedrine, Adderall), methamphetamine and methylphenidate

Schedule III/IIIN

- Intermediate abuse potential (less than schedule I and II but more than schedule IV)
- Currently accepted medical use
- Examples include:
Hydrocodone/acetaminophen, anabolic steroids, Ketamine, Fiorinal

Schedule IV controlled substances

- Low potential for abuse relative to schedule 3 drugs, abuse potential more than schedule V
- Examples Alprazolam, clonazepam, zolpidem, clorazepate, valium, lorazepam, temazepam, triazolam, tramadol, phentermine, Librium, lunesta, modafinil, phenobarbital

SCHEDULE V

- Medications with the least potentials for abuse among the controlled substances
- Examples : cough suppressants, appetite suppressants, CBD marijuana-derived pharmaceutical formulation (Epidiolex) Cannabidiol derived from industrial hemp remains schedule I

Resurgence of Research

- Rick Strassman (1990-1995)
- Melatonin and N,N-dimethyltryptamine (DMT)
- 400 DMT doses to 60 healthy volunteers
- Psychedelic Renaissance



But What is Going On?

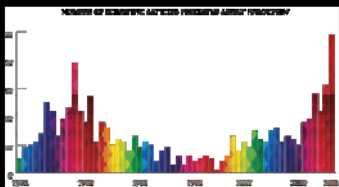
- Pineal Gland?

But What is Going On?

- Natural Human Ability

Non-Drug Methods

Controlled Substance Act



- Beckley Foundation

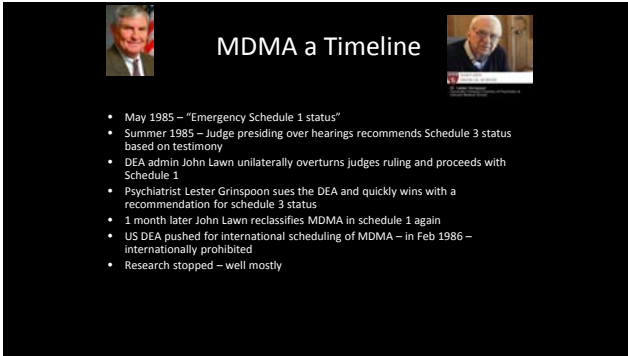
What illnesses hope to benefit?

- Anxiety disorders
- Autism
- Obsessive-Compulsive Disorders
- Addiction
- Psychosomatic disorders
- PTSD

MDMA a Timeline

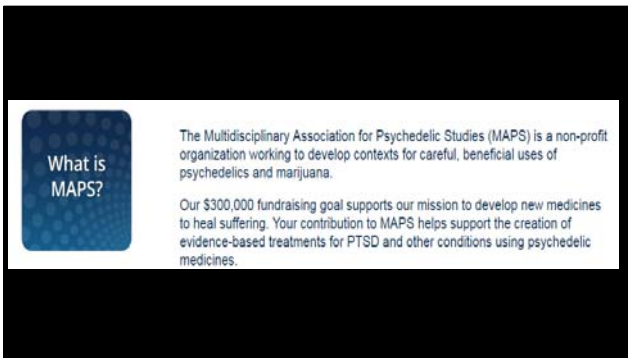
- First Synthesized by MERCK in 1912/1914 – patented to “stop abnormal Bleeding”
- 1953-1954 studies by US Military in animals for toxicity along with others (mescaline derivatives)
- 1965 – Alexander “Sasha” Shulgin synthesized while working at DOW Chemicals – did not test it
- 1970 – Shulgin sent instructions to a colleague at the Las Angeles Chemical Company – subsequently sent to Chicago around 1970 (first known recreational use)
- 1975-1976 – Shulgin Learns of “Amphetamine like content” from a grad student – tries it “Low calorie martini”





MDMA a Timeline

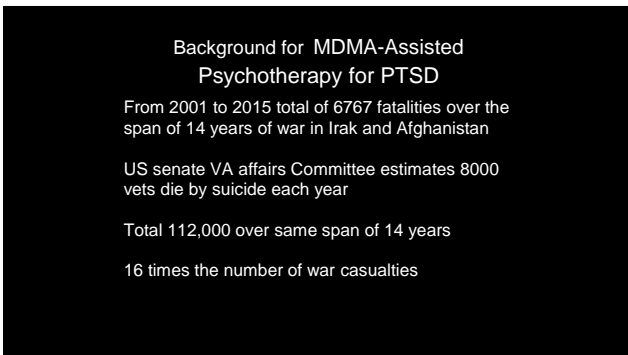
- May 1985 – “Emergency Schedule 1 status”
- Summer 1985 – Judge presiding over hearings recommends Schedule 3 status based on testimony
- DEA admin John Lawn unilaterally overturns judges ruling and proceeds with Schedule 1
- Psychiatrist Lester Grinspoon sues the DEA and quickly wins with a recommendation for schedule 3 status
- 1 month later John Lawn reclassifies MDMA in schedule 1 again
- US DEA pushed for international scheduling of MDMA – in Feb 1986 – internationally prohibited
- Research stopped – well mostly



What is
MAPS?

The Multidisciplinary Association for Psychedelic Studies (MAPS) is a non-profit organization working to develop contexts for careful, beneficial uses of psychedelics and marijuana.

Our \$300,000 fundraising goal supports our mission to develop new medicines to heal suffering. Your contribution to MAPS helps support the creation of evidence-based treatments for PTSD and other conditions using psychedelic medicines.




Background for MDMA-Assisted Psychotherapy for PTSD

From 2001 to 2015 total of 6767 fatalities over the span of 14 years of war in Irak and Afghanistan

US senate VA affairs Committee estimates 8000 vets die by suicide each year

Total 112,000 over same span of 14 years

16 times the number of war casualties



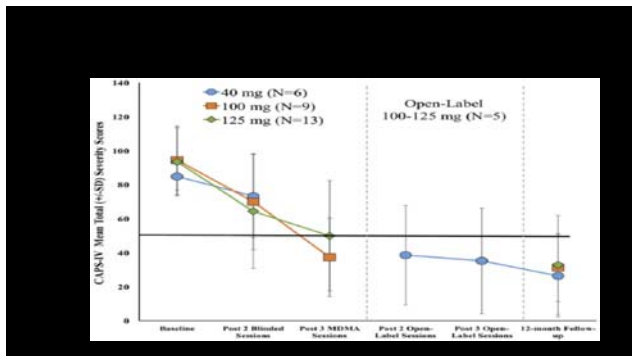
The FDA designated MDMA-assisted psychotherapy for PTSD as a Breakthrough Therapy in August 2017. By granting Breakthrough Therapy Designation, the FDA has agreed that this treatment may have a meaningful advantage and greater compliance over available medications for PTSD.

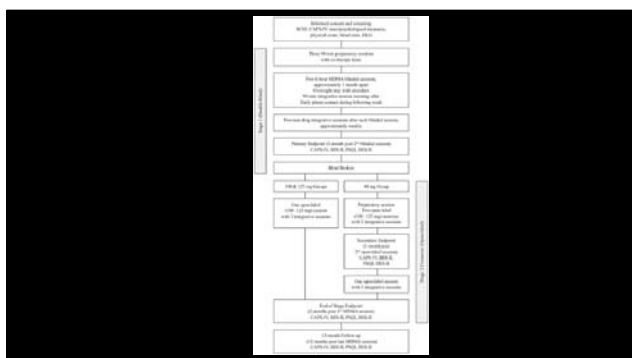
MDMA Breakthrough Therapy Designation

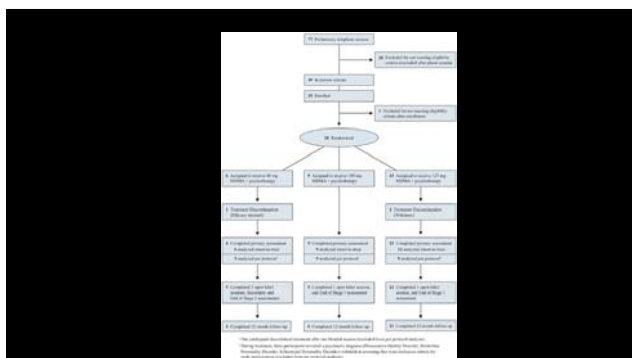
- Granted by FDA only given for drugs that have data indicating they work better and/or more safe than current medication for a life-threatening illness
- New Phase 2 trial in Boulder CO; N=28; randomized blinded protocol; 40mg (placebo), 100mg or 125mg (active doses)
- 61 points symptom reduction on CAPS-IV score
- At 12-months, 76% of participants did not meet PTSD criteria.

MDMA-Assisted Psychotherapy for PTSD

- Three 90 min preparation sessions with co-therapy team
- Two 8-hour MDMA blinded sessions, 1 month apart overnight stay with attendant, 90 min integrative session morning after;
- Two non-drug integrative sessions weekly after each blinded session







Phase 3 Trials

The first FDA-regulated Phase 3 trial of MDMA-assisted psychotherapy for PTSD began enrolling subjects this month, and we are currently seeking funding in support of MAPS' mission to make psychedelic therapy a legal treatment around the world.

FDA Grants 'Breakthrough' Status to Psilocybin Mushroom Therapy for Untreatable Depression

Psilocybin

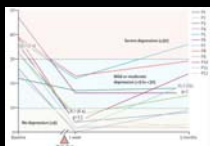
- The approval comes just weeks after researchers from Johns Hopkins researchers [published an article](#) calling for psilocybin mushrooms to be reclassified from a schedule I drug—one with no known medical potential—to a schedule IV drug such as prescription sleep aids, but with tighter control.

Psilocybin

- Treatment-resistant depression is a huge unmet need, affecting 100 million people around the world who do not respond to existing treatments. Depression is one of the fastest growing health problems we face today, and mental health disorders are the leading cause of ill-health and disability worldwide. The Breakthrough Therapy designation for psilocybin therapy highlights the importance of supporting early research that can be translated to clinically meaningful outcomes.

Psilocybin with psychological support for Treatment resistant depression

- Cahart-Harris et al., Lancet Psychiatry, 2016
 Open label
 12 patients
 2 oral doses (10 and 25 mg, 7 days apart)
 Reduction of BDI

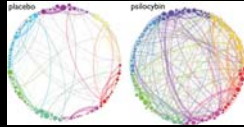


Melancholy, Edvard Munch, 1894

Psilocybin

- Studies in animals and humans both show low potential for abuse, the researchers say. When rats push a lever to receive psilocybin, they don't keep pushing the lever like they do for drugs such as cocaine, alcohol or heroin. When it comes to human studies, people who have used psilocybin typically report using it a few times across their lifetime.

Psilocybin: Other

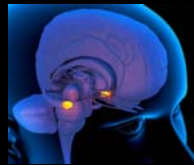


- Homological scaffolds of brain functional networks
G. Petri, et al. Journal of the Royal Society Interface Oct. 2014.

Psilocybin

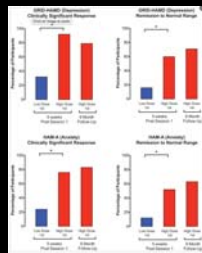
Psilocybin: Amygdala

- Psilocybin decreases amygdala reactivity and generates empathy improves mood in healthy volunteers (Kraehenmann, 2015)



Psilocybin for Anxiety in Advanced Cancer

- Grob et al. JAMA Psych., 2011, 12 patients, double blind cross over, placebo vs. high dose
- Griffith et al., J. Psychopharm., 2016: 51 patients, double blind randomized cross over, microdose vs. high dose
- Phase III Clinical Trial: NYU and the Heftler Institute



Psilocybin: Other

- Tobacco dependence: Open label, 15 patients, 80% abstinence at 6 month follow up
- Alcohol dependence: Open label, 9 patients, reduced drinking days and craving
- Obsessive Compulsive Disorder (OCD), Double blind, 9 patients (low, moderate, high dose), reductions from 23 to 100 % in YBOCS in all subjects after one week



Psilocybin

Psilocybin: Microdosing

- Case reports suggest may improve mental health
- 0.3 mg every 3 days
- Proposals:
 - Open label: 15 patients with TRD for eight weeks to assess tolerance and possible antidepressant effect
 - Double blind: Psilocybin at microdoses vs. SSRI vs. Placebo



Ayahuasca or Yage

- Concoction of two plants: Psychotria viridis (DMT) a serotonin and sigma-1 receptor agonist and Banisteriopsis caapi rich in reversible MAO inhibitor such as harmine, harmaline
- Is not addictive

Ayahuasca in Depression

- Ayahuasca: Dimethyltryptan (DMT) - (agonist 5HT2A) + Harmin-(MAOI)
- Depression
- Two studies:
 - Osorio et al., Open Label, 6 patients with recurrent MDD, one session with improvement in MADRS after 1, 7 and 21 days post treatment
 - Palhano-Fontes, Double blind, ayahuasca vs. placebo, 35 patients with TRD and high comorbidity of BRD, high improvement of MADRS to ayahuasca and placebo at D1 but at D7 (64% vs. 27%)



Also Thought to be Caused by DMT



Dreams



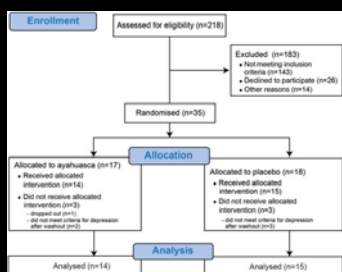
Near Death Experiences

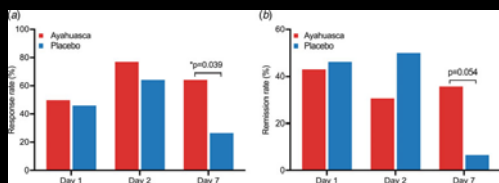


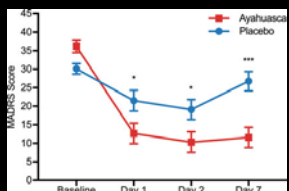
Alien Abductions

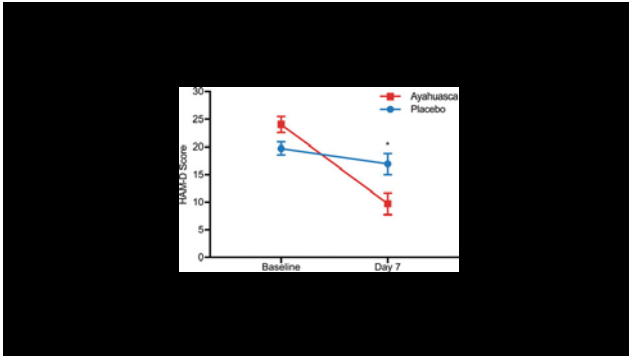
Ayahuasca

- Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial
- *Psychological Medicine: Palhano-Fontes F et al (2018)*





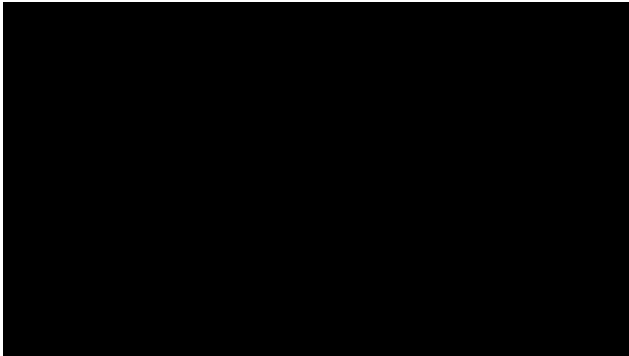




Medical Marijuana

- Dronabinol, the active ingredient in FDA approved Marinol® capsules and generic equivalents, is synthetic delta-9-tetrahydrocannabinol (THC). Dronabinol is approved as a prescription drug product in many countries for the treatment of anorexia associated with weight loss in patients with AIDS, as well as for nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.
- [Sativex®](#), a standardized cannabis extract containing THC and cannabidiol (CBD), is approved as a pharmaceutical product for the treatment of MS Spasticity in over 25 countries, but not the U.S.
- Epidiolex®, an oral solution containing CBD, is in late stage clinical development for the treatment of certain seizure disorders.





CANNABIS

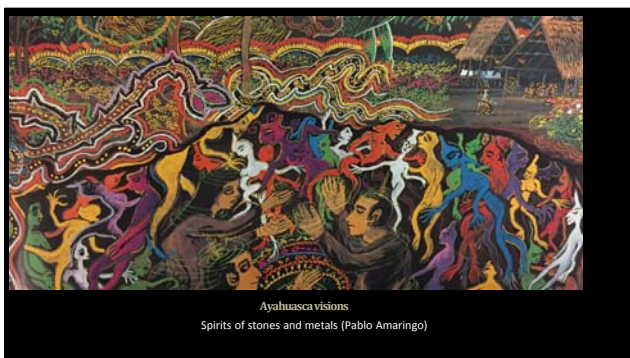
- What is CBD oil?
- Answer:
- For the purpose of the University of Mississippi's R&D program, "CBD oil" is referred to as "CBD extract oral solution." It is prepared from the plant extract, which is formulated for pharmaceutical use, and is suitable for oral administration. The current product version contains 50 mg/ml CBD, or cannabidiol, and not more than 2.5 mg/ml of THC.
- UM's CBD oil product is prepared from a concentrated extract of Cannabis [CBD-enriched Cannabis extract] with a high ratio of CBD to THC, or tetrahydrocannabinol.
- Note that the term "CBD oil" is used fairly indiscriminately by marketers and users, and may refer either to concentrated oily residues of the plant, or to many derived products with different oils added. These products may vary highly in CBD content, quality, purity and in the content of other cannabinoids.

CANNABIS

- What is the difference in marijuana and hemp?
- Answer:
- The scientific name *Cannabis sativa* L. describes a single species of the cannabis plant that has multiple varieties that may be identified by their physical and chemical characteristics. The terms "marijuana" and "hemp" describe varieties having high and low levels of tetrahydrocannabinol (THC) respectively.
- While both have medicinal value, marijuana has traditionally been abused for its psychoactive effects, while hemp has traditionally been used for industrial purposes such as seeds and fiber products. Both have been considered DEA Schedule-I controlled substances for decades in the U.S., but the 2018 Farm Bill includes amendments to the Controlled Substance Act (21 U.S.C. 812) which makes the hemp variety (with <0.3% THC content) no longer a controlled substance. Marijuana, however, remains as Schedule-I.

CANNABIS

- Is the University of Mississippi the only legal marijuana grower in the U.S.?
- Answer:
- Under the 1961 international Single Convention on Narcotic Drugs and the 1970 Controlled Substances Act, the federal government is the single "agent" allowed to provide marijuana for research. As of now, the DEA has only authorized one grower, the University of Mississippi, which grows marijuana under contract with the National Institute on Drug Abuse. As part of this contract, UM holds a DEA Schedule-I Bulk Manufacturer registration to cultivate plants for this purpose.
- However, in 2016 DEA announced a [new interpretation](#) of the Single Convention to allow other growers to cultivate marijuana to supply researchers. As of July 2017, UM is unaware of any growers who have been approved under this new program.



Ayahuasca visions
Spirits of stones and metals (Pablo Amaringo)

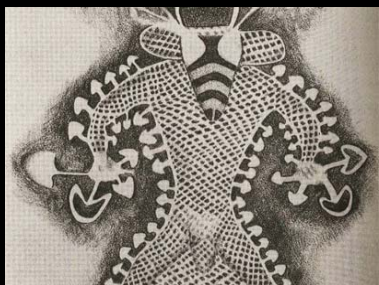
Ibogaine

- Psychedelic with dissociative properties
- Inhibits reuptake of serotonin, Kappa receptor agonist and weak mu receptor agonist
- Proposed for treatment of opioid withdrawal since 1998
- Brown and Alper, Am J Alcohol and Drug Abuse, 2018:
 - 30 subjects, Observational study
 - Subjective Opioid Withdrawal Scale (SOWS) decreased from 31 to 14.8
 - 50% remission at 1 month, sustained at 3 and 12 months



Ketamine/Esketamine

- Schedule III , blocking glutamate reuptake; N-methyl-D-aspartate (NMDA) receptor blocker
- Approved only as injectable anesthetic for pain and also for treatment resistant depression.
- Esketamine ; nasal spray
- Side effects: cistitis, dissociative episodes



Tassili Cave Drawing (Southern Algeria) 6000 B.C.
Bee-Faced Mushroom Shaman (Terence McKenna, *Food of the Gods*)

Language in human evolution

- Language initially developed not as a means of communication with others but rather as a means to hold a personal dialogue with ourselves . (Gould, Steven Jay; *Evolution*; 1997)
- At a later point in evolution the internal thoughts became externalized speech and communication
- In psilocybin neuroimaging you see a closing of the eyes and an opening to the inner world of mind

Paradise found?

- The Tassili in central Sahara may well have been the Garden of Eden
- They brought a cult of cattle, domestication of animals and plants and Great Goddess into pre-Dynastic Egypt
- A lost golden age of plenty, partnership and social balance a nostalgia for the lost paradise
- In this milieu the psilocybin-containing mushrooms were encountered, consumed and deified.
- Pastoral people moved out of Africa due to the drought

one million years of psilocybin

- Opposing thumbs
- Bipedalism
- Binocular vision
- Throwing arm
- Above all language and spirituality

Prehistory and History

- Most of the time that people has lived on earth has been during what we call PREHISTORY
- Today we live during the time period known as HISTORY
- When did one end and the other begin?
- In one word WRITING
- 3500bc writing is invented in Mesopotamia

From the book of Genesis (1200 BC)

•When the woman saw that the fruit of the tree was good to eat, and that it was pleasing to the eye and pleasing to contemplate, she took some and ate it. She also gave her husband some and he ate it. Then the eyes of both of them were opened and they discovered that they were naked, so they stitched fig leaves together and made themselves loin-cloth.

Book of Genesis

3.22. The Lord God made tunics of skin for Adam and his wife and clothed them. He said "The man has become like one of us, knowing good and evil; what if he now reaches out his hand and takes fruit from the tree of life also, eats it and lives forever?" So the Lord God drove him out of the Garden of Eden to till the ground from which he had been taken. He cast him out, and to the east of the Garden of Eden he stationed the cherubim and a sword whirling and flashing to guard the way to the tree of life.

Book of Exodus 16:14

- Then said the Lord unto Moses, Behold, I will rain bread from heaven for you; and the people shall go out and gather a certain rate every day, that I may prove them, whether they will walk in my law or not.
- And when the dew that lay was gone behold, upon the face of the wilderness there lay a small round thing, as small as the hoar frost on the ground.
- And when the children of Israel saw it, they said one to another It is manna: for they wist not what it was. And Moses said unto them. This is the bread which the Lord hath given you to eat

LET'S TAKE A LOOK

- THE BOOK OF GENESIS
- THE BOOK OF EXODUS
- THE RIG VEDA

Soma and the Rig Veda

- The cult to Soma it is described in the earliest Indo-European spiritual writings, the Vedas
- Soma was a juice extracted out of the swollen fibers of a plant, purified and poured through a woolen filter and then was mixed with milk
- Rig Veda is a collection of hymns to Soma of praise for the magical plant; composed in the north-western of India between 1700-1100 B. C.

why only one million years?

- From Homo Africanus to Homo Erectus took five million years
- From Homo Erectus to Homo Sapiens took only a million years
- Homo Erectus lived with and around their cattle
- From simple cave-dwelling hunter-gatherers to farmers and keeper of animals
- Where there are cattle, there are cow pats and where there are cow pats there are mushrooms
- Mushrooms will force the cave-people go within the inner world of mind, induce feeling of oceanic unity

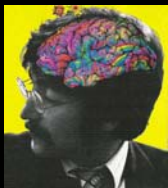
Ninth Mandala (Rig Veda)

- It is drunk by the sick man as medicine at sunrise; partaking of it strengthens the limbs, preserves the legs from breaking, wards off all disease and lengthens life. Then need and trouble vanish away; the poor man, in the intoxication of the Soma, feels himself rich; the draught impels the singer to lift his voice and inspires him for song; it gives the poet supernatural power, so he feels himself immortal

Mushrooms and McKenna

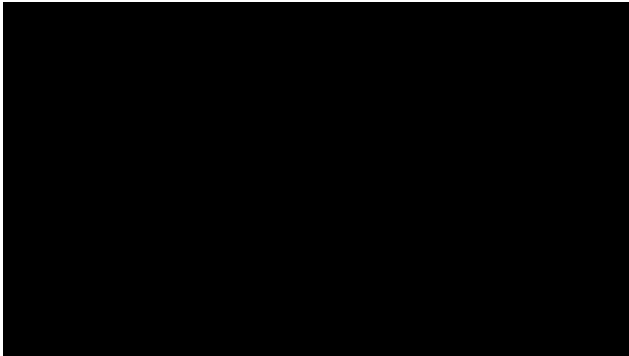
- Gave us thought and thinking gave us language
- Gave us spirituality, cognitive development , religion and shamanism but also gave us alcohol

Thank You!



• Manuel Morales

• manuel.morales@tmcmed.org



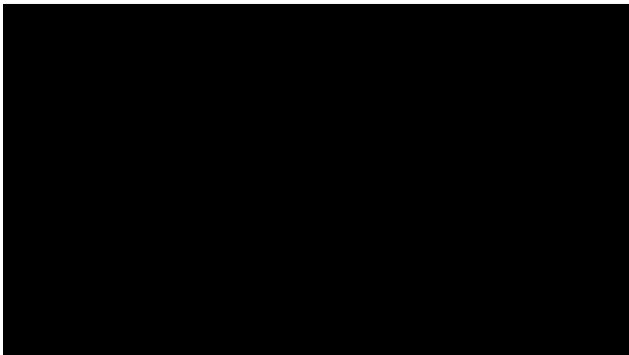
MDMA for Treatment Resistant PTSD

- Randomized triple blind protocol
- 3 Arms: 125mg, 75mg, Placebo=30mg all allowed to take a second half dose.
- Data from Phase-II clinical trials:
- N=107; avg. of 28 years with PTSD
- 63% no longer met criteria for PTSD two months after study (67% at one year follow up).
- Effect size = 0.9 (large).

(Mithoefer MAPS, 2017)

Group	Baseline (N=107)	12-Month Follow-up (N=86)
Placebo	85.8	69.7
Active Dose	81.3	37.8

(48 point drop)



RECOMMENDED BOOKS

- "THE CHALICE AND THE BLADE" By Riane Eisler
- "THE PSYCHEDELIC RENAISSANCE" By Ben Sessa
- "PSYCHEDELIC DRUG TREATMENTS" By Ben Sessa
- "FOOD OF THE GODS" By Terence McKenna
- "AYAHUASCA VISIONS" By Pablo Amaringo and Luis Luna
-
