Psychedelics in Psychiatry

Nicole Fox, MD, MPA, FAPA

Board Certified Psychiatrist and Lifestyle Medicine Physician

President-Elect, Idaho Psychiatric Association

Clinical Assistant Professor, University of Washington

Associate System Medical Director, Behavioral Health, St. Luke's Health System
Disclosures

• I have no disclosures.
"What we ordinarily call ‘reality’ is merely that slice of total fact which our biological equipment, our linguistic heritage and our social conventions of thought and feeling make it possible for us to apprehend."

-Aldous Huxley
Agenda

- Definitions
- History
- Psychedelic Renaissance
- Highlights
  - Classical psychedelics
  - Entactogens / Empathogens
  - Dissociative substances
- Session Overview
- Challenges
- Research Directions
The Psychedelics: 
a few definitions

- **psychomimetic**: drug or substance that produces psychological and behavioral changes resembling those of psychosis.
- **mind altering substances**: something that changes a mood or perceptions.
- **psychosis inducer**: a substance that produces psychosis.
- **entheogens**: a substance, typically of plant origin, that is ingested to produce a non-ordinary state of consciousness for religious or spiritual purposes.
History

Ancient Times and Indigenous Use

Early Science

Prohibition

Renaissance
Ancient Times and Indigenous Use

- Evidence points to the use of psychedelic plants as early as 3500 BCE
- Traditional uses were tied to religious ceremonies, used for pain control and to prepare for battle
- Cacti including peyote, san pedro and peruvian torch containing mescaline which can be dried and smoked or infused into water or alcohol (mescal)
- Psilocybin, a mushroom native to the Americas ingested through chewing or creating a tea, to treat pain and participate in ceremonies
- Cannabis, typically from the marijuana plant, which has milder psychedelic properties
- Ayahuasca, a brew made from plants in the Amazon rainforest; contains the potent psychedelic DMT
- Salvia, a flowering plant which is a dissociative whose leaves can be smoked, chewed or made into a tea
Early Science: late 1800s-1960s

- 1895 first scientific trial involving peyote in Washington, DC at (now) George Washington University
- 1912 Anton Köllisch, a German chemist, became the first person to synthesize MDMA
- 1919 Ernst Spath synthesizes mescaline
- 1931 Richard Manske, a Canadian chemist, is the first to synthesize DMT
- 1938 chemist Albert Hoffman created d-lysergic acid diethlamide, aka LSD
- 1943 Hoffman self administers; starts to publish on methodologies and findings
- 1947 Sandoz Laboratories markets LSD and distributes it to psychiatrists to study effects on mental disorders
- 1958 Hofmann isolates and figures out the structure of psilocybin and psilocin
- 1960s Stanislav Grof, MD, PHD carried out more than 4,000 LSD-assisted therapy sessions
- 1966 ban on manufacturing and sales of peyote, mescaline, LSD, and DMT were prohibited in the US
- 1968 ban on personal use or possession for any reason
- 1970 Controlled Substances Act- schedules
Timeline of LSD

1938
Albert Hoffman synthesized LSD; searching for ergot-alkaloid derivatives useful for medicinal purposes

1943
Hoffman used himself as the first human test study, ingesting 250 micrograms

1947
Sandoz began producing LSD

1950s
CIA starts ‘project “MK Ultra”; administers LSD to subjects to monitor response: military, government agents, physicians, mentally ill patients, prostitutes, and the public

1963
Sandoz patent expires; US classifies LSD as “investigational drug” creating restrictions on medical and scientific use

1968
Possession of LSD made illegal in US; research ban

1970
Controlled Substances Act; Schedules
Schedule 1 substance

1) Is deemed to have a high abuse potential

2) Has no legitimate medical use and treatment

3) There is a lack of accepted safety for its use under medical supervision

“the DEA’s definition for high potential for abuse really means that people will take it without a prescription. It doesn’t necessarily mean that it has the possibility of people getting addicted”

–David Nichols, PhD, Professor of Medical Chemistry and Molecular Pharmacology
What Happened?

- Before LSD was banned, the NIH funding more than 130 studies into the use of LSD for a variety of mental health conditions including anxiety, depression and alcohol use disorder.

- Led to rapid advancements in brain science.

- Adoption by the public of recreational use, and association with Vietnam era anti-war sentiments, led to fear, altered political landscape and ultimately banning of further study.
Psychedelics Renaissance: Current State of Study

- The efforts of a dedicated few early on, paved the way to the recent resurrection of psychedelics study and renaissance
- Roland Griffiths et al discovered that a dose of psilocybin led to enduring improved mood and sense of well being when administered therapeutically
- Neuroimaging studies by Carhart-Harris and Nutt found that psilocybin dosing produced alterations in brain function, particularly in the default mode network, similar to an anti-depressant effect
- Studies paved the way for further investigation into depression, anxiety, substance use disorders, etc
- Likely future state, licensed for medicinal use in approved diagnoses

Psychedelics Renaissance Timeline

- **1998** Franz Vollenweider discovers LSD and psilocybin bind 5-HT2A receptor
- **1999** Roland Griffiths, PhD establishes research at Johns Hopkins University to study the effects of psilocybin
- **2006** Griffiths publishes paper showing that psilocybin can induce mystical experiences
- **2009** Robin Carhart-Harris, PhD studies psilocybin in the UK
- **2011** Charles Grob, MD, publishes research on psilocybin reducing anxiety in cancer patients
- **2014** Petri et al demonstrates with imaging that psilocybin increases neuronal connectivity.
- **2016** Robin Carhart-Harris, PhD publishes on LSD increasing connectivity
- **2018** Study illustrates that ayahuasca leads to significant decreases in symptoms of depression
- **2019** Imperial College London launches Centre for Psychedelics Research*
- **2019** Launch of Hopkins Center for Psychedelic and Consciousness Research*
Current Wave

PSYCHEDELICS TAKE FLIGHT

Over the past decade, there has been an increase in clinical trials testing psilocybin, MDMA and LSD for use in psychiatric conditions, including depression, drug dependency and anorexia nervosa.

- Black = 1 trial
- Light blue = Psilocybin
- Orange = MDMA
- Blue = LSD


17 trials

Paused
### Psychiatric indications* under evaluation

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* Non-psychiatric indications under study as well including neurodevelopmental disorders (autism spectrum disorders), neurodegenerative disorders (Alzheimer’s, Parkinson’s, MS), pain conditions like headache, phantom limb and fibromyalgia, etc
Psychedelic medicine: a re-emerging therapeutic paradigm

Kenneth W. Tupper PhD, Evan Wood MD PhD, Richard Yensen PhD, Matthew W. Johnson PhD
Psychedelic drugs—a new era in psychiatry?

David Nutt, DM, FRCP, FRCPsych, FMedSci
Psychedelic Research for Mass Mental Health

At MAPS, we've been dedicated to psychedelic research since 1986. Now, we're shifting perceptions to give medicine and our society the tools needed to heal—no matter who you are.
Classic Psychedelics

- Examples: LSD, Psilocybin, DMT (N,N-dimethyltryptamine)
- Serotonergic hallucinogens
- Full or partial agonists of serotonergic 5-HT2a receptors
- Induce a state of altered perception, thought and feeling
Empathogens / Entactogens

- Example: MDMA aka ecstasy (3,4-methylenedioxymethamphetamine)
- Mixed serotonin and dopamine reuptake inhibitors and releasers
- Induce a sense of emotional connectivity and increased sociability
Dissociatives

- Example: Ketamine
- Reduces excitation, causes sedation and perceptual distortion
- Overly simplified: antagonism at NMDA receptor
- Leads to an increase in glutamate in the PFC
- Glutamate cascade stimulate receptors downstream that may increase expression of synaptic proteins leading to remodeling, e.g., increased synaptic plasticity
Book Excerpt:

“I received my first license to practice clinical psychology in 1966 while teaching psychology at the University of Michigan in Ann Arbor. One evening a colleague invited me to his home where he offered me the opportunity to experience DMT (dimethyltryptamine). I took one puff of the normal appearing cigarette, immediately closed my eyes, lay back, and explored the very deepest core of my consciousness and the very borders of the universe.

I had a clear sense that within the infinite universes I was smaller than what I see while using an electron microscope. I experienced being and nothingness. The experience lasted about twelve minutes. I sat up and asked for another puff. Once again I embarked on inner-space travel. I became a dematerialized inner-space traveler transcending time. I soared through the universe in search of the Source. I had a clear sense that I was a part of, and expression of, the whole of it all. My journey had begun.”

-Dr. Richard Louis Miller, Psychedelic Medicine: the healing powers of LSD, MDMA, psilocybin and ayahuasca
Sessions

- A preparation session with a trained therapist, known as a guide is typical
- Explores the potential experience and approaches to any challenges
- In session, the patient may be offered eye shades and headphones with music compiled in advance
- Psilocybin sessions may last 4-5 hours
- The guide is present for assurance; however, the patient is not typically expected have significant engagement with the therapist
- Patients will typically experience an inner journey into visions, memories, thoughts
- Post session follow up: integration of experience + plan for ongoing psychotherapy
Challenges?

- Substances highly regulated: scheduled as dangerous, illegal drugs.
- How do you train an adequate number of therapists to act as guides?
- How do you ensure fidelity to good practice through structured, manaulized treatment?
- How do you keep patients safe from those who would take advantage of “the next best thing?” without adequate training and knowledge?
- What is that necessary training and knowledge?
- How do you monitor outcomes in non-study environments?
- How do you prevent another prohibition?
- Other challenges you’ve identified?
Future Research Directions

Can psychedelics provide therapeutic effects without the “trip”; e.g., can the hallucinogenic and “mind-altering properties” be disentangled from the inner journey or is it the inner journey that provides therapeutic benefit?

But how do they really work?

What is consciousness?

What is reality?

How does my view of the world inform my response to it?
“Consciousness does not just passively reflect the objective material world; it plays an active role in creating reality itself.”

- Stanislav Grof, MD, PhD
References


• FDA grants Breakthrough Therapy designation for MDMA-assisted psychotherapy for PTSD, agrees on special protocol assessment for phase 3 Trials. News release. Multidisciplinary Association for Psychedelic Studies; August 26, 2017.


Thank You