

# Psychedelics and the use of psilocybin for psychological and existential distress at end-of-life

*Dr. Ryan Patchett-Marble, MD, CCFP  
Assistant Professor, NOSM*

**Preamble**

**Psychedelics  
Presentation**

**Tracey's  
Story**

# Financial Disclosures

*Disclosure of Affiliations, Financial Support, and Mitigating Bias*  
*Speaker Name: Dr. Ryan Patchett-Marble*

**Affiliations:**

I am a volunteer clinical advisor for the non-profit patient advocacy group TheraPsil

**Financial Support:**

This session/program has not received financial or in-kind support.

**Mitigating Potential Bias:**

Referencing peer-reviewed publications



# Objectives

By the end of this session, participants will be able to:

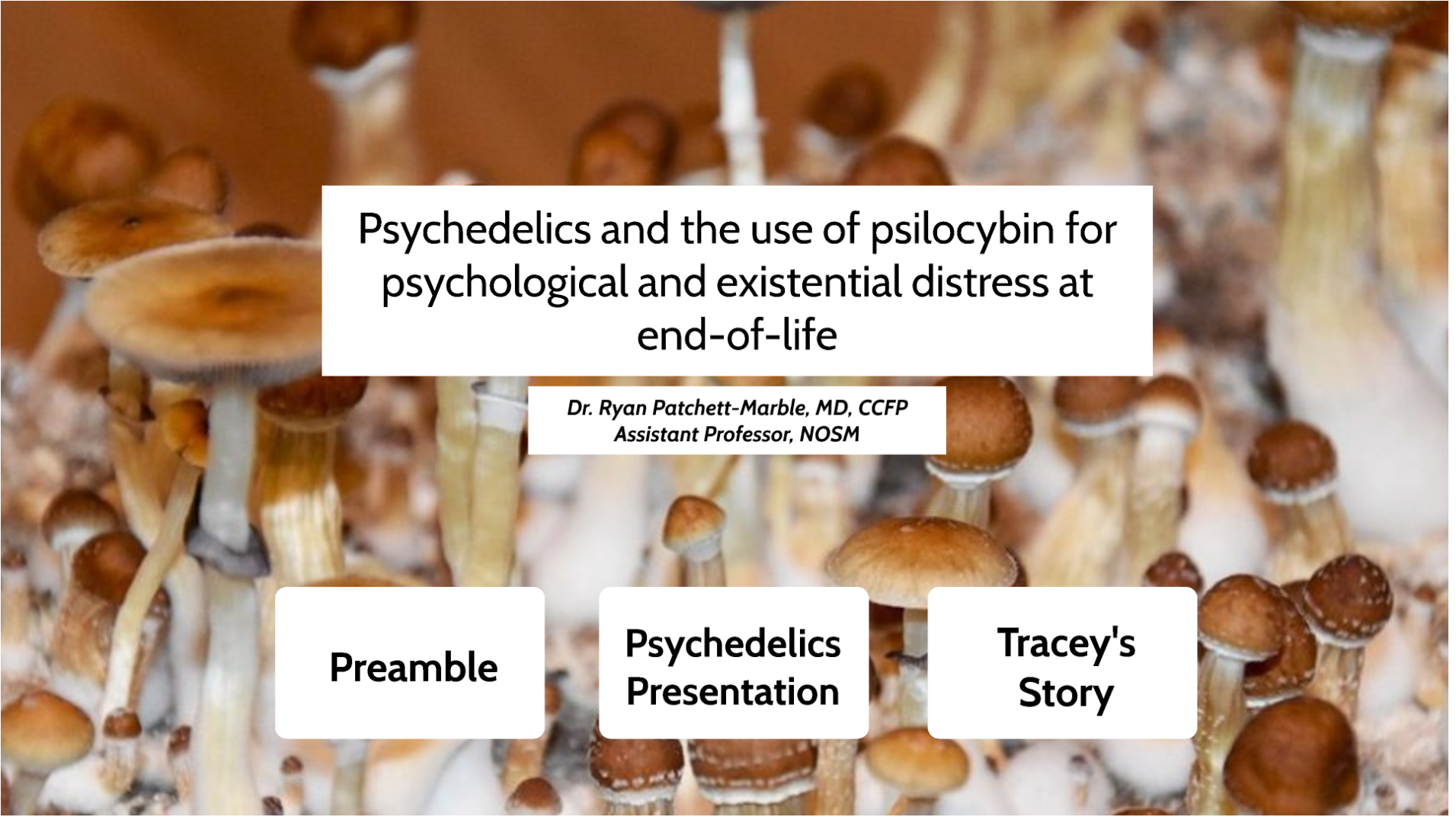
- 1** Describe the terminology and relevant history of psychedelic medicine
- 2** Summarize the medical evidence for psilocybin at end-of-life
- 3** Apply knowledge to direct patient care

# My Background

Clinical work/interests

Psychedelics

- Training
- Clinical experience



# Psychedelics and the use of psilocybin for psychological and existential distress at end-of-life

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The background of the slide is a close-up photograph of several mushrooms, likely psilocybin mushrooms, with light-colored stems and brown, gilled caps. The image is slightly blurred, creating a soft, naturalistic feel.

**Background**

**Clinical  
Research**

**Psychedelics and the use of  
psilocybin for psychological and  
existential distress at end-of-life**

**Mechanisms  
of Action**

**Treatment  
Process**

**Summary**



A close-up photograph of several mushrooms with light brown caps and stems, growing on a bed of dry leaves. The image is slightly blurred, creating a soft, naturalistic background.

# Psychedelics

*Background*

**What are  
they?**

**History of  
Psychedelics**

# Psychedelic Substances

## *Terminology*

### Psychedelic

- "psyche" = mind/soul/spirit
- "deloun" = reveal/manifest/appear/make clear
- "mind-manifesting capability, revealing useful or beneficial properties of the mind" (Osmond, 1957)

# Psychedelic Substances

## *Classification*

- Classic Psychedelics
  - Psilocybin, LSD, Mescaline, DMT
- Dissociative Anaesthetics
  - Ketamine, Dextromethorphan, Nitrous Oxide
- Empathogen/Entactogen
  - MDMA
- Other
  - Cannabis and many more...

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# Psychedelics

*Background*

**What are  
they?**

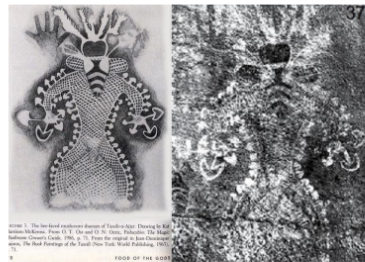
**History of  
Psychedelics**



# History of Psychedelics

*A long time ago...*

- Used across the world for centuries, or even millennia (Nichols 2016)
- Bee shaman 6000-9000 years ago





# History of Psychedelics

*The Science...*

1943 - LSD-25 properties discovered



1957 - "Magic Mushrooms" brought to America

1959 - Psilocybin isolated

# History of Psychedelics

*The Science...*

*This was not a quickly rejected and forgotten fad. Between 1950 and the mid-1960s there were more than a thousand clinical papers discussing 40,000 patients, several dozen books, and six international conferences...it aroused the interest of many psychiatrists who were in no sense cultural rebels or especially radical in their attitudes.*

- Grinspoon 1979



# History of Psychedelics

*The Dark Days?*

1960s - "Hippie" Counterculture Movement



early 1970s - psychedelics made illegal in Canada

# History of Psychedelics

*The Dark Days?*



# History of Psychedelics

*Rebirth...*

1990s - small studies resume

2000s-2010s - RCTs at prestigious research institutions

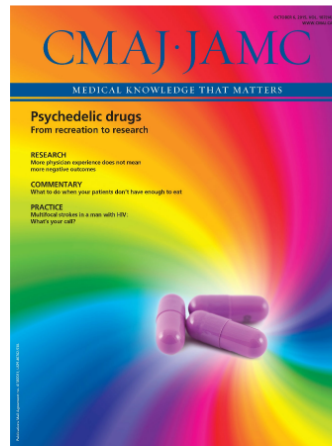


For the history of Psychedelics and Palliative care, see *Psychedelics and Dying Care: A Historical Look at the Relationship between Psychedelics and Palliative Care* (Dyck 2019)

# History of Psychedelics

*Present day*

- In the news...





## Psychedelic drugs

From recreation to research

### More physician experience does not mean more negative outcomes

### What to do when your patients don't have enough to eat

### Multifocal strokes in a man with HIV: What's your call?





# Denver becomes the first city to decriminalize hallucinogenic mushrooms



By [Nicole Chavez](#) and [Ryan Prior](#), CNN

⌚ Updated 4:25 PM ET, Thu May 9, 2019



GETTY IMAGES

More from CNN



The Ki  
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## NEWS

# Oakland in California decriminalizes magic mushrooms and peyote

Elizabeth Weise and Marco della Cava USA TODAY

Published 2:40 a.m. ET Jun. 5, 2019 | Updated 2:27 p.m. ET Jun. 5, 2019



SAN FRANCISCO – First pot, now ‘shrooms. Oakland City Council in California on Tuesday voted unanimously to decriminalize hallucinogenic fungi, otherwise known as “magic mushrooms.”


The vote makes Oakland the second U.S. city to decriminalize the natural



LIVE

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# Canada Is Allowing Dying People to Do Psychedelic Mushrooms

Health Minister Patty Hajdu has granted four people with terminal cancer access to psilocybin mushrooms through an exemption to the Controlled Drugs and Substances Act.



By [Manisha Krishnan](#)  
TORONTO, CANADA

5.8.20



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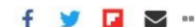


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# Ann Arbor Decriminalizes Magic Mushrooms, Psychedelic Plants

The city of Ann Arbor has decriminalized psychedelic plants and fungi, including magic mushrooms, and police officers will no longer make them an enforcement focus.

By Associated Press, Wire Service Content Sept. 26, 2020, at 10:57 a.m.



## Heart Racing & Short of Breath

A man presents to his PC physician because of shortness of breath and racing of his heart.

Medscape.com

OPEN



HEALTH AND SCIENCE

# Oregon becomes first state to legalize magic mushrooms as more states ease drug laws in 'psychedelic renaissance'

PUBLISHED WED, NOV 4 2020•10:55 AM EST | UPDATED FRI, NOV 6 2020•6:31 AM EST



Will Feuer  
@WILLFOIA

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## KEY POINTS

- Oregon on Wednesday became the first state to legalize the active ingredient in so-called magic mushrooms on an election night that saw more states ease restrictions on drugs across the country.



Spor

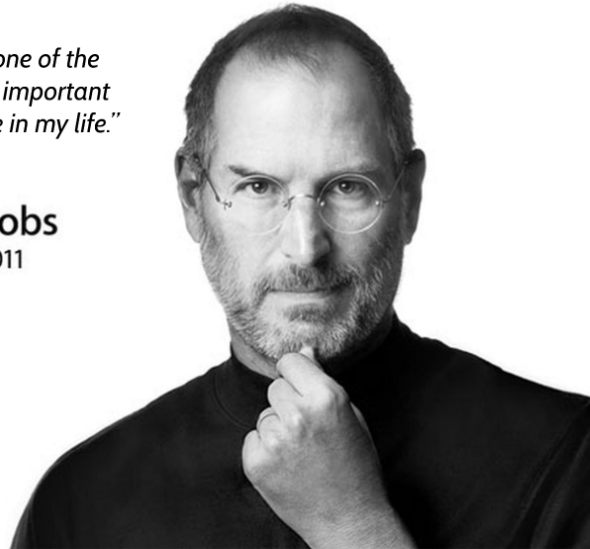
# History of Psychedelics

*Present day*

- pop culture...

*Taking LSD was "one of the  
two or three most important  
things I have done in my life."*

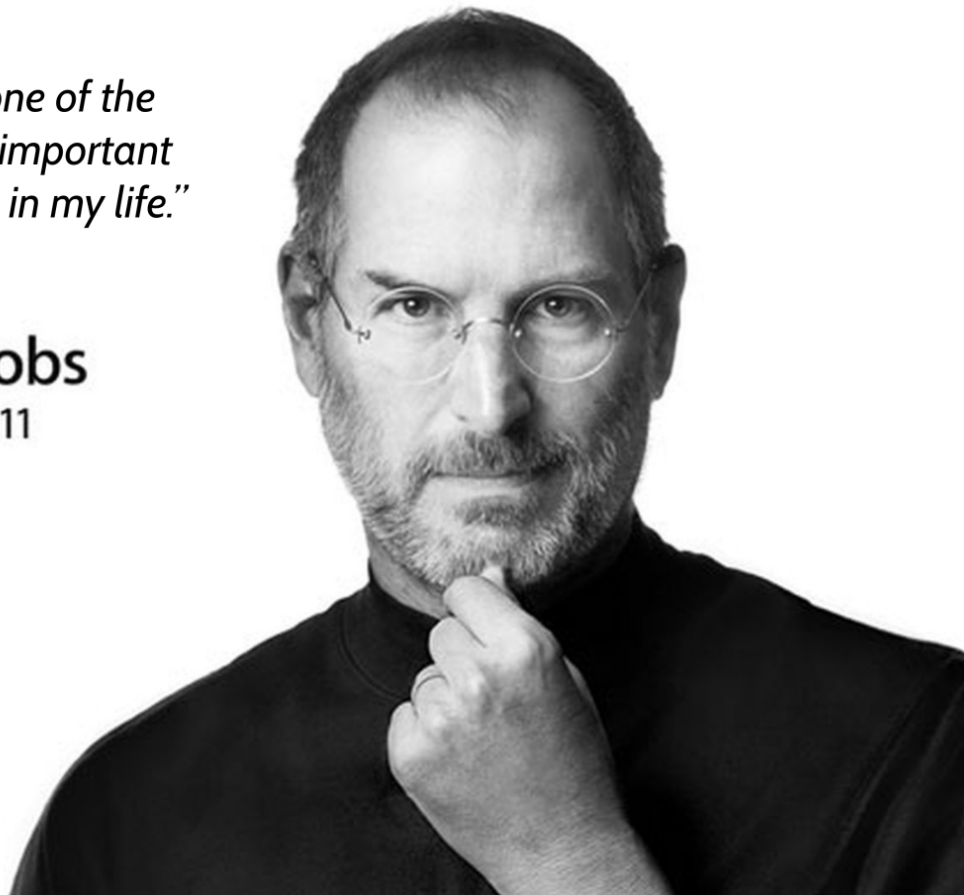
**Steve Jobs**  
1955-2011

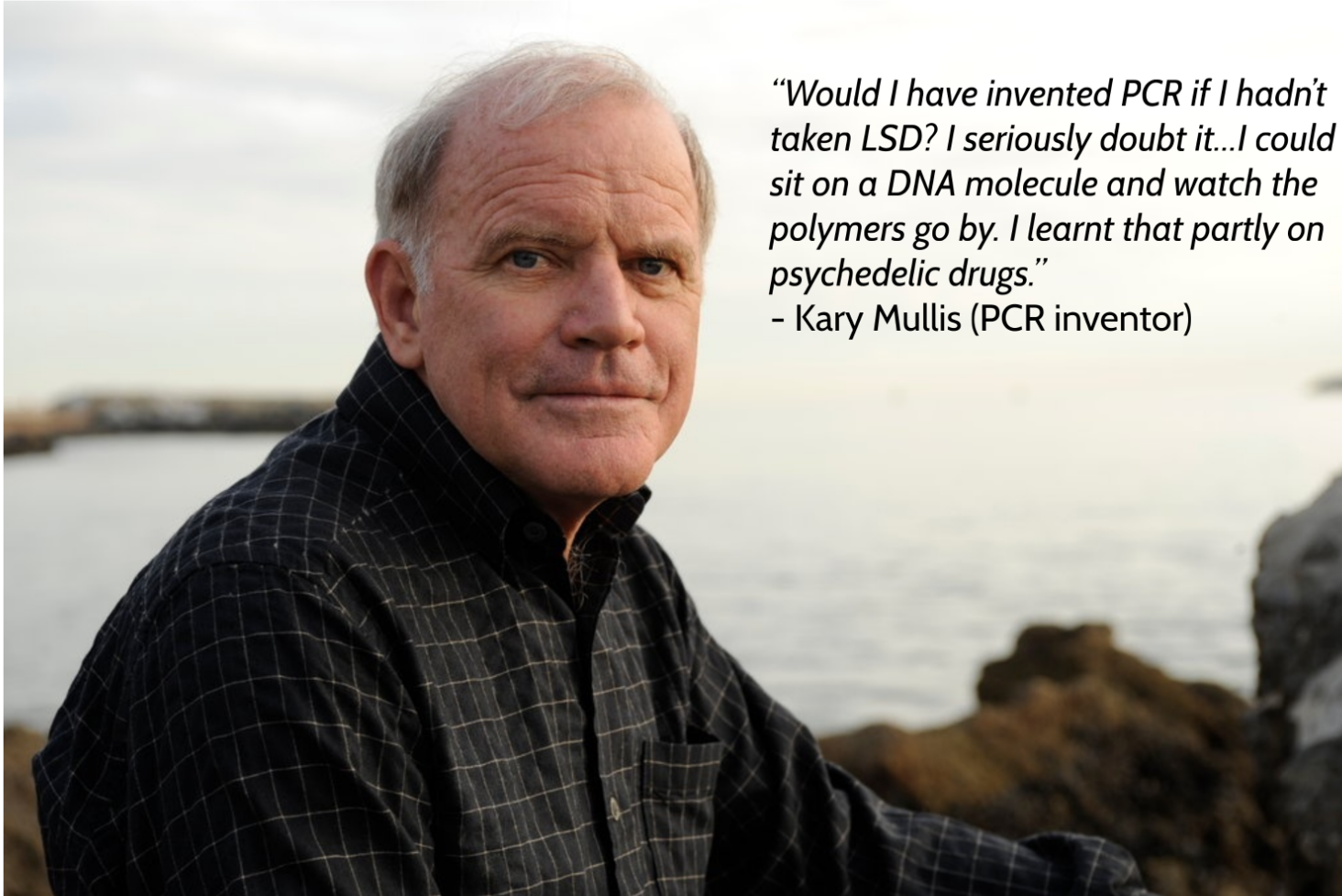




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**Steve Jobs**  
1955-2011





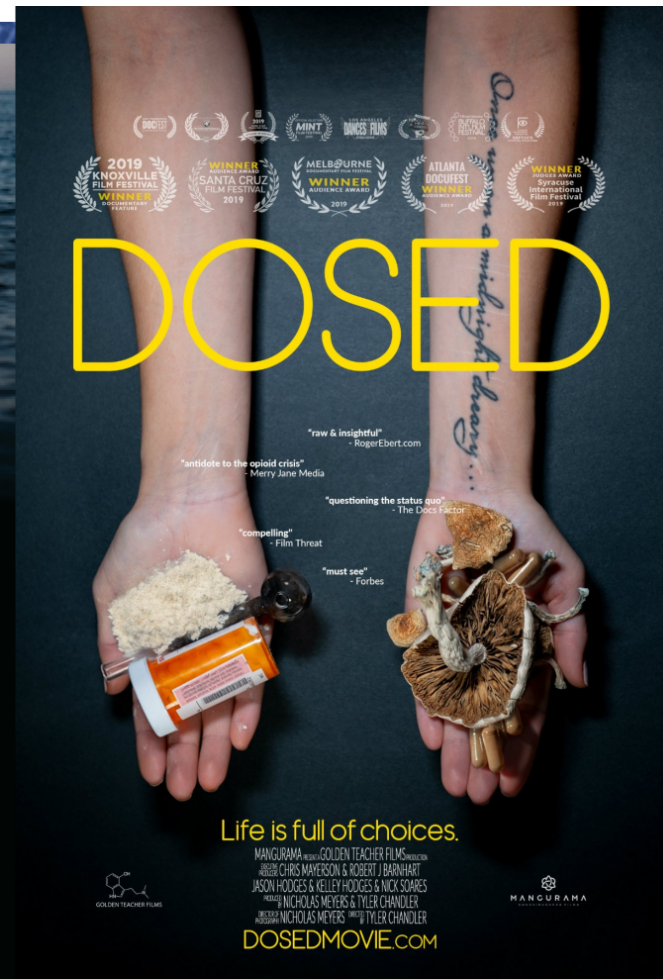
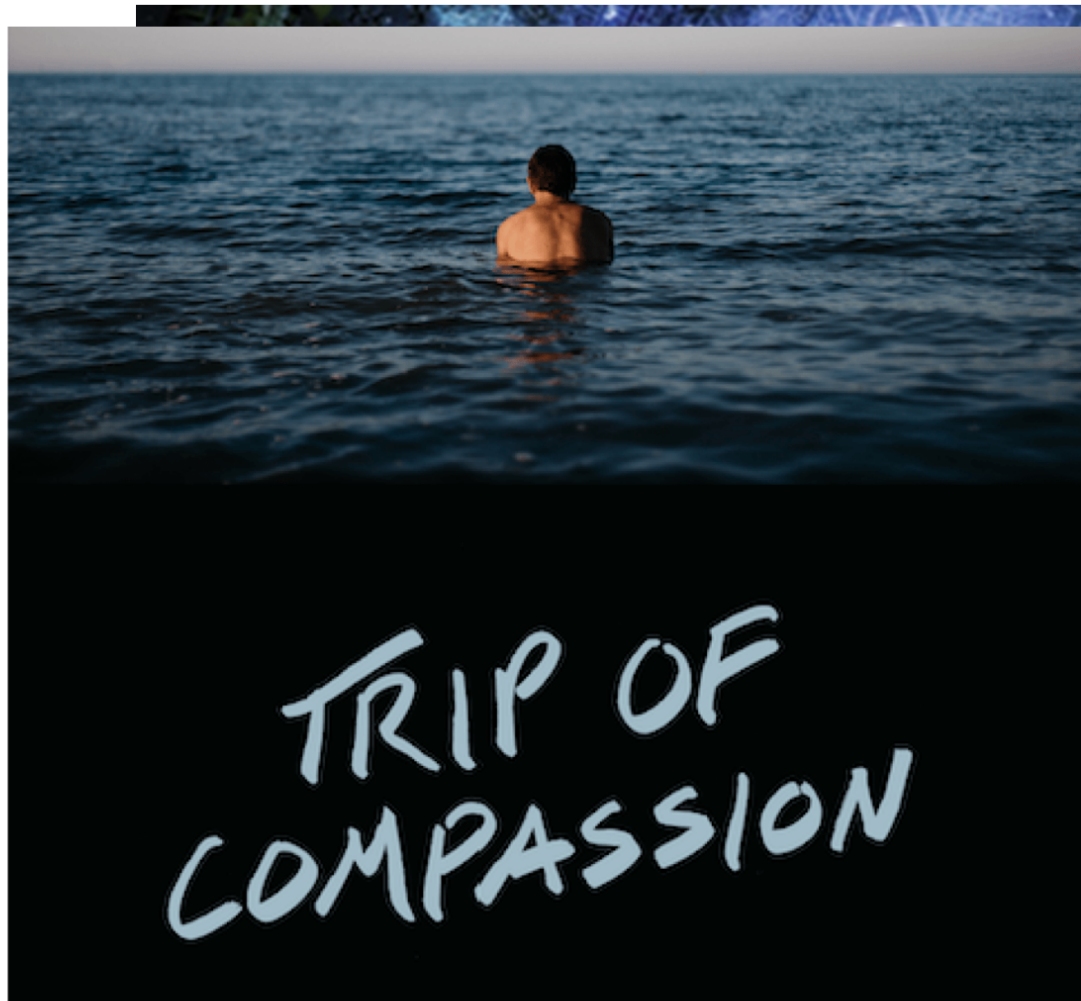
*"Would I have invented PCR if I hadn't taken LSD? I seriously doubt it...I could sit on a DNA molecule and watch the polymers go by. I learnt that partly on psychedelic drugs."*

- Kary Mullis (PCR inventor)

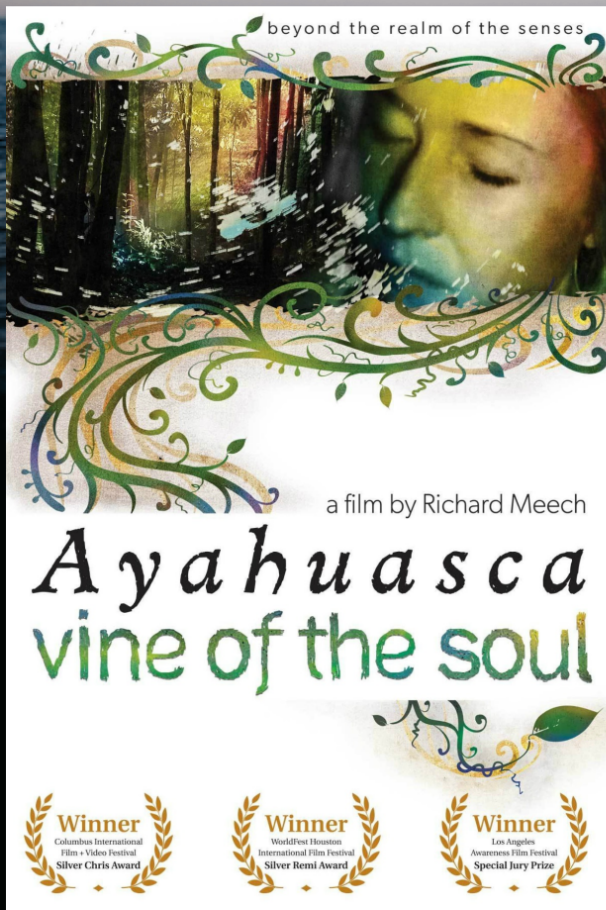


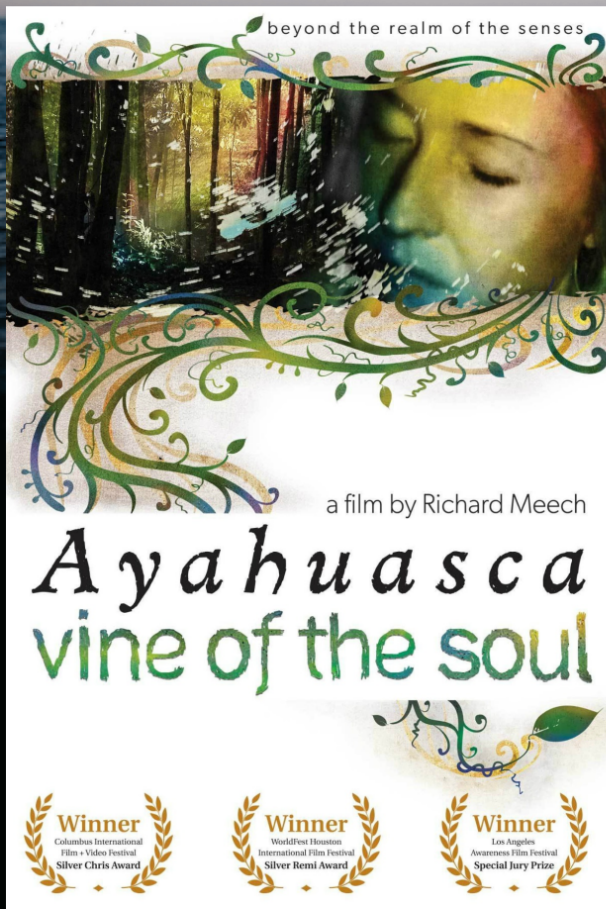




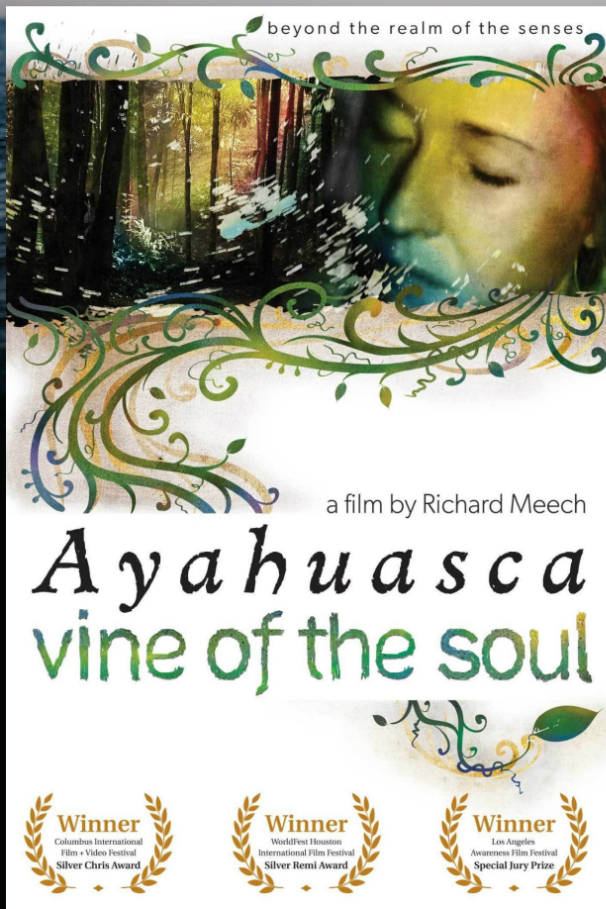












## How to Change Your Mind

What the New Science of Psychedelics Teaches Us About Consciousness, Dying, Addiction, Depression, and Transcendence

Michael Pollan

Author of *The Omnivore's Dilemma*

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**Background**

**Clinical  
Research**

**Psychedelics and the use of  
psilocybin for psychological and  
existential distress at end-of-life**

**Mechanisms  
of Action**

**Treatment  
Process**

**Summary**



# Psychedelic Clinical Research

*What does the medical evidence show?*

**"Palliative  
Care"**

**Depression**

**Addiction**

**PTSD**

**Spirituality**

**Other**

# Psychedelics and Palliative Care

## *Overview of Clinical Trials*

Only four recent RCTs (2011-2020), two largest studies (n=80):

<b>Population</b>	Life-threatening cancer
<b>Intervention</b>	Moderate to high-dose psilocybin (one session)
<b>Comparison</b>	Very low-dose psilocybin, or niacin
<b>Outcome measures</b>	<b>Psychological and Existential Distress</b>

*(Grob 2011, Gasser 2014, Griffiths 2016, Ross 2016, Agin-Liebes 2020)*



# Psychedelics and Palliative Care

## *Results of Clinical Trials*

- From largest study (JHU - Griffiths 2016)
  - 2/3 of patients had one of the top 5 most spiritually significant, and/or personally meaningful, experience of their lives
  - Over 80% said psilocybin increased well-being or life-satisfaction moderately or very much at 6-month study completion
  - "psilocybin produced large and significant decreases in depression, anxiety or mood disturbance, and increases in measures of quality of life, life meaning, death acceptance, and optimism. These effects were sustained at 6 months."

# Psychedelics and Palliative Care

## *Results of Clinical Trials*

- From 2nd largest study (NYU - Ross 2016):
  - (Essentially the same results at 6 month follow-up)*
  - \* In addition, results sustained at 4.5y (Agin-Liebes 2020)

# Psychedelics and Palliative Care

## *Results of Clinical Trials - Adverse Events*

- Short-term effects (Johns Hopkins study):
  - No serious adverse events attributed to psilocybin administration occurred
  - Elevated BP (34% vs 17%) Nausea or vomiting (15%), Physical discomfort (21% vs 8%), Psychological discomfort (32% vs 12%), Anxiety (26% vs 15%)
- Psilocybin has been administered to human participants over 2000 times since the 1990s, in controlled academic settings, reporting no serious adverse events (Studerus 2011).



# Psychedelics and Palliative Care

## *Conclusions of Clinical Trials*

- RCTs suggest that psilocybin-assisted psychotherapy leads to immediate and substantial improvement in QOL and psychological/existential distress (Griffiths 2016, Ross 2016)
  - Results sustained to study completion (up to 4.5y in one RCT) (Agin-Liebes 2020)
- Clinical outcomes appear to be mediated by the degree of mystical experience (Griffiths 2016, Ross 2016)



# Psychedelic Clinical Research

*What does the medical evidence show?*

**"Palliative  
Care"**

**Depression**

**Addiction**

**PTSD**

**Spirituality**

**Other**

# Psychedelics and Depression

*What do we know from the Medical Literature?*

*Beyond scope of discussion today*



# Psychedelic Clinical Research

*What does the medical evidence show?*

**"Palliative  
Care"**

**Depression**

**Addiction**

**PTSD**

**Spirituality**

**Other**

# Psychedelics and Addiction

*What do we know from the Medical Literature?*

*Beyond scope of discussion today*



# Psychedelic Clinical Research

*What does the medical evidence show?*

**"Palliative  
Care"**

**Depression**

**Addiction**

**PTSD**

**Spirituality**

**Other**

# Psychedelics and PTSD

*What do we know from the Medical Literature?*

*Beyond scope of discussion today*





# Psychedelic Clinical Research

*What does the medical evidence show?*

**"Palliative  
Care"**

**Depression**

**Addiction**

**PTSD**

**Spirituality**

**Other**

# Psychedelics and Spirituality

*What do we know from the Medical Literature?*

*Beyond scope of discussion today*



# Psychedelic Clinical Research

*What does the medical evidence show?*

**"Palliative  
Care"**

**Depression**

**Addiction**

**PTSD**

**Spirituality**

**Other**

# Psychedelics and Other Indications

*What do we know from the Medical Literature?*

*Beyond scope of discussion today*



# Psychedelic Clinical Research

*What does the medical evidence show?*

**"Palliative  
Care"**

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Psychedelics and the use of  
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**Summary**



# Psychedelics

*Mechanisms of Action*

**Neurological**

**Experiential**

# Psychedelics

## *Neurological Mechanism of Action*

- Neurochemistry:
  - “Classic” psychedelics are full or partial agonists at the serotonin 2A (5-HT2A) receptor (Glennon 1984)
  - 5-HT2A receptors are abundant throughout the neocortex (Carhart-Harris 2014)

# Psychedelics

## *Neurological Mechanism of Action*

- Default Mode Network (DMN):
  - network of brain structures - neurological basis for "self"? (Andrews-Hanna 2012)
- DMN implicated in depression, GAD, PTSD, and many others (Buckner 2008)
- Psychedelics (and meditation) reduce the activity of DMN (Milliere 2018)



# Psychedelics

*Mechanisms of Action*

**Neurological**

**Experiential**



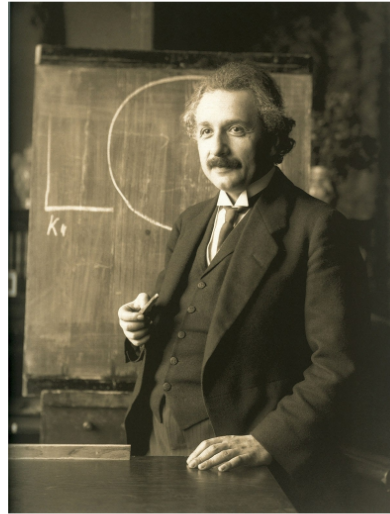
# Psychedelics

## *Experiential Mechanisms of Action*

What experience does a psychedelic induce?

- See Dr. Stanislav Grof's extensive work, including cartography of the psyche
- One domain of experience is the "mystical" experience...

# Mystical Experiences



*The most beautiful and profound emotion we  
can experience is the sensation of the mystical.*  
- Albert Einstein

# Mystical Experiences

*What are they?*

- Direct experience of a transcendent reality (sometimes called spiritual/religious/sacred experience)
- "Mystics" may be considered “empirical” theologians (Huxley, 1947)
- Numerous definitions for trying to qualify a "mystical experience"
  - Pahnke 1963 - nine criteria...

# **Mystical Experiences**

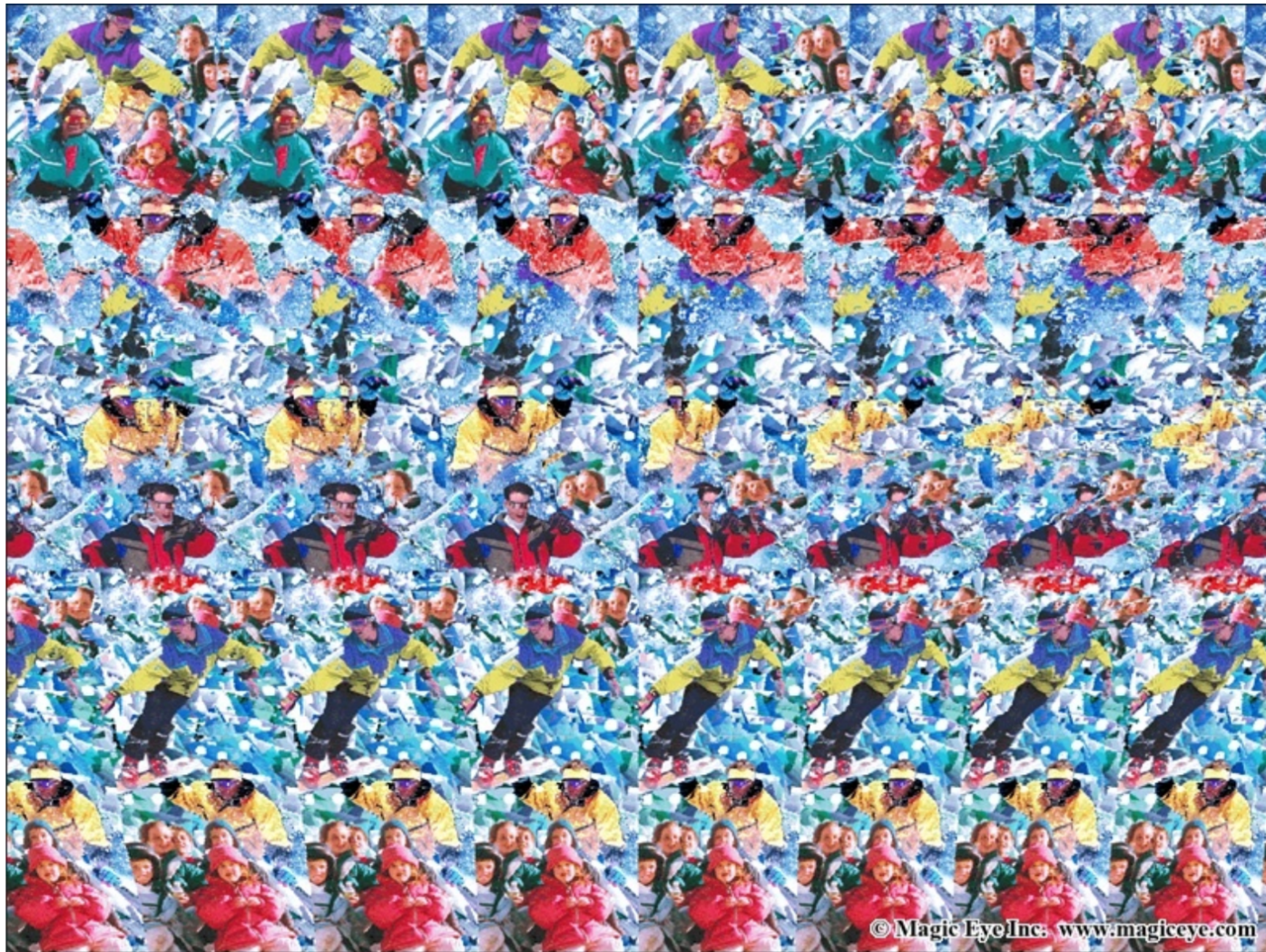
*Definition and Core features*

# Mystical Experiences

*Definition and Core features*









# Mystical Experiences

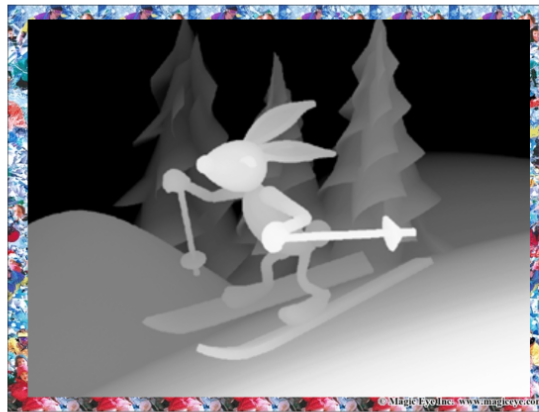
*Definition and Core features*

*Doesn't see "It":*



*"There's nothing there"*

*"You're crazy..."*



*Sees "It":*



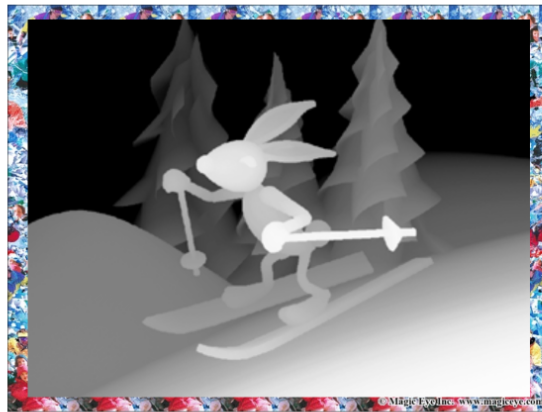
*"Wow! It's so obvious!"*

*"You can't convince me  
it's not there."*

# Mystical Experiences

*Definition and Core features*

*Doesn't see "It":*



*Sees "It":*

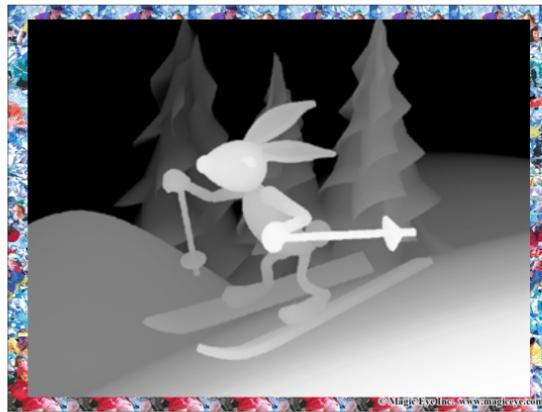
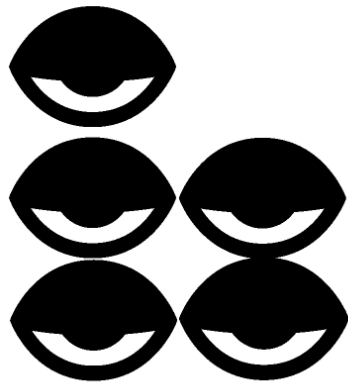




# Mystical Experiences

*Definition and Core features*

*Doesn't see "It":*



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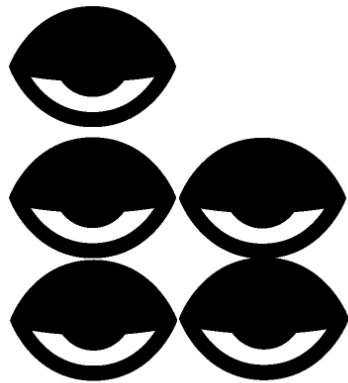


# Mystical Experiences

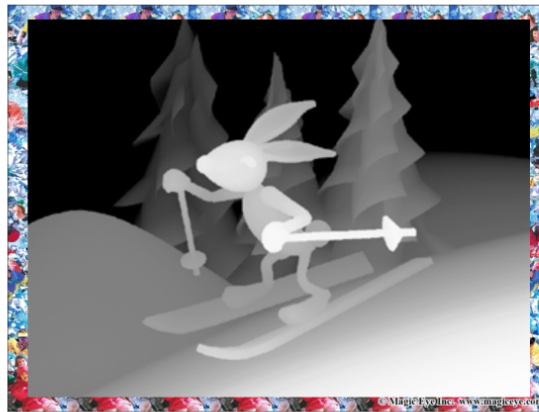
*Definition and Core features*

## 1 Noetic Quality ("Ultimate Truth")

*Doesn't see "It":*



*"There's nothing there"*



*Sees "It":*



*"You STILL can't  
convince me it's not  
there."*

# Mystical Experiences

*Definition and Core features*

- 2 Alleged Ineffability
- 3 Unity
- 4 Transcendence of Time and Space
- 5 Sacredness (Awe, humility, wonder)

# Mystical Experiences

## *Definition and Core features*

- 6 Deeply felt positive mood
- 7 Transiency
- 8 Paradoxicality
- 9 \*Persisting positive changes in attitude and behaviour

# Mystical Experiences

*Why are they important?*

- associated with abrupt, substantial, and sustained changes in behavior and perception (Miller 2001)
- unpredictable and low probability of occurring "naturally" (Griffiths 2018)

# Mystical Experiences

## *Induction with Psychedelics - The Good Friday Experiment*

Can a psychedelic induce a mystical experience in predisposed subjects?  
(Pahnke 1963, Doblin 1991)

- Prior to Good Friday service, 20 divinity students at Harvard were double-blinded to psilocybin 30mg or niacin (control)
- Almost all of psilocybin group reported profound religious experiences
- In follow-up (6 months and 25 years), psilocybin group rated persisting positive changes that they attributed to their psilocybin experience
- At 25y f/u, 6/7 participants from psilocybin group described the experience as a “genuine” mystical experience, and one of the “high points” of their spiritual lives

# Mystical Experiences

*Induction with Psychedelics - The Good Friday Experiment*

"...the most powerful cosmic homecoming I have  
ever experienced."

- Huston Smith



# Mystical Experiences

## *Induction with Psychedelics - Recent Clinical Trials*

What about more recent clinical trials - how effective are psychedelics at inducing a "complete" mystical experience?

Healthy volunteers - **61%** (Griffiths 2006), **58%** (Griffiths 2008 f/u study)

Healthy volunteers - **72%** at doses of 20mg and/or 30mg (Griffiths 2011)

Smoking cessation study - **60%** (Garcia-Romeu 2014)

*\*When administered under supportive conditions*



# Psychedelics

*Mechanisms of Action*

**Neurological**

**Experiential**

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**Background**



**Clinical  
Research**



**Mechanisms  
of Action**



**Treatment  
Process**

**Summary**

Psychedelics and the use of  
psilocybin for psychological and  
existential distress at end-of-life

A close-up photograph of several mushrooms with brown caps and light-colored stems, growing on a white surface. The mushrooms are in various stages of growth, with some showing gills and others being more rounded.

# **Psychedelic Treatment Process**



A close-up photograph of several mushrooms with brown caps and light-colored stems, growing on a white surface. The image is slightly blurred, creating a soft, ethereal atmosphere.

**Patient  
Interest?**

# **Psychedelic Treatment Process**

# Psychedelic Treatment Process

## *Assessing Patient Interest*

Options for patients wondering if psilocybin treatment is for them:

- 1 Knowledgeable healthcare providers
- 2 Other patients
- 3 Books, online resources, published papers, etc. (see handout)



The background of the slide is a close-up photograph of several mushrooms with brown caps and light-colored stems, growing on a white surface. The mushrooms are slightly out of focus, creating a soft, textured background.

# Psychedelic Treatment Process

Patient  
Interest?



Medical  
Assessment

# Psychedelic Treatment Process

## *Medical Assessment*

### Medical history

- Includes spiritual history and detailed biographical history

### Contraindications?

#### Pertinent exclusion criteria from **clinical trials**:

- personal or family history of schizophrenia/bipolar, cancer with known CNS involvement, hepatic dysfunction, uncontrolled HTN
- SSRIs, etc.

### Informed consent

# Psychedelic Treatment Process

Patient  
Interest?



Medical  
Assessment



Section 56  
Application



Preparation

# Psychedelic Treatment Process

*Preparation for psychedelic session(s)*

- Set
  - expectations and intentions of the patient
- Setting
  - the physical/social/cultural environment

# Psychedelic Treatment Process

Patient  
Interest?



Medical  
Assessment



Section 56  
Application



Preparation

# Psychedelic Treatment Process

Patient  
Interest?



Medical  
Assessment



Section 56  
Application



Preparation



Psychedelic  
Session



# Psychedelic Treatment Process

*Psychedelic session*



# Psychedelic Treatment Process

Patient  
Interest?



Medical  
Assessment



Section 56  
Application



Preparation



Psychedelic  
Session



Integration

# Psychedelic Treatment

*Integration of psychedelic session(s)*



*I'm like an ant that's gotten into the granary...and trying to lug  
out a grain that's way too big*

- Rumi

# Psychedelic Treatment

*Integration of psychedelic session(s)*

Critical component of treatment is what to do afterward ("integration"):

- 1 What rises up?
- 2 What does it mean for my life?

# Psychedelic Treatment Process

Patient  
Interest?



Medical  
Assessment



Section 56  
Application



Preparation



Psychedelic  
Session



Integration

