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

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Assistant Professor, NOSM

January 20, 2022

Preamble

Psychedelics Presentation

Tracey's Story

Land Acknowledgement

We acknowledge that the lands on which we are hosting this workshop include the traditional territories of many nations. I am joining you from the traditional territory of the Anishnawbe people and the unceded territory of the Ojibway peoples of Biigtigong First Nation, in the Robinson Superior treaty territory.

We recognize that the many injustices experienced by the Indigenous Peoples of what we now call Canada continue to affect their health and well-being. I invite all of us to reflect on the territories you are calling in from, and what contribution we can make to reconciliation in our various roles in healthcare (and beyond).

Financial Disclosures

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

Affiliations:

Advisory: 2020-21 volunteer clinical advisor for the non-profit patient advocacy group TheraPsil.

Research: Investigator for psilocybin qualitative research involving patients with life-threatening disease, caregivers and therapists

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

General clinical practice

Psychedelics

- Training
- Clinical experience
- Personal experience

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

Background → Clinical Research → Mechanisms of Action → Treatment Process → Summary

Psychedelics

Background

What are they?

How are they unique?

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
  - Ibogaine and many more...

Psychedelic Substances

How are they unique?

- approach to discomfort
- underlying causes
    - widespread application
- mechanism of action

Psychedelic Substances

How are they unique?

- discordance between opinions and evidence
- psychedelic therapist skillset
- the next "magic bullet" people will come to for "fixing"?

History of Psychedelics

A long time ago...

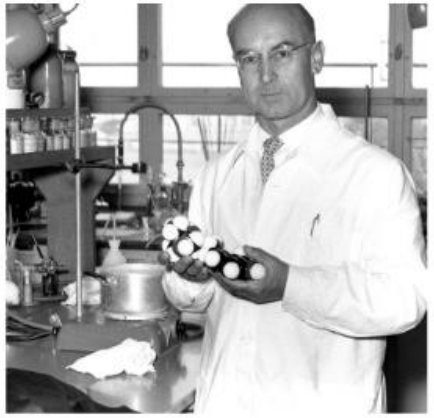
- Shamanism ~30-40K years old
- Naturally occurring psychedelics have been employed across the world for centuries, or even millennia (Nichols 2016)
- Non-ordinary states have been developed and used in Hinduism, Buddhism, Jainism, Taoism, Islam, Judaism, and Christianity (Grof 2019)

History of Psychedelics

The Science...

1897 - Mescaline first isolated and identified

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

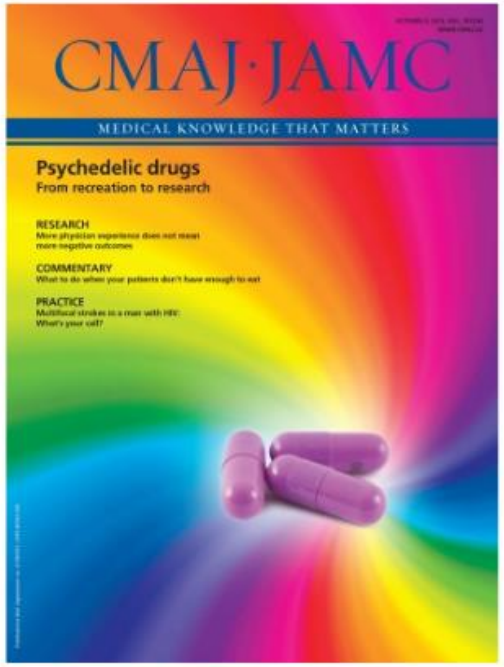
2000s-2010s - RCTs at prestigious research institutions

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...



CNN US Crime + Justice Energy + Environment Extreme Weather Space + Science LIVE

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

More from CNN

The Ka
conte

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
ize
from CNN
The Ka

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 SHARE TWEET Snap

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

SHARE

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.

Sp

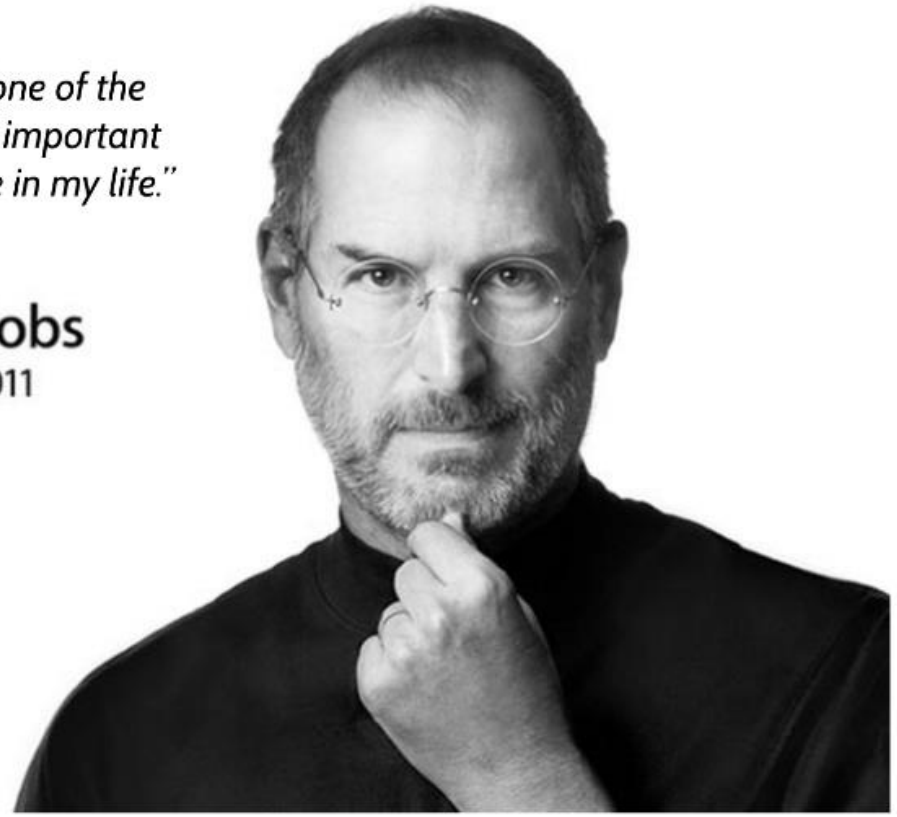
History of Psychedelics

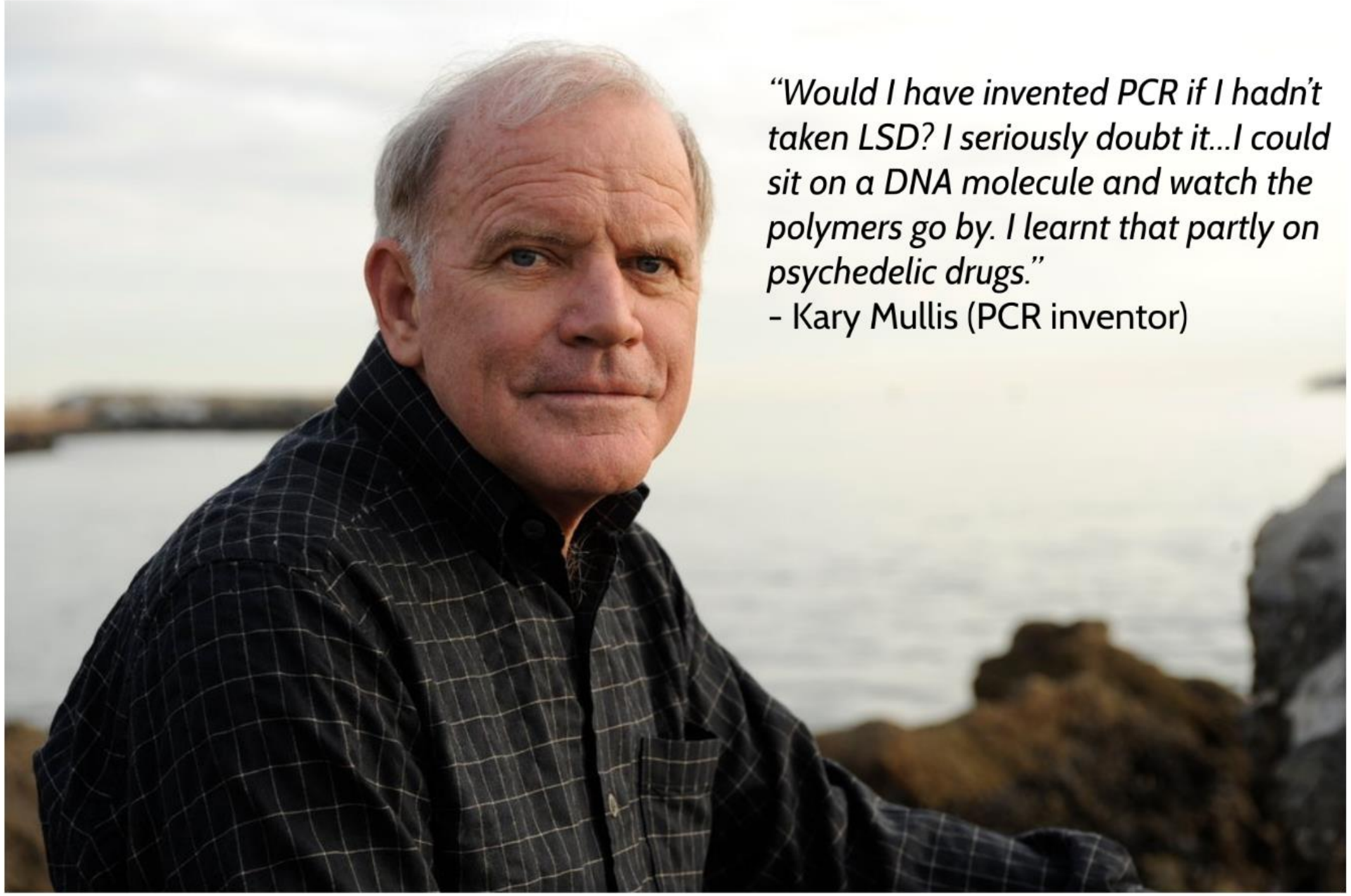
Present day

- pop culture...

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

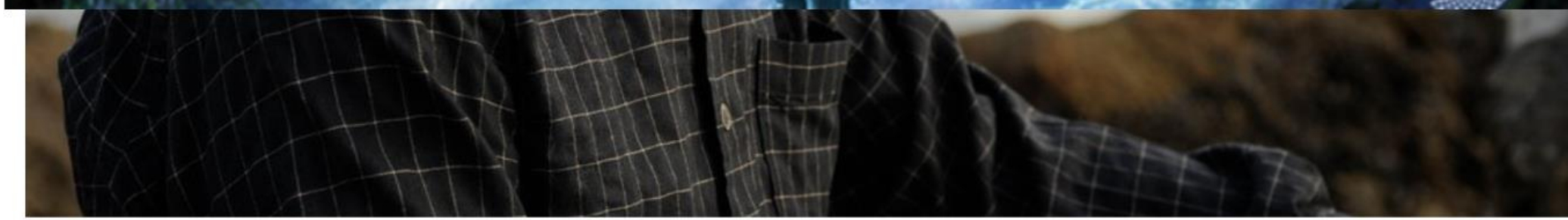
Steve Jobs
1955-2011




"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)

FROM SHOCK TO AWE

HEALING PTSD WITH AYAHUASCA, MDMA, AND CANNABIS



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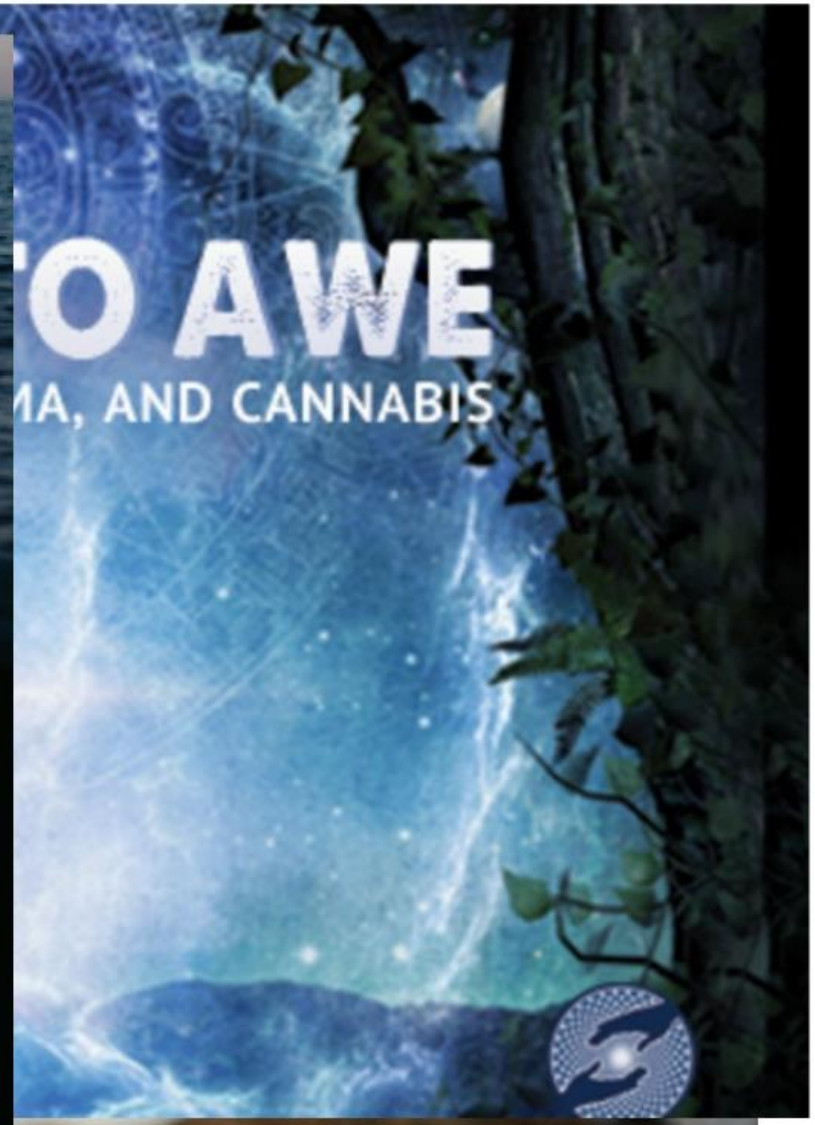

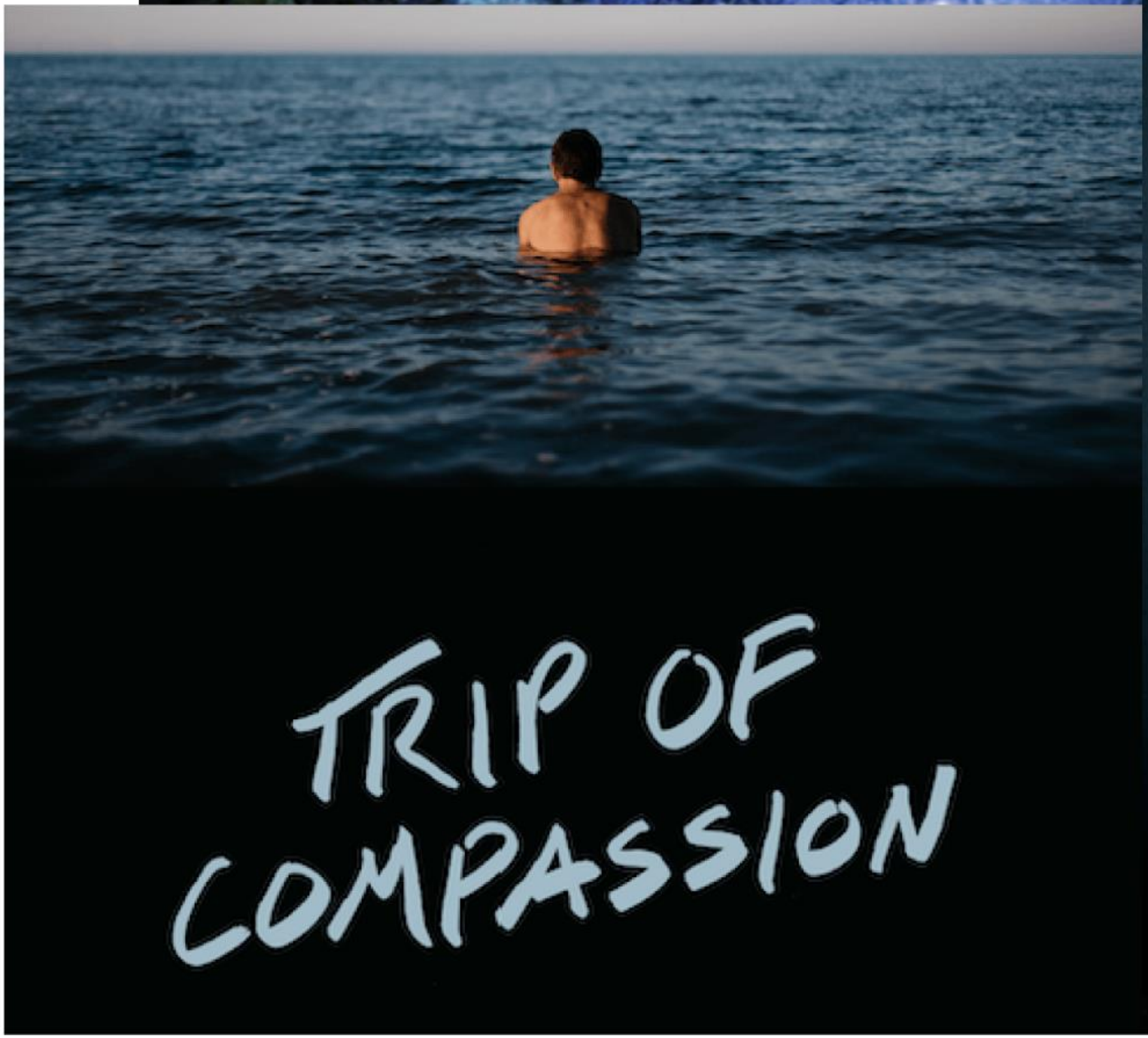
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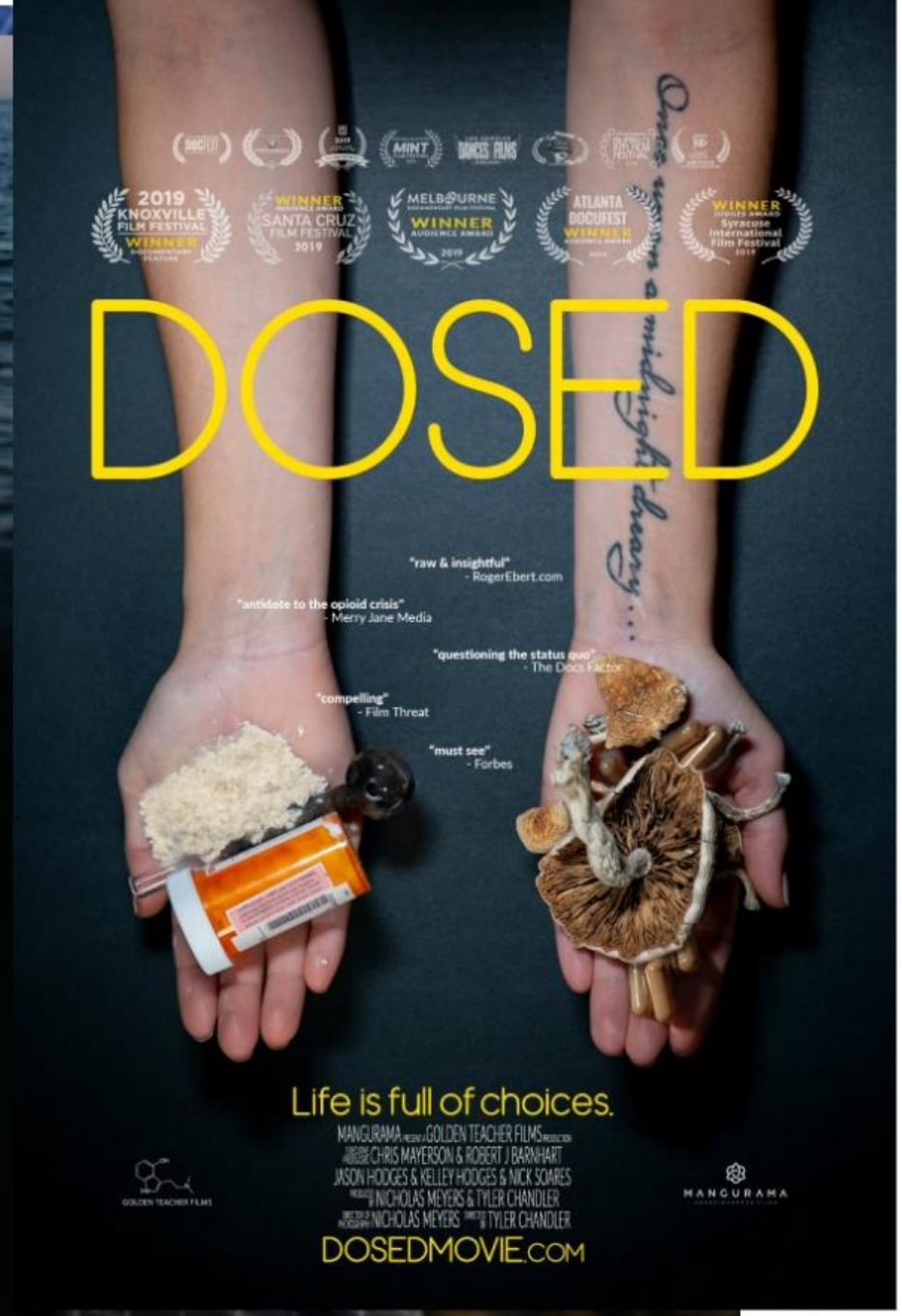
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"antidote to the opioid crisis" - Merry Jane Media
"questioning the status quo" - The Docs Factor
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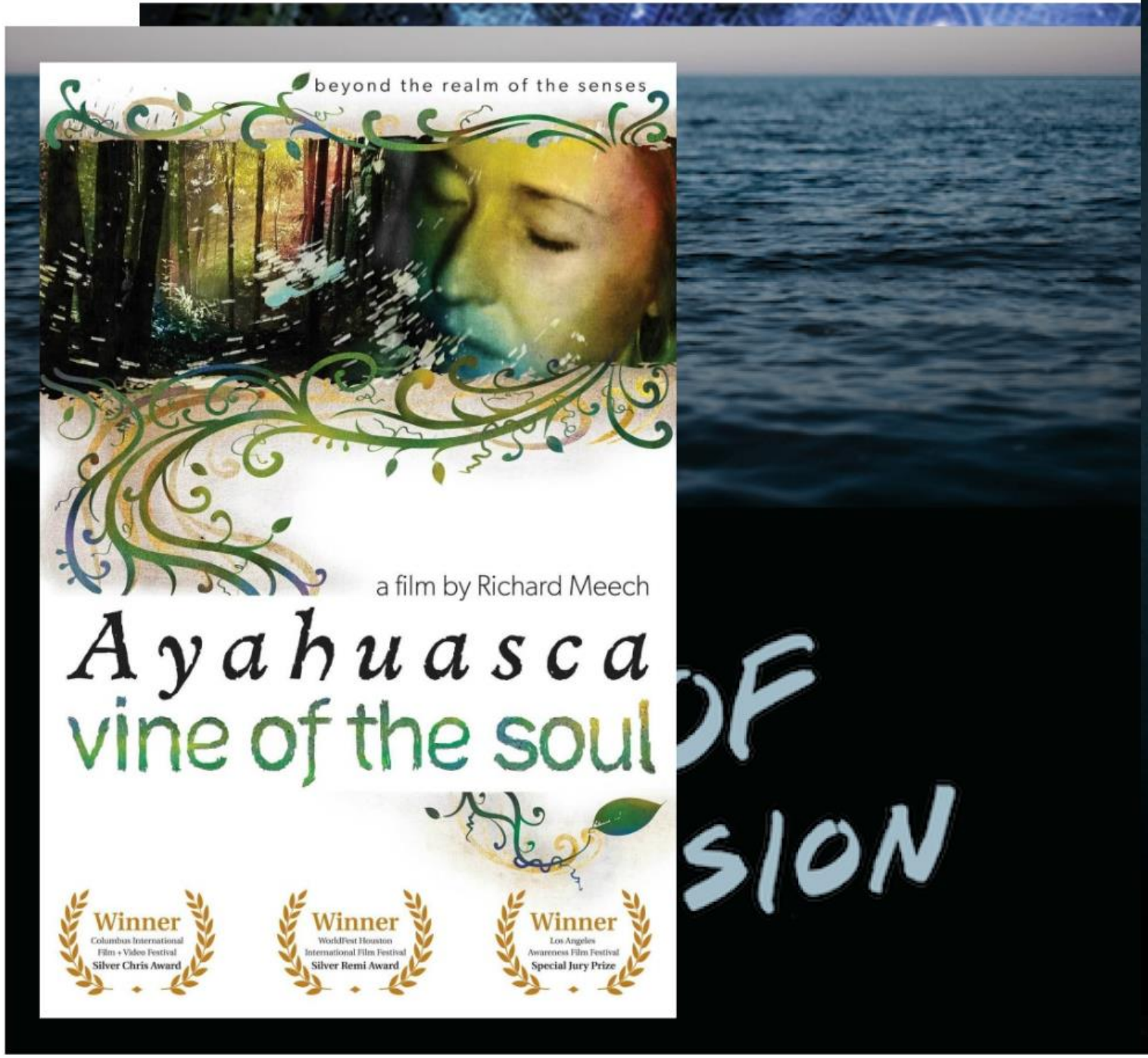
beyond the realm of the senses
a film by Richard Meech
Ayahuasca
vine of the soul
Winner
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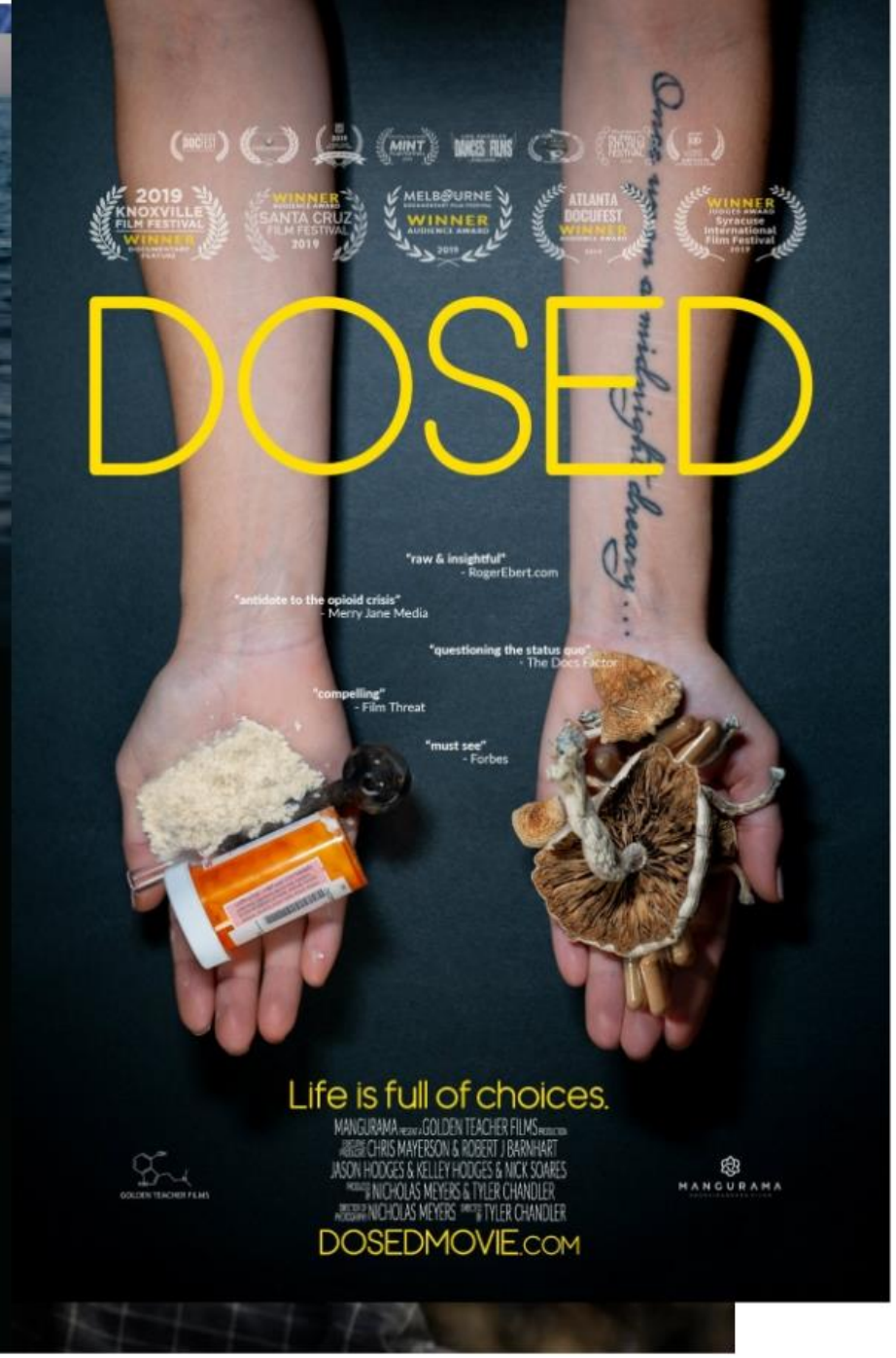
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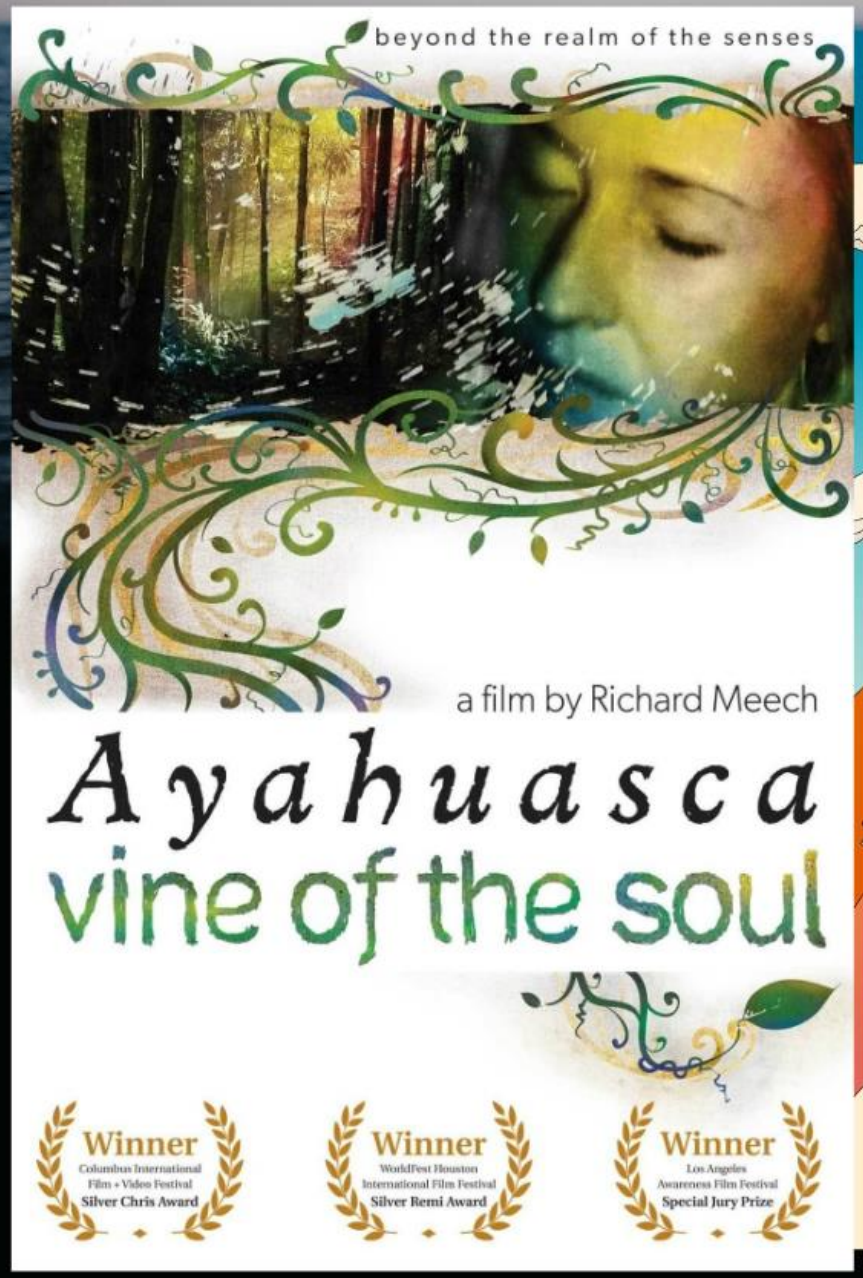
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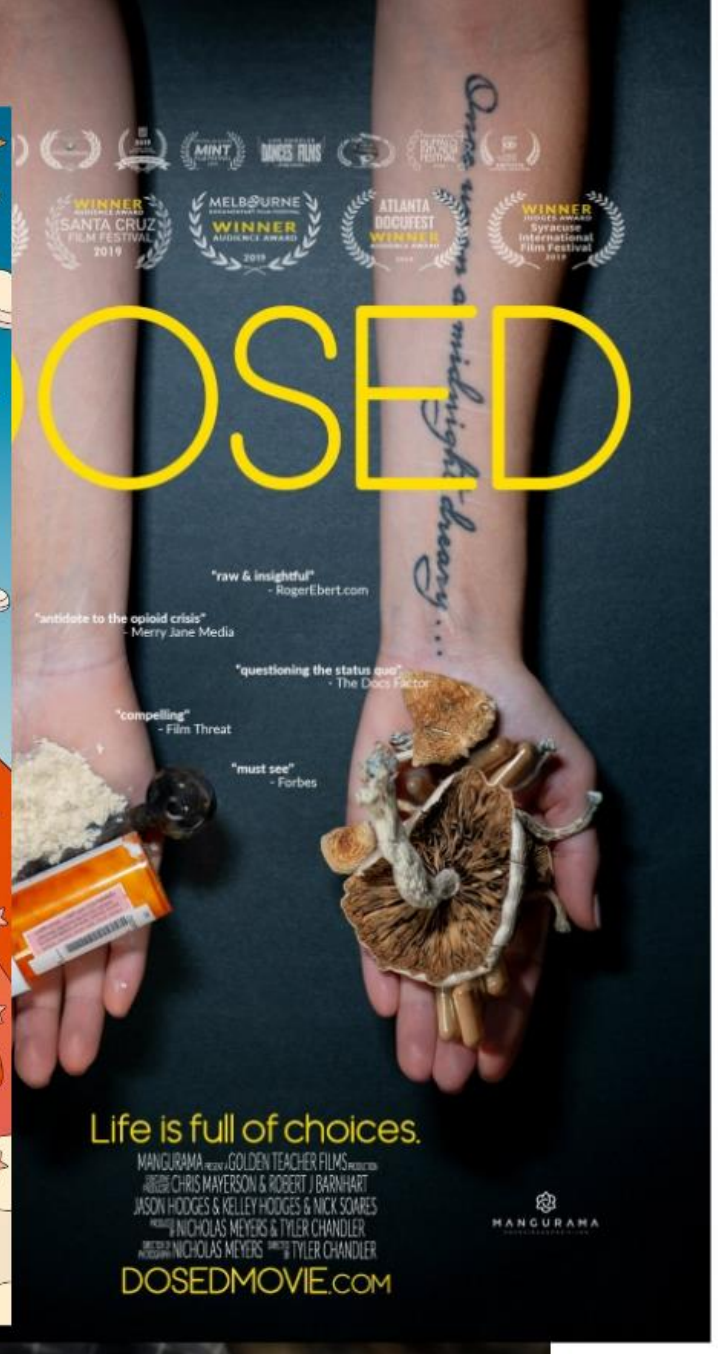
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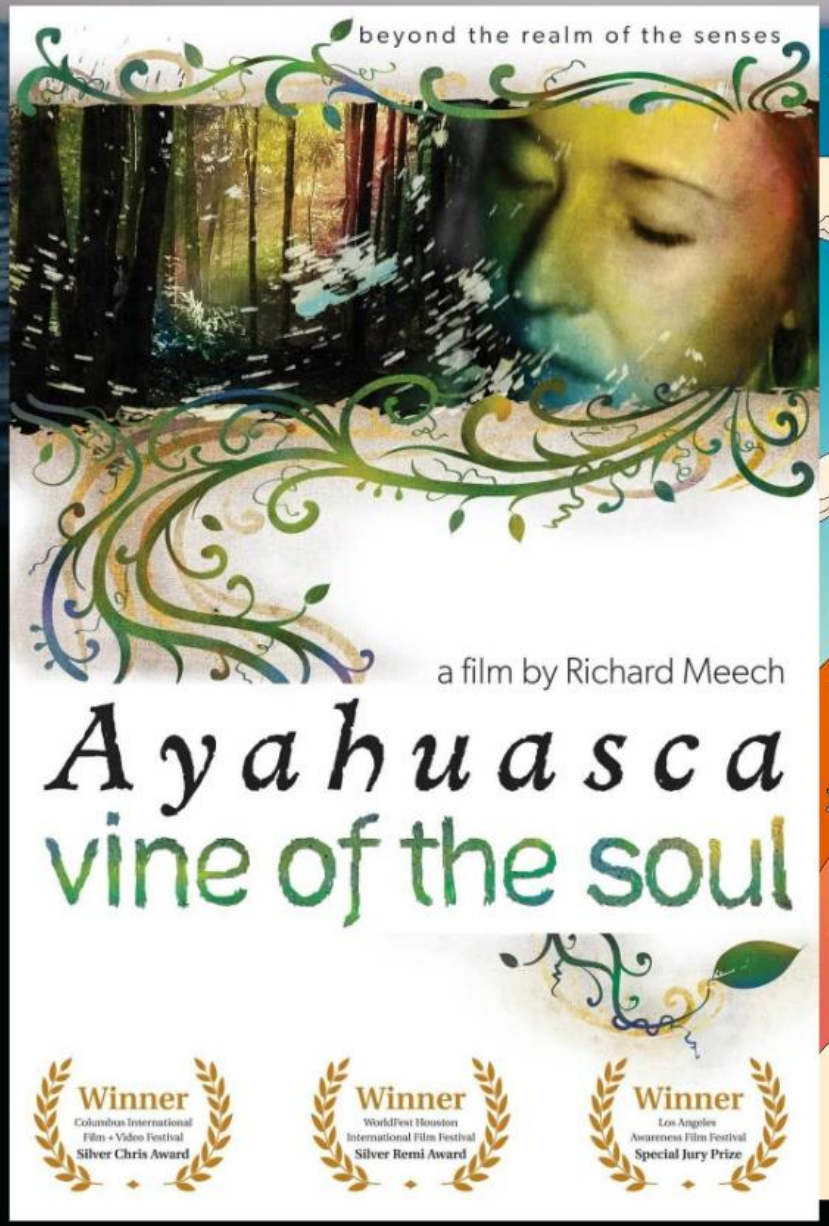
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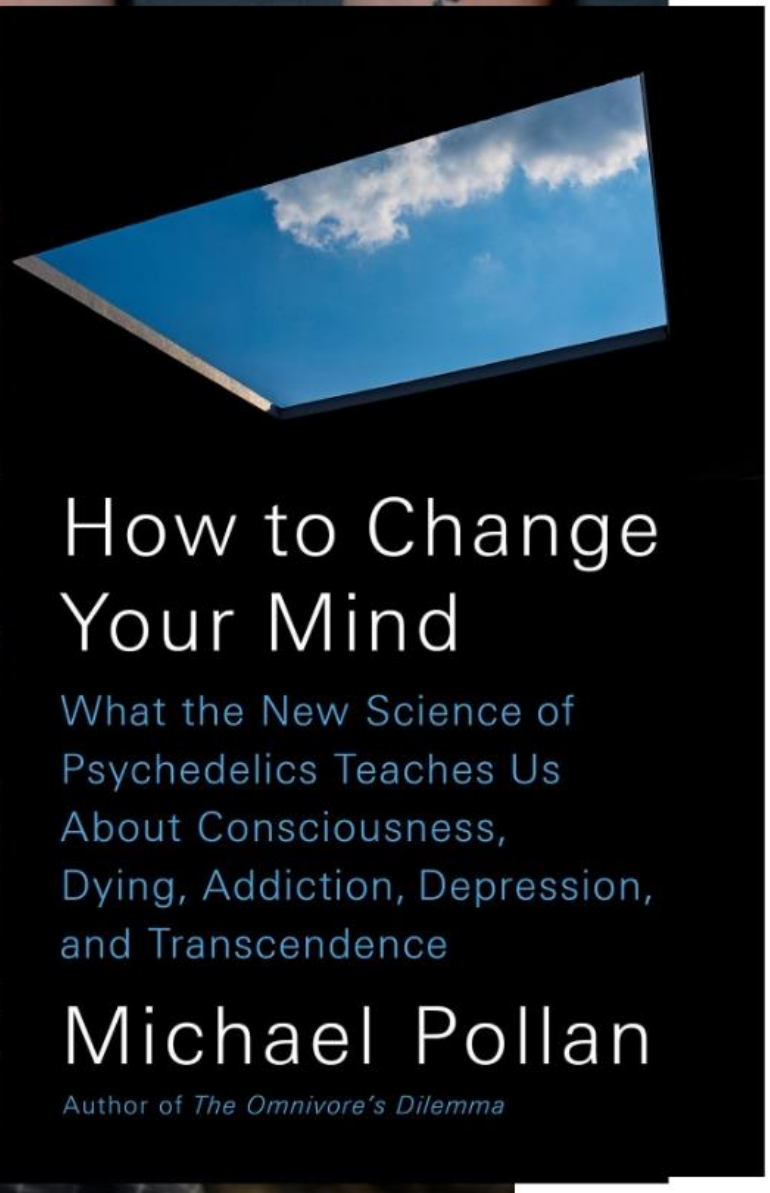
How to Change Your Mind
What the New Science of Psychedelics Teaches Us About Consciousness, Dying, Addiction, Depression, and Transcendence
Michael Pollan
Author of The Omnivore's Dilemma

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

Background → Clinical Research → Mechanisms of Action → Treatment Process → Summary

Psychedelic Clinical Research

What does the medical evidence show?

Clinicial Trials

Clinicial Trials

clinicaltrials.gov, active or completed/terminated (2021)

Psilocybin

MDD

TRD

BAD II

Anxiety/depression in cancer

Demoralization in LTAS

EtOH Use Disorder

Tobacco Use Disorder

Opioid Use Disorder

Cocaine Use Disorder

OCD

Anorexia Nervosa

Body Dysmorphic Disorder

Headache

MDMA

PTSD

EtOH Use Disorder

Anxiety in Serious Illness

Anxiety in Cancer

Social Anxiety in Autism

Ayahuasca (DMT)

TRD

LSD

MDD

Anxiety in Serious Illness

Headache

Ibogaine

Methadone detoxification

Clinicial Trials

clinicaltrials.gov, active or completed/terminated (2021)

Psilocybin
MDD
TRD

MDMA
PTSD

LSD

Anxiety/depression in cancer

Ibogaine

EtOH Use Disorder
Tobacco Use Disorder

Ayahuasca (DMT)

N>50?

Clinicial Trials

clinicaltrials.gov, active or completed/terminated (2021)

Psilocybin
MDD

MDMA
PTSD

LSD

Anxiety/depression in cancer

Ibogaine

Ayahuasca (DMT)

N>50 AND published?

Psychedelic Clinical Research

What does the medical evidence show?

"Palliative Care"

Depression

Addiction

PTSD

Spirituality

Other

Psychedelics and Palliative Care

Background

- Life-threatening disease associated with psychological and existential distress (Reiche 2018)
- Growing consensus that existential distress is a core determinant of QOL in palliative care (Reiche 2018)
- Conventional treatments are largely ineffective (Chochinov 2005, Lemay 2008, Iovieno 2011, Laotidis 2013, Grassi 2014,Ostuzzi 2018)

Psychedelics and Palliative Care

Overview of Clinical Trials

2011-2020: Only four recent RCTs. Three looked at psilocybin:

Population	Life-threatening cancer
Intervention	Moderate to high-dose psilocybin (one session)
Comparison	Very low-dose psilocybin, or niacin
Outcome measures	Depression, anxiety, death anxiety, death acceptance, quality of life, life meaning/satisfaction, optimism, demoralization, spiritual well being.

Psychedelics and Palliative Care

Overview of Clinical Trials

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Intervention	Moderate to high-dose psilocybin (one session)
Comparison	Very low-dose psilocybin, or niacin
Outcome measures	Psychological and Existential Distress

*(Grob 2011, *Gasser 2014 (LSD), 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):
    - 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)

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

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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)

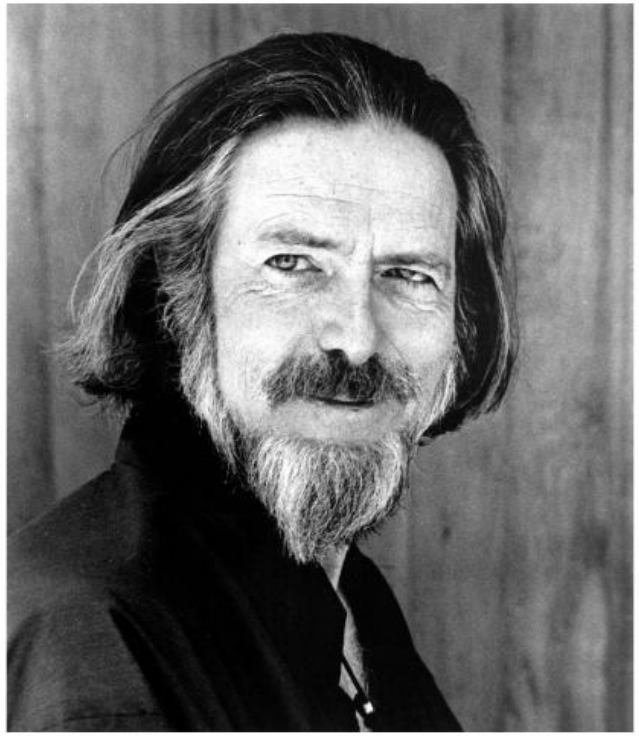
For more information on neurological mechanism of action, check out:
i) Robin Carhart-Harris (numerous articles/talks)
ii) Nichols 2016

Psychedelics

Experiential Mechanisms of Action

- what types of experiences do psychedelics induce?
    - see Dr. Stanislav Grof's extensive work, including cartography of the psyche
    - one domain of experience is the "mystical" experience...

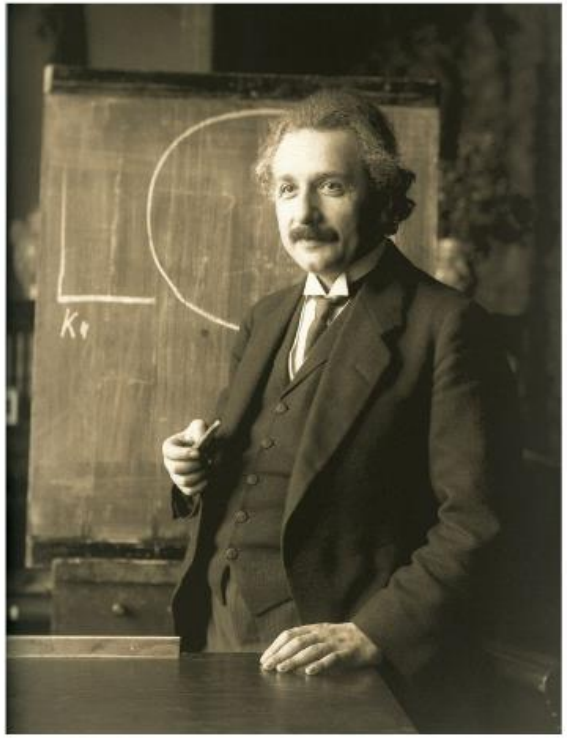
Mystical Experiences



"[Mystical experiences are] those peculiar states of consciousness in which the individual discovers himself to be one continuous process with God, with the Universe, with the Ground of Being, or whatever name he may use by cultural conditioning or personal preference for the ultimate and eternal reality."

- Alan Watts

Mystical Experiences



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

Mystical Experiences

By trying to say these things,
you conceal them.
- Rumi

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

© Magic Eye Inc. www.magiceye.com

Mystical Experiences

Definition and Core features

Doesn't see "It":

"There's nothing there"

"You're crazy..."

Sees "It":

"Wow! It's so obvious!"

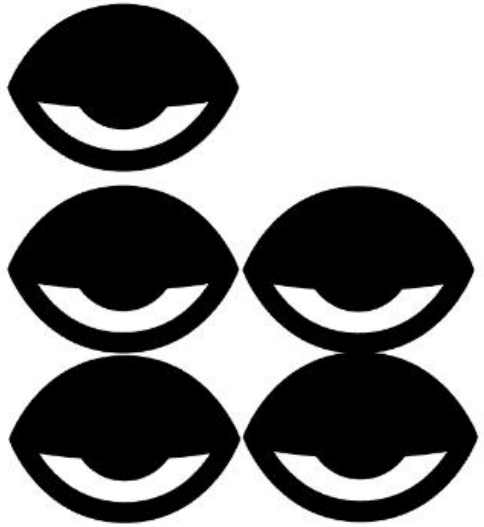
"You can't convince me it's not there."

Mystical Experiences

Definition and Core features

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. *Persistenting 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 - Clinical Trials

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

Healthy volunteers - **61%** (Griffiths 2006)

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

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

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Psychedelic Treatment Process

in Canada

Patient Interest → Medical Assessment → Legal Access

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)

Psychedelic Treatment Process

Medical Assessment

- Medical history
    - Includes spiritual history and detailed biographical history
- 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

Legal Access

Option A: Section 56 Exemption

Option B: Special Access Program

Option A: Section 56 Exemption

- Route since Aug 2020: We have some sense of what to expect
- Slow responses…
- Psilocybin only
- Patient applies
- Patient responsible for sourcing

Option B: Special Access Program

"serious or life-threatening condition where conventional treatments have failed, are unsuitable, or are not available in Canada"

"level of scientific evidence, including evidence pertaining to safety and efficacy...for the treatment of the patient's specific condition"

Option B: Special Access Program

- New route for psychedelics (Jan 5/22)
- Psilocybin, MDMA, others?
- Prescriber applies to Health Canada
- Prescriber responsible for sourcing
- "Requests are generally processed within 1–2 working days following receipt"

https://www.gazette.gc.ca/rp-pr/p2/2022/2022-01-05/html/sor-dors271-eng.html

Psychedelic Treatment Process

Legal Access

Option A: Section 56 Exemption

- Route since Aug 2020: We have some sense of what to expect
- Slow responses...
- Psilocybin only
- Patient applies
- Patient responsible for sourcing

Option B: Special Access Program

- New route for psychedelics (Jan 5/22)
- Psilocybin, MDMA, others?
- Prescriber applies to Health Canada
- Prescriber responsible for sourcing
- "Requests are generally processed within 1–2 working days following receipt"

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Psychedelic Treatment Process

in Canada

Psychedelic Treatment Process

Preparation for psychedelic session(s)

- cultivation of radical openness
- set and setting

Psychedelic Treatment Process

Psychedelic session

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?
3. How do I integrate this into my day-to-day life?

For more information: www.psychedelic-integration.org and others

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

Background → Clinical Research → Mechanisms of Action → Treatment Process → Summary

Summary

Psychedelics, Psilocybin and End-of-life

- discordance between opinions and evidence
- psychedelic medicine challenges conventional paradigms:
    - approach to suffering, underlying causes, mechanism of action for healing
- Life-threatening illness
    - small RCTs suggest psilocybin is safe and effective for existential and psychological distress
- Canada leading the world in opening up access?
- psychedelic research is exploding...stay tuned!
- *next "magic bullet" people will come to for "fixing"?

Thank you

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Recommended Books

- ***Overview of psychedelics (non-medical)***: *How to Change your Mind (Michael Pollan)*
- ***Psychedelic medicine:*** *Handbook of Medical Hallucinogens (Grob and Grigsby)*
- ***Psychedelics and mystical experiences:*** *Sacred Knowledge (William Richards)*
- ***Non-ordinary states of Consciousness:*** *The Way of the Psychonaut Volume 1 and 2 (Stanislav Grof)*
- ***First-person description of psychedelic experience:*** *Joyous Cosmology (Alan Watts)*

Tracey's Story...

The Personal

The Medical

Tracey's Story: A Case Presentation

Pearls

Patient Interest → Medical Assessment → Legal Access → Preparation → Psychedelic Session → Integration → Preparation

Case Presentation

Integration

1 Week Post Session

1 month Post Session

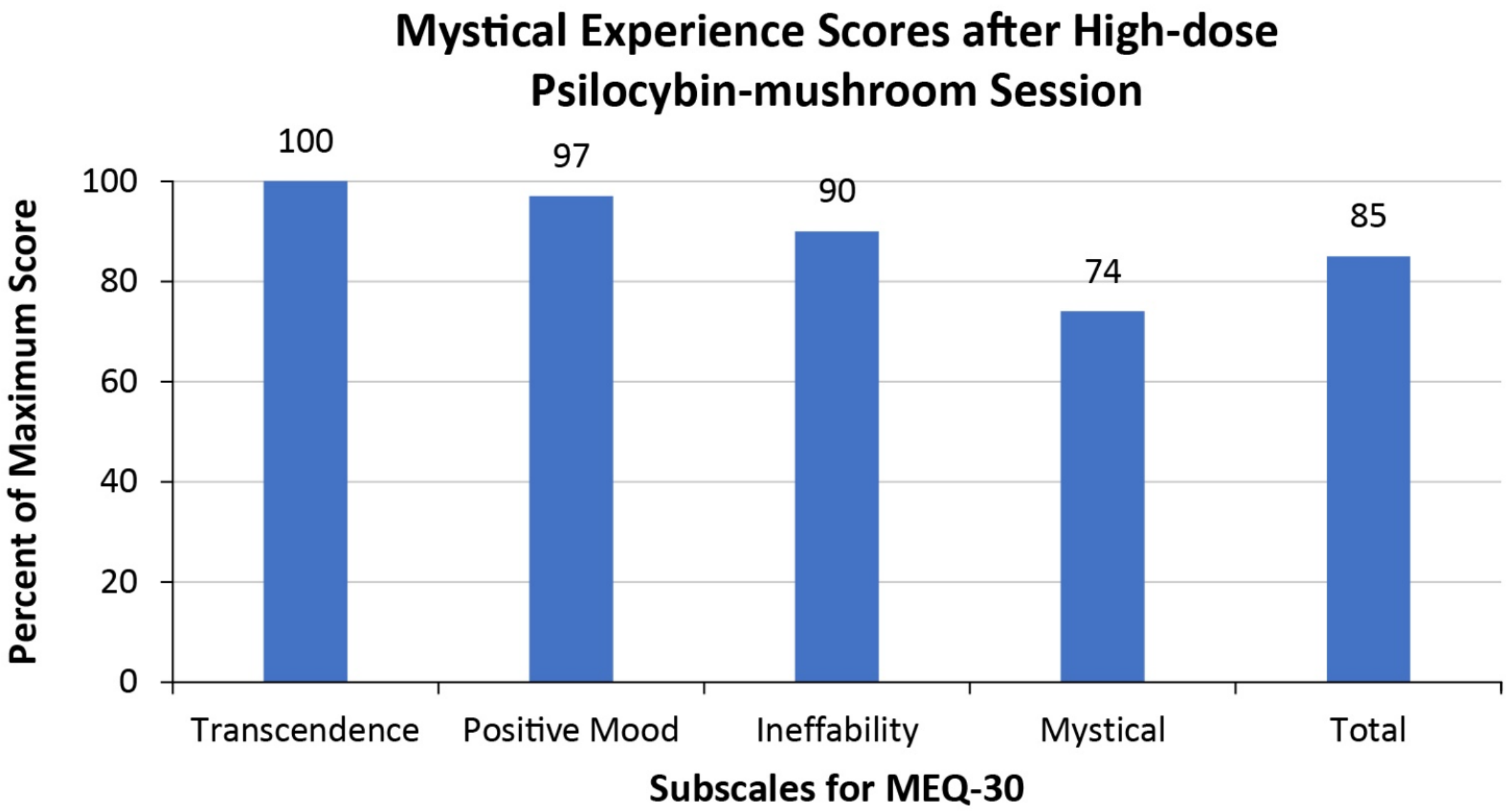
2 months Post Session

3 months Post Session

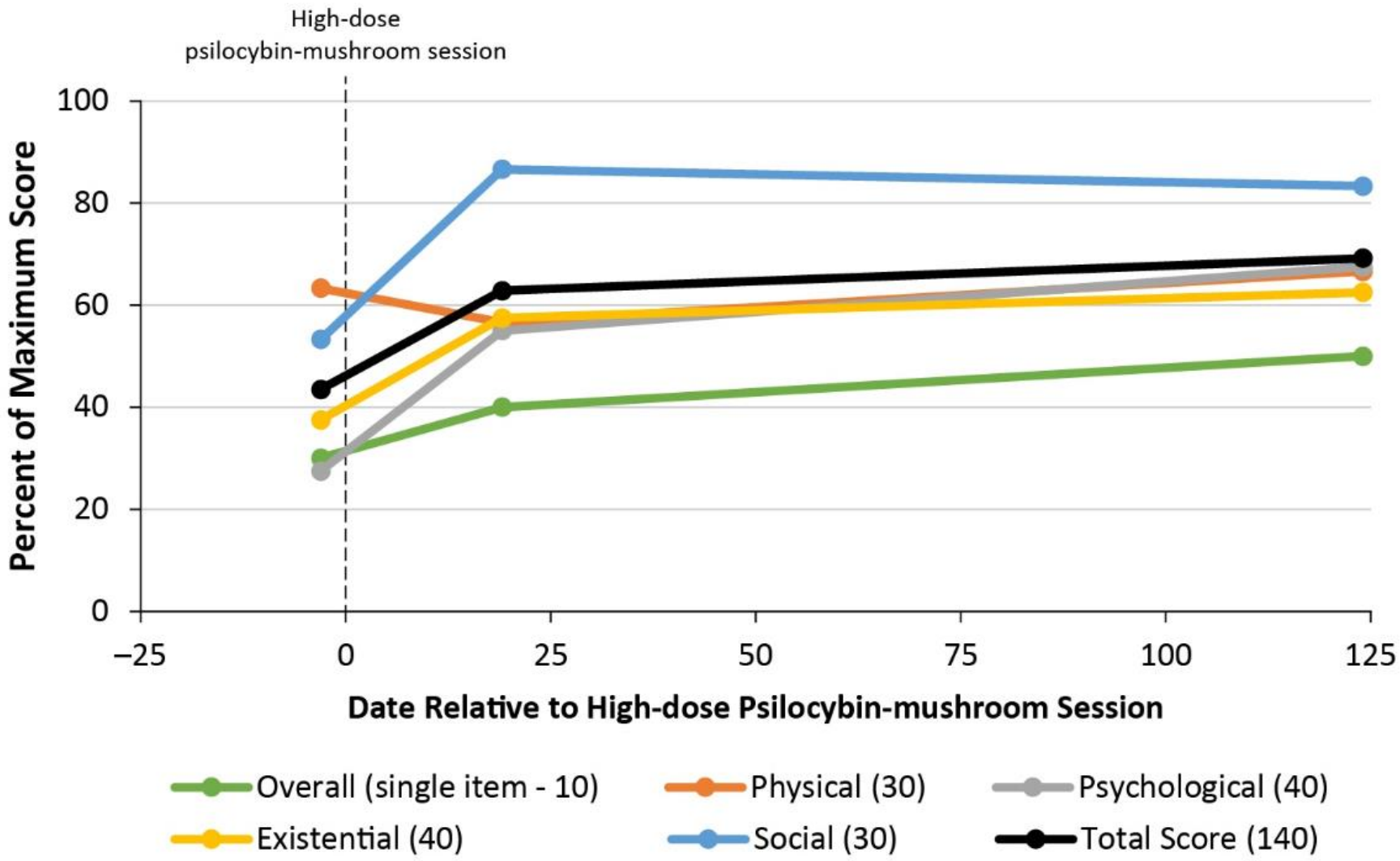
4 months Post Session

5 months Post Session

Questionnaire Scores

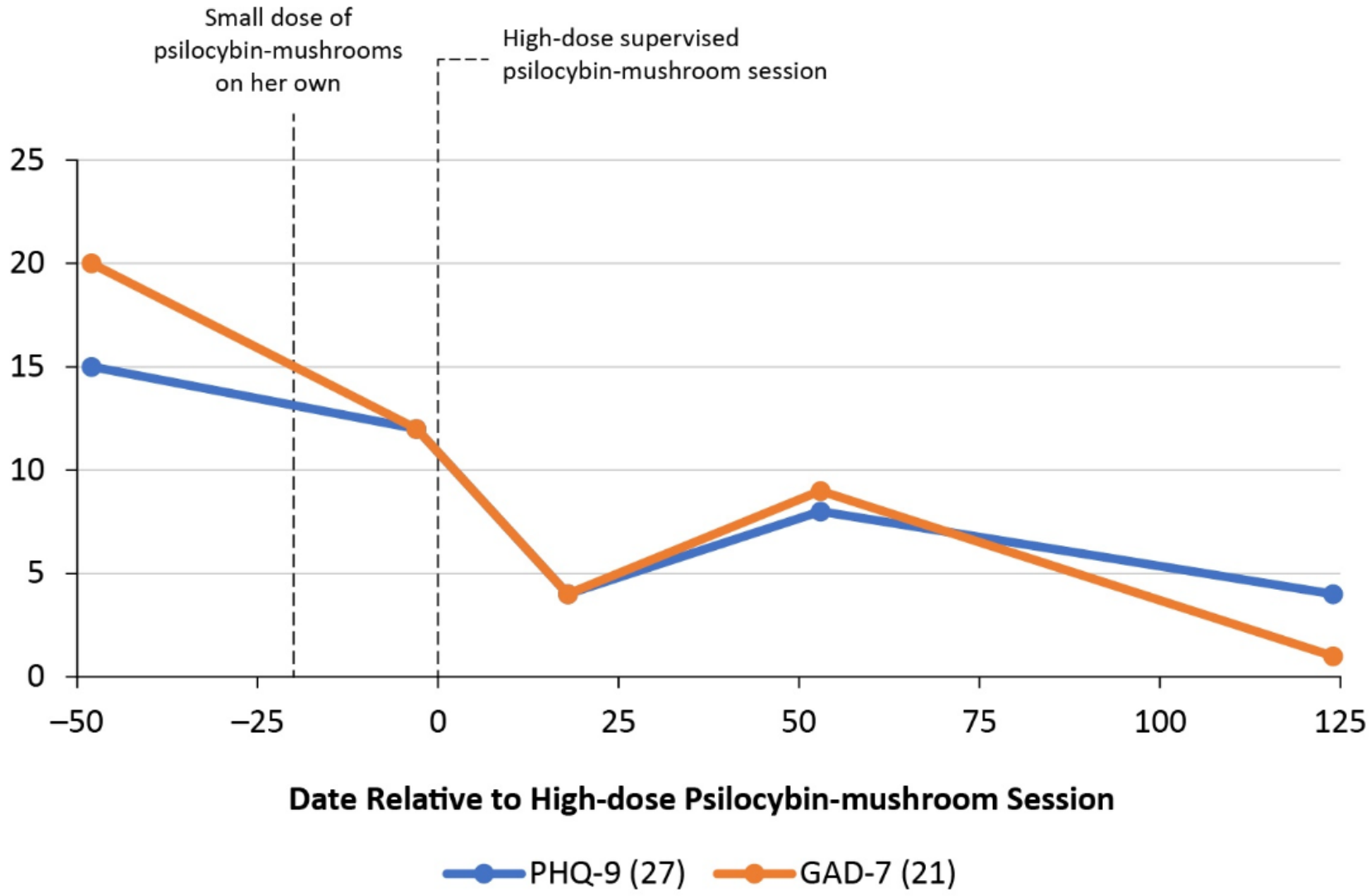

Mystical Experience Scores after High-dose Psilocybin-mushroom Session
Percent of Maximum Score
100
80
60
40
20
0
100
97
90
74
85
Transcendence
Positive Mood
Ineffability
Mystical
Total
Subscales for MEQ-30

Quality of Life Scores Before and After High-dose Psilocybin-mushroom Session



(maximum score in brackets)

Depression and Anxiety Scores Before and After High-dose Psilocybin-mushroom Session



(maximum score in brackets)

Validated Questionnaires:

Date relative to treatment	PHQ-9 (27)	GAD-7 (21	MQOL-R					
			Overall (single item - 10)	Physical (30)	Psychological (40)	Existential (40)	Social (30)	Total Score (140)
~-2 months	15	20						
-3 days	12	12	3	19	11	15	16	61
Treatment day								
~3 weeks	4	4	4	17	22	23	26	88
~ 2 months	8	9						
~4 months	4	1	5	20	27	25	25	97

Case Presentation

Questionnaire Scores

Persisting Effects Questions (4 months post-psilocybin):

How **personally meaningful** were the experiences? *(Select the highest number that applies)*

1. no more than routine, everyday personally meaningful experiences
2. similar to personally meaningful experiences that occur on average once or more a week
3. similar to personally meaningful experiences that occur on average once a month
4. similar to personally meaningful experiences that occur on average once a year
5. similar to personally meaningful experiences that occur on average once every 5 years
6. among the 10 most personally meaningful experiences of my life
7. among the 5 most personally meaningful experiences of my life
8. the single most personally meaningful experience of my life

Case Presentation

Questionnaire Scores

Persisting Effects Questions (4 months post-psilocybin):

PEQ-5	
Personally meaningful	Single most of life
Spiritually significant	Top 5 of life
Psychologically challenging	Single most of life
Psychologically insightful	Single most of life
Change in personal well-being and life satisfication	Very much

Tracey's Story: A Case Presentation

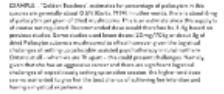
Pearls

Patient Interest → Medical Assessment → Legal Access → Preparation → Psychedelic Session → Integration → Preparation

Case Presentation

Pearls for Psychedelic Therapists

- seek mentorship and/or a community of practice
- documentation
    - "case reviewed with..."
    - cite scientific evidence



EXAMPLE: ...“Golden Teachers”...estimates for percentage of psilocybin in this species are generally about 0.6% (Gartz, 1994). In other words, there is about 6mg of psilocybin per gram of dried mushrooms. This is an estimate since this supply is of course not regulated. Recommended dose would therefore be 3-5g based on previous studies. Some studies used lower doses (20mg/70kg or about 3g of dried Psilocybe cubensis mushrooms) to effect however given the logistical challenges of setting up psilocybin assisted psychotherapy in rural northern Ontario at all - when we are 7h apart – this could present challenges. Namely, given that she has an aggressive cancer and there are significant logistical challenges of expeditiously setting up another session, the higher-end dose seems warranted to give her the best chance of achieving her intention and having a mystical experience.

Case Presentation

Pearls for Psychedelic Therapists

- seek mentorship and/or a community of practice
- documentation
    - "case reviewed with..."
    - cite scientific evidence
    - informed consent very explicit
    - use validated tools

Case Presentation

Pearls for Psychedelic Therapists

- involve family members (and secondary therapist) early
- do your own inner work
- beware of "magic bullet" phenomenon