Far Out Therapies: Psychedelics in Palliative Care

By Dr. Hayden Rubensohn
Disclosures

Dr. Rubensohn is a paid research therapist for the Multidisciplinary Association for Psychedelic Studies (MAPS); affiliated with the BC Centre for Substance Use (BCCSU)
Outline

- Case
- Psychological issues in life-limiting illness
- Psychedelics
  - What do they do? How do they work
  - Review of data
- Empathogens
  - What do they do? How do they work
  - Review of data
- Relationship between psychedelics and MAiD
Objectives

By the end of this session I hope you will:

- Understand what psychedelics are
- Understand why psychedelics might work
- Understand what psychedelics could be used for
- Consider the possible intersection between psychedelic medicine and MAiD
Case: Mrs. AD

- 52 year old female, previously healthy
  - No prior psychiatric history

- Diagnosed 4 years ago with triple negative breast cancer
  - Treatment has included mastectomy, chemo, radiation
  - Stable stage III disease without mets
  - Declined further chemo due to fear of side effects and impact on quality of life
Case: Mrs. AD

- Symptoms include fatigue, managed pain, occasional nausea
- Most bothered by persistent anxiety and hopelessness about her illness and its course, sadness for missing future events
  - Concerned about the dying process
  - Worried that her life has been meaningless by dying so young
  - Often wonders “why me?” and wonders if she’s being punished
Case: Mrs. AD

- Psychiatry says that Mrs. AD has an Adjustment Disorder with Mixed Anxiety and Depressed Mood
- Cognitive therapy only provides partial relief
- A 3 week trial of bupropion worsens her anxiety
- A 2 week trial of paroxetine results in somnolence
- Reluctantly, Mrs. AD agrees to a trial of citalopram which after 8 weeks has mild to moderate benefit
Case: Mrs. AD

What if there were other options for this patient?
Emotional Distress

- Significant complication in those diagnosed with cancer and life limiting chronic illness
- High rates of depression, anxiety, other psychiatric disorders

- Impact on health outcomes
  - QoL, Treatment adherence, Morbidity, Mortality

- Limited efficacy of currently available therapies
  - Psychotherapies
  - Pharmacotherapies

Psychedelics

- **Etymology:** *psyche-delose* (mind-revealing)

- **Classic Psychedelics – 5HT2A Agonists**
  - Psilocybin
  - Others... beyond the scope of this talk

- **Non-Classic Psychedelics**
  - MDMA – 5HT releaser
  - Others... beyond the scope of this talk

Psilocybin

- Tryptamine alkaloid found in various species of mushrooms

- Rapidly metabolized to psilocin (structural similarity to 5HT)
Psilocybin

- Tryptamine alkaloid found in various species of mushrooms

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Psilocybin

- Active at 5-10mg with a dose related response
- Oral activity begins in 30-60 minutes, with a peak effect at 2 hours, and a total duration of action from 4-8 hours

https://www.erowid.org/plants/mushrooms/mushrooms_effects.shtml
Classic Psychedelics

Subjective Effects

- Maintenance of a clear sensorium
- Change in perception, cognition processing
- States of ecstasy and elevated mood
- Visual illusions and internal visionary experiences
- Dissolution of ego boundaries
- Experiences of union with others and the natural world

https://www.erowid.org/plants/mushrooms/mushrooms_effects.shtml
Why Would Psychedelics Work

- A deeper look at psychosocial distress
  - Total Pain
  - Existential Suffering

- Biological Plausibility
  - Mystical Experiences
  - The Default Mode Network
Total Pain

Figure 4.17. Total Pain Graphic. Nociceptive pain is worsened, depicted by inward arrows, by emotions such as anxiety, anger and depression. There is also circular interaction with, for example, anger or depression heightening anxiety. Thus, both inward and circular components contribute to the total pain perceived by the patient. M Downing.
Existential Suffering

Terminal diagnoses may trigger existential crises at patients try to make sense of their mortality.

Spiritual emergencies

“The aspect of humanity that refers to the way individuals seek and express meaning and purpose… they way they experience connectedness to the moment, to the self, to others, and to the sacred”

Breitbart et al. “concepts of adequate end of life care must be expanded beyond symptom control alone to include psychiatric, psychosocial, existential and spiritual domains."
Why Would Psychedelics Work

Grob et. al: “the [psychedelic] treatment model is the only approach that potentially facilitates a radical shift in consciousness yielding transpersonal, transcendental, spiritual, and mystical experiences”

Potential to engender an ontological shift with the capacity to change assumptions and beliefs about the meaning of life and death

Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance

R. R. Griffiths • W. A. Richards • U. McCann • R. Jesse

Received: 20 January 2006 / Accepted: 27 May 2006
© Springer-Verlag 2006
Mystical Experiences Model
Conclusions When administered under supportive conditions, psilocybin occasioned experiences similar to spontaneously occurring mystical experiences. The ability to occasion such experiences prospectively will allow rigorous scientific investigations of their causes and consequences.

MYSTICISM SCALE

2 Months after 1st Session

2 Months after 2nd Session
### Mystical Experiences Model

**Conclusions** When administered under supportive condi-

<table>
<thead>
<tr>
<th>Questionnaire Items</th>
<th>1 Month after Sessions</th>
<th>14 Month Follow-up (20 or 30 mg/70 kg)**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td><strong>How personally meaningful was the experience?</strong></td>
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<td>Single most meaningful experience of life</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Top 5 most meaningful, including single most</td>
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<td>11.1</td>
</tr>
<tr>
<td><strong>How spiritually significant was the experience?</strong></td>
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<td><strong>Did the experience change your sense of well-being or life satisfaction?</strong></td>
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<tr>
<td>Increased well-being/life satisfaction (very much)</td>
<td>5.6</td>
<td>27.8</td>
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<tr>
<td>Increased well-being/life satisfaction (moderately or very much)</td>
<td>38.9</td>
<td>55.6</td>
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</tbody>
</table>

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*Note: † indicates 2 Months after 1st Session, ‡ indicates 2 Months after 2nd Session.*
Mystical Experiences Model

Mystical and spiritually meaningful experiences may mediate the beneficial effects of psychedelic based therapies.

Deeply interpersonal experiences without fear and with renewed trust may mediate the beneficial effects of empathogen based therapies.

Mystical Experiences Model

- Mystical and spiritually meaningful experiences may mediate the beneficial effects of psychedelic based therapies.

14 months after the final session. The significant increase in the Religious subscale of the Death Transcendence Scale is notable in this group of healthy volunteers because questions in this subscale assess a sense of continuity after death (e.g., Death is a transition to something even greater than this life; Death is never just an ending, but a part of a process). This effect may be relevant to the proposed palliative effects of psilocybin and similar hallucinogens in treating existential anxiety in terminal illness (Kast 1967; Richards et al. 1972; Grob et al. 2011).

- Deeply interpersonal experiences without fear and with renewed trust may mediate the beneficial effects of empathogen based therapies.
The Default Mode Network

- Self Referential Thinking – at rest
The Default Mode Network

- Disturbance in connectivity – with psychedelics

- Medial node interference: reduced associative and sensory processing → ego dissolution
- Lateral node interference: enhanced Timelessness and spacelessness


Comprehensive Psychedelic Model

Existential Suffering
Anxiety
Depression
Comprehensive Psychedelic Model

Existential Suffering
Anxiety
Depression

Supportive Therapy
Existential Suffering
Anxiety
Depression
Classic Psychedelics
Supportive Therapy
Comprehensive Psychedelic Model

- Existential Suffering
  - Anxiety
  - Depression

- Classic Psychedelics

- Supportive Therapy

- Predictable neurobiological alterations
Comprehensive Psychedelic Model

Existential Suffering
Anxiety
Depression

Classic Psychedelics

Supportive Therapy

Predictable neurobiological alterations

Transcendental mystical experiences
Comprehensive Psychedelic Model

Existential Suffering
Anxiety
Depression

Supportive Therapy

Predictable neurobiological alterations

Fuller lives
Better deaths

Classic Psychedelics

Transcendental mystical experiences
Therapy Structure and Conduct

- Participant meets study therapists
- Introductory and preparatory sessions occur (2-3)
Therapy Structure and Conduct

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- Experimental sessions occur (full day experience; 2-3)
  - Typically 1-2 months after first introductory meeting
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- Follow up with study therapists (integration):
  - Day after in-person
  - Phone calls (~7)
  - Weekly meetings (2-3)
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- Follow up with study therapists (integration):
  - Day after in-person
  - Phone calls (~7)
  - Weekly meetings (2-3)
- Longer term follow up
  - 2 month
  - 6-12 month

Long-term follow up includes:

- 2 month
- 6-12 month
Therapy Sessions

- Aesthetically pleasing environment
- Two co-therapists present
- Non-directive, supportive model of therapy employed
  - “Trust, let go and be open”
  - “The inner healer”
- Full day sessions
Johns Hopkins Study - Design

Published in 2016; follow up to a 2011 published pilot study

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial

Roland R Griffiths¹,², Matthew W Johnson¹, Michael A Carducci³, Annie Umbricht¹, William A Richards¹, Brian D Richards¹, Mary P Cosimano¹ and Margaret A Klinedinst¹
Johns Hopkins Study - Design

- Published in 2016; follow up to a 2011 published pilot study
- 51 subjects with potentially life threatening cancer diagnoses (65% metastatic/recurrent) and a DSM-IV diagnosis involving anxiety and/or mood disturbance
- Double-blind, randomized, crossover study
  - Two sessions per participant
    - High dose (20-30mg/70kg) → low dose; or
    - Low dose (1-3mg/70kg) → high dose
Johns Hopkins Study - Results

- Adverse events: no serious adverse events
  - No hallucinogen persisting perception disorder, psychosis

- Primary outcomes measures:
  - Significant and sustained evidence of clinical response and symptom remission after high dose session
Johns Hopkins Study - Results

Mystical Experiences and Death Acceptance
Published in 2016

Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial

Stephen Ross¹,²,³,⁴,⁵,⁶, Anthony Bossis¹,²,⁴, Jeffrey Guss¹,²,⁴, Gabrielle Agin-Liebes¹⁰, Tara Malone¹, Barry Cohen⁷, Sarah E Mennenga¹, Alexander Belser⁸, Krystallia Kalliontzi², James Babb⁹, Zhe Su³, Patricia Corby² and Brian L Schmidt²
NYU Study - Design

- Published in 2016

- 29 subjects with potentially life threatening cancer diagnoses (62% Stage III/IV) and a DSM-IV diagnosis involving anxiety

- Double-blind, randomized, active-placebo controlled, crossover study

- Two sessions per participant
  - Psilocybin (0.3mg/kg) → niacin (250mg); or
  - Niacin (250mg) → Psilocybin (0.3mg/kg)
NYU - Results

- Adverse events: no serious adverse events
  - No hallucinogen persisting perception disorder, psychosis

- Primary outcomes measures:
  - Significant reductions in both anxiety and depression, mediated by psilocybin exposure
NYU - Results

Mystical Experiences and Death Transcendence
Numerous studies in the literature have proposed that this population experiences stresses related to the diagnosis of the disease, and/or to the challenges of living with the illness that are much like how survivors of violent crime or natural disasters relate to their traumatic experiences (Cordova, Studts, Hann, Jacobsen, & Andrykowski, 2000; Jackson et al., 2007).

Similar lack of efficacy for currently available psychotherapies and pharmacotherapies
MDMA

3,4-methylene-dioxy-n-methyl amphetamine – a substituted amphetamine

Sub-classified as an empathogen: to generate empathy
MDMA

- VMAT inhibitor, SERT reverser: efflux of serotonin from the axon terminal

MDMA

- VMAT inhibitor, SERT reverser: efflux of serotonin from the axon terminal

- Synaptic cleft is flooded with 5-HT resulting in a unique profile of subjective effects

MDMA

- Active at 75-100mg with a dose related response
- Oral activity begins in 30-60 minutes, with a peak effect at 2 hours, and a total duration of action from 4-6 hours

https://erowid.org/chemicals/mdma/mdma_effects.shtml
Empathogens

- Subjective Effects
  - Enhanced inner awareness
  - Elevated mood, euphoria
  - Increased desire and willingness to communicate
  - Diminished fear and anxiety
  - Feelings of love, empathy
  - Forgiveness for self and others
  - Reduced pain

https://erowid.org/chemicals/mdma/mdma_effects.shtml
Why Would Empathogens Work

A Method of Conducting Therapeutic Sessions with MDMA™

George R. Greer, M.D.* & Requa Tolbert, M.S.N.**

“... comfortable [for patients] to be aware of, to communicate, and to remember thoughts and feelings... usually accompanied by fear and anxiety...”

Why Would Empathogens Work

- Facilitate deepened and more intimate intra- and interpersonal relationships at a time of isolation, reflection, and introspection
Comprehensive Psychedelic Model

Existential Suffering
Anxiety
Depression

Classic Psychedelics

Supportive Therapy

Predictable neurobiological alterations

Transcendental mystical experiences

Fuller lives
Better deaths
Comprehensive Psychedelic Model

- Empathogens
- Supportive Therapy
  - Predictable neurobiological alterations
  - Transcendental mystical experiences
- Classic Psychedelics
- Existential Suffering
- Anxiety
- Depression
  - Fuller lives
  - Better deaths
Comprehensive Psychedelic Model

Existential Suffering
Anxiety
Depression

Classic Psychedelics
Supportive Therapy

Empathogens
Predictable neurotransmitter flux

Predictable neurobiological alterations
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Existential Suffering  
Anxiety  
Depression

Classic Psychedelics

Supportive Therapy

Empathogens

Predictable neurotransmitter flux

Transcendental mystical experiences

Predictable neurobiological alterations

Integrative interpersonal experiences

Fuller lives

Better deaths

Total pain

Physical  
Psychological  
Social  
Spiritual
Not yet published

107 pooled subjects with treatment refractory PTSD (failure to respond to pharmaco- and psychotherapy)

Multiple study designs
  Vancouver:
    Double-blind, randomized, placebo controlled, crossover study
    Three sessions per participant
    MDMA 125mg +/- 62.5mg booster dose
    Placebo → MDMA 125mg +/- 62.5mg booster dose
MDMA-PTSD Study - Results

- Adverse events: 5 reported serious AEs
  - 1x PVCs, 2x Fractures, 1x Syncope, 1x Suicidal ideation

- Primary outcomes measures:
  - Significant reduction in PTSD severity following MDMA administration

![Graph showing PTSD Severity for Participants Across Study](image-url)

*Placebo Stage 1
*MDMA Stage 1

Multidisciplinary Association for Psychedelic Studies. (2016). *Briefing Packet End of Phase 2 Meeting.*
MDMA-PTSD Study - Results

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  - 1x PVCs, 2x Fractures, 1x Syncope, 1x Suicidal ideation

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  - Significant reduction in PTSD severity following MDMA administration

PTSD Severity for Participants Across Study

Multidisciplinary Association for Psychedelic Studies. (2016). Briefing Packet End of Phase 2 Meeting
Mrs. AD signs up for a clinical trial examining the use of psilocybin in anxiety disorders related to life limiting illnesses.

During her treatment she sees a vision of herself and her husband, wrapped in a yellow cloak, walking towards a great glass tower; she is pulsing with a profound love, fueled by the experiences of her life.

Her husband is unable to enter the tower, and Mrs. AD wraps him in the yellow cloak as she ascends the tower. She radiates love down from the tower, and watches over her husband who is comforted by the cloak.
Mrs. AD

- She does not resume her citalopram, continues to meet with her psychedelic therapist weekly to discuss her experience and vision.

- When energy allows, she paints pictures inspired by her vision, and shares them with her husband.

- When she is admitted to hospice, she comments on not being afraid because she will be watching over her husband from the glass tower, knowing that she has shared her life and love with him.

- Her husband comments: “My greatest concern was that she would be scared and worried until the moment she died, she deserved peace, and through psilocybin she found it. I’m glad we shared those last few months together.”
Current State of the Medicines

- Psychedelics – scheduled – illegal to use
  - Ongoing Phase II and Phase III studies planned

- MDMA – scheduled – illegal to use
  - MAPS Sponsored Phase III study to begin in 2018
  - Target FDA approval date: 2021

- Ketamine – scheduled – legal for use
Current State of the Medicines

Orenda Institute

KETAMINE ASSISTED PSYCHOTHERAPY TRAINING

A Foundation Course For Clinicians

Cortes Island, BC 2018

Inquiries: Email ryensen@orenda.org
Subject line: “Orenda Institute Ketamine Training”
Psychedelics and MAiD

Eligibility

- Age 18 or older
- Capable of making health care decisions
- Having a **grievous and irremediable medical condition**
- Voluntary request
- Able to provide informed consent
Psychedelics and MAiD

- Grievous and irremediable medical condition:
  - Serious and incurable medical illness, disease, disability
  - Advanced state of irreversible decline in capabilities
  - **Enduring physical or psychological suffering**, caused by the medical condition or the state of decline, the is **intolerable** to the person
  - Natural death has become reasonably foreseeable
### Psychedelics and MAiD

**Table 4: Occurrence in themes and subcategories of unbearable suffering among patients**

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<th>Subcategory</th>
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<td>Pain</td>
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<td>Feeling miserable</td>
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<td>Loss of social significance</td>
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* n, number of patients who mentioned the theme, category, or code.

### Physical symptoms: 94%


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* n, number of patients who mentioned the theme, category, or code.
Psychedelics and MAiD

Physical symptoms: 94%

Pain: 21%

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* n, number of patients who mentioned the theme, category, or code.
Psychedelics and MAiD

Table 4: Occurrence in themes and subcategories of unbearable suffering among patients

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| Psycho-emotional       | 29 | Loss of self              | 17 |                       |   |
|                        |    | Negative emotions         | 17 |                       |   |
|                        |    | Biographical aspects      | 1  |                       |   |
|                        |    | Fear of future suffering  | 5  |                       |   |
|                        |    | Dependency                | 12 |                       |   |
|                        |    | Loss of autonomy          | 18 |                       |   |
|                        |    | Being worn out            | 16 |                       |   |

| Socio-environmental    | 20 | Loss of social significance | 1  |                       |   |
|                        |    | Communication problems     | 3  |                       |   |
|                        |    | Discontent with residential situation or quality of care | 5 |                       |   |
|                        |    | Being a burden            | 13 |                       |   |
|                        |    | Loneliness                | 8  |                       |   |

| Existential            | 31 | Hopelessness               | 30 |                       |   |
|                        |    | Limitation of activities  | 23 |                       |   |
|                        |    | Pointlessness              | 17 |                       |   |
|                        |    | Tired of life             | 17 |                       |   |

Psycho-emotional: 94%

Psychedelics and MAiD

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Psychedelics and MAiD

# Psychedelics and MAiD


## Table 4: Occurrence in themes and subcategories of unbearable suffering among patients

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Psychedelics and MAiD
Correlates of Existential Suffering

- Chochinov et al.
  - Loss of will to live, Loss of dignity, Sense of self-perceived burden

- Breitbart et al.
  - Diminished sense of Meaning and Peace increases depression, suicidal ideation

- Rodin et al.
  - Hopelessness, which was further identified as a risk factor for desire for hastened death

Psychedelics and MAiD
Correlates of Existential Suffering

- Kissane et al.
- Demoralization syndrome – hopelessness, loss of meaning, existential distress

Psychedelics and MAiD
Correlates of Existential Suffering

- Kissane et al.
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Psychedelics and MAiD

- Lack of empirical evidence for the effect of psychedelics on the rates of request for, or completion of MAiD

- But what if...?
Questions?