Taking Psychedelics Seriously

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DISCLOSURE OF FINANCIAL RELATIONSHIPS

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  o Heffter Research Institute
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• None of my slides and/or handouts contain any advertising, trade names or product-group messages. Any treatment recommendations I make will be based on clinical evidence or guidelines.
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• Dr. Byock has no financial relationships to disclose

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Learning Objectives

1.) Identify types of suffering of psychological, emotional, social, spiritual, or existential nature that are potential indications for supervised therapy involving psychedelic medications, as well as important contraindications to this class of drugs.

2.) Apply findings from the evidence base of clinical research of psychedelic therapies to the treatment of persistent depression, existential suffering in terminal illness, and severe PTSD (post-traumatic stress disorder.)

3.) Discuss the public health concerns ethical, and socio-political issues pertinent to research and clinical use of psychedelics.
Background

Santa Is A Psychedelic Mushroom
New York Times December 21, 2017

https://www.nytimes.com/2017/12/21/opinion/santa-christmas-mushrooms.html?_r=0
Ethnobotany of Psychedelics

The Ethnobotany of Psilocybin
The Anthropology of Psilocybin

Sacramental use for 7,000+ years

- Religious and medicinal uses
- Used by widely diverse cultures
- Influenced religion, philosophy, art

Background

Dr. Albert Hofmann in 2003
CIA Experiments

Early Clinical Studies
Patients with Advanced-Stage cancer

Kast, Eric C. 1964. 
Lysergic acid diethylamide as an analgesic agent in cancer patients, Anesthesia and Analgesia, 43:285-291.

• Several hundred advanced-stage cancer patients studied
• No preparation
• Superior analgesia compared to hydromorphone and meperidine (several days as opposed to several hours)
• Pain reduced for several weeks
• Theory of “attenuation of anticipation”
• Additional findings included: relief of depression, improved sleep, lessened fear of death
• The occurrence of “happy, oceanic feelings” lasting up to 12 days following treatment.

Patients with Advanced-Stage cancer


• 17 dying patients administered LSD after appropriate therapeutic preparation.
• Variables examined included “tension”, depression, pain and fear of death.
• One-third improved “dramatically”.
• One-third improved “moderately”.
• One-third unchanged.
Patients with Advanced-Stage cancer


“The most dramatic effects came in the wake of a . . .mystical experience.”

• Decrease in fear, anxiety, worry and depression  
• Sometimes, need for pain medications lessened mainly because the patient was able to tolerate pain more easily  
• Increase in serenity, peace, and calmness  
• Decrease in the fear of death

Patients with Advanced-Stage cancer

LSD-assisted psychotherapy in patients with terminal cancer.  
*International Pharmacopsychiatry*, 8:129-144.

• 60 terminal cancer patients studied pre and post-treatment.  
• 29% dramatically improved  
• 41.9% moderately improved  
• 22.6% unchanged  
• 6.4% had global indexes showing a decrement in post-treatment ratings
Patients with Advanced-Stage cancer

LSD-assisted psychotherapy in patients with terminal cancer.
International Pharmacopsychiatry 8:129-144

- Changes in the attitude toward and concept of death
- Increased acceptance of death usually followed sessions in which the patients reported deep religious and mystical experiences
- Improvement of the emotional condition and relief of pain frequently observed even after sessions with predominantly psychodynamic content

Summary of Early Clinical Studies

“Over a thousand clinical papers were published in the professional literature during the 1950s and 1960s discussing the experiences of 40,000 patients treated with hallucinogens.”

— Grinspoon and Bakalar, 1979
Summary of Early Clinical Studies

Treatment applications included:

- Alcoholism and drug addiction
- Psychosomatic disorders
- Chronic post-traumatic stress
- Obsessive-compulsive disorder
- Anti-social behavior
- Autism
- Existential anxiety in terminal cancer

20th Century Culture & Psychedelics

by Judy Balaban & Cari Beauchamp
Vanity Fair, August 2010
20th Century Culture & Psychedelics

THE DOORS OF PERCEPTION

aldous huxley

20th Century Culture & Psychedelics

TIMOTHY LEARY
THE HARVARD YEARS

Edited and introduced by James Penner
20th Century Culture & Psychedelics

Turn On, Tune In, Drop Out
An antiwar demonstrator places flowers into the barrels of rifles while blocking the Pentagon on Oct. 21, 1967. (Bernie Boston/The Washington Star Collection)
The Need

Treating Depression and Demoralization Syndrome

Reduce medications which can exacerbate depression

Counseling
CBT, meaning making (logotherapy), life review, life completion, Dignity Therapy, Outlook Interventions, legacy work

Medications
Psychostimulants // anxiolytics // antidepressants // Psychedelics

The Need

Treating Depression and Demoralization Syndrome

Meaning Making

- Developmental counseling
- Story telling & life review
- Prayer
- Ritual
- Celebration
- Entheogens & empathogens
The Need

Why People Choose to Hasten Their Deaths

<table>
<thead>
<tr>
<th>End-of-life concerns</th>
<th>2016 (n=133)</th>
<th>Total 1998-2016 (n=1,127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Losing autonomy</td>
<td>89.5%</td>
<td>91.4%</td>
</tr>
<tr>
<td>• Less able to enjoy life</td>
<td>89.5%</td>
<td>89.7%</td>
</tr>
<tr>
<td>• Loss of dignity</td>
<td>65.4%</td>
<td>77.0%</td>
</tr>
<tr>
<td>• Losing control bodily functions</td>
<td>36.8%</td>
<td>46.8%</td>
</tr>
<tr>
<td>• Burden on others</td>
<td>48.9%</td>
<td>42.2%</td>
</tr>
<tr>
<td>• Inadequate pain control or concern about it</td>
<td>35.3%</td>
<td>26.4%</td>
</tr>
<tr>
<td>• Financial implications</td>
<td>5.3%</td>
<td>3.4%</td>
</tr>
<tr>
<td>• Referred for psychiatric eval</td>
<td>3.8%</td>
<td>5.1%</td>
</tr>
</tbody>
</table>


The Need

Why People Choose to Hasten Their Deaths

California Kaiser 1st year experience with End-of-Life Options Act

“Similar to Oregon’s experience, patients’ end-of-life concerns appear difficult to palliate with the most common cited reasons for pursuing EOLOA being existential suffering, inability to enjoy life, and loss of autonomy.”

Huong Q. Nguyen, Eduard J. Gelman, Tracey A. Bush, Janet S. Lee, Michael H. Kanter. Characterizing Kaiser Permanente Southern California’s Experience With the California End of Life Option Act in the First Year of Implementation JAMA Internal Medicine December 26, 2017
The Need

Why People Choose to Hasten Their Deaths

Feeling
- Hopeless
- Undignified
- Worthless
- Out of control
- A burden to others
- Pain – physical suffering or fear of future suffering
- Isolated and lonely
- Bored
- Life not worth living

Clinical Considerations

- Potential benefit and risk
- Patient selection
- Preparation - “Set and Setting”
- Supervision
- Environment of experience
- Adverse effects
- “Emotional contagion”
Clinical Considerations

Medication Selection

Entheogens & Empathogens

• Psilocybin
• LSD
• MDMA
• Ketamine
• Ayahuasca
• Peyote
• Amanita

Subjective Effects of Psilocybin

This state is marked by:

• Stimulation of affect
• Enhanced ability for introspection
• Similar to dream and hypnogogic states
• Perceptual changes (e.g., illusions, synaesthesias, affective activation and alterations of thought and time)
Subjective Effects of Psilocybin

Characteristics Of The Psychedelic Peak Experience
(Pahnke and Richards, 1966)

- Sense of unity or oneness
- Transcendence of time and space
- Deeply felt positive mood
- Sense of awesomeness and reverence

Subjective Effects of Psilocybin

Characteristics Of The Psychedelic Peak Experience
(Pahnke and Richards, 1966)

- Meaningfulness of psychological and/or philosophical insight
- Ineffability
- Paradoxicality
- Transiency
Clinical Effects of Psilocybin

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

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

Received 20 January 2006 / Accepted 27 May 2006 © Springer-Verlag 2006

Results Psilocybin produced a range of acute perceptual changes, subjective experiences, and labile moods including anxiety. Psilocybin also increased measures of mystical experience. At 2 months, the volunteers rated the psilocybin experience as having substantial personal meaning and spiritual significance and attributed to the experience sustained positive changes in attitudes and behavior consistent with changes rated by community observers.

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.

Annie L., 53-year-old woman with metastatic ovarian cancer

Charles S. Grob, Anthony P. Bossis, Roland R. Griffiths
B.I. Carr and J. Steel (eds.), Psychological Aspects of Cancer, Springer 2013
“I had lost my faith because of anxiety, and I was just terrified. I was so anxious that it was hard to think about anything else. I didn’t think I was so worried about death as I was about the process of dying.

About suffering and being in pain and having all kinds of medical procedures. I was becoming so irritable with my husband. I was just so anxious... I was not enjoying my life at all.

Comments  6 months after her participation in a Harbor-UCLA psilocybin cancer-anxiety study.

As soon as it (the psilocybin) started working I knew I had nothing to be afraid of... It connected me with the universe... It was very gentle... And there were people (the treatment team) right there if I got upset...

I thought about being involved with people I loved, things I would do with people I knew, things I would tell them... I had an amazing spiritual experience. It re-connected me to the universe.

Comments  6 months after her participation in a Harbor-UCLA psilocybin cancer-anxiety study.
**“Annie’s mood remained greatly improved for some time after the treatment. She also had much less anxiety, and her fear of getting sicker and her fear of the dying process also diminished a great deal. Beyond that, she and I got along much better after her psilocybin treatment ... I have no doubt that the treatment Annie went through was of great value to her ...”**

*Comments from Annie L.’s husband 4 months after her death*

Charles S. Grob, Anthony P. Bossis, Roland R. Griffiths
B.I. Carr and J. Steel (eds.),
Psychological Aspects of Cancer, Springer 2013

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The Chemistry of Psilocybin
The Biochemistry of Psilocybin

- $\text{C}_{12}\text{H}_{17}\text{N}_2\text{O}_4\text{P}$
- Tryptamine family of indoles
- Close resemblance to serotonin
- Low toxicity
- 4-phosphoryloxy-N,N-dimethyltryptamine
- Substituted indolealkylamine/hallucinogenic tryptamine
- 5-HT 2A and 5-HT 2C receptor agonists
- Medium dose psilocybin (12-20 mg.) produces a well-controlled altered state of consciousness.
- Effects last from 4 to 6 hours

Figure a. Time-course of plasma levels for psilocybin after 0.226 mg/kg body weight psilocybin p.o. (+/-SD)^2

Figure b. Mean urine excretion over time after 5.204 mg/kg psilocybin p.o. (+/-SE)^2
Neurobiology of Psilocybin

Study Methodology & Approval Process

Harbor-UCLA/LA BioMed

Psilocybin Treatment of Advanced-Cancer Anxiety
Study Methodology

Experimental treatment

- 12 subjects
- Metastatic cancer
- Anxiety
- Ages 18 – 70

- Preparatory psychotherapy
- Double-blind, placebo-controlled methodology
- Niacin 250 mg.
- Psilocybin 0.2 mg/kg
- GCRC setting
- Follow-up evaluation and integration

Hospital room used for study
(Before decorating)
Study Methodology

Hospital room used for study
(After decorating)

Study Methodology - Instruments

<table>
<thead>
<tr>
<th>Instrument Chart Schedule</th>
<th>2 wks before</th>
<th>1 day before</th>
<th>Just before drug</th>
<th>4 hrs after</th>
<th>6 hrs after</th>
<th>1 day after</th>
<th>2 wks after</th>
<th>monthly X 6 mos</th>
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<tbody>
<tr>
<td>POMS-SB (Profile of Mood States-Brief)</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>STAI (State Trait Anxiety Inventory)</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>BDI (Beck Depression Inventory)</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>SDS (Symptom Distress Scale)</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>SCL-90 (Derogatis)</td>
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<td>X</td>
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<td>BPRS (Brief Psychiatric Rating Scale)</td>
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<td>X</td>
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<td>BPI-SF (Brief Pain Inventory-Short Form)</td>
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<td>X</td>
<td>X</td>
<td>X</td>
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<td>MSAS (Memorial Symptom Assrt Scale)</td>
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<th>1 day after</th>
<th>2 wks after</th>
<th>monthly X 6 mos</th>
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<tr>
<td>MSKCC (Sloan Kettering Pain Cant)</td>
<td>Daily</td>
<td>Daily</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Daily</td>
<td>Daily until 2 wks after</td>
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<tr>
<td>WHOQOL brief 26 Qs</td>
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<td>X</td>
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<td>WHOQOL: SRPB 32 Qs</td>
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<td>X</td>
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<td>Additional SRPB 12 Qs</td>
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<td></td>
<td>X</td>
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<td>Importance SRPB 11 Qs</td>
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<td></td>
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<td>X</td>
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<tr>
<td>KAST SQs</td>
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<td>Extra Questions</td>
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Demographics

<table>
<thead>
<tr>
<th>Subject #</th>
<th>Age</th>
<th>Gender</th>
<th>Primary Diagnosis</th>
<th>Duration Cancer</th>
<th>Metastatic Disease</th>
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<tbody>
<tr>
<td>1</td>
<td>54</td>
<td>Female</td>
<td>Peritoneal Cancer</td>
<td>2 yrs</td>
<td>Liver</td>
</tr>
<tr>
<td>2</td>
<td>58</td>
<td>Female</td>
<td>Colon Cancer</td>
<td>1 yr</td>
<td>Liver</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>Female</td>
<td>Colorectal Cancer</td>
<td>3 yrs</td>
<td>Lymphatic, Liver</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>Female</td>
<td>Ovarian Cancer</td>
<td>12 yrs</td>
<td>Lung, Liver</td>
</tr>
<tr>
<td>5</td>
<td>47</td>
<td>Female</td>
<td>Breast Cancer</td>
<td>2 mos</td>
<td>Bone, Eye</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>Female</td>
<td>Breast Cancer</td>
<td>17 yrs</td>
<td>Liver, Lung, Bone</td>
</tr>
<tr>
<td>7</td>
<td>49</td>
<td>Female</td>
<td>Breast Cancer</td>
<td>6 yrs</td>
<td>Lung, Bone</td>
</tr>
<tr>
<td>9</td>
<td>53</td>
<td>Female</td>
<td>Salivary Gland Cancer</td>
<td>18 yrs</td>
<td>Lung, Bone, Lymphatic</td>
</tr>
<tr>
<td>10</td>
<td>53</td>
<td>Female</td>
<td>Ovarian Cancer</td>
<td>5 yrs</td>
<td>Abdomen</td>
</tr>
<tr>
<td>11</td>
<td>54</td>
<td>Female</td>
<td>Breast Cancer</td>
<td>2 yrs</td>
<td>Liver, Lung, Bone</td>
</tr>
<tr>
<td>12</td>
<td>36</td>
<td>Male</td>
<td>Colon Cancer</td>
<td>1 yr</td>
<td>Liver, Lymphatic</td>
</tr>
<tr>
<td>13</td>
<td>49</td>
<td>Female</td>
<td>Multiple Myeloma</td>
<td>8 yrs</td>
<td>Abdomen, Tongue, Vagina</td>
</tr>
</tbody>
</table>
Heart Rate and Blood Pressure

Heart Rate (bpm)

Placebo vs. Psilocybin 0.2 mg/kg

Placebo
○ Psilocybin 0.2 mg/kg

**p<0.01

Systolic Blood Pressure (mm Hg)

Diastolic Blood Pressure (mm Hg)

* p<0.05, ** p<0.01
Beck Depression Inventory

Assessment Time Point

1 Day Before 1 Day After 2 Weeks After

BDI Score

Placebo Psilocybin

Beck Depression Inventory

BDI Score

1 Day Before Month 1 Month 2 Month 3 Month 4 Month 5 Month 6

*p<0.05
**STAI State**

- Placebo
- Psilocybin 0.2 mg/kg

**STAI Trait**

- Placebo
- Psilocybin 0.2 mg/kg

*p<0.05, **p<0.01*
Study Results


Clinical Effects of Psilocybin
Clinical Effects of Psilocybin

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

Roland R Griffiths, Matthew W Johnson, Michael A Casucci, Annie Uembricht, William A Richardson, Brian D Richards, Mary P Cosimano and Margaret A Klineinst

Abstract
Cancer patients often develop chronic, clinically significant symptoms of depression and anxiety. Previous studies suggest that psilocybin may decrease depression and anxiety in cancer patients. The effects of psilocybin were studied in 51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety. This randomized, double-blind, cross-over trial investigated the effects of a very low (placebo-like) dose (1 or 3 mg/70 kg) vs. a high dose (21 or 30 mg/70 kg) of psilocybin administered in counterbalanced sequence with 3 weeks between sessions and a 4-month follow-up.

Harbor-UCLA Psilocybin Research:

www.clinicaltrials.gov
www.heffter.org
Looking Ahead
Will We Be Using Psychedelic Therapeutically?

- Legal and Regulatory barriers
- Political considerations
- Compassionate use / expanded access
- Right-to-try laws
- Business / financial
- Cultural puritanism

“We can give you enough medication to alleviate the pain, but not enough to make it fun.”
Looking Ahead
Will We Be Using Psychedelic Therapeutically?

“Death must become a more human experience. To preserve the dignity of death and prevent the living from abandoning or distancing themselves from the dying is one of the great dilemmas of modern medicine”.

Sidney Cohen
LSD and the anguish of dying.