Psychedelic-Assisted Psychotherapy
Dr. Joe Flanders
Mindspace
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Dr. Joe Flanders is the Founder and Director of Mindspace Wellbeing and the Vice-President of Psychology at Numinus Wellness. He is a licensed psychologist and an Assistant Professor (Professional) at McGill University. He has an active practice as a psychotherapist, psychedelic-assisted psychotherapist, and mindfulness teacher—in addition to his role as the head of Practitioner Relations at Numinus. He appears frequently in the media as an expert in mental health, mindfulness, and psychedelics.
Disclosures/Conflicts of Interest

- Employee of and shareholder in Numinus Wellness, a corporation developing psychedelic compounds, conducting research on psychedelic-assisted psychotherapy and providing psychedelic-assisted psychotherapy services.
- Mindspace Wellbeing is a subsidiary of Numinus Wellness.
Learning Objectives

● Describe the history of psychedelic therapies in the West
● List the most common psychedelic compounds
● Discuss the key studies driving the psychedelic renaissance
● Explain current hypotheses about the mechanisms of action in psychedelic therapy
The problem

There is a mounting crisis in mental health

Instances of anxiety, depression and other mental health disorders have been on a steady rise for the last 30 years, and coronavirus pandemic has now created an even greater crisis; prescriptions for anti-anxiety and anti-depression medication have spiked 20% during the lockdown.

Unfortunately, there have been very few new developments with medication in this time span, with increasing evidence that existing treatments are ineffective (with high relapse rates), or worse, simply exacerbate the problem, turning potentially treatable issues into long-term chronic conditions at a huge cost to society’s collective well-being.
The Psychedelic Renaissance

Web of science psychedelic publication count by year, searching for “LSD,” “PSILOCYBIN,” “PSYCHEDELICS,” or “HALLUCINOGENS”
## Psychedelic research

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<th>Psilocybin-assisted Psychotherapy</th>
<th>MDMA-assisted Psychotherapy</th>
<th>Wellness</th>
</tr>
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<tr>
<td>Smoking cessation</td>
<td>Treatment-resistant PTSD</td>
<td>Creativity</td>
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<tr>
<td>Alcohol use disorder</td>
<td>Anxiety related to end of life</td>
<td>Spirituality</td>
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<td>Cocaine use disorder</td>
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<tr>
<td>Anxiety &amp; depression in patients with advanced-stage cancer</td>
<td>Alcohol use disorder</td>
<td>Prosocial attitudes &amp; behaviours</td>
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<tr>
<td>Treatment-resistant depression</td>
<td>Treatment resistant depression</td>
<td>Train openness</td>
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<tr>
<td>Distress associated with loss due to HIV/AIDS</td>
<td>Heroin use disorder</td>
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</tbody>
</table>

**Ketamine**
- Alcohol use disorder
- Treatment resistant depression
- Heroin use disorder

**Planned trials**
- Anorexia Nervosa (psilocybin)
- Opioid use disorder (psilocybin)
- Emotional distress in early Alzheimer's (psilocybin)
- Group therapy
- Microdosing
Recent FDA Breakthrough Therapies in Psychiatry (150 total)

April 2016: Pimavanserin for Parkinson’s Disease Psychosis
April 2017: Valbenazine for Tardive Dyskinesia
August 2017: Deutetrabenazine for Tardive Dyskinesia
August 2017: MDMA-assisted psychotherapy for PTSD
October 2018: Psilocybin (COMPASS) for treatment-resistant depression
March 2019: Brexanolone for postpartum depression
March 2019: Esketamine for treatment-resistant depression
November 2019: Psilocybin (Usona) for major depressive disorder
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: definition

- Coined in 1953 by Canadian psychiatrist Humphrey Osmond
- From the Greek *psyche* (mind/soul) and *delos* (reveal/manifest).
- A diverse group of molecules that produce profoundly altered states of consciousness
- Classical Psychedelics:
  - LSD, psilocybin, ayahuasca (DMT + MAOI), peyote
  - 5-HT2A agonists
- Empathogens: MDMA
- Others:
  - Ketamine/Esketamine
  - Ibogaine
  - Cannabinoids?
- Origins can be traced variously to:
  - 6,000 BC North Africa
  - Aztec Rituals
  - 20th Century Switzerland
Mechanism of action

Biological
- 5HT2A receptor action
- Anti-inflammatory effects
- Oxytocin release

Psychological
- Sense of awe
- Interconnectedness
- Positive mood
- Autobiographical memory access
- Emotional release

Interaction
- Set & setting
- PAP
Entropic brain hypothesis

placebo

psilocybin
Use & Risks

Lifetime prevalence:
- 32 million in US in 2010
- 17% of people 21-64 years
- Highest rate among 30-34 year olds (20%; 26% male, 15% female)
- Jump from 4% to 8% of US college students

Recognized risks:
- Hallucinogen Persisting Perception Disorder
- Substance (Hallucinogen) Induced Psychosis

Anecdotal evidence
- Increased anxiety
- Lower mood
- Dramatic shifts in relationships and value systems
- Somatic symptoms
- “Psychedelic Trauma”
Harm profile

Image credit: The 2010 Lancet study’s official rankings. Alcohol is by far the most dangerous drug. Nutt et al./Lancet
The history of psychedelics

**Early evidence**
- **DMT**
  - 2130 BCE - Earliest evidence of DMT usage in form of entheogenic Yopo snuffs derived from Anadenanthera seeds in NW Argentina.
  - 1931 - DMT is first synthesized by Richard Maniske.
- **MDMA**
  - 1912 - MDMA is first synthesized and patented by the German pharmaceutical company Merck in Darmstadt.
- **LSD**
  - 1938 - Swiss chemist Albert Hofmann working at Sandoz Pharmaceuticals, first synthesized LSD.
  - 1943 - Hofmann accidentally discovered its psychedelic properties.
- **Peyote**
  - 1897 - German chemist Arthur Hoffmann isolated Meselaine from Peyote.
- **Salvia**
  - Little is known about it’s traditional use as an entheogen.
  - 1938 - Jean B. Johnson wrote about Salvia divinorum (Hikoba Mario) in his publications about the Mazatec shamans.
- **Psilocybin**
  - 7000 to 9000 BCE - N. Africa
  - Psilocybin use traces back to very prehistoric times.
  - 6000 BCE - Spain
  - Earliest mescal of suspected Psilocybin Mushroom rituals.
- **Ayahuasca**
  - 1851 - English botanist Richard Spruce encountered the use of an intoxicating beverage among Tupi-Indians of the Rio Lapes in Brazil; this was the first non-published scientific discovery of Ayahuasca.
- **Iboga**
  - Possibly used for thousands of years; roots of Iboga are used during initiation rites in the Bwiti/Religion in Gabon, Africa.

**Mid 1960s prohibition**
- **LSD**
  - 1950s and 1960s scientific research
    - Dr. Oscar Janiger
      - Psychologist in Los Angeles
      - Substance: LSD
      - Period: 1954 till 1962
      - Participants: 900
    
    - Around 40,000 patients
    - 6 international conferences
    
    - Conclusion: LSD can be safely administered in controlled doses to healthy humans by researchers trained in psychotherapy.
  
  - Expansion of the hippie movement, which promoted the use of psychedelic drugs such as marijuana and LSD as harmless and non-addictive, in order to explore the altered states of consciousness.

**All scientific psychedelic research on humans banned in U.S.**
- 
  - Summer of Love - San Francisco
    - Around 100,000 people gathered; influenced by the movement and lifestyle.
  
  - Second Summer of Love - Britain
    - A renaissance of acid house music and rave parties.
    - Supported MDMA and LSD use.

- LSD was considered as having a negative impact on the values of the Western middle class and declared a controlled substance in California.
- The rest of the world followed.
- After that, the LSD black market emerged.

**Controlled Substances Act**
- Declares that these drugs have “no currently accepted medical use”.
- However, researchers were unable to further explore their therapeutic potential because they are banned.
Lysergic Acid Diethylamide (LSD)

Albert Hofmann synthesizes LSD for the first time in 1938
- Ergot a fungus growing on rye
- Discovers psychoactive properties in 1943
- Distributed widely by Sandoz
- Research took off in the 1950s
  - Exploring psychosis
  - Adjunct for psychotherapy
Harvard Psilocybin Project (1960-62)

Psilocybin research
- Timothy Leary & Richard Alpert
- Concord Prison Experiment & Marsh Chapel Experiment
- Ethics controversy
- Fired from Harvard in 1963
- Set & Setting
- “Turn on, tune in, drop out”
Prohibition

Psychedelics go underground
- 1962 FDA starts regulating research
- 1963 LDS hits the streets
- 1970 Controlled Substances Act
- 1976 research comes to a halt
Alexander Shulgin synthesizes MDMA in 1976
- Tried it himself
-Introduced it to psychotherapists who used it for anxiety, trauma & couples therapy
- 70s & 80s “Ecstasy”/”Molly” becomes a popular street/rave drug
- 1985 it was added to Schedule I
Multidisciplinary Association for Psychedelic Science (MAPS)
- Founded by Rick Doblin in 1986
- To organize and mobilize the response to the DEA’s restrictions on MDMA through research
- 2017 FDA grants “breakthrough stats” for MDMA-assisted treatment of PTSD
- 3 trials underway
Psychedelic-Assisted Psychotherapy

- The utilisation of a psychedelic molecule in order to facilitate psychotherapy
- Characterized by:
  - Several preparatory psychotherapy sessions
  - 1-3 treatment (“high-dose”) sessions creating non-ordinary states of consciousness
  - “Journeys” are characterized by heightened internal and external environmental sensitivity
  - 3-12 integration sessions debriefing the experience, consolidating insights, aiming for lasting change
  - Trust of patient’s “inner healing intelligence”
MDMA-Assisted Psychotherapy for PTSD

TREATING PTSD WITH MDMA-ASSISTED THERAPY

Phase 3 Trial Results Published

67% of participants in the MDMA-assisted therapy group no longer had PTSD after 3 sessions, compared to 32% in the placebo with therapy group.

- Lost PTSD diagnosis: 21%
- Clinically meaningful response: 12%
- No response: 30%

Mitchell 2021, Nature Medicine

The Multidisciplinary Association for Psychedelic Studies (MAPS) is a 501(c)(3) non-profit research organization working to develop MDMA-assisted therapy into an FDA-approved prescription treatment. The safety and efficacy of MDMA-assisted therapy is currently under investigation. It has not yet been approved by the FDA, does not work for everyone, and carries risks even in therapeutic settings. Learn more about our research at maps.org.
Psilocybin-Assisted Psychotherapy for Depression

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 Carducci1, Annie Umbricht1, William A Richards1, Brian D Richards1, Mary P Cosimano1 and Margaret A Klinedinst1

Randomized, double-blind, cross-over trial
- Psilocybin administered to 51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety.
- Very low dose vs. high dose
- 5 weeks between sessions
Psilocybin-Assisted Psychotherapy for Depression

- Large decreases: in clinician- and self-rated measures of depressed mood and anxiety
- Increases in
  - quality of life
  - life meaning
  - optimism
  - Peace with death
- At 6-month follow-up:
  - 80% of participants show clinically significant decreases in depressed mood and anxiety


...were treated with either a high dose of psilocybin or an active placebo

Improvements in Depression

- Psilocybin group: 92% at 6 months
- Control group: 79% at 6 months

Improvements in Anxiety

- Psilocybin group: 76% at 6 months
- Control group: 83% at 6 months

Percent of patients showing clinically significant response rate to treatment. (Griffiths et al. 2016)
## Psilocybin versus Escitalopram for Depression

### Phase 2, Double-Blind, Randomized, Controlled Trial

<table>
<thead>
<tr>
<th>Adults with moderate-to-severe major depressive disorder</th>
<th>Psilocybin (two 25-mg doses 3 wk apart) + placebo (microcrystalline cellulose)</th>
<th>Escitalopram (10 mg daily [3 wk], then 20 mg [3 wk]) + placebo (psilocybin, 1-mg doses 3 wk apart)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=30</td>
<td>N=29</td>
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### Change in QIDS-SR-16 depressive symptom score at 6 wk (range, 0–27; higher score = greater depression)

- **Psilocybin**: −8.0±1.0
- **Escitalopram**: −6.0±1.0

Difference, −2.0 points (95% CI, −5.0 to 0.9)

Overall incidence of adverse events was similar in the two groups.

No significant difference between psilocybin and escitalopram in QIDS-SR-16 score change from baseline.

R. Carhart-Harris et al. 10.1056/NEJMoa2032994
Ketamine

- “Dissociative” anesthetic
- Extremely popular ER drug for sedation since 1990s
- Scheduled in 1999 by FDA following widespread use as club drug
- First used for TRD in 2000
Takeaways

- Psychedelics are powerful molecules that can create non-ordinary states of consciousness.
- The effects of these NOSCs can range from profoundly healing to traumatizing. Use with care.
- Early research into psychedelic-assisted psychotherapy suggests enormous potential for helping alleviate the current mental health crisis in our society. And perhaps more...


Additional references available upon request.
Q&A

• We will now discuss questions that were submitted via the Q&A feature throughout the presentation.
• Due to time constraints, we will not be able to address every question asked.
Thanks for your attention.

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