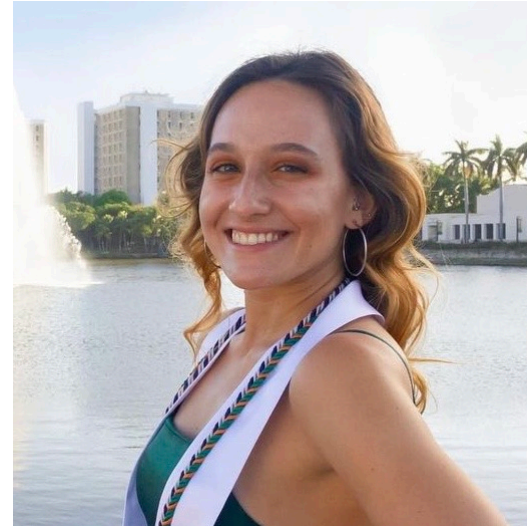


PSYCHEDELICS: CURRENT RESEARCH AND THERAPEUTIC POSSIBILITIES

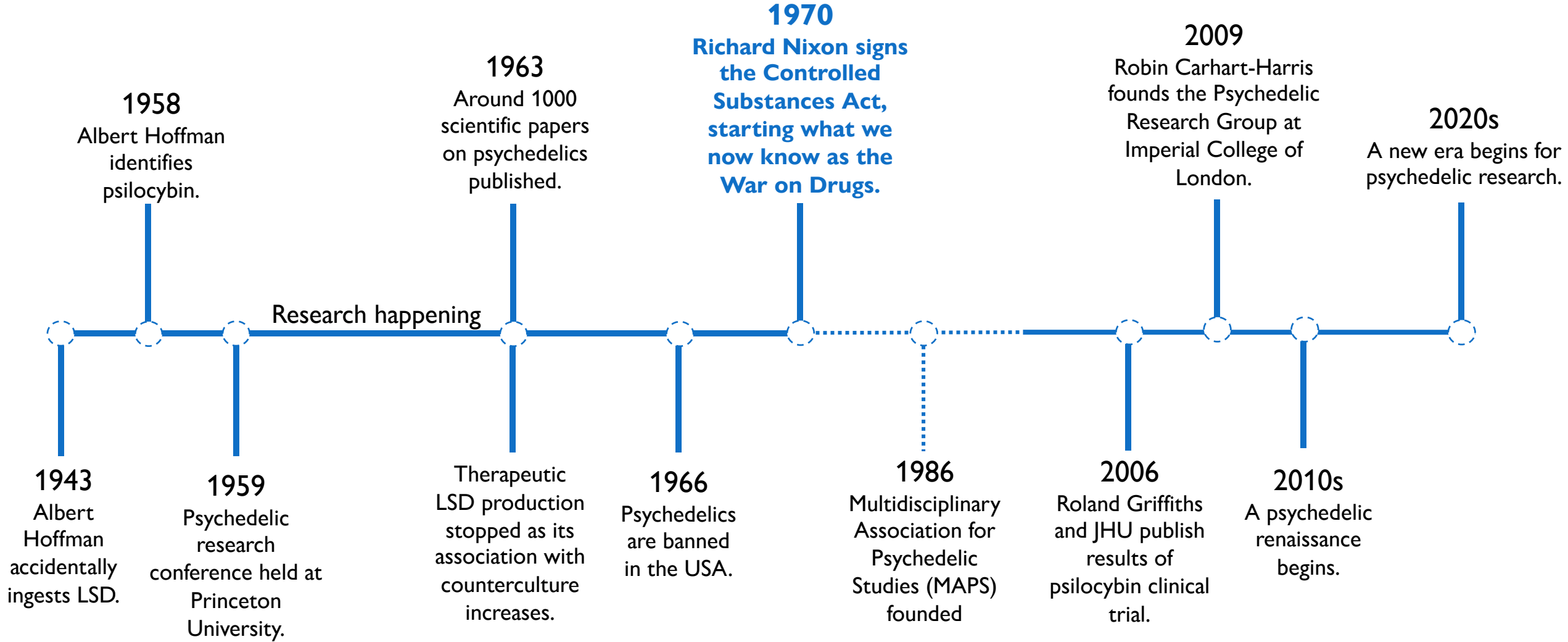
Angelica DeFalco, B.S.
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ABOUT ME

- Originally from Marlboro, NJ
- Lab Manager for BEAVERS-Lab
- Undergraduate degree from University of Miami
- Next step: PhD in Clinical Psychology
- Fun fact: I am trilingual!



RESEARCH TIMELINE



OVERVIEW

MDMA	Psilocybin	LSD	Ketamine
<ul style="list-style-type: none"> • PTSD treatment, treatment of social anxiety in autistic adults and eating disorders studies • Currently in Phase III Clinical Trials 	<ul style="list-style-type: none"> • Used in end-of-life anxiety, depression, and substance use disorders (SUDs) treatment studies • Currently in Phase II Clinical Trials 	<ul style="list-style-type: none"> • Used end-of-life anxiety (Gasser et al., 2014), depression and (most prominently) alcohol use disorder (see Fuentes et al., 2019) treatment studies • Took place mostly in the 1970s, with renaissance occurring recently • Current research taking place in Europe 	<ul style="list-style-type: none"> • Used in treatment of addiction (Krupitsky et al., 2002), depression (Dore et al., 2019) , and PTSD (Halstead et al., 2021)

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GENERAL STUDY INCLUSION / EXCLUSION CRITERIA

Inclusion	Exclusion
<ul style="list-style-type: none">• Have clinically diagnosed levels of anxiety / depression / PTSD / substance use depending on the clinical trial• 18 years+	<ul style="list-style-type: none">• Familial history of psychotic symptoms / disorders (e.g., schizophrenia, bipolar disorder)• Actively taking anti-depressants or other contraindicated medications (e.g., SSRIs)• History of seizures, hypertension, high blood pressure, or other heart or circulatory problems• Pregnancy• Use of hallucinogens on 10 or more occasions

GENERAL STRUCTURE OF CLINICAL TRIALS

1. Eligibility, screening and informed consent
2. Preparatory Sessions
 - 2-3 preparatory sessions with guides to establish rapport and build trust
 - Discuss intention for treatment session, how to react to frightening visuals or feelings (should any occur), the general flow of the day of treatment, etc.
3. Treatment Sessions
 - 2-3 dosing sessions (depending on trial), spaced out by a few weeks
 - Double-blind and randomized
 - 6-8 hours
 - Always someone in the room / on-call with participant
 - 1 MD, 1 PhD and 2 trained guides

GENERAL STRUCTURE OF CLINICAL TRIALS

4. Integration Sessions

- Take place between and after treatment sessions
- Discuss with therapist what occurred during the dosing session and try to incorporate what may have been felt or learned from the experience into participant's life
- Psychotherapy

5. Follow up

- Take place 2-6 months post-treatment to collect retention of treatment data

**NOTE: THE PROPOSED
TREATMENT IS DRUG-
ASSISTED
PSYCHOTHERAPY. NOT
JUST DRUG
ADMINISTRATION!**

PSILOCYBIN

AKA: Magic Mushrooms, Shrooms

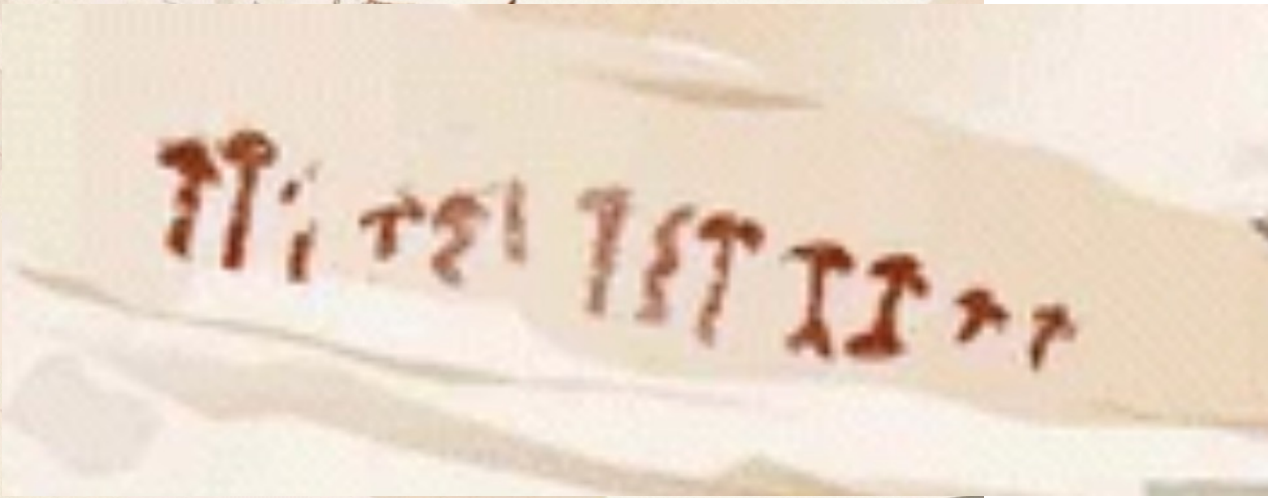
HISTORY

- Though Western civilization only became familiar with "magic mushrooms" in the 1950s, it is likely that they were used all over the world by indigenous tribes long before



~5000 – 10,000 BCE: Sandawe (a) and Bradshaw (b) tribes cave art depictions of a psilocybin trance in Australia

WALL ART



Psilocybe hispanica

MESOAMERICAN STONES



~1500 BCE: Mesoamerican mushroom stones

HOW DOES IT WORK?

- Metabolized into *psilocin*
- Targeting serotonin 5-HT_{2A} receptors in the brain
- Prevents reuptake of serotonin, increasing its concentration; boost in mood, sensory alteration
- Acts as serotonin **agonist**
- Activating new neural pathways – inability to plan (focus on the moment) and ability to “think outside the box” is increased

IN THEORY, PSILOCYBIN ALLOWS THE INDIVIDUAL TO...

Think of (and feel) their experiences in new
ways

Focus on how they are feeling in the moment

Momentarily disconnect from looping
thought patterns and ruminations and
reapproach their emotions more
compassionately

WHICH SERVE AS A PRETTY GOOD AIDE IN THERAPY!

JOHNS HOPKINS UNIVERSITY

- Center for Psychedelic and Consciousness Research led by Roland Griffiths
- Psilocybin-assisted psychotherapy in end-of-life anxiety, depression and drug addiction
- Published in various journals, including *Journal of Psychopharmacology*, *Psychopharmacology*, and *Frontiers in Psychiatry*
- Awarded a \$3.9M NIH grant for clinical research on psilocybin-assisted psychotherapy to treat tobacco addiction.

PILOT STUDY: NICOTINE CESSATION

- Open-label
- 15-week smoking cessation protocol; 2 drug sessions
- $N = 15$
- Biomarkers (i.e., urine analysis) of smoking status and self-report
- Results
 - 12 of 15 (80%) showed at least seven-day abstinence at 6-month follow up – better efficacy than some FDA approved medications
 - 11 of 15 quit on target quit date (confirmed by biomarkers during treatment)

Johnson et al., 2014

NICOTINE CESSATION RESULTS

- When asked how this trial helped participants quit:
 - 73% said that they realized long-term benefits were more important than immediate desires
 - 73% said it strengthened their belief in their own ability to quit
 - 68% said it helped change their life priorities/values, or that smoking was not more important than quitting
- Future clinical trials: pre- and post-MRI scans

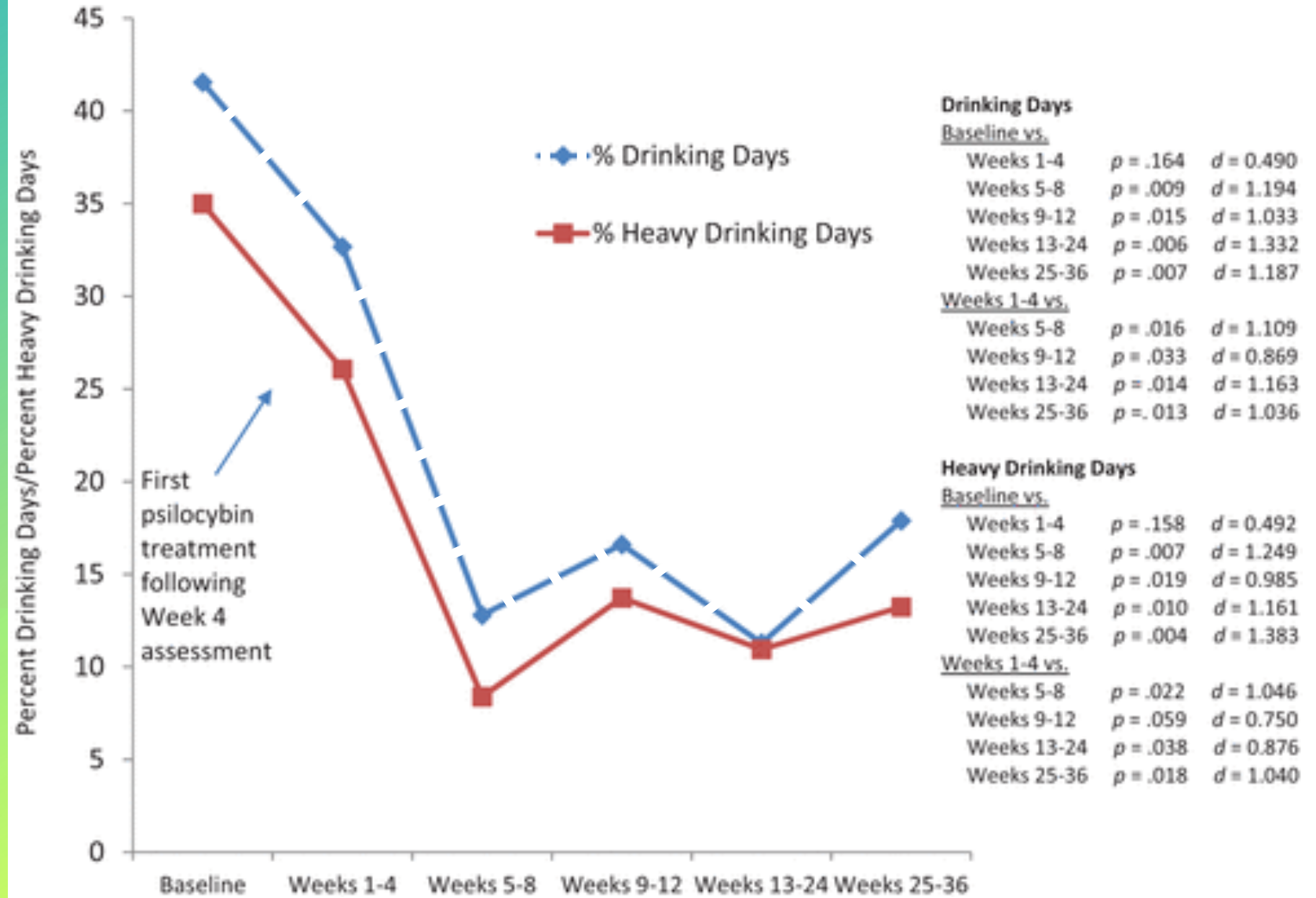
Johnson et al., 2014

UNIVERSITY OF NEW MEXICO: AUD PILOT

- 10 participants meeting DSM criteria for alcohol dependence
- 12-week program with Motivational Enhancement Therapy (MET) and 2 dosing sessions
- First dosing session occurred at the end of week 4, second occurred during week 8

Bogenschutz, 2015, 2018

RESULTS



BALLOT MEASURE 109

- As part of Ballot Measure 109 in 2020, Oregon legalized the use of psilocybin in therapeutic settings.
- Oregon has established a Psilocybin Advisory Board as part of the Oregon Health Authority (OHA)
- By January 2, 2023, the OHA will begin taking applications for licensing of people to manufacture psilocybin products, operate a psilocybin service center, facilitate psilocybin services and test products

<http://oregonvotes.org/irr/2020/034text.pdf>

STRUGGLES, SKEPTICISMS AND CRITIQUES

SMALL SAMPLE SIZES

- May amplify or diminish an effect that may or may not actually exist
- Larger samples / more research is needed to understand how the proposed mechanisms impact a broader population
- Underpowered studies

DIFFICULTY WITH BLINDING

- Participants in the “control” group tend to be more aware that they are not receiving the drug
- Greater drop-out rates in “control” groups
- Expectancy effects

STIGMA

- Since the War on Drugs began, psychedelics have earned a bad reputation in the general public (and among researchers)
 - “They put holes in your brain”
 - “You’ll never come back”
 - “You’ll go crazy”

CONTROVERSIAL RESEARCHERS

- Some individuals conducting this research are controversial and are not practicing rigorous scientific procedures
 - Unethical and questionable actions toward patients
 - Mistreatment of patients and employees
 - P-hacking
 - Lack of preregistration

NEW AND UNVALIDATED PROTOCOLS

- New protocols are being developed for treatment alongside drug administration
- This often means that they are not yet validated
- A solution may be to conduct research with well-validated forms of psychotherapy in parallel with novel ones to start to create some comfort around these new techniques
- **Of note:** many studies make note of (and specifically include) individuals who have been resistant to other types of treatments (e.g., other types of therapy, medication, etc.)

MISUNDERSTANDING OF PROTOCOLS

- Many people are under the impression that these clinical trials are **ONLY** administering drugs to people, but this is **not the case**
- It is not “MDMA therapy”, rather “MDMA-*assisted* therapy”
- Headlines can be misleading!

IN THE MEDIA

PODCASTS

- Psychedelics Today
- MAPS Podcast
- The Psychedelic Therapy Podcast
- Psychedelic Medicine Podcast with Dr. Lynn Marie Morski

DOCUMENTARIES

- Fantastic Fungi
- Neurons to Nirvana: Understanding Psychedelic Medicines
- How to Change Your Mind (based on the book by Michael Pollan)
- A New Understanding: The Science of Psilocybin

TED TALKS

- [Rick Doblin: The future of psychedelic-assisted psychotherapy](#)
- [Frederick Streeter Barrett: The neuroscience of psychedelic drugs, music and nostalgia](#)
- [Fabian Oefner: Psychedelic science](#)
- [Roland Griffiths: The science of psilocybin and its use to relieve suffering](#)