

Psychedelic-Assisted Therapy in Substance Use Disorders

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06-12-2022 @ European Parliament, Brussels



Structure

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2. Burden of disease of SUDs
3. Psychedelic Renaissance also for SUDs
4. Clinical studies of PAT for SUDs:
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 - c. Opioids
 - d. Cocaine
 - e. Private development
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7. Why PATs might be a promising future treatment for SUDs?
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9. Bibliography
10. Q&A

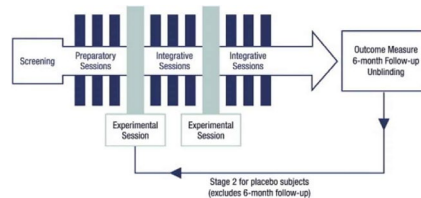
Psychedelic-Assisted Therapies

Psychedelic substances (former "hallucinogens")

- Classic: Psilocybin (magic mushrooms), LSD, DMT (Ayahuasca), Mescaline,...
- Atypical: MDMA, Ketamine, ibogaine,...

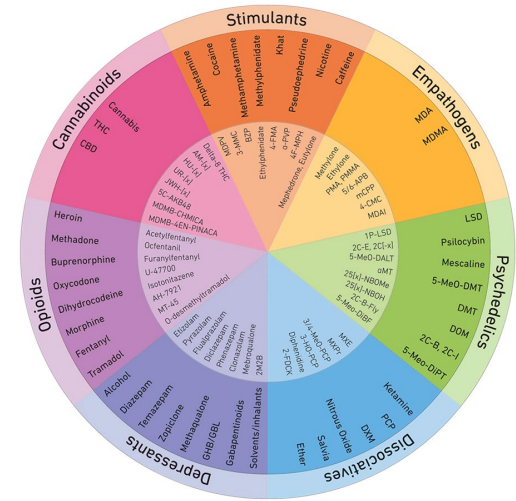
PAT= Therapy + psychedelic

- It is not a symptomatic treatment like current psychoactive drugs.
- The psychedelic is intended to act as a catalyst for a transformative experience, not treat the symptoms by chronic use.
- 1-3 acute administrations of the substance during a complete treatment, always under medical supervision.
- Lasting results for months-years.
- Previous screening, preparation for the experience and subsequent integration.
- During the psychedelic, introspection is invited with closed eyes and music.



The Drugs Wheel

A new model for substance awareness



Burden of disease SUDs

- 11.8 million deaths a year are attributed to tobacco, alcohol and other drugs, and the loss of 130 million DALYs.
- Tobacco use is the single largest cause of preventable death worldwide (6.6 million people a year). None of the established treatments aimed at smoking cessation work for a majority of smokers.
- Alcohol is the cause of 3.3 million deaths a year. Current treatments are ineffective in many cases and even abrupt discontinuation could lead to big risks.
- Behavioural addictions are on the rise (gambling, social media, internet, videogames, pornography, sex,...), specially post-pandemic.



Psychedelic Renaissance also for SUDs

The New York Times

The Next Big Addiction Treatment

Several psychedelic drugs are touted as effective treatments for drug and alcohol abuse. But psilocybin combined with therapy is emerging as the most effective.

 **NEWS**

Psychedelic drug helped people with alcohol use disorder reduce drinking, study shows

Psilocybin, the ingredient in magic mushrooms, along with talk therapy, showed significant benefit in the largest clinical trial of its kind.

the
PHARMACEUTICAL JOURNAL
Psychedelics: entering a new age of addiction therapy

Psilocybin, the compound that makes mushrooms magic, is showing promise as a treatment for several psychiatric illnesses.

SCIENTIFIC AMERICAN
MIND
MEDICINE

Treating Addiction with Psychedelics

Researchers see some promise in ibogaine, a well-known hallucinogen, and related compounds

RESEARCH | May 24, 2022

\$2.7M grant to find new addiction treatments related to psychedelics

(SACRAMENTO) Evidence from human and animal testing suggests the brain-altering effects of psychedelics could be repurposed for treating addiction.

 **NEWS**

NIH-funded psychedelic trial will study whether hallucinogen can help smokers quit

Early research has found that psilocybin, the psychedelic compound found in "magic mushrooms," helped smokers kick the habit.



4. a. Clinical studies on PATs for SUDs: ALCOHOL (AUD)

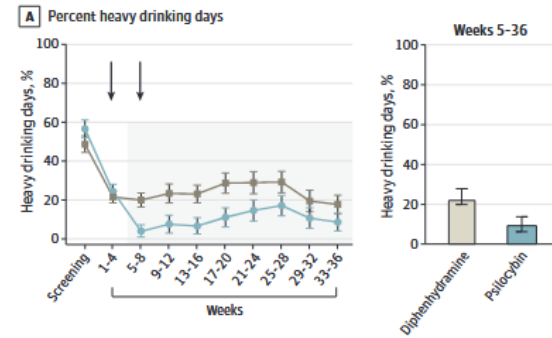
- Randomized controlled trial (inactive placebo = diphenhydramine)
- 93 participants
- Two doses of psilocybin (25 mg/70 kg & 25-40 mg/70 kg)
- Paired with 12-week manualized psychotherapy
- Percentage of heavy drinking days during the 32-week double-blind period was 9.7% for the psilocybin group and 23.6% (P = .01)
- Mean daily alcohol (drinks per day) lower in the psilocybin group

JAMA Psychiatry | Original Investigation

Percentage of Heavy Drinking Days Following Psilocybin-Assisted Psychotherapy vs Placebo in the Treatment of Adult Patients With Alcohol Use Disorder A Randomized Clinical Trial

Michael P. Bogenschutz, MD; Stephen Ross, MD; Snehal Bhatt, MD; Tara Baron, MA; Alyssa A. Forcehimes, PhD; Eugene Laska, PhD; Sarah E. Mennenga, PhD; Kelley O'Donnell, MD, PhD; Lindsey T. Owens, MA; Samantha Podrebarac, MA; John Rotrosen, MD; J. Scott Tonigan, PhD; Lindsay Worth, MA

Figure 2. Effects of Treatment on Continuous Drinking Outcomes



Clinical studies on PATs for SUDs: ALCOHOL (AUD)

On-Going

Clinical and Mechanistic Effects of Psilocybin in Alcohol Addicted Patients

- University of Zurich
- ClinicalTrials.gov Identifier: NCT04141501

Psilocybin Treatment of Major Depressive Disorder with Co-occurring Alcohol Use Disorder

- Johns Hopkins University School of Medicine



Clinical studies on PATs for SUDs: ALCOHOL (AUD)

On-Going

Psilocybin-assisted Therapy for Treatment of Alcohol Use Disorder

- Copenhagen University
- ClinicalTrials.gov Identifier: NCT05416229P

Psilocybin-assisted Psychotherapy for Treatment of Alcohol Use Disorder

- University of Iowa
- ClinicalTrials.gov Identifier: NCT05421065



Clinical studies on PATs for SUDs: TOBACCO (NUD)

- Open-Label study
 - 12 of 15 (80%) showed biologically confirmed abstinence at 6 months
 - (current behavioral and/or pharmacological therapies are about 35% effective)
- 12 month: 67% abstinent
- ≥16 months: 60% abstinent

Johnson et al., 2014, Journal of Psychopharmacology

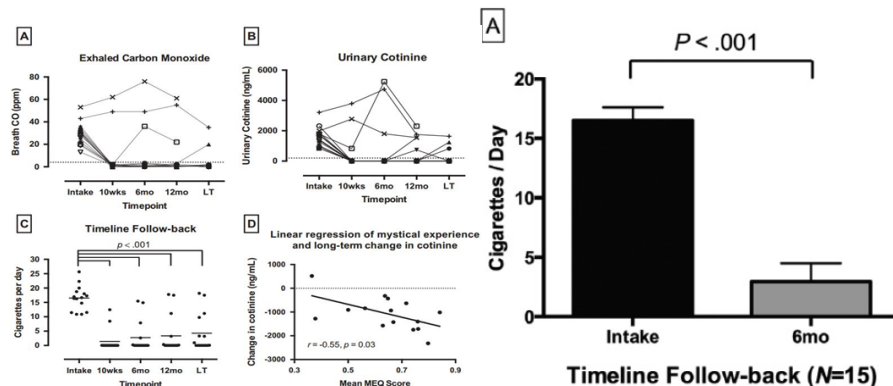
Original Paper

Pilot study of the 5-HT_{2A}R agonist psilocybin in the treatment of tobacco addiction

Matthew W Johnson¹, Albert Garcia-Romeu¹, Mary P Cosimano¹ and Roland R Griffiths^{1,2}

Psychopharm

Journal of Psychopharmacology
2014, Vol. 28(11) 983–992
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DOI: 10.1177/0269881114548296
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4.b. Clinical studies on PATs for SUDs: TOBACCO (NUD)

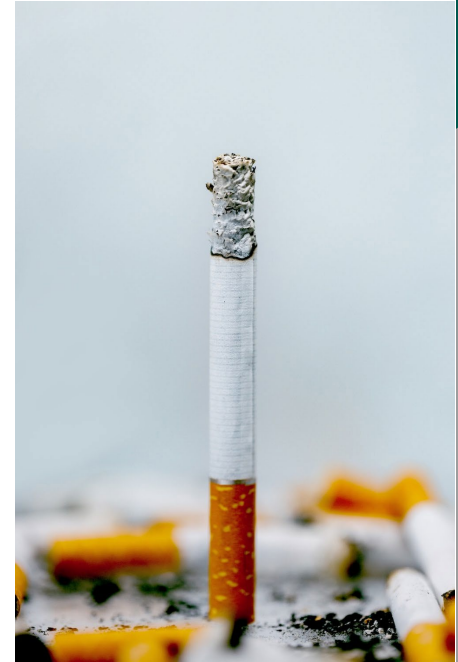
ONGOING STUDIES

Psilocybin-facilitated Smoking Cessation Treatment: A Pilot Study

- Johns Hopkins University School of Medicine
- Open Label (continuation of study just shown)
- ClinicalTrials.gov Identifier: NCT01943994

5-HT2A Agonist Psilocybin in the Treatment of Tobacco Use Disorder

- Johns Hopkins University School of Medicine
- Randomized controlled trial (inactive placebo = niacin)
- ClinicalTrials.gov Identifier: NCT05452772



Clinical studies on PATs for SUDs: OPIOIDS

ONGOING STUDIES

Preliminary Efficacy and Safety of Ibogaine in the Treatment of Methadone Detoxification

- Hospital de Reus & ICEERS

Psilocybin for Opioid Use Disorder

- Johns Hopkins University School of Medicine
- Randomized Clinical Trial

Adjunctive Effects of Psilocybin and Buprenorphine

- University of Wisconsin
- Randomized Clinical Trial



Clinical studies on PATs for SUDs: COCAINE (CUD)

ONGOING

Psilocybin-facilitated Treatment for Cocaine Use: A Pilot Study

- University of Alabama, Birmingham
- ClinicalTrials.gov Identifier: NCT02037126



Clinical trials on PATs for SUDs: PRIVATE DEVELOP.

Awakn™

Alcohol use disorder

MDMA

II

B.More

Alcohol use disorder

Psilocybin

II


DemeRx

Opioid use disorder

DMX-NB1

II


DemeRx

Opioid use disorder

DMX-1002

I / II

ENTHEON

(Unspecified) Substance use disorder

DMT

I

journey colab

Alcohol use disorder

JOUR-001

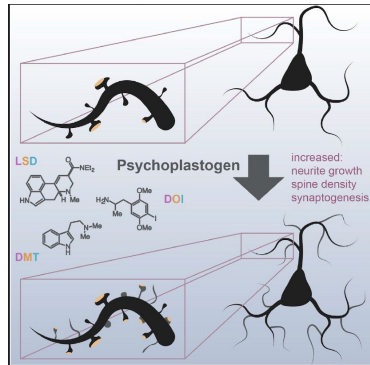
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Mechanisms for its therapeutic effect

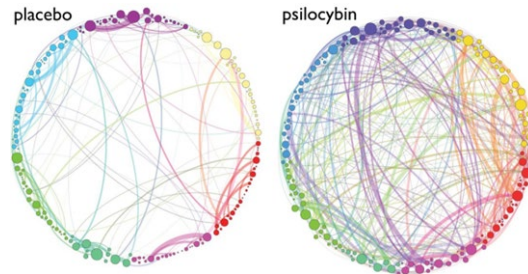
NEURONAL

- 5-HT2a agonism
- Neuroplasticity



NETWORKS / BRAIN:

- Reduces amygdala activation
- Reduces DMN activity
- Unify brain activity
- Thought Pattern disruption (“reset button”)



PSYCHOLOGICAL / PHENOMENOLOGICAL:

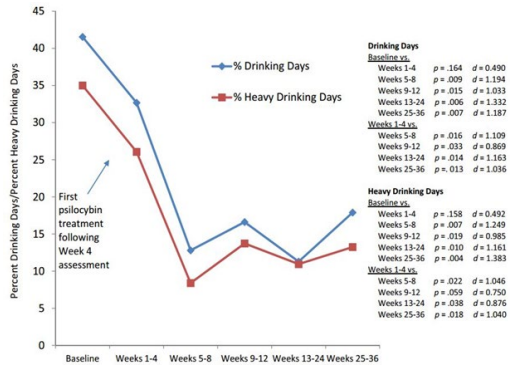
- New way to see the world and the problem
- Insight
- “Mystical experience”



Why PATs might be a promising future treatment for SUDs ?

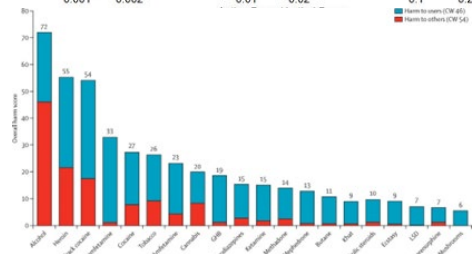
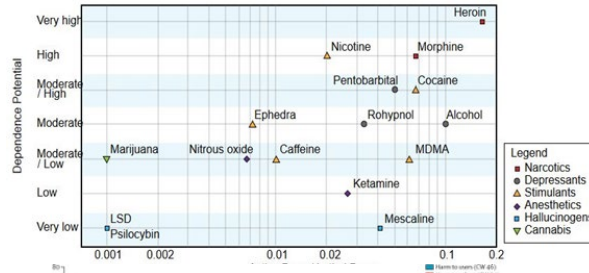
EFFECTIVE

- Great efficacy, even in treatment-resistant patients.
- Lasting results (weeks, months, even years)



SAFE (in clinical settings)

- Non-addictive
- Low toxicity
- Manageable psychological risks



EFFICIENT

- Single or small exposure required
- Lasting therapeutic effect
- Cheap substances
- Work for very debilitating and expensive conditions
- Save of DALYs, resources and human suffering

Outcome	LSD, single dose		Naltrexone, daily		Acamprosate, daily		Disulfiram, daily	
	Benefit difference (95% CI)	NNT	Benefit difference (95% CI)	NNT	Benefit difference (95% CI)	NNT	Benefit difference (95% CI)	NNT
Improvement on alcohol misuse, or return to heavy drinking	16% (8%, 25%)	6	11% (7%, 15%)	9	1% (-2%, 5%)	100	Not reported	
Maintained abstinence, or return to any drinking	15% (4%, 25%)	7	3% (1%, 6%)	33	11% (7%, 15%)	9	11% (-1%, 22%)	9

Conclusions and considerations for future implementation

- Big opportunity for European R&D and public health, but needs support.
- A few doses under direct supervision have fast and lasting therapeutic effect: different business model and investment requirements. Need of public investment.
- Only to be used by trained therapists, with screened patients and under direct supervision.
- Not take-home treatment, not to be sold in pharmacies. Only to be used in Hospitals and specialized clinics.
- Second line, for treatment-resistant patients.
- Great savings for public health systems.
- PATs for behavioral adictions? (Gambling, eating, sexual, social media, internet,...)

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Thank you!

Q & A

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