





Terminology

Psychedelics: mind manifesting (Greek) drugs

Hallucinogens: cause perceptual change

Psychomimetics: psychosis-like

Entheogens: mystical, spiritual experience

Tryptamines

Psilocybin, semi-synthetic LSD, DMT

Phenylethylamines

Mescaline (peyote), MDMA, phencyclidine, ketamine



Psilocybin

A friend or a foe?

Suthimon Thumtecho, MD

Division of Toxicology, Department of Medicine
Chulalongkorn University and King Chulalongkorn Memorial Hospital

History

3000 BC: Maya and Aztec: teonanácatl (flesh of god)

Xochipilli, Aztec god of flowers, replica in Washington DC



Photo by Nancy Cotner.

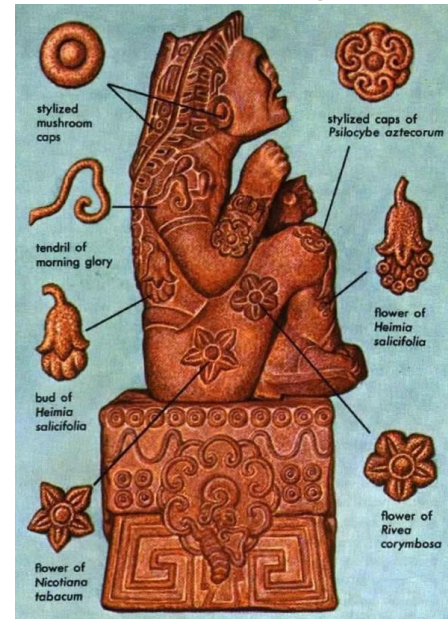
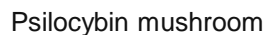


Photo by Richard Evans Schultes.

1955 LIFE magazines: “Magic mushroom”

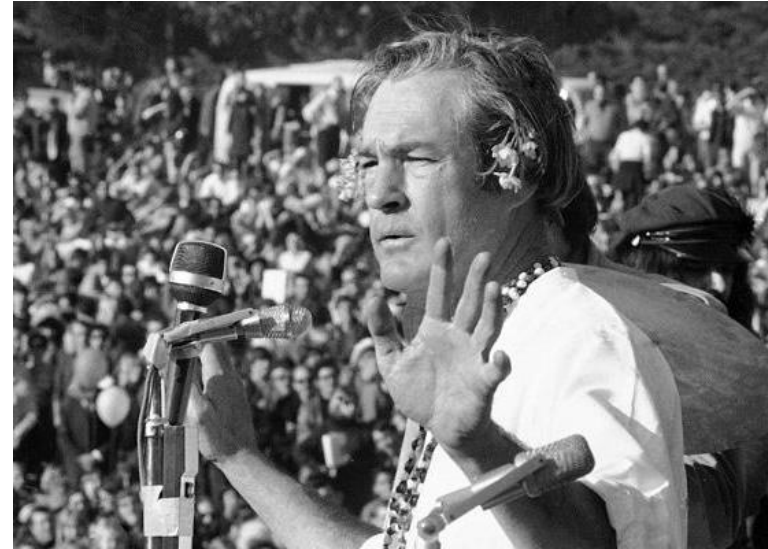


History

3000 BC: Maya and Aztec: teonanácatl flesh of god

1955 LIFE magazines: “Magic mushroom”

Timothy Leary: Tune in, turn on, and drop-out



<https://alumni.berkeley.edu/>

History

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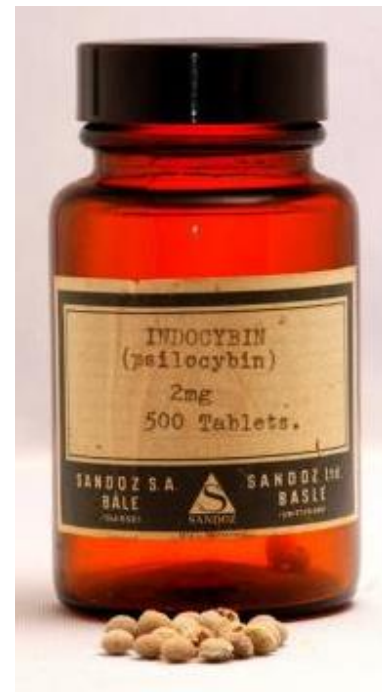
1955 LIFE magazines: “Magic mushroom”

Timothy Leary: Tune in, turn on, and drop-out

Sandoz chemist: Albert Hoffman

LSD (1938)

Extraction of psilocybin from *Psilocybe mexicana* (1957)



<https://psychedelicreview.com/event/sandoz-pharmaceutical-manufactures-indocybin/>

History

1965 Magic mushroom gain public consciousness

1968 War on drug began (USA)

1970s Schedule I of the Controlled Substances Act



The Magic Mushroom

- Psilocybin-containing mushrooms (Magic mushroom)
 - *Psilocybe cyanescens*, *Psilocybe cubensis*
 - *Conocybe cyanopus*
 - *Panaeolus cyanescens*
 - *Gymnopilus spectabilis*
 - *Psathyrella foenisecii*
- The habit of consuming magic mushroom may have been taught to the native Thai.



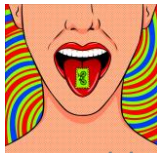
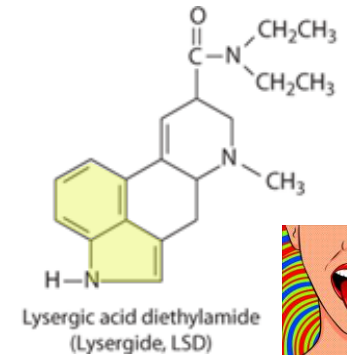
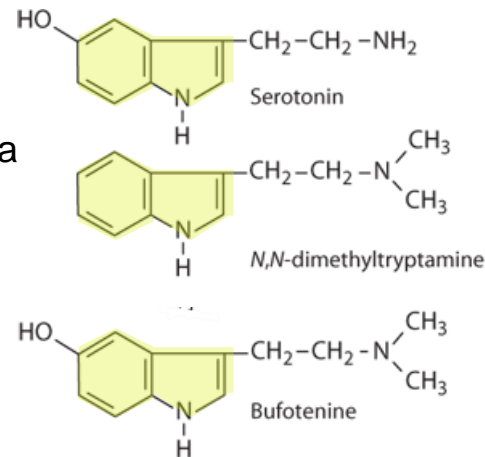
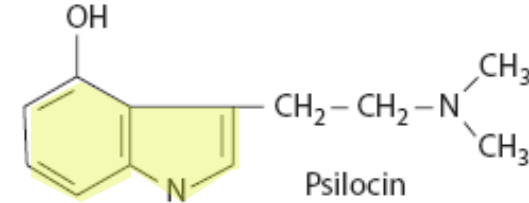
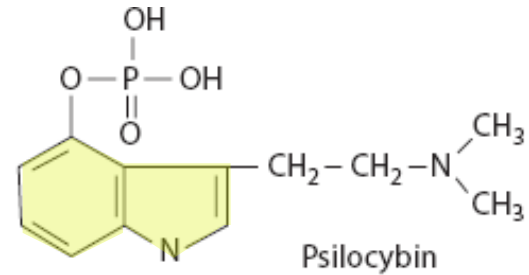
Psilocybe cubensis

เห็ดขี้ควาย/เห็ดเมา/เห็ดโอสถหลวงจิ

Buffalo dung Mushroom

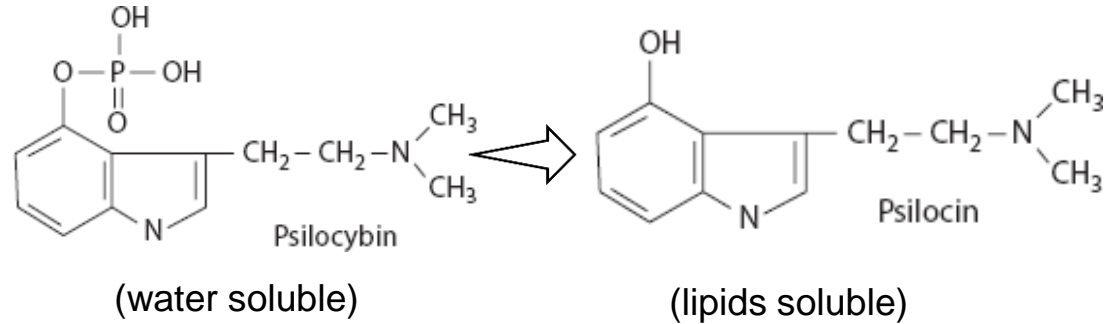
Psilocybin

- Active substances: psilocybin, psilocin
- Heat stable
- Structure similar to
 - Serotonin
 - Bufotenine
 - Dimethyltryptamine (DMT) - Ayahuasca
 - Lysergic acid diethylamide (LSD)



Pharmacodynamics

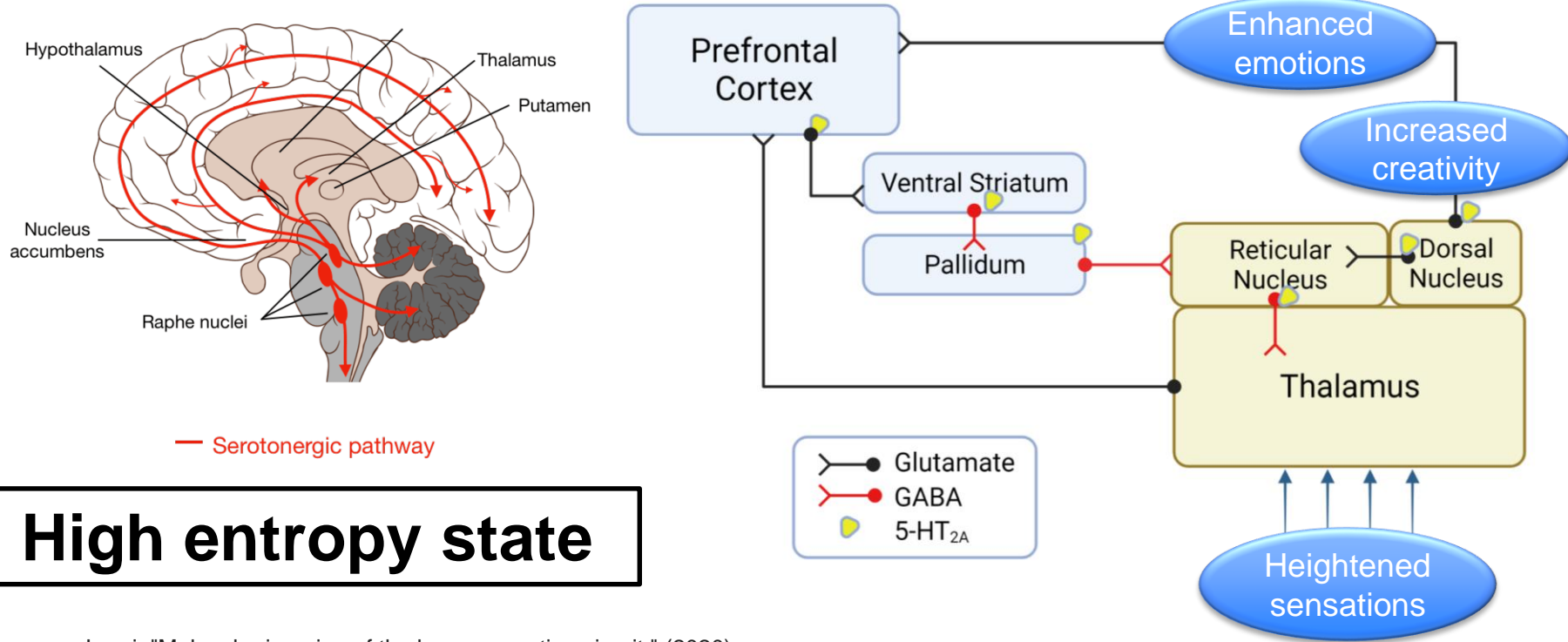
- Bioavailability 52.7%
- Metabolism
 - Stomach: acid
 - Intestine: alkaline phosphatase, non-specific esterase
 - Hepatic: UDP-glucuronosyltransferase (80%)
- Plasma half life: 2.5-6 h
- Elimination: Majority compounds are excreted within 3 h



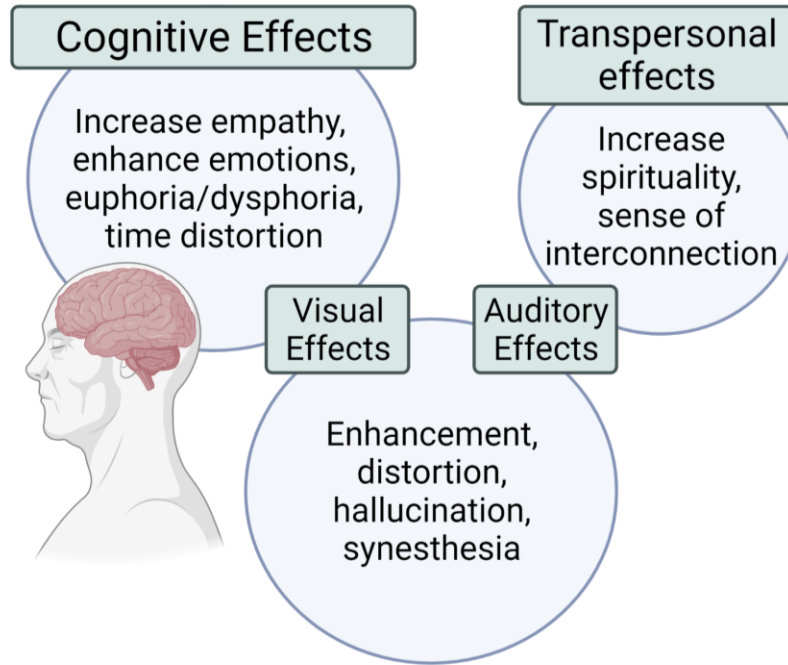
Onset 20-40 min
Peak 60-90 min
Duration 4-6 h

Mechanism of action

- High affinity to serotonin 5-hydroxytryptamine (5-HT) receptor: 5-HT_{1A}, 2A, 2C



Effects



Very much based on **set and setting**



Increase patience

Priorities shifting

Increase core senses of self

*Increase compassion, gratitude,
love and forgiveness for self
and others*

Mushroom composition

Psilocybe cubensis/subcubensis

Psilocin 0.14-0.42% (whole), **0.17-0.78% (cap)**, 0.09-0.3% (stem)
(4-hydroxy-N,N-dimethyltryptamine)

Psilocybin 0.37-1.30% (whole), **0.44-1.35% (cap)**, 0.05-1.27% (stem)
(N-phosphoryloxy-N,N-dimethyltryptamine)

May contain other substances such as serotonin, phenylethylamine

Other species (ex. *Copelandia* spp.) have different ratios

Dose-dependent effects

Psilocybin: 8-25 mg oral, 1-2 mg IV

Moderate = 0.2 mg/kg (0.25 mg)

High = up to 40 mg/70 kg

10 to 50 milligrams → 20 to 30 g fresh mushrooms/ 1 to 2 g dried mushroom



<https://limitlessmushrooms.com/>



<https://www.canadamushrooms.ca/>



<https://mungus.com/>

Drawbacks

1. Profound change in perceptions

- “Bad trips”, illusions, intensification of colours, proprioceptive change (feel gigantic, synesthesia)
- Alteration and intensification of emotions, alteration of time and space
- Accidents
- Inappropriate behaviors

Drawbacks

Rare deaths

Very few serious complications

2. Toxic Psychotic reaction and pro-psychotic potential

- Anxiety, paranoia, derealization, depersonalization, psychosis
- Low risk after a single dose is very low, especially in educated subjects in a safe environment (set-setting)

3. Flashbacks = Hallucinogen persisting perception disorder (HPPD)

- Usually with coingestion with alcohol, marijuana

Reported serious outcomes

Rare deaths

Takotsubo cardiomyopathy (17 yo, *P. semilanceata*)

Nef HM, et al. Int J Cardiol 2009; 134(1) e39-41.

Arrhythmia, myocardial infarction (18 yo, *P. semilanceata*)

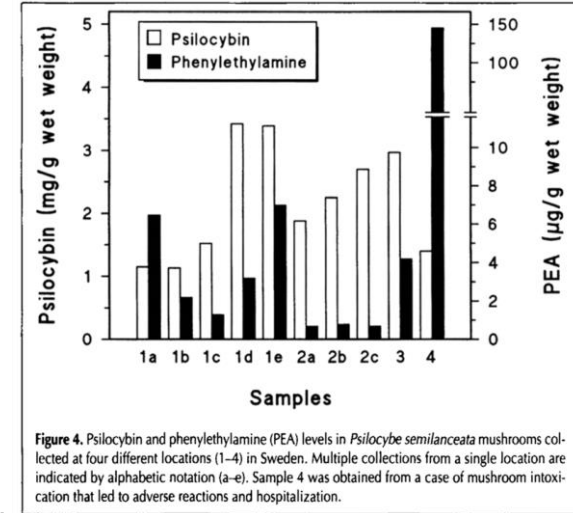
Borowiak KS, et al. J toxicol Clin Toxicol 1998;36:47-9.

Renal failure

Bickel M, et al. Eur J Emerg Med 2005;12:306-8.

Seizure, hyperthermia, renal failure, rhabdomyolysis (coingestion)

Raff E, et al. Can Med Asso J 1992;147:1339-441.



P. semilanceata
Beck O, et al. J Anal Toxicol. 1998;22(1):45-49.

Drug interaction

“Enhance the trip”

Mono amine oxidase (MAO) inhibitor

Acetaldehyde (metabolite of ethanol) inhibits MAO

Tobacco lowers brain MAO

“Risk of seizure”

Lithium

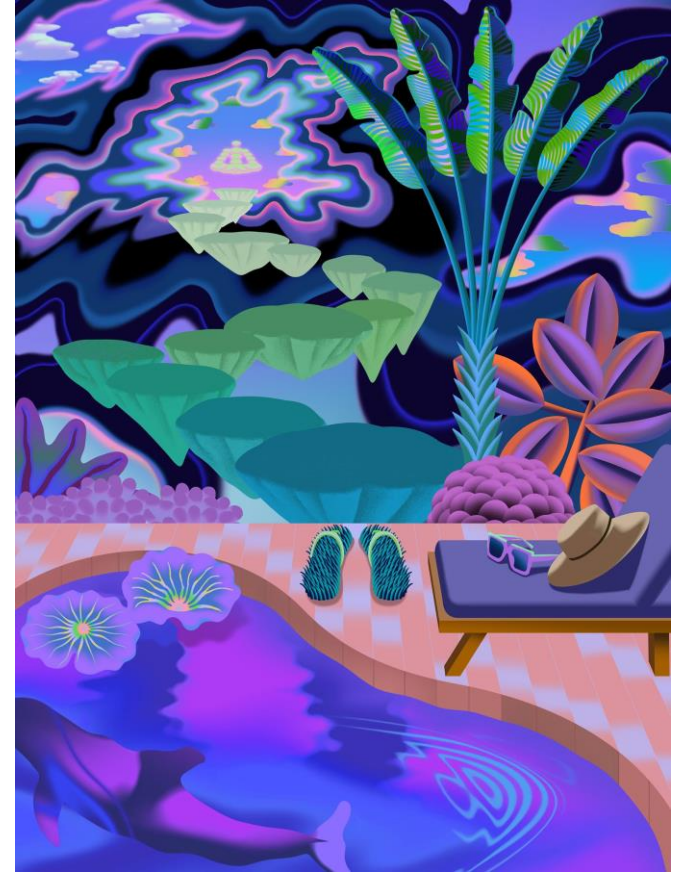


Illustration: Saiman Chow

Drug abuse and tolerance

No dependence

No addiction: Fail to stimulate dopamine release

Katzung's Basic and Clinical Pharmacology, 15th edition

Prone to abuse other drugs: cocaine, ecstasy, opiate, psychotropics, LSD

Hallock RM, et al. Drug Alcohol Depend 2013;130:245-8.

Back to the future: Research in 21th century

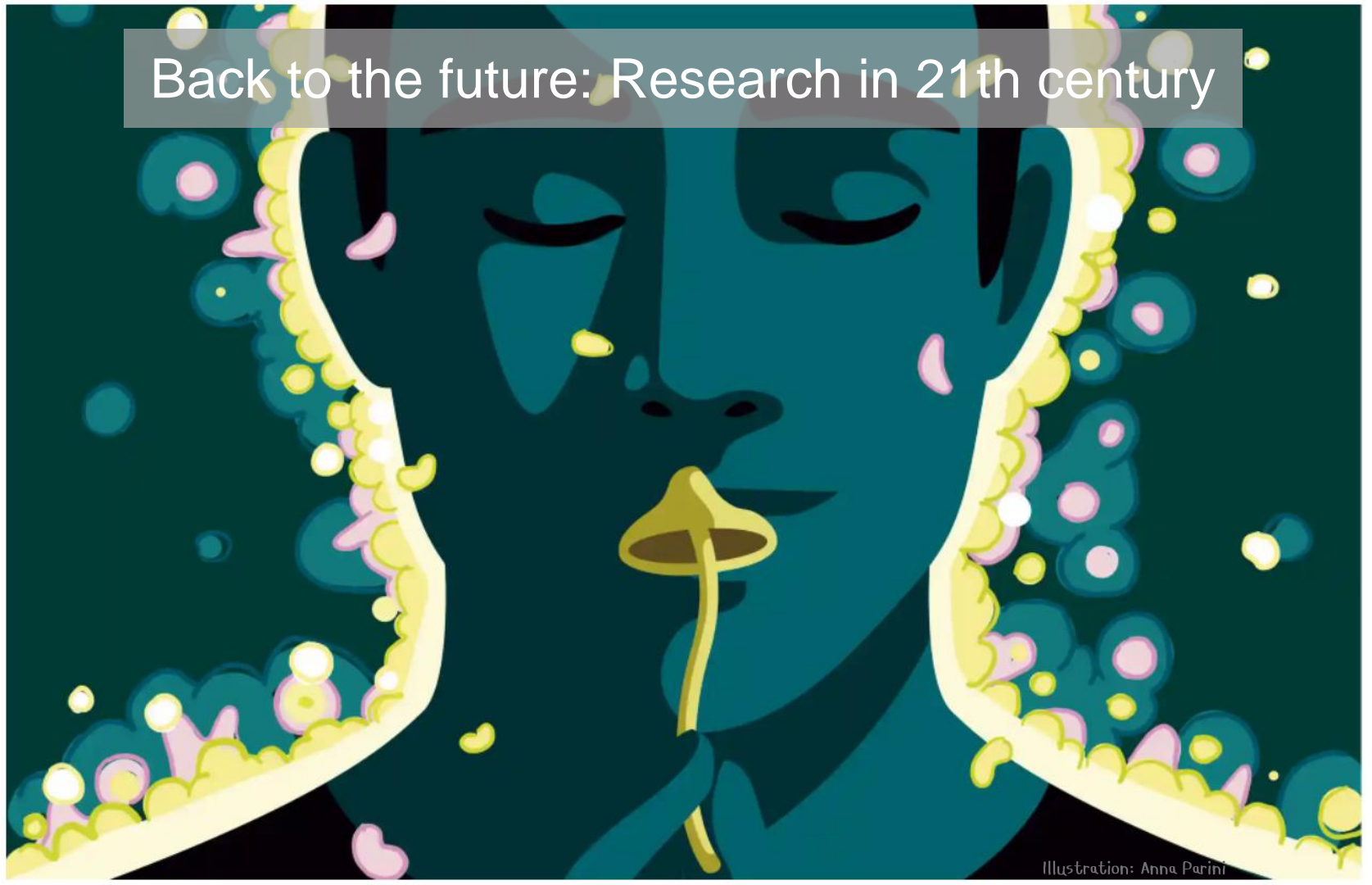
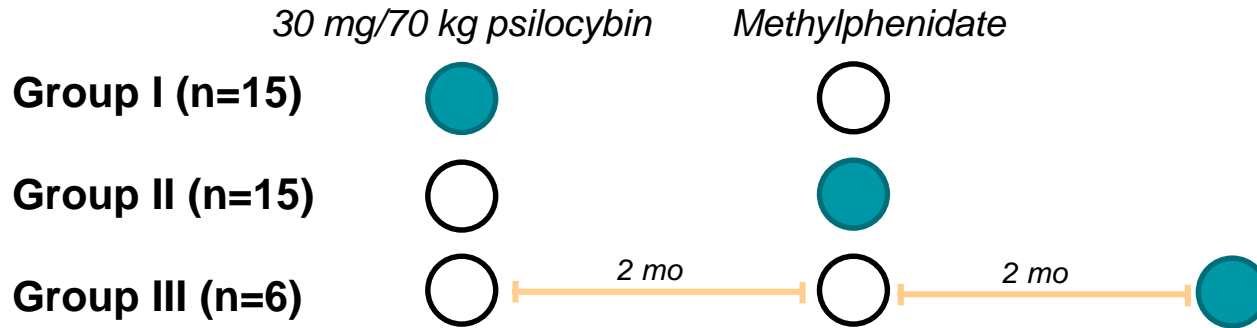


Illustration: Anna Parini

Healthy volunteers



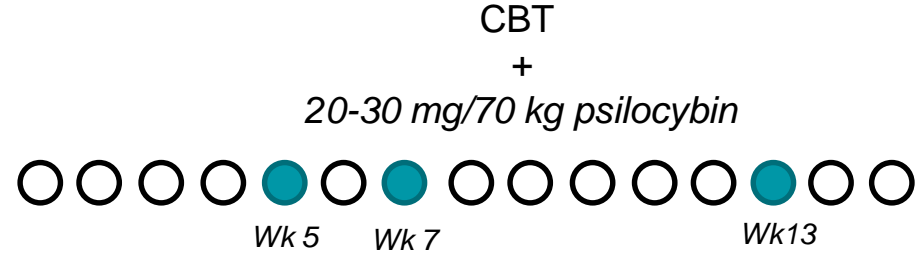
At 14th month

- 58% among five most personally meaningful experience
- 67% among five most spiritually significant experiences of their lives
- 64% the experience increased well-being or life satisfaction
- 58% met criteria for having had a 'complete' mystical experience

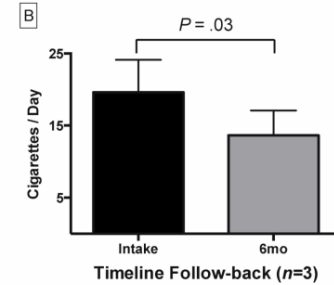
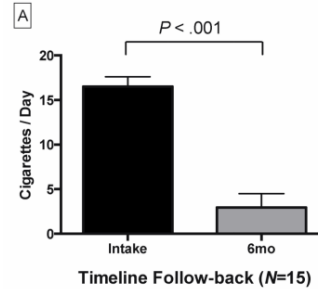


Tobacco cessation

15 nicotine-dependent smokers (psychiatrically healthy)



- 80% Abstinent at 6th-month follow-up
- 67% Abstinent at 12th-month follow-up
- 60% Abstinent at 2 ½th-year follow-up
- Mystical experiences induced were linked to positive changes



Cancer study – Depression and Anxiety

12 Life-threatening Cancer Patients + Anxiety

0.2 mg/kg Psilocybin



Niacin 250 mg



- Minimal change in BP, HR
- Sustained decrease in anxiety at 1st, 3rd month
- Sustained decrease in depression at 6th month

Cancer study – Depression and Anxiety

51 Life-threatening Cancer Patients + Depression + Anxiety

Group I (n=25)

1-2 mg/70 kg psilocybin

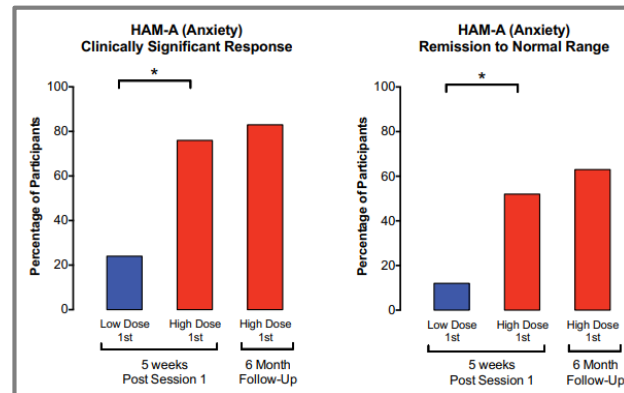
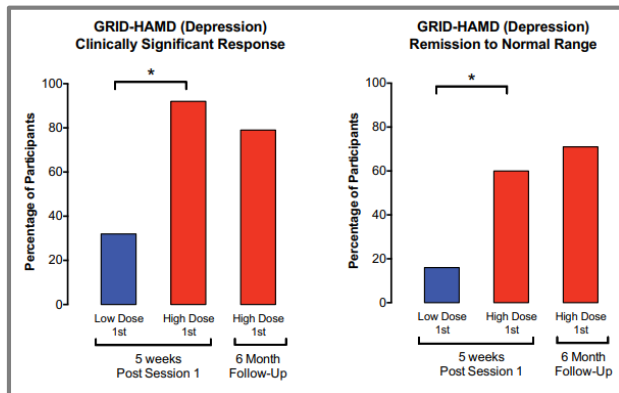


Group II (n=26)

22-33 mg/70 kg psilocybin



5 wk



Cancer study

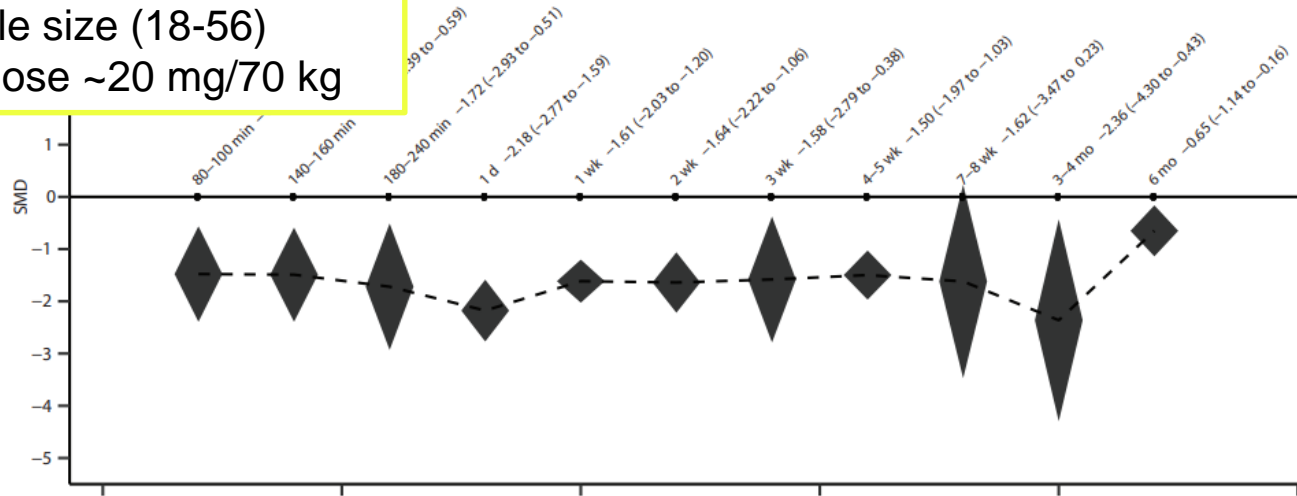
At 6th month

- 60-80% Clinically significant decreased in depression and anxiety
- 67% One of the top 5 meaningful experiences in their lives
- 70% One of the top 5 spiritually significant experience in their lives
- 82% Significant increased sense of personal well-being or life satisfaction
- “Highly correlated with the participants’ mystical or spiritual experience”
- “Improvements in attitudes toward death”

Suicidality – meta-analysis

Figure 2. Meta-Analysis of Standardized Mean Differences (SMDs) for Pooled Suicidality Scores for Each Time Point Compared to Baseline^a

7 RCTs (last search: Nov 2020)
Trials that assess suicidality
Small sample size (18-56)
Psilocybin dose ~20 mg/70 kg



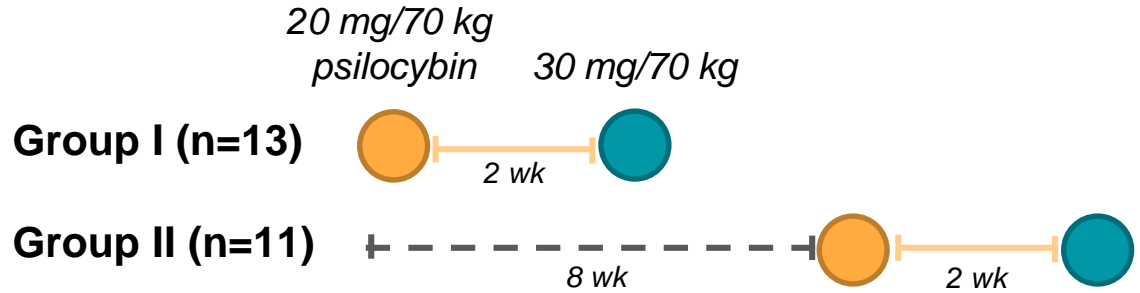
- Acute and sustained reductions in suicidality
- Rare acute and post-acute elevations in suicidality

Depression study

24 mod-severe MDD

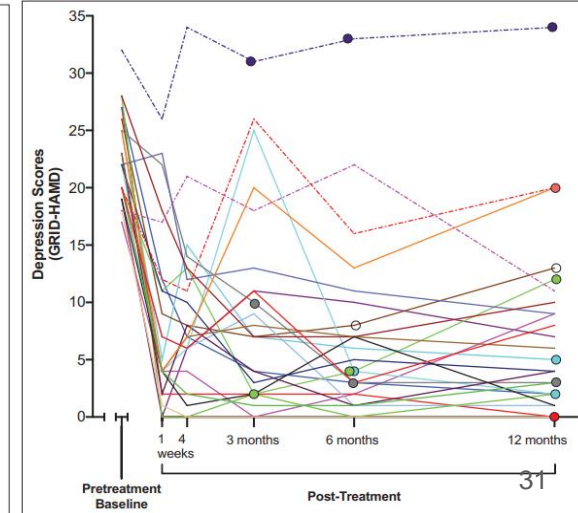
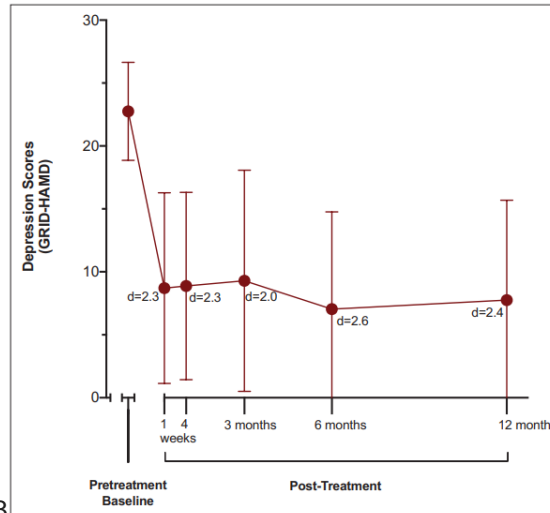
Age 21-75

RCT, unblind



At 12th month

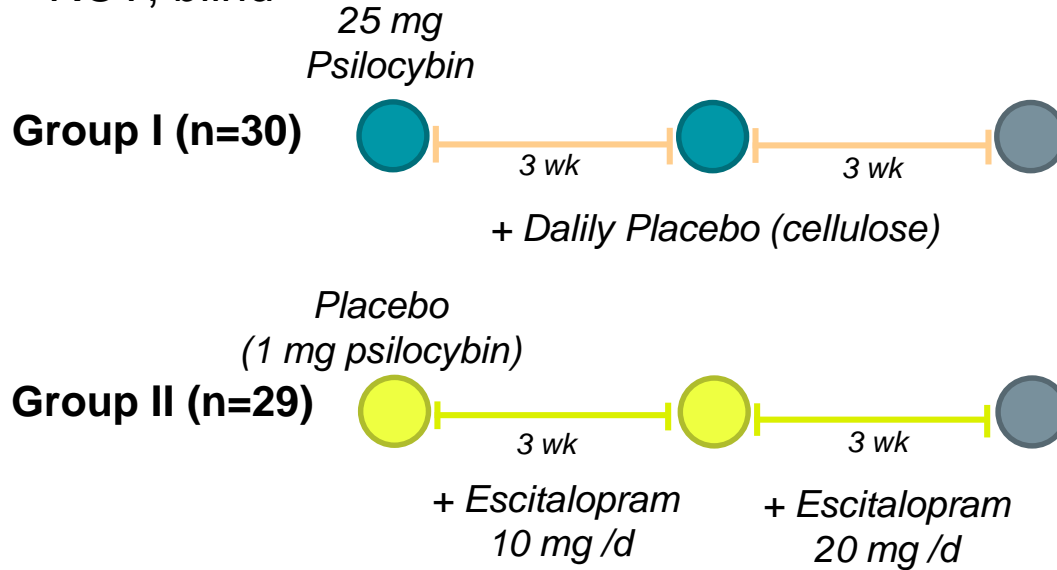
- Treatment response 75%
- Remission 58%



Depression study

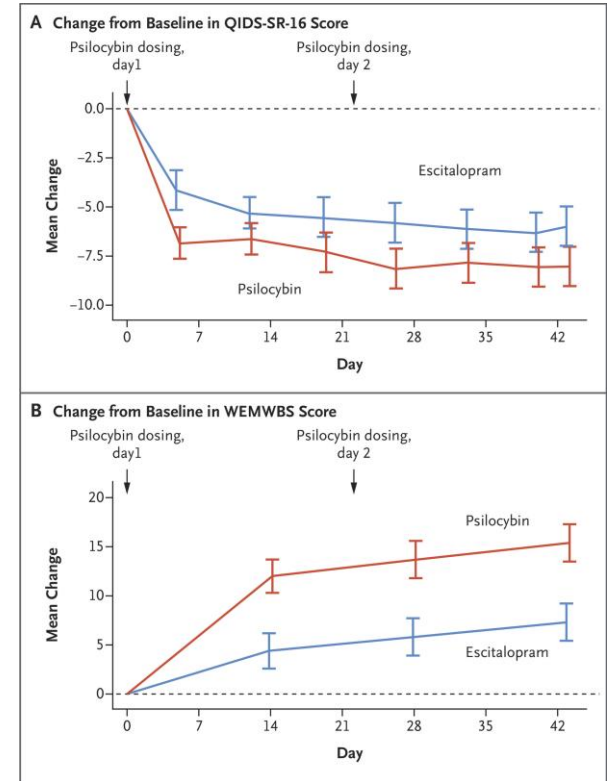
59 mod-severe MDD

RCT, blind



At 6th week

- No significant difference (QIDS-SR-16)
- 70% response, 57% remission in psilocybin group (vs 48%, 28%)



Back to the future: Research in 21th century

- Healthy volunteer
- Smoke addiction
- Depression and anxiety in advanced cancer patients
- OCD
- Alcohol addiction



Low entropy state

Ongoing studies

- PTSD
- Anorexia nervosa
- Early-stage Alzheimer's
- Opioid addiction

Things to consider: Legalization



**ดันเร็กเก้บาร์เกาะพะงัน จับเห็ดขี้ควาย ปั่นขาย นทท. ช่วง
ฟูมุ่น**

ไทยรัฐออนไลน์ ข่าว > ทัวไทย > ใต้

19 ก.ค. 2559 16:30 น. แชร์ บันทึก

ตร.เกาะพะงัน นำกำลังเข้าดันเร็กเก้บาร์ ยึดเห็ดขี้ควาย 2 กก. ผู้ดูแลร้าน รับซื้อมากิโลละ 5 พัน เตรียมนำ
มาปั่นผสมเครื่องดื่ม ขาย นทท. ช่วงฟูมุ่น คุ่มตัวดำเนินคดี ...

- Plants containing psilocybin or psilocine: Schedule 5 (Narcotics Drug Act 1979)
- Psilocybin and psilocine: Schedule 1 (Psychotropic Substance Act 1975)

Things to consider: Setting

Controlled contexts!!!

Volunteer selection

Study personnel

Physical environment

Preparation: how to handle the effect

Volunteer safety

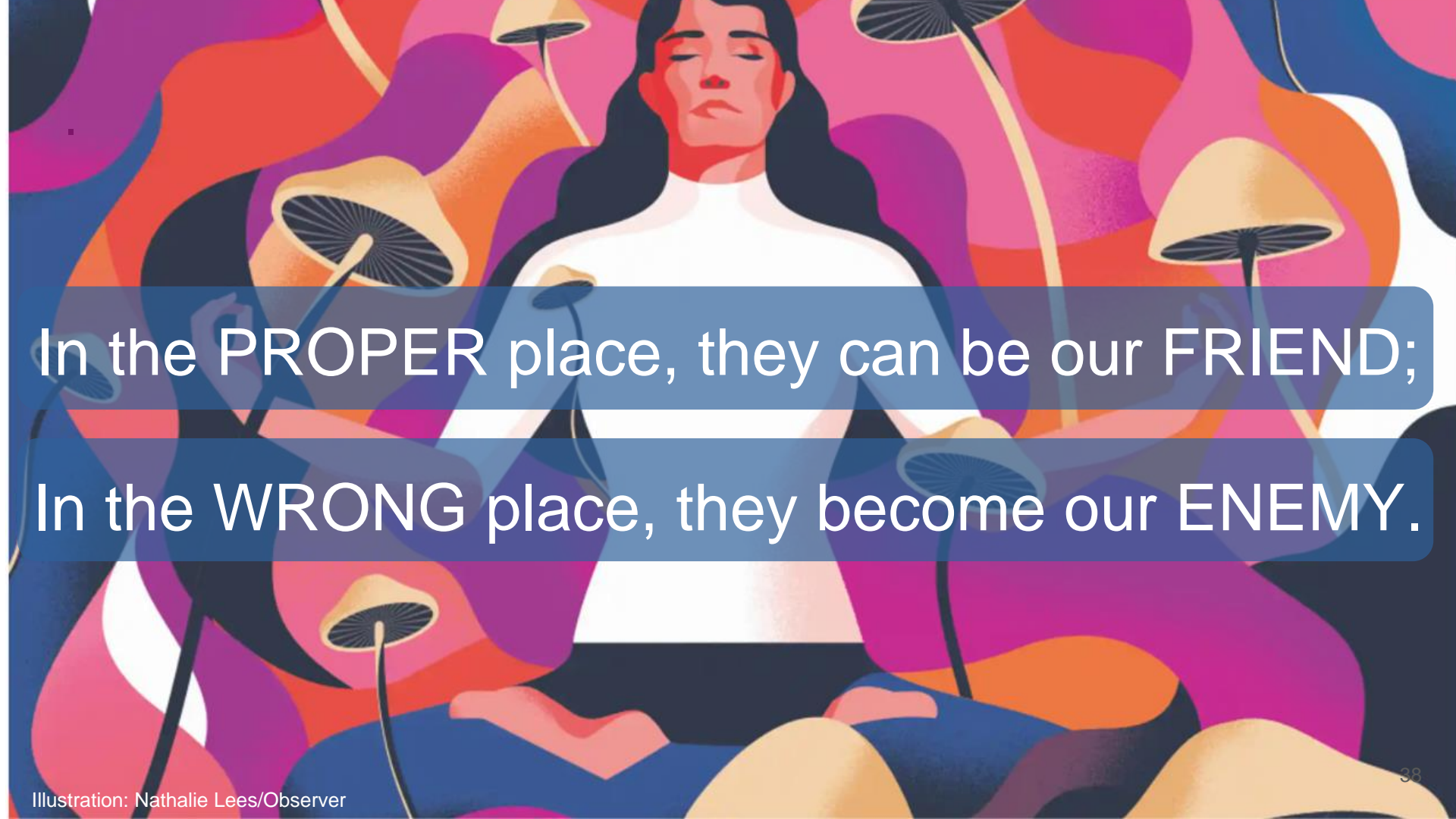


Johnson M, et al. J Psychopharmacol. 2008 Aug;22(6):603-20.



Things to consider: Adulteration

- Hallucinogenic mushrooms sold on the street are often non-psychoactive mushrooms that have been adulterated with LSD or phencyclidine (PCP).



In the PROPER place, they can be our FRIEND;
In the WRONG place, they become our ENEMY.