

Psilocybine

Généralités et applications cliniques en psychiatrie

présentation par Charles Dauré

06/01/2025



Biosynthèse de la psilocybine dans le mycélium

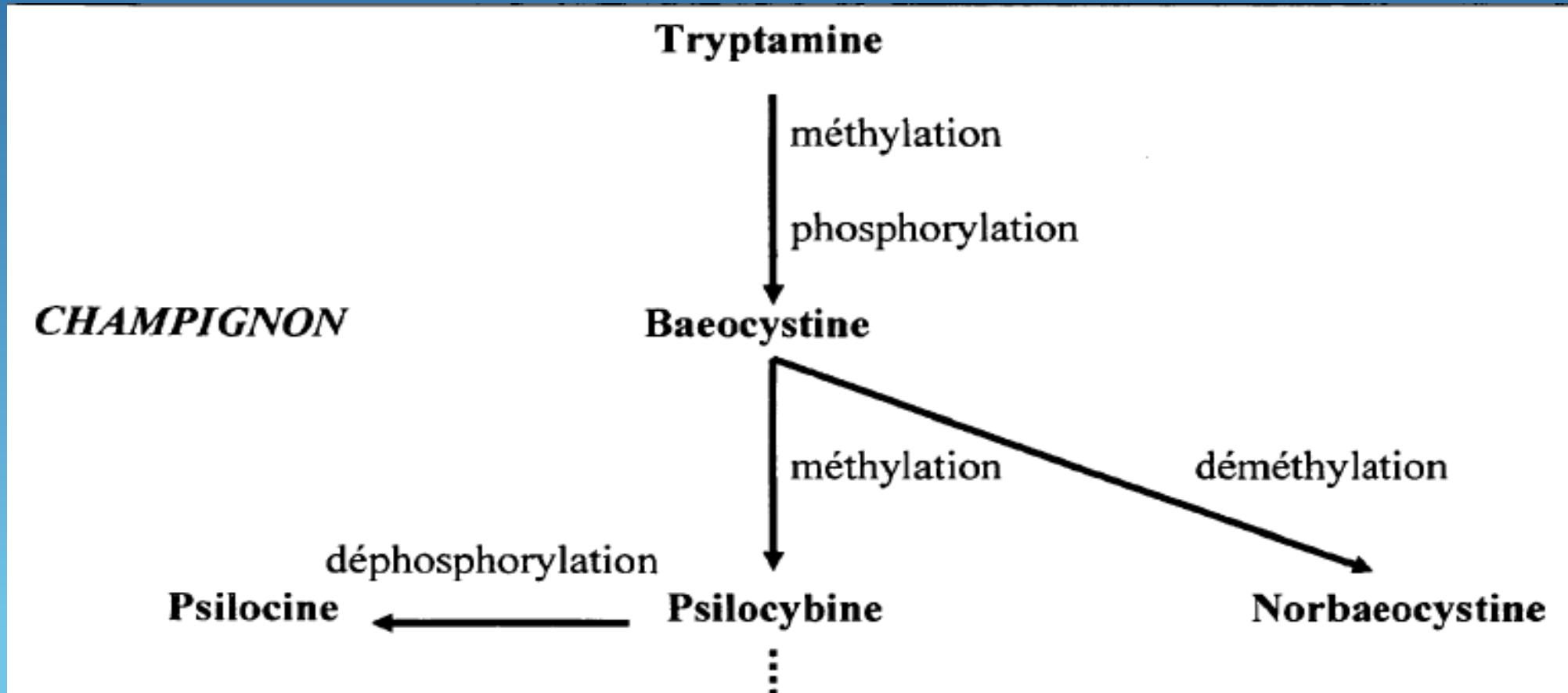


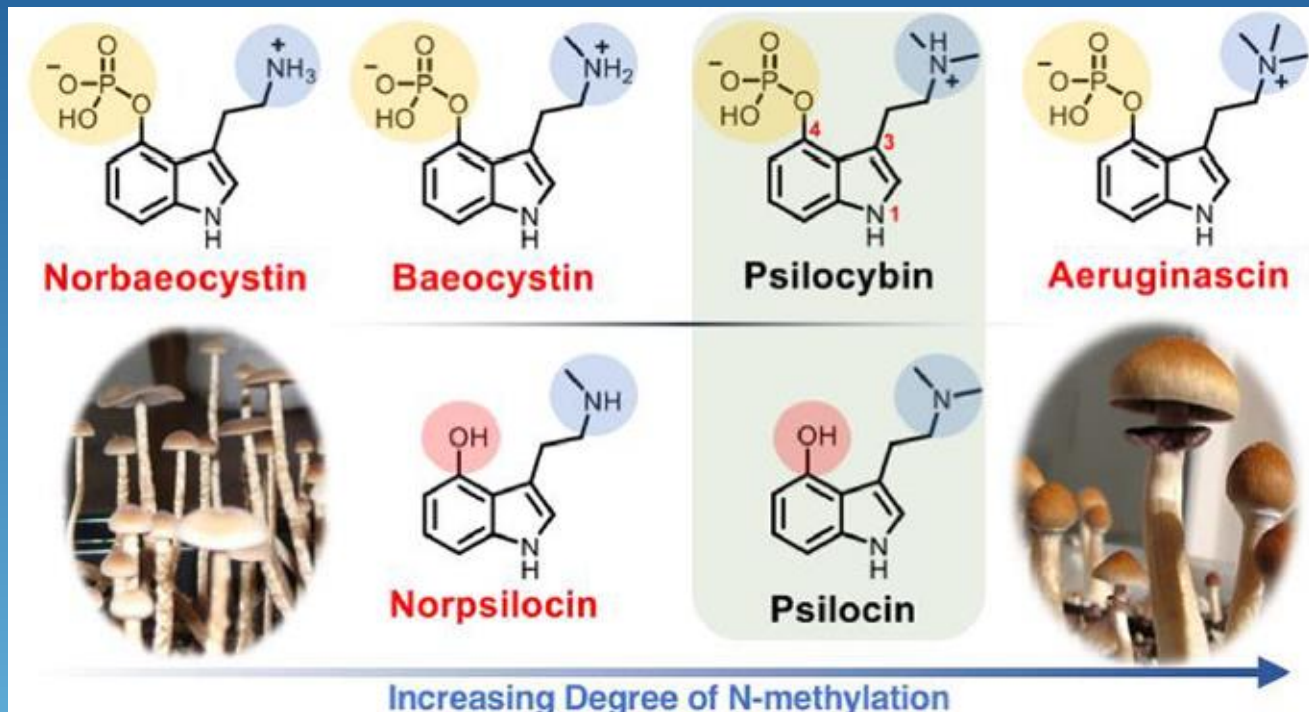
Table 1 Systematic classification and the selected representatives of mushrooms containing psilocybin. Representatives of species currently freely distributed in the SmartShop network in the Netherlands are depicted in bold.

Mushrooms containing psilocybin

Division	Class	Order	Family	Genus	Best know representative
Basidiomycotina	Hymenomycetes	Agaricales	Bolbitiaceae	Conocybe	<i>Conocbe cyanopus</i>
			Copriniaceae	Copelandia	<i>Copelandia cyanescens</i>
				Panaeolina	<i>Panaeolus africanus</i>
			Cortinariaceae	Panaeolus	<i>Panaeolus subbalteus</i>
				Gymnopilus	<i>Gymnopilus Purpuratus</i>
				Galerina	
			Plutaceae	Inocybe	<i>Inocybe aeruginascens</i>
				Pluteus	<i>Pluteus salicinus</i>
			Strophariaceae	Psilocybe	<i>Psilocybe azurescens</i>
				(115 representatives)	<i>Psilocybe bohemica</i>
					<i>Psilocybe cubensis</i>
					<i>Psilocybe cyanescens</i>
	<i>Psilocybe mexicana</i>				
	<i>Psilocybe semilanceata</i>				
	<i>Psilocybe tampanensis</i>				
Tricholomataceae	Hypholoma				
	Gerronema				
	Mycena				

Table 2 Content of psilocybin and psilocin in the dry state of selected representatives of psychoactive mushrooms, x=content is not known.

Species	Psilocybin (%)	Psilocin (%)	Study
<i>Psilocybe azurens</i>	1.78	0.38	Stamets and Gartz (1995)
<i>Psilocybe bohemica</i>	1.34/0.78/ 0.85	0.11/0.01/ 0.02	Gartz and Moller (1989) and Gartz (1993, 1994)
<i>Psilocybe semilanceata</i>	0.98/0.96	x/x	Gartz (1994, 1993)
<i>Psilocybe baeocystis</i>	0.85	0.59	Repke et al. (1977) and Beug and Bigwood (1982)
<i>Psilocybe cyanescens</i>	0.85/0.45/ 0.32	0.36/0.06/ 0.51	Repke et al. (1977), Stijve and Kuyper (1985), and Gartz (1993, 1994)
<i>Psilocybe tampanensis</i>	0.68	0.32	Gartz (1993)
<i>Psilocybe cubensis</i>	0.63	0.6	Gartz (1994) and Stijve and De Meijer (1993)
<i>Psilocybe mexicana</i>	0.3	0.05	Hofmann et al. (1959)
<i>Psilocybe hoogshagenii</i>	0.6	0.1	Heim and Hofmann (1958)
<i>Psilocybe stuntzii</i>	0.36	0.12	Repke et al. (1977) and Beug and Bigwood (1982)
<i>Psilocybe cyanofibrillosa</i>	0.21	0.04	Stamets et al. (1980)
<i>Psilocybe liniformans</i>	0.16	x	Stijve and Kuyper (1985)
<i>Gymnopilus Purpuratus</i>	0.34	0.29	Gartz (1994)
<i>Inocybe aeruginascens</i>	0.40	x	Gartz (1994)
<i>Copelandia cyanescens</i>	0.32	0.51	Barceloux (2012)
<i>Panaeolus subbalteus</i>	0.39	x	Gartz (1993)
<i>Conocbe cyanopus</i>	0.88	0.15	Gartz (1993)
<i>Pluteus salicinus</i>	1.09	x	Gartz (1993)

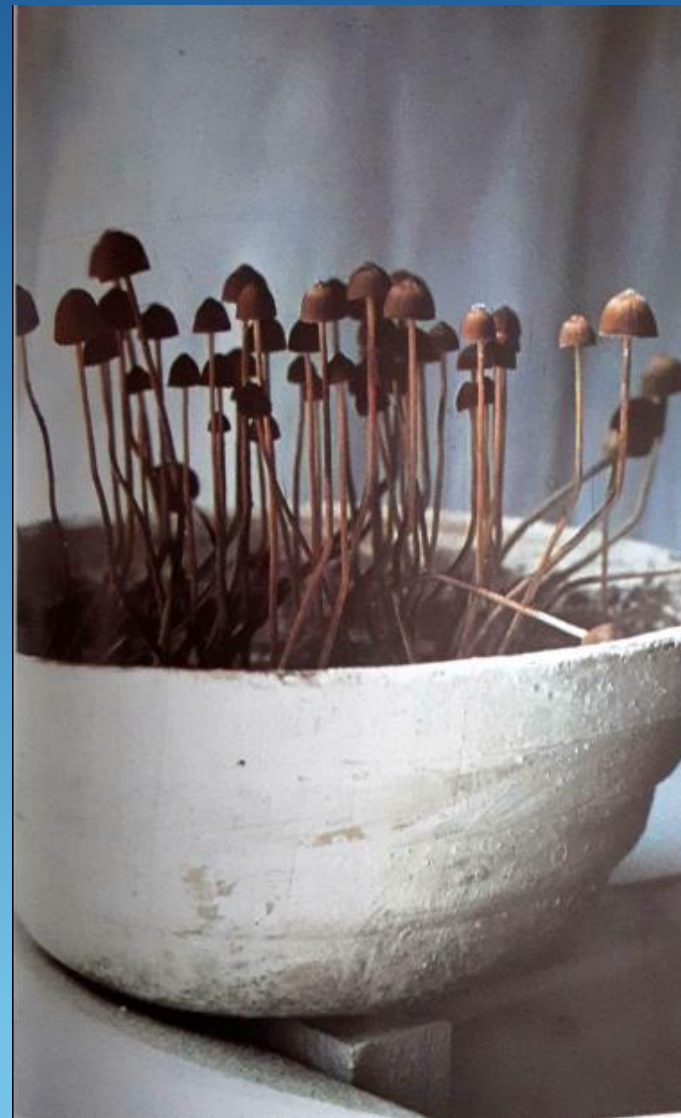


Sherwood et al., J. Nat. Prod, 2020

Simultaneous Production of Psilocybin and a Cocktail of β -Carboline Monoamine Oxidase Inhibitors in “Magic” Mushrooms

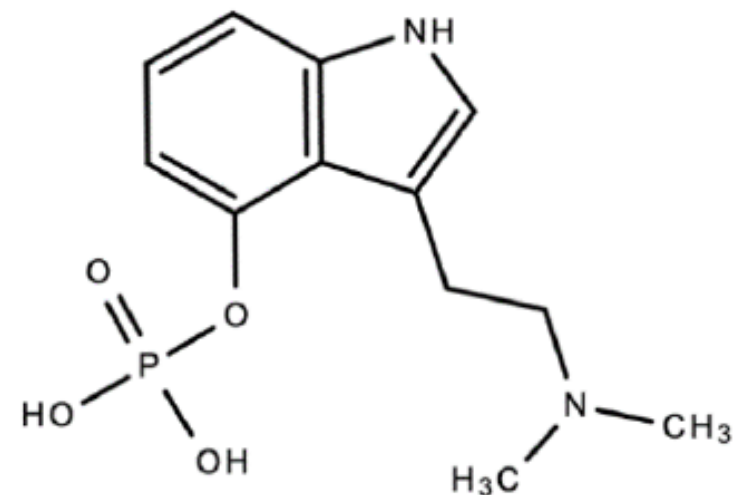
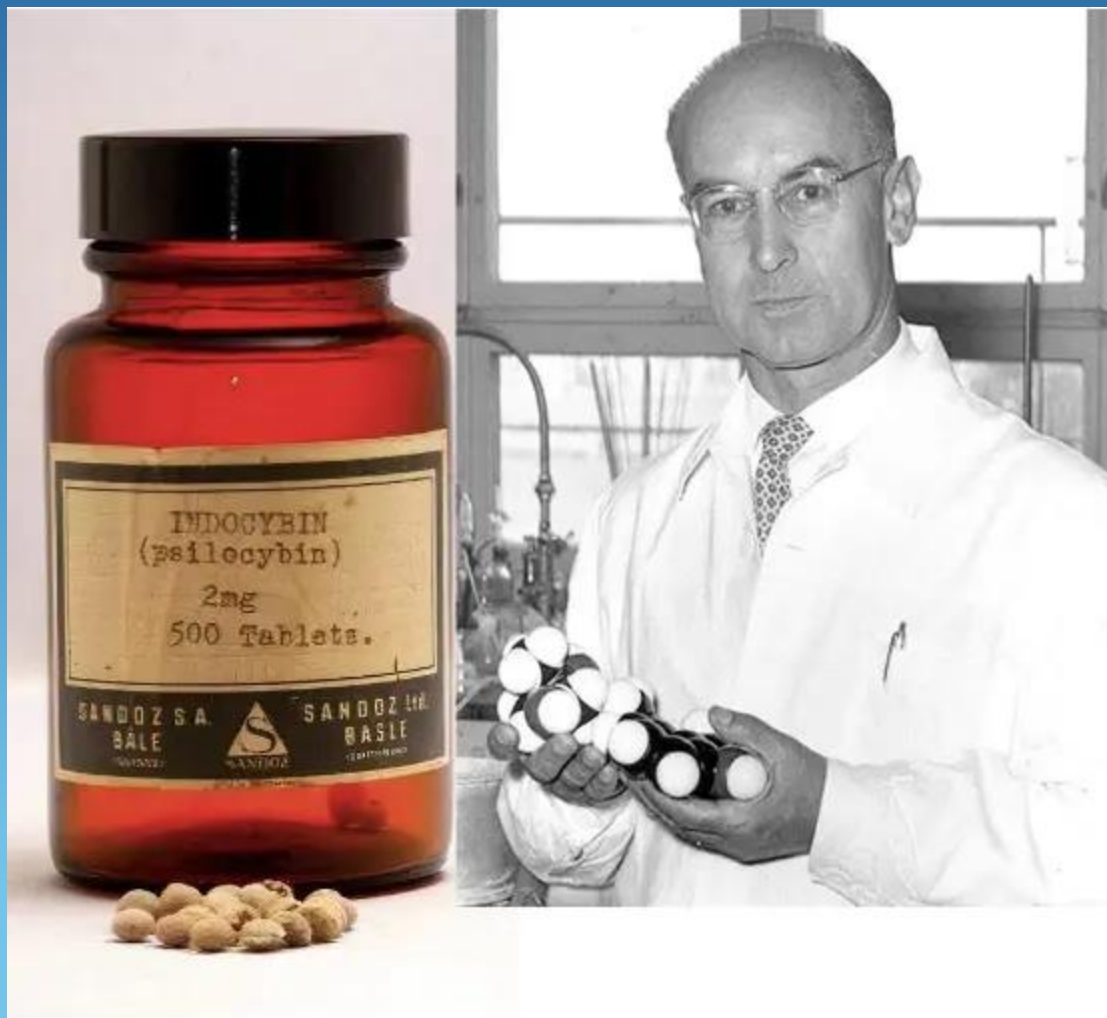
Felix Blei⁺,^[a] Sebastian Dörner⁺,^[a] Janis Fricke,^[a] Florian Baldeweg,^[a] Felix Trottmann,^[b] Anna Komor,^[b] Florian Meyer,^[c] Christian Hertweck,^[b, d] and Dirk Hoffmeister*^[a]

Chem Eur J, 2020



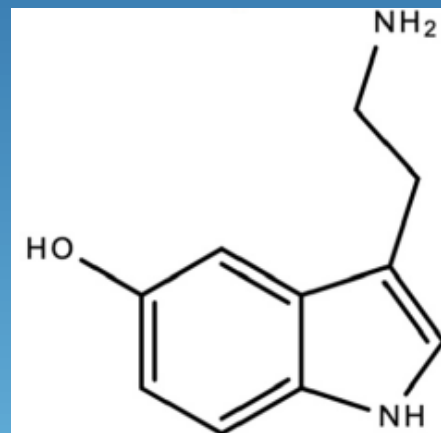
Roger Heim,
Les champignons
toxiques et
hallucinogènes
Boubée, 1978

Roger Heim with a culture of *Psilocybe mexicana* at the cryptogamy laboratory of the MNHN in Paris, c. 1958.



Psilocybin

(4-phosphorloxy-N,N-dimethyltryptamine)



Serotonin

1958 : synthèse de la psilocybine par Albert Hoffman

FACULTÉ DE MÉDECINE DE PARIS

ANNÉE 1960

N°

THÈSE

POUR LE

DOCTORAT en MÉDECINE

(DIPLOME D'ÉTAT)

PAR

QUÉTIN Anne-Marie

née le 31 janvier 1931, à Aurillac (Cantal)
Ancien Externe des Hôpitaux de Paris
Interne des Hôpitaux Psychiatriques de la Seine
(Médaille d'or)

Présentée et soutenue publiquement le 10 juin 1960



**LA PSILOCYBINE EN PSYCHIATRIE
CLINIQUE ET EXPERIMENTALE**

In: Heim, R., Wasson, R.G.: Les champignons hallucinogènes du Mexique.
Ed. Muséum nation. hist. natur., Paris 1958, p. 287-309.

ÉTUDE PSYCHO-PHYSIOLOGIQUE ET CLINIQUE DE LA PSILOCYBINE

par

JEAN DELAY, PIERRE PICHOT, THÉRÈSE LEMPERIÈRE,
PIERRE J. NICOLAS-CHARLES et ANNE-MARIE QUÉTIN

<https://bibliography.maps.org/citation/600>

<https://societepsychedelique.fr/fr/blog/la-psylocybine-en-psychiatrie-clinique-et-experimentale>

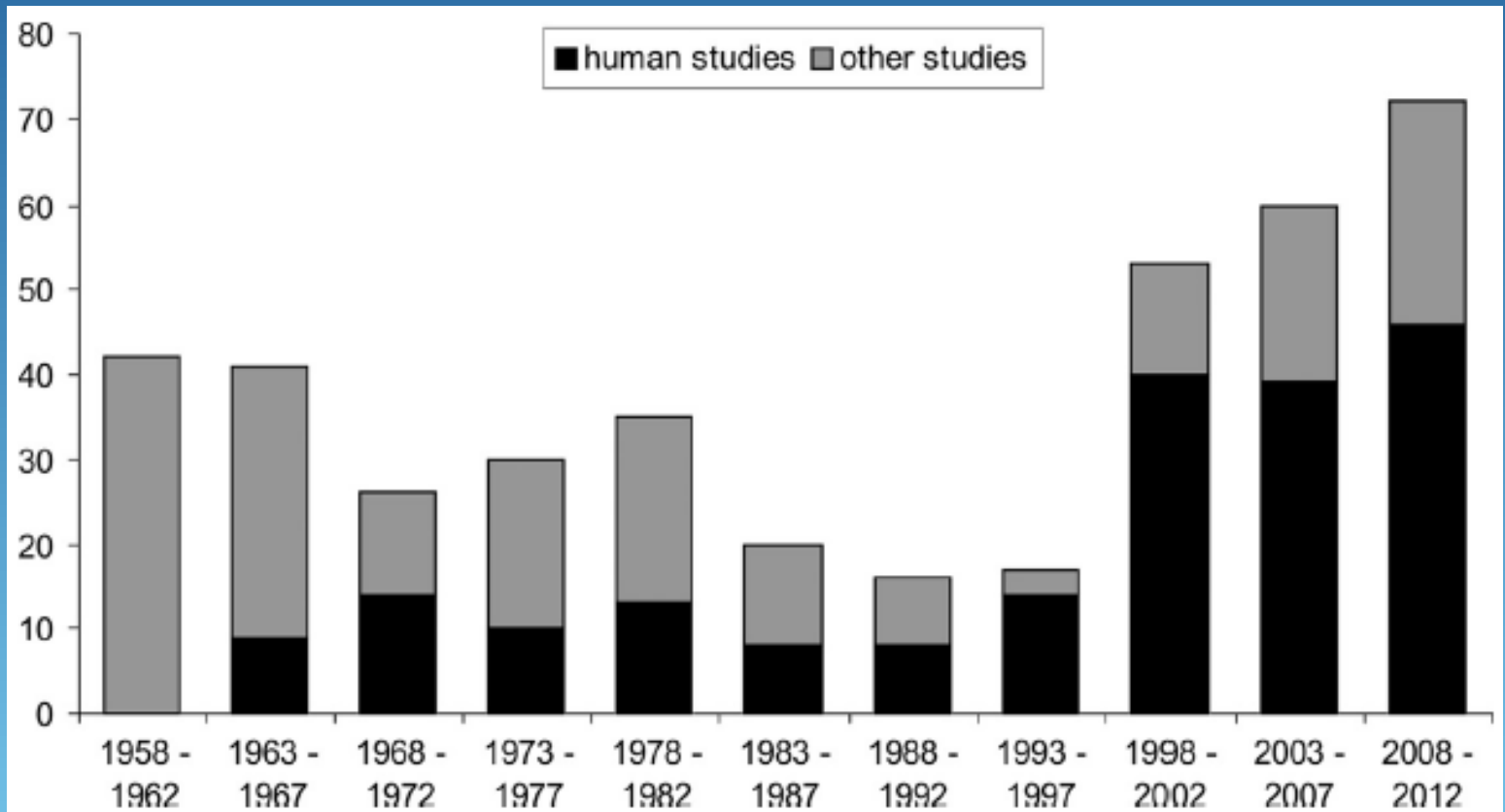


Figure 1 Number of publications dealing with psilocybin/psilocin (y axis) in five-year intervals

Tylš et al., European neuropsychopharmacology, 2014

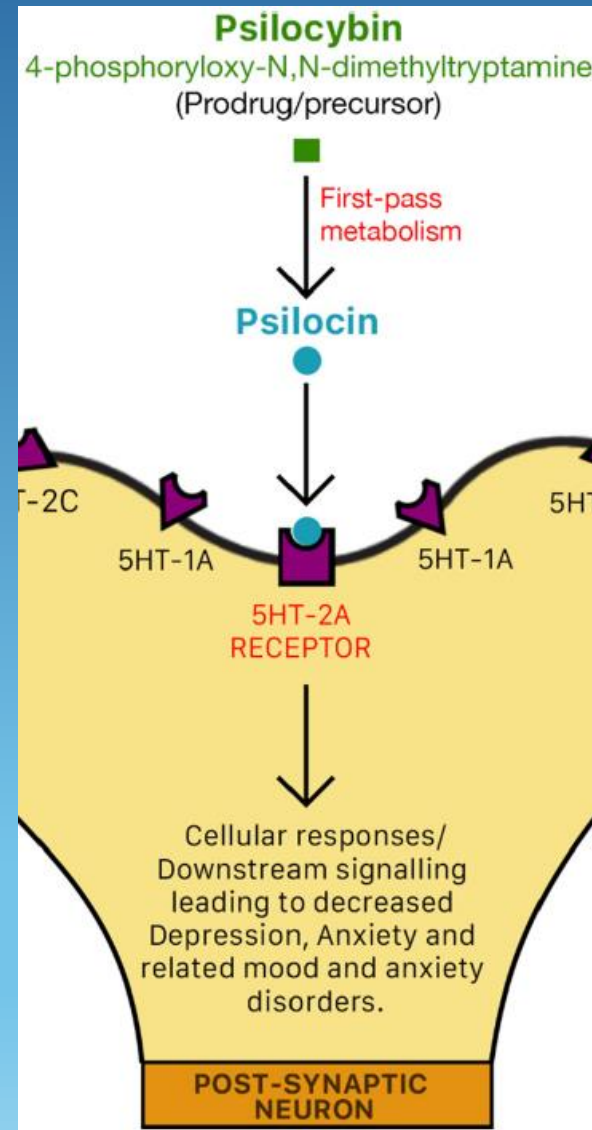
1990-2000s : renaissance psychédélique

NeuroReport 9, 3897–3902 (1998)

Psilocybin induces schizophrenia-like psychosis in humans via a serotonin-2 agonist action

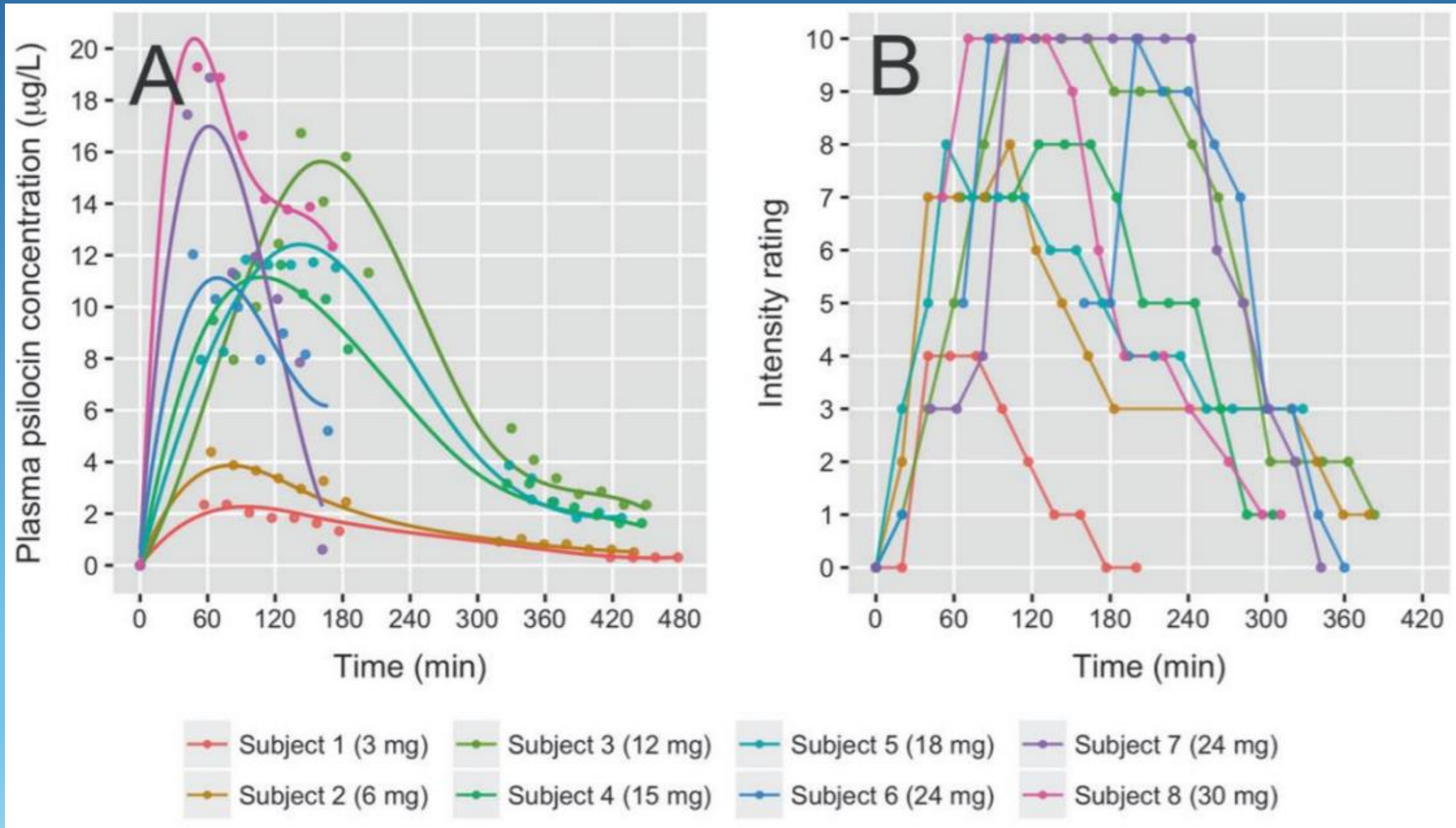
Franz X. Vollenweider,^{CA} Margreet F. I. Vollenweider-Scherpenhuyzen,¹ Andreas Bäbler, Helen Vogel and Daniel Hell

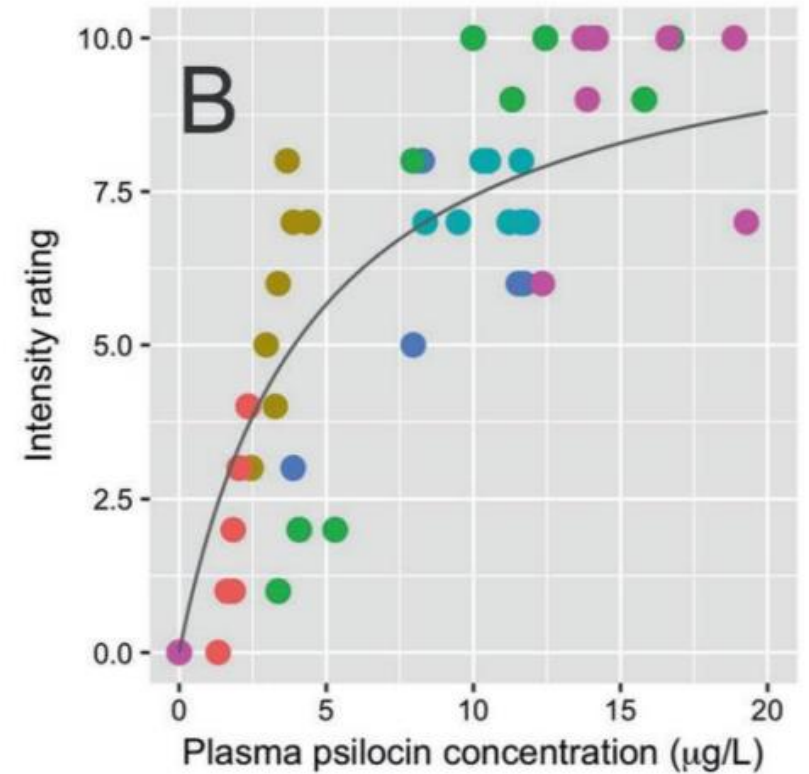
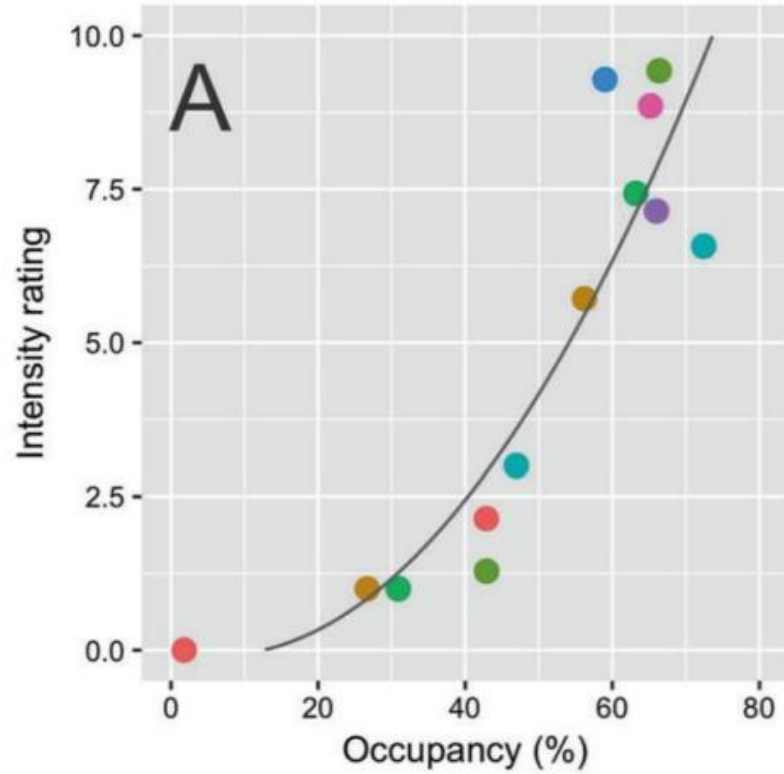
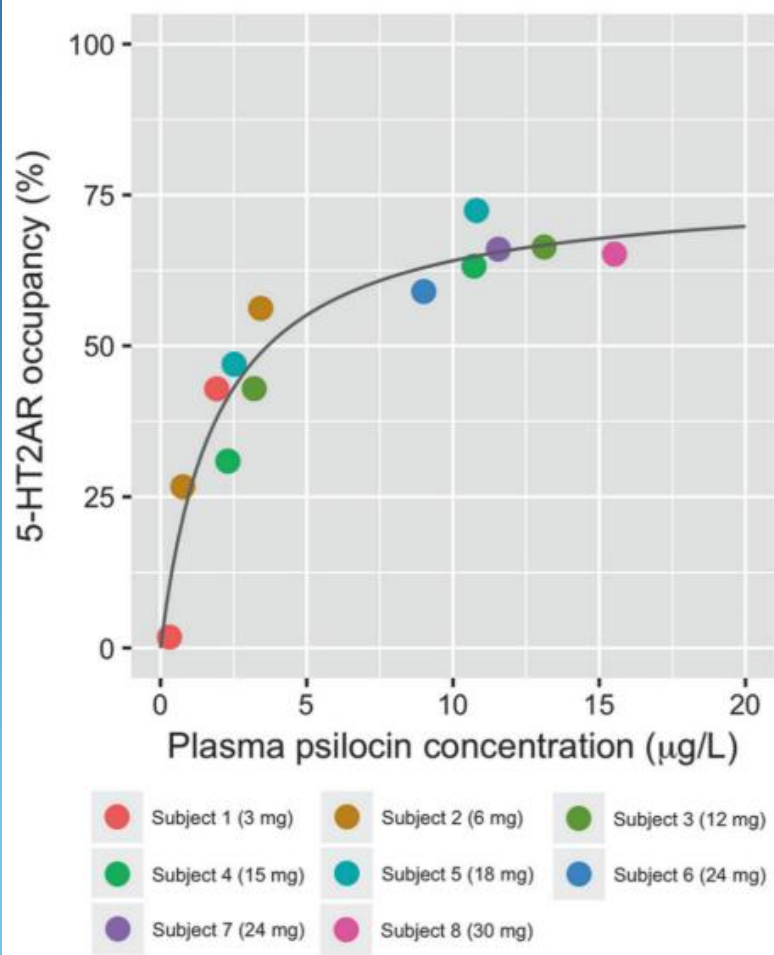
Research Department, Psychiatric University Hospital Zürich, Box 68, CH-8029 Zürich; Department of Anesthesiology, University Hospital of Zürich, Zürich, Switzerland




Lowe et al., Molecules, 2021

Concentration de psilocine et intensité des effets





Emotions and brain function are altered up to one month after a single high dose of psilocybin

Frederick S. Barrett ^{1*}, Manoj K. Doss¹, Nathan D. Sepeda¹, James J. Pekar^{2,3} & Roland R. Griffiths^{1,4}

Barrett et al., Sci Rep, 2020

↘↘ affects négatifs à 1 semaine post-psilocybine

Fenêtre de neuroplasticité++

- Début des effets : 20-40 min
- Pic : 60-90min
- Disparition des effets à 6h

Hasler et al., Psychopharmacology, 2004

Effets Sensoriels : distorsions visuelles, illusions, synesthésie

Cognitifs : altération perception temps/espace, visions intérieures, relâchement de l'association des idées, intuitions/révélation.

Émotionnels : émerveillement, extase, anxiété/peur

Transpersonnels : connection à une puissance supérieure, connaturalité divine, unité avec le Tout.

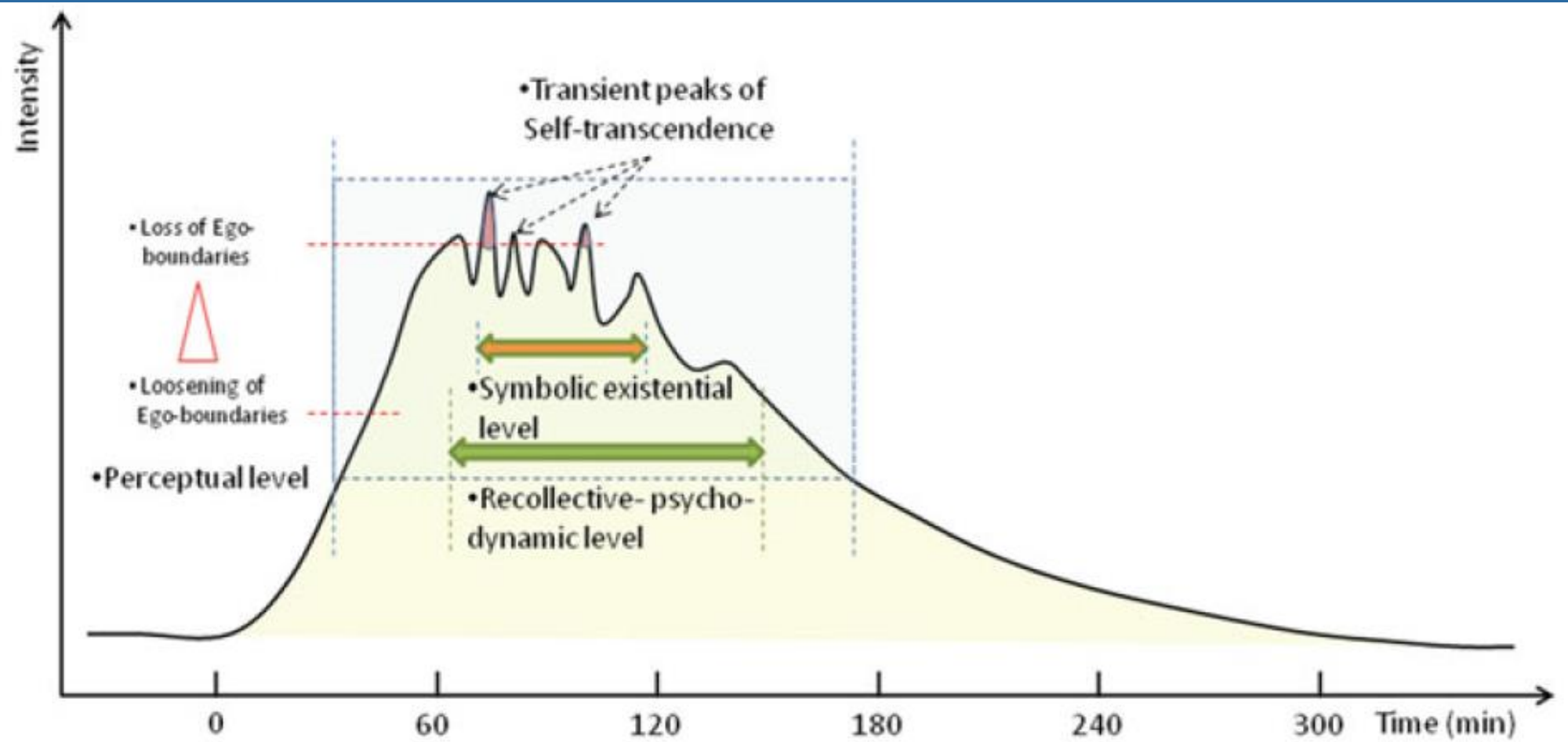


Fig. 3 Temporal dynamics and stages of a psilocybin-induced psychedelic experience (adapted from Leuner 1962)

Quid de la toxicité de la psilocybine ?

Acute psychological and physiological effects of psilocybin in healthy humans: a double-blind, placebo-controlled dose-effect study

Hasler, Felix ; Grimberg, Ulrike ; Benz, Marco A ; Huber, Theo ; Vollenweider, Franz X

Psychopharmacology, 172(2):145-156. (2004)

- Pas de modification de l'électrocardiogramme
- Pas de changement de température corporelle
- Augmentation modérée de la PA
- Paramètres sanguins normaux *« Les états modifiés de conscience induits par la psilocybine sont généralement bien tolérés et intégrés par les sujets sains »*
- Excrétion rénale des 2/3 de la psilocine après 3h (Passie et al., Addiction Biology 2002)
- Absence de neurotoxicité (Tylš et al., European neuropsychopharmacology, 2014)
- Absence de génotoxicité (Passie et al., Addiction Biology, 2002)
- Potentiel addictif très faible (Nichols, Pharmaco Ther, 2004)
- Overdose rarissime (Lim et al., Internal medicine journal, 2012 ; Gerault, Picard., Bull.Soc.Mycol. Fr, 1996)

effets indésirables somatiques
bénins et transitoires

Table S6. Acute adverse drug effects

	Placebo			15 mg psilocybin			30 mg psilocybin		
	0h	0-12h	12-24h	0h	0-12h	12-24h	0h	0-12h	12-24h
Fatigue	7	16	11	8	23	18	4	25	17
Headache	1	8	6	1	14	10	0	18	14
Lack of concentration	0	0	0	0	17	1	0	15	3
Lack of energy	0	1	2	0	11	3	0	16	10
Dullness	1	3	1	0	12	2	0	12	7
Feeling of weakness	1	2	0	0	10	2	0	14	6
Loss of appetite	0	0	0	0	7	0	0	18	4
Dry mouth	0	1	0	0	9	1	0	9	3
Balance disorders	0	0	0	0	9	0	0	16	1
Rapid exhaustibility	0	1	0	0	8	0	0	15	5
Excessive need for sleep	0	3	2	0	8	5	0	7	5
Brooding	0	0	0	0	6	1	0	9	2
Neck and shoulder pain	3	3	4	2	3	4	2	8	6
Inner restlessness	0	0	0	1	4	0	0	9	1
Inner tension	0	0	0	0	8	1	0	8	1
Excessive perspiration	0	0	0	1	4	2	1	7	2
Low back and back pain	3	4	3	2	3	2	3	5	3
Hypersensitivity to certain odours	0	0	0	0	5	0	0	8	2
Nausea	0	0	0	1	7	0	0	9	2
Forgetfulness	0	0	0	0	5	0	0	8	0
Trembling	0	0	0	0	2	0	0	5	0
Feeling of limpness	1	1	1	3	4	1	2	6	3
Tendency to cry	0	0	0	0	4	0	0	11	0
Frequent urination	0	1	2	0	6	4	0	6	1
Hot flashes	0	1	1	0	3	0	0	6	3
Freezing	0	1	0	0	7	0	0	7	0
Fizziness	0	0	0	0	7	0	0	9	0
Bruxism	0	0	0	0	2	0	0	1	0
Restless legs	0	0	0	0	5	1	0	4	1
Anxiety	0	0	0	0	2	1	0	6	1

Toxicité à long terme

- Valvulopathie ?

Serotonin 5-HT_{2B} receptor agonism and valvular heart disease: implications for the development of psilocybin and related agents

Roger S. McIntyre^{a,b,c*}

EXPERT OPINION ON DRUG SAFETY
2023, VOL. 22, NO. 10, 881-883

The risk of chronic psychedelic and MDMA microdosing for valvular heart disease

Michael Tagen¹, Daniel Mantuani^{2 3}, Liron van Heerden^{2 3}, Alex Holstein^{2 3},
Linda E Klumpers^{1 4}, Richard Knowles^{2 3}

J Psychopharmacol. 2023 Sep;37(9):876-890.

Effets indésirables psychologiques et psychiatriques

- « bad trip » (anxiété/paranoïa/confusion)
- Les évènements psychiatriques graves sont rares++:

Réaction psychotique prolongée

Trouble du comportement/suicide : environnement non sécurisé,
usage associé de substances psycho-actives

Syndrome post-hallucinatoire persistant

Manie/psychose




<u>Case number</u>	<u>Author, year</u>	<u>Length of adverse event</u>	<u>Psychedelic substance</u>	<u>Polysubstance use during event/prior</u>	<u>Mania &/or psychosis</u>	<u>One time or repeated psychedelic use</u>	<u>Bipolar history or family history?</u>	<u>Additional factors</u>	<u>Did the symptoms resolve?</u>
3	Hyde et al., 1978	5 - 10 days	Psilocybin	None indicated	Psychosis and possible mania	Mutiple times over course of a week plus large dose	No previous diagnosis or family history noted	Very large dose	After 10 days
4	Davies, 1979	hospitalized for 5 weeks	Psilocybin	No; polysubstance use history	Psychosis and possible mania	Repeated	No previous diagnosis or family history noted	Not clear that symptoms tied to mushroom use	5 weeks, but continued depression
5	Dewhurst, 1980	hospitalized for 10 weeks	Psilocybin	None indicated during episode but frequent	Both mania and psychosis	One time large dose; followed by	No previous diagnosis or family history	Very large dose	Possibly at 10 weeks
8	Bickel et al., 2005	1 month, possibly longer	Psilocybin	No; polysubstance abuse use history	Psychosis and possible mania	One time	No previous diagnosis or family history noted	Long history of heroin, opiate, and cannabis abuse; unclear from description if symptoms are definitely mania	At 6 month visit no symptoms
16	Hendin and Penn, 2021	1 week	Psilocybin	Cannabis, but not immediately	Psychosis and mania	One time	Father and paternal		About 1 week

Syndrome post-hallucinatoire persistant



Review

Hallucinogen Persisting Perception Disorder: Etiology, Clinical Features, and Therapeutic Perspectives

Giovanni Martinotti ^{1,2}, Rita Santacrose ^{1,2,*} , Mauro Pettorruso ³ , Chiara Montemitto ¹ ,
Maria Chiara Spano ¹, Marco Lorusso ¹, Massimo di Giannantonio ¹ and Arturo G. Lerner ^{4,5}

« HPPD is a rare and poorly understood condition »

2018



Halpern et al., Curr Topics Behav Neurosci, 2016

RESEARCH ARTICLE

Extended difficulties following the use of psychedelic drugs: A mixed methods study

Jules Evans¹, Oliver C. Robinson^{2*}, Eirini Ketzitidou Argyri³, Shayam Suseelan², Ashleigh Murphy-Beiner⁴, Rosalind McAlpine⁵, David Luke², Katrina Michelle⁶, Ed Prideaux⁷

Plos one, 2023

- Difficultés émotionnelles++ : anxiété, peur
cognitives
existentielles
perceptuelles : flashback, HPPD
sociales : isolement

Adverse effects of psychedelics: From anecdotes and misinformation to systematic science

Anne K Schlag^{1,2,3} , Jacob Aday^{1,4,5} , Iram Salam¹, Jo C Neill^{1,6} 
and David J Nutt^{1,2}



Journal of Psychopharmacology

1–15

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DOI: [10.1177/02698811211069100](https://doi.org/10.1177/02698811211069100)

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Dépistage comorbidités psychiatriques
Importance de la préparation, supervision,
intégration
Alliance thérapeutique
Expérience du thérapeute
Environnement sécuritaire

↘ ↘ risques d'effets
indésirables
psychiatriques

Indications thérapeutiques de la psilocybine

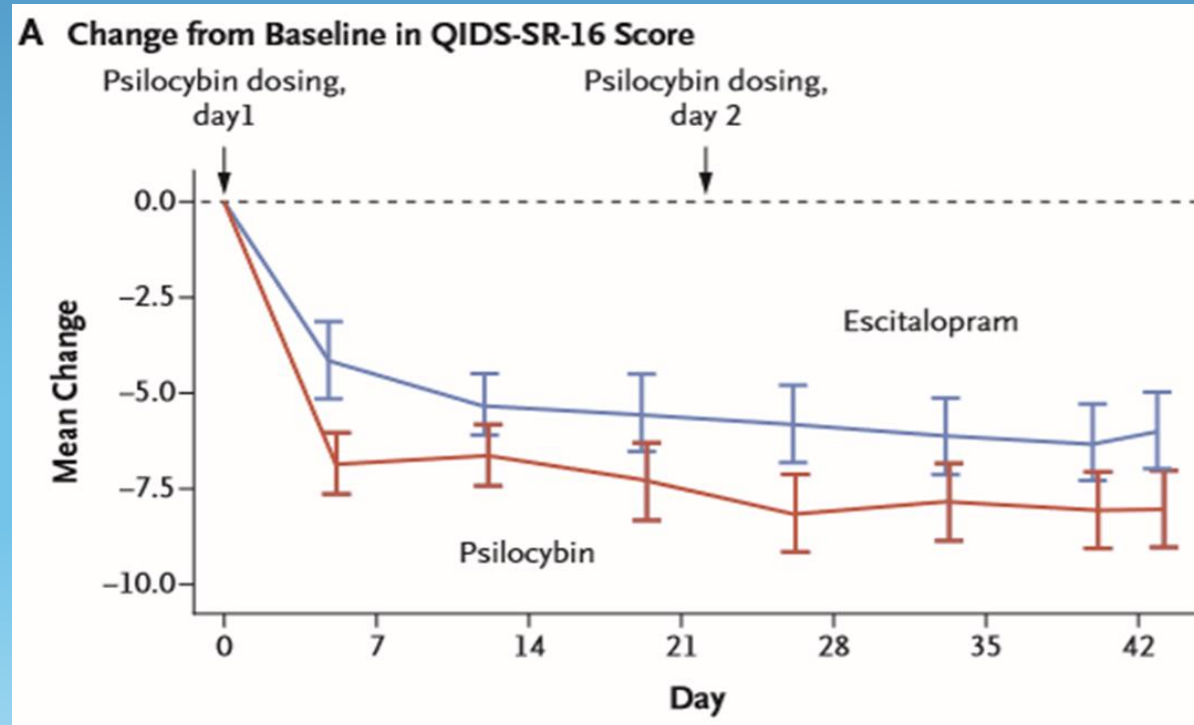
- Dépression
- Anxiété de fin de vie
- Trouble lié à l'usage d'alcool
- Trouble obsessionnel compulsif

Trial of Psilocybin versus Escitalopram for Depression

Robin Carhart-Harris, Ph.D., Bruna Giribaldi, B.Sc., Rosalind Watts, D.Clin.Psy.,

N Engl J Med 2021

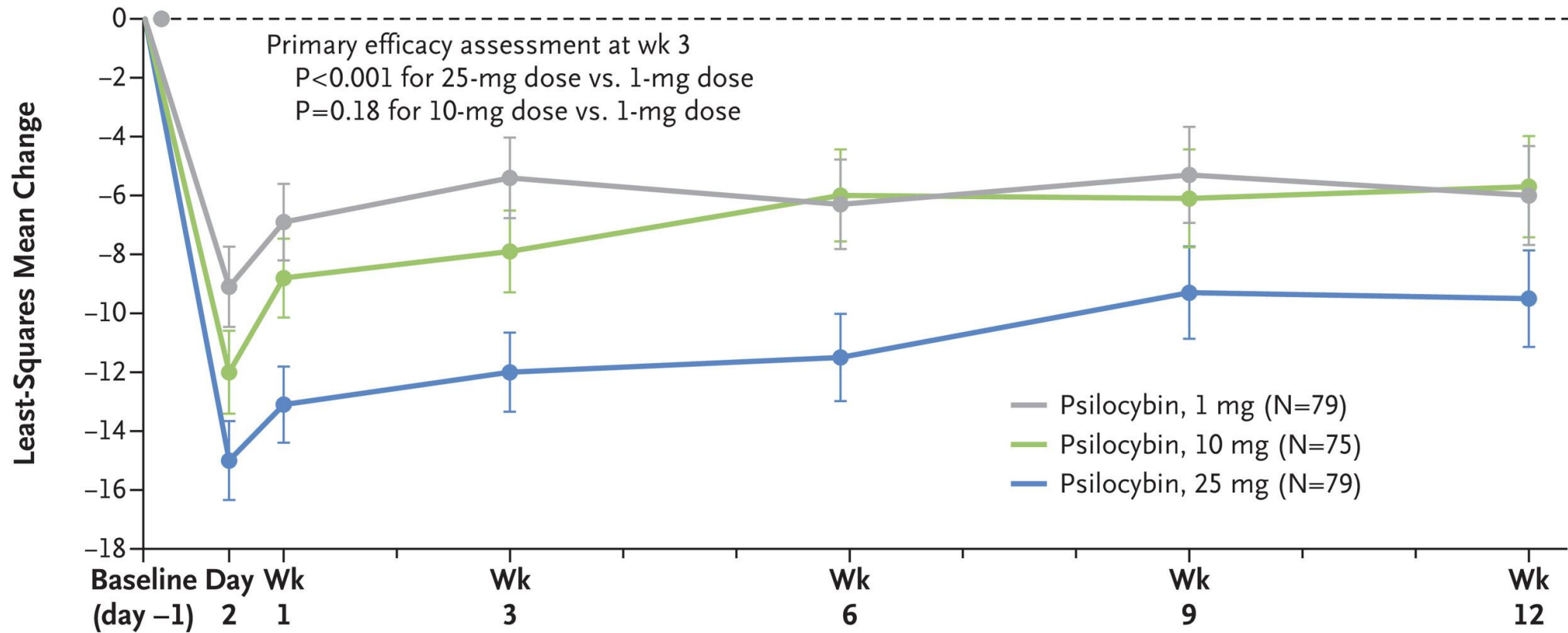
- N= 59 patients
- Psilocybin 25 mg per os two doses + 6 weeks daily placebo vs
- Psilocybin 1 mg per os two doses + 6 weeks daily escitalopram



Single-Dose Psilocybin for a Treatment-Resistant Episode of Major Depression

Goodwin GM et al. DOI: 10.1056/NEJMoa2206443

The NEW ENGLAND JOURNAL of MEDICINE



Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial

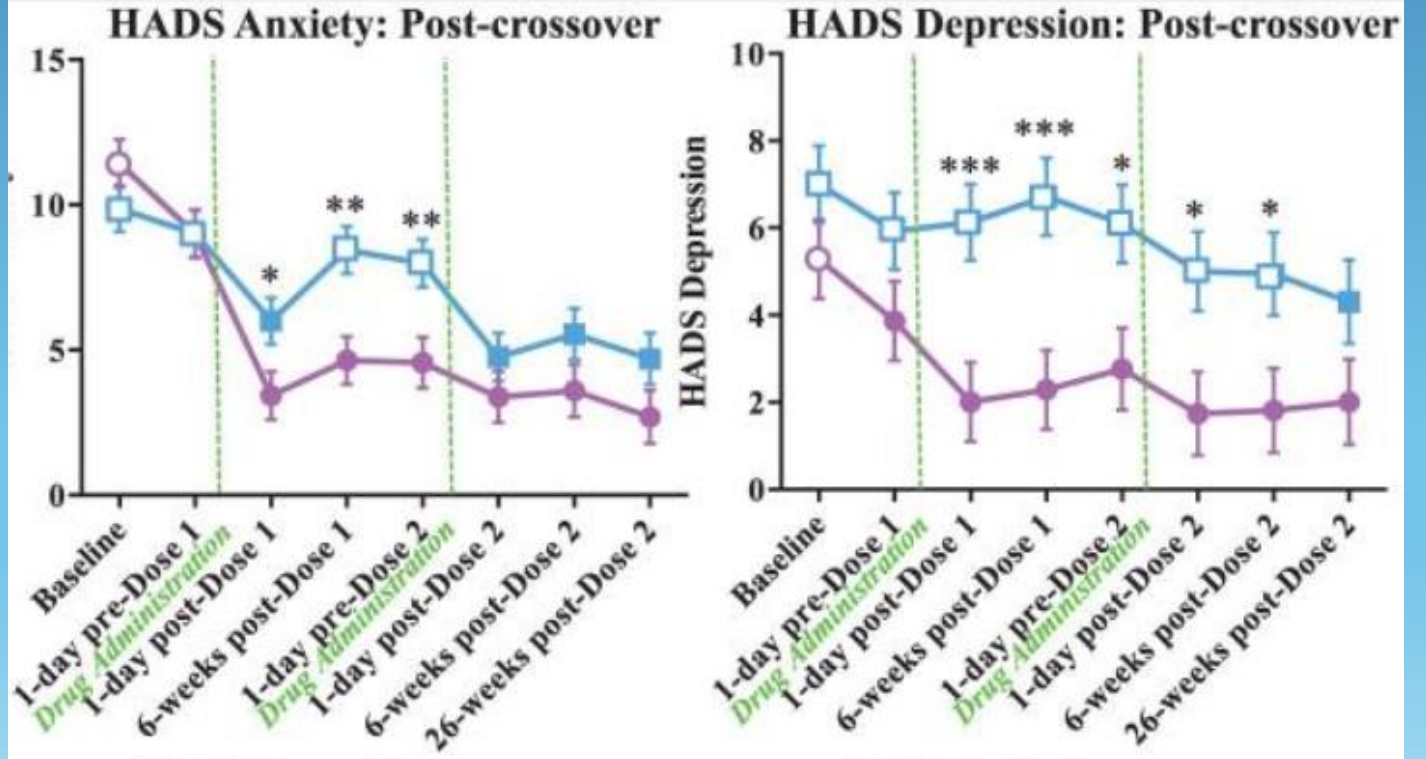
Stephen Ross^{1,2,3,4,5,6}, Anthony Bossis^{1,2,4}, Jeffrey Guss^{1,2,4}, Gabrielle Agin-Liebes¹⁰, Tara Malone¹, Barry Cohen⁷, Sarah E Mennenga¹, Alexander Belser⁸, Krystallia Kalliontzi², James Babb⁹, Zhe Su³, Patricia Corby² and Brian L Schmidt²

Psychopharm

Journal of Psychopharmacology
2016, Vol. 30(12) 1165–1180
© The Author(s) 2016



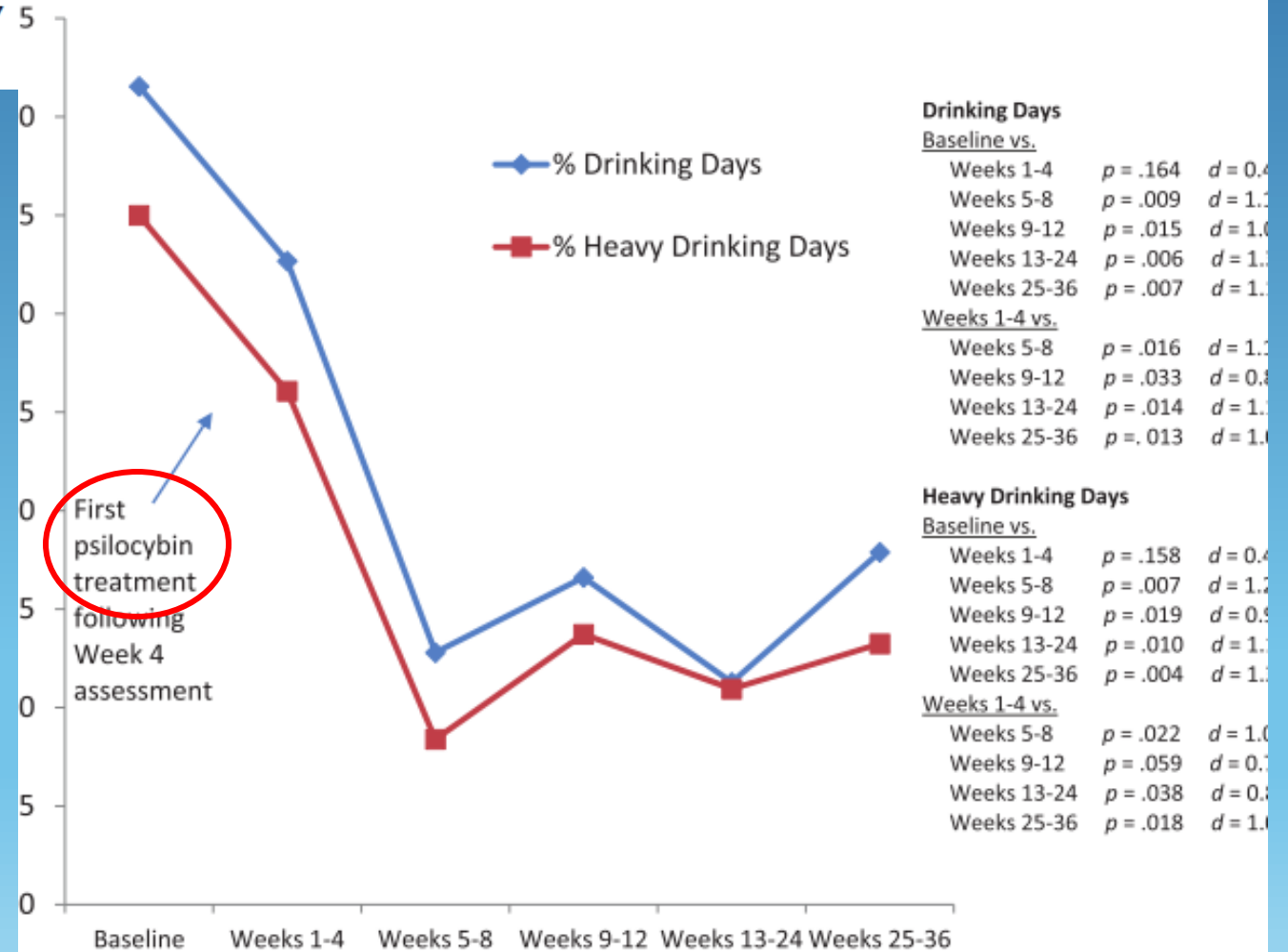
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DOI: 10.1177/026988111667
jop.sagepub.com



Psilocybin-assisted treatment for alcohol dependence: A proof-of-concept study

Michael P Bogenschutz¹, Alyssa A Forcehimes¹, Jessica A Pommy¹,
 Claire E Wilcox¹, PCR Barbosa² and Rick J Strassman¹

Journal of Psychopharmacology
 1-11
 © The Author(s) 2015



Drinking Days
 Baseline vs.

Weeks 1-4	$p = .164$	$d = 0.4$
Weeks 5-8	$p = .009$	$d = 1.1$
Weeks 9-12	$p = .015$	$d = 1.0$
Weeks 13-24	$p = .006$	$d = 1.1$
Weeks 25-36	$p = .007$	$d = 1.1$

Weeks 1-4 vs.

Weeks 5-8	$p = .016$	$d = 1.1$
Weeks 9-12	$p = .033$	$d = 0.8$
Weeks 13-24	$p = .014$	$d = 1.1$
Weeks 25-36	$p = .013$	$d = 1.0$

Heavy Drinking Days
 Baseline vs.

Weeks 1-4	$p = .158$	$d = 0.4$
Weeks 5-8	$p = .007$	$d = 1.2$
Weeks 9-12	$p = .019$	$d = 0.9$
Weeks 13-24	$p = .010$	$d = 1.1$
Weeks 25-36	$p = .004$	$d = 1.1$

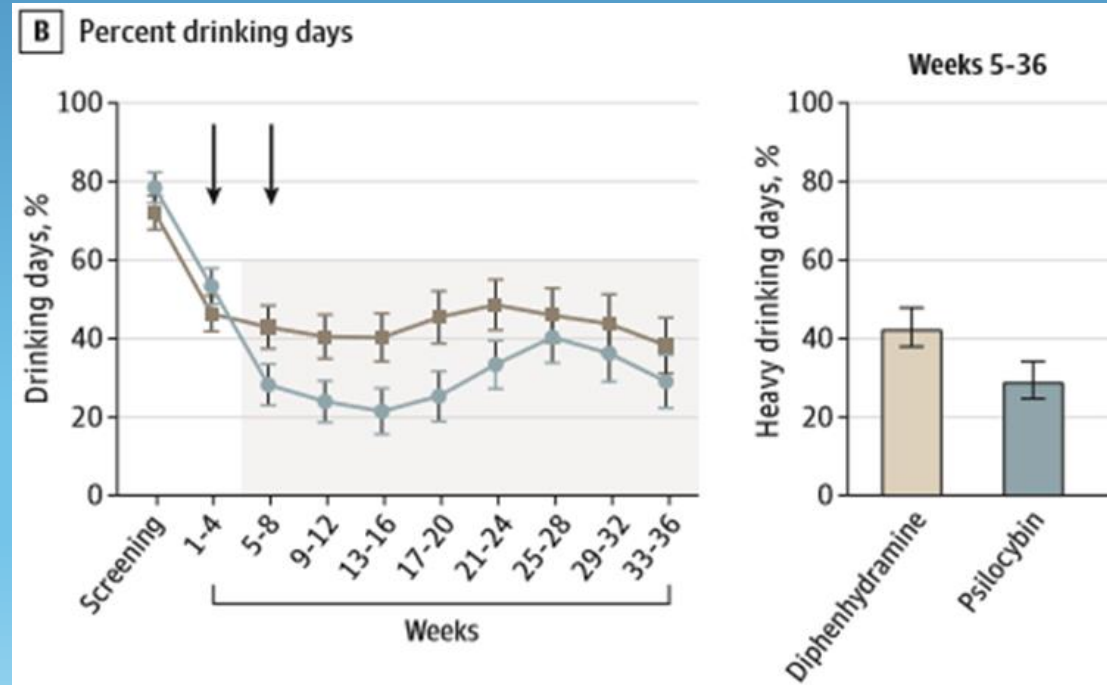
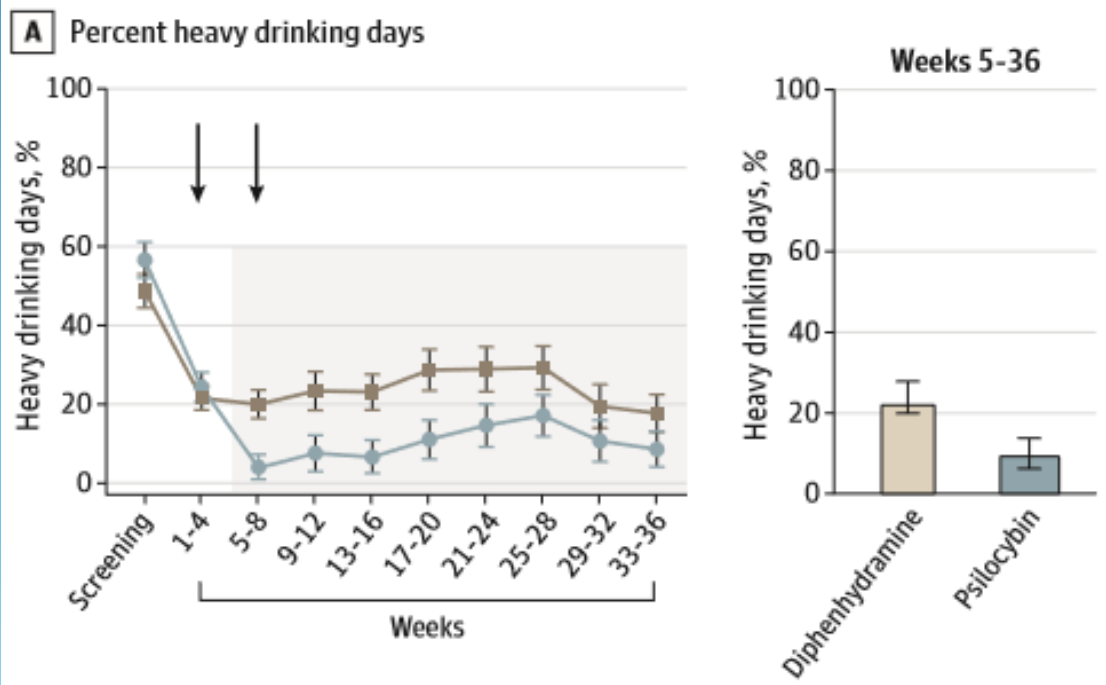
Weeks 1-4 vs.

Weeks 5-8	$p = .022$	$d = 1.0$
Weeks 9-12	$p = .059$	$d = 0.7$
Weeks 13-24	$p = .038$	$d = 0.8$
Weeks 25-36	$p = .018$	$d = 1.0$

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

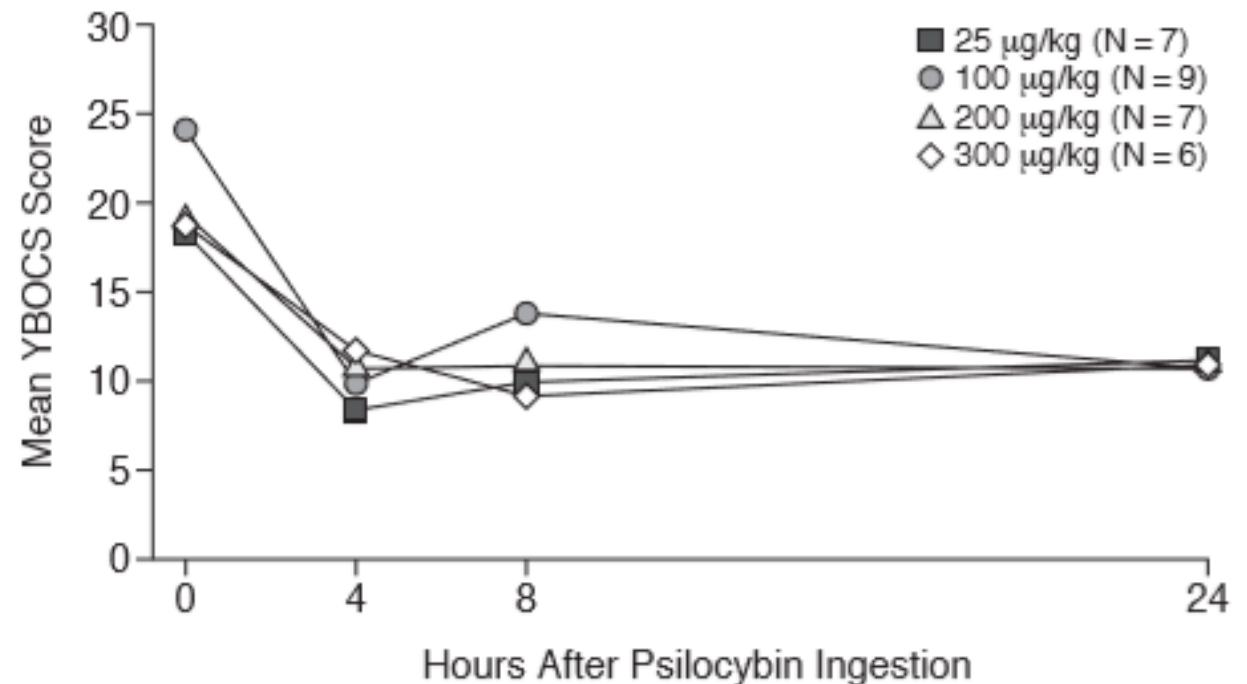


Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients With Obsessive-Compulsive Disorder

Francisco A. Moreno, M.D.; Christopher B. Wiegand, M.D.;
E. Keolani Taitano, Ph.D.; and Pedro L. Delgado, M.D.

J Clin Psychiatry, 2006

Figure 1. Effects of Psilocybin on Obsessive-Compulsive Symptom Severity^a



Actualités en France

Démarrage de l'étude COMP006 sur la psilocybine pour la dépression résistante

Cette étude évalue l'efficacité de la psilocybine (principe actif des champignons hallucinogènes) dans le traitement de la dépression résistante.

<https://www.ghu-paris.fr/fr/actualites/demarrage-de-letude-comp006-sur-la-psilocybine-pour-la-depression-resistante>

Etude PAD

30 patients seront accueillis à l'Hôpital du Grau-du-Roi dans la première étude en France testant l'efficacité de la psychothérapie assistée par les psychédéliques

Psilocybine dans le trouble lié à l'usage de l'alcool avec symptômes dépressifs

Étude pilote contrôlée randomisée en double aveugle

<https://www.chu-nimes.fr/actu-cht/etude-pad.html>