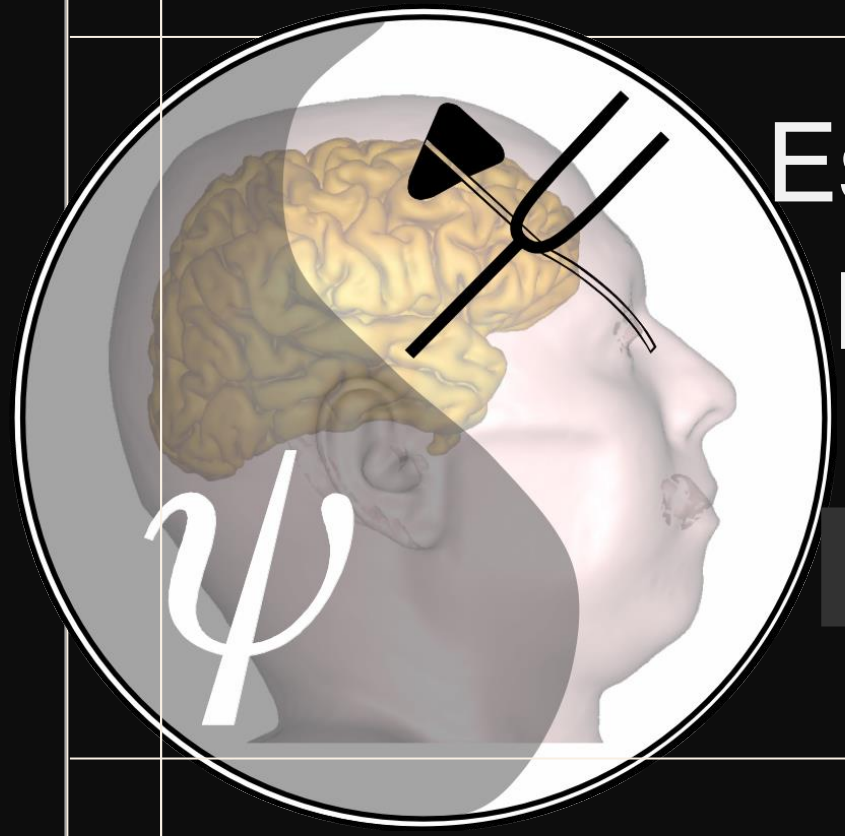


Essais cliniques : les psychédéliques soignent-ils ?

Journée de la Psychiatrie de l'Est

Ludovic Dormegny-Jeanjean

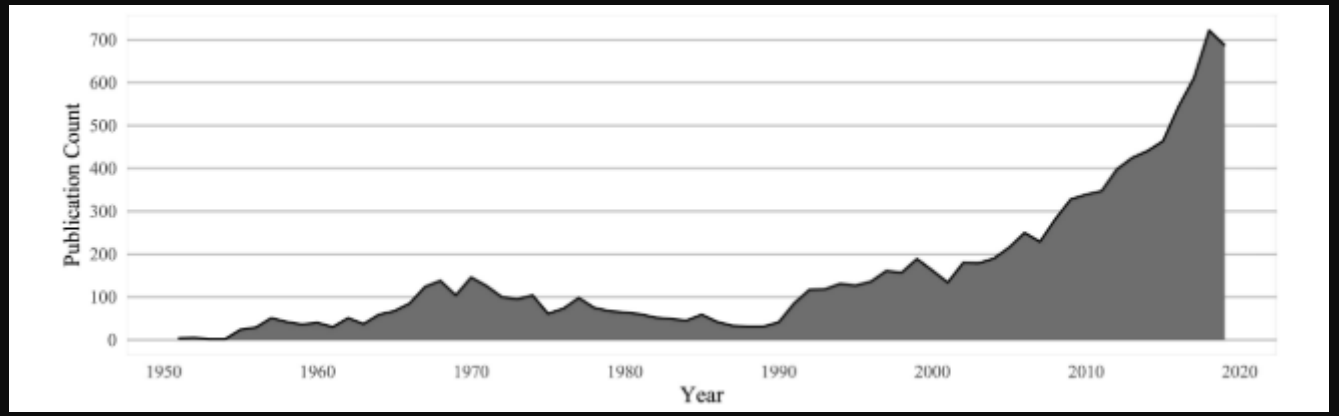
CEMNIS – Centre de Neuromodulation Non-Invasive de Strasbourg
UMR 7357 iCube – Université de Strasbourg

lundi 8 mai 2023

Bibliométrie

"Psylocybin" et/ou "LSD" = 965 publications en 2022

- rTMS = 1919
- Kétamine = 1602
- SSRI = 389
- ECT = 637



(Petranker et al, 2020)

ClinicalTrials.gov

105 études en cours

- *dépression, anxiété, burn-out*
- *ALZ*
- *Addictologie*
- *OCD, TCA…*

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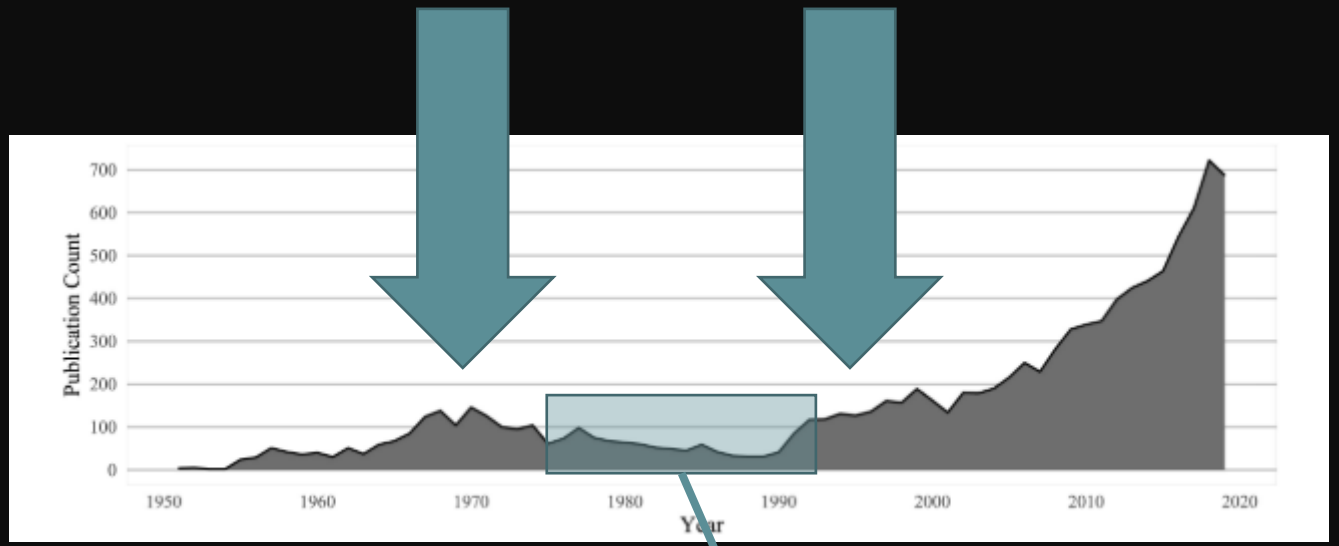

(Petranker et al, 2020)

Période de creux

- Causes : pénalisation, méthodologies discutables
- Lobbies +++ (+-3 G$)

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-Liebes[10], Tara Malone[1], Barry Cohen[7],

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2016 - 2 essais en cross-over → symptômes psy – maladie grave

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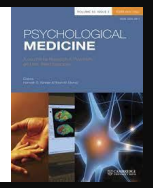

Fernanda Palhano-Fontes[1,2], Dayanna Barreto[2,3], Heloisa Onias[1,2],

2019

JAMA Psychiatry | Original Investigation

Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder
A Randomized Clinical Trial

JAMA Psychiatry

Alan K. Davis, PhD; Frederick S. Barrett, PhD; Darrick G. May, MD; Mary P. Cosimano, MSW; Nathan D. Sepeda, BS; Matthew W. Johnson, PhD; Patrick H. Finan, PhD; Roland R. Griffiths, PhD

2021

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2022

4 essais cliniques → dépression

- Contrôlés, randomisés, double aveugle
- Accompagnement psychothérapeutique

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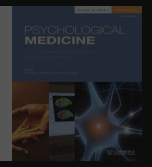

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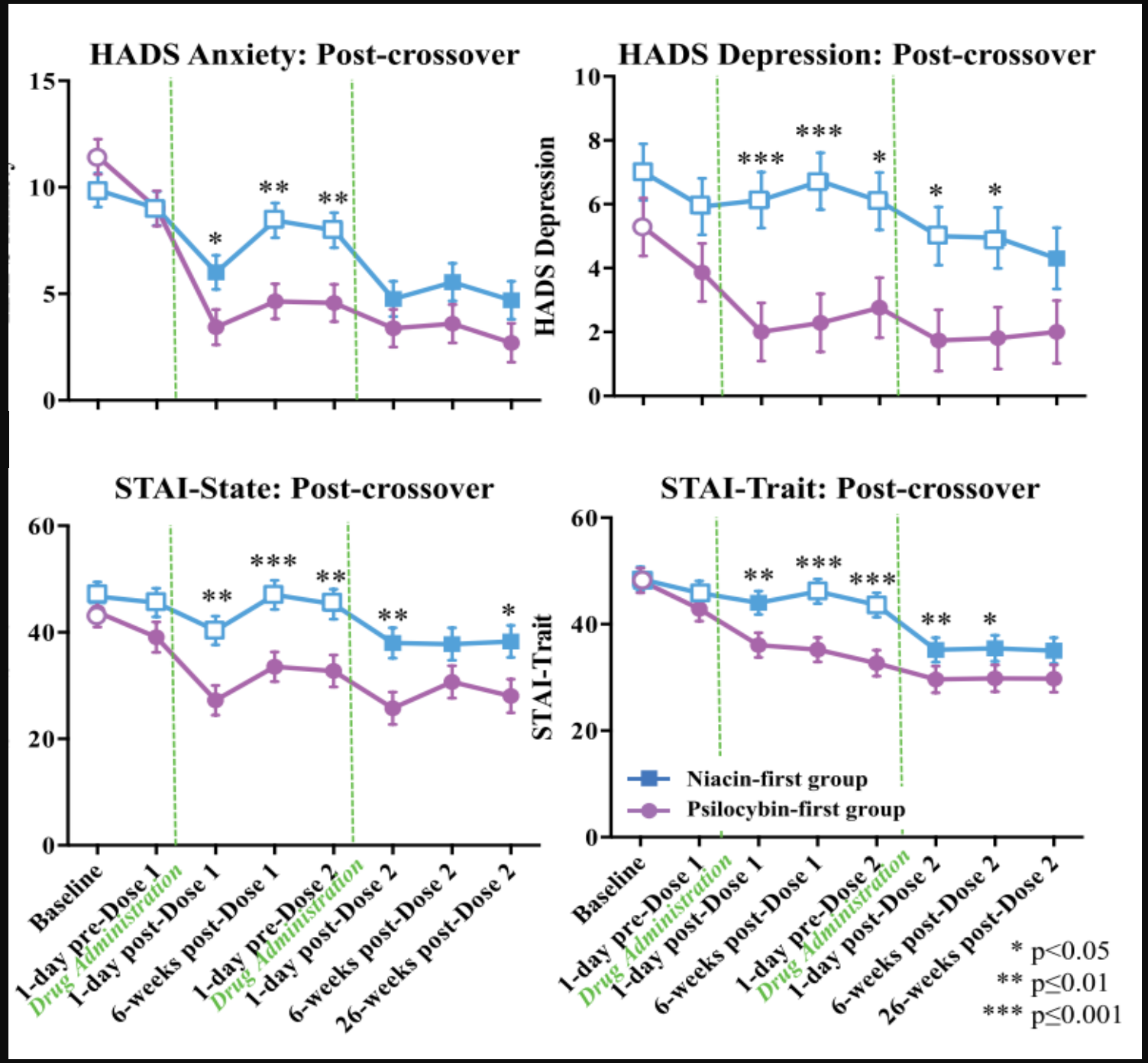
Essai randomisé, cross over
patients anxiété / dep + cancer
(incluant les rémissions)

31 patients randomisés
- 28% avec dépression
- 55% déjà utilisé hallucinogènes

Active : PCB 0,3mg/kg
Placebo : niacine (vit B3)


HADS Anxiety: Post-crossover
HADS Depression: Post-crossover
HADS Depression
STAI-State: Post-crossover
STAI-Trait: Post-crossover
STAI-Trait
Niacin-first group
Psilocybin-first group
Baseline
1-day pre-Dose 1
Drug Administration
1-day post-Dose 1
6-weeks post-Dose 1
1-day pre-Dose 2
Drug Administration
1-day post-Dose 2
6-weeks post-Dose 2
26-weeks post-Dose 2
* p<0.05
** p≤0.01
*** p≤0.001

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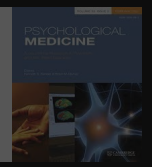

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Design +-similaire

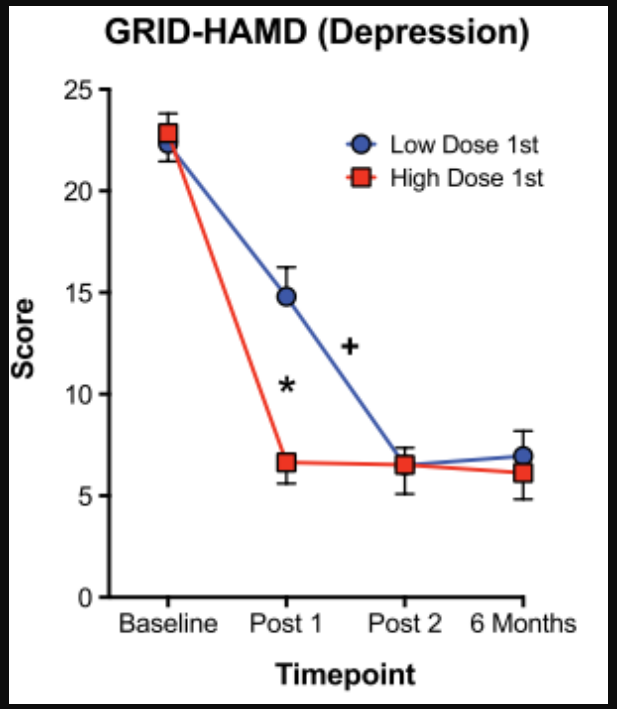
51 patients randomisés

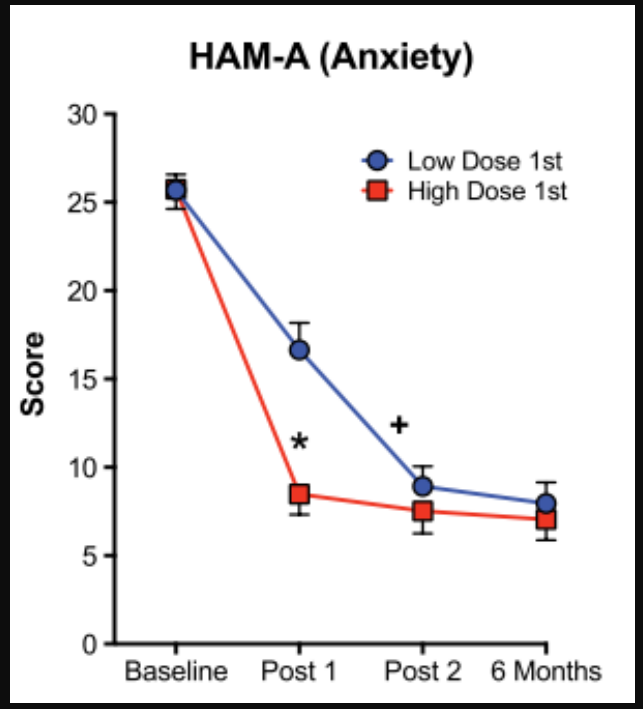
- 35% avec dépression
- 45% déjà utilisé hallucinogènes

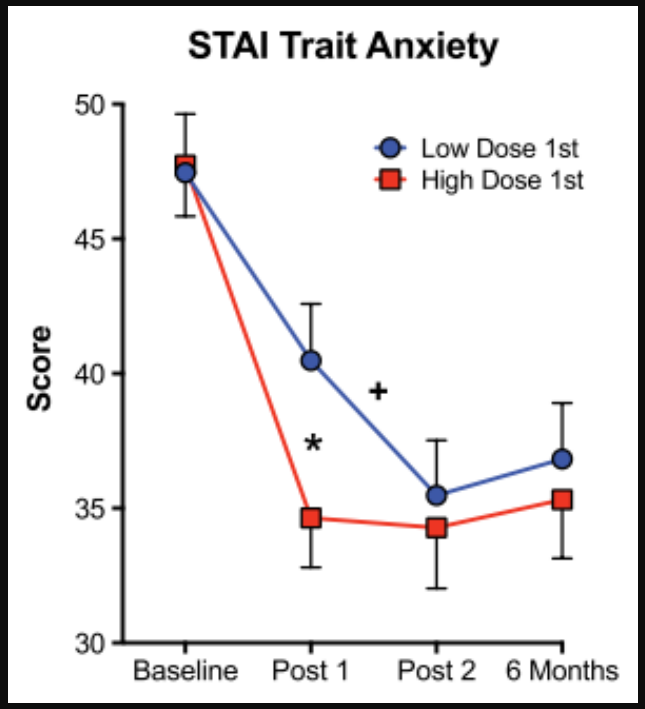
Active : PCB 30/22mg DU
Contrôle : PCB 1mg DU

Infléchissement dans le bras contrôle

- Effet biologique ?
- Effet placebo ++++ ?







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Essai randomisé en double aveugle contre placebo
N = 29, R à deux lignes
76% tble perso – cluster B
+ stresseurs environnementaux

Active : 0,36mg/kg –N-DMT
Placebo : neutre, imite gout et propriétés dig

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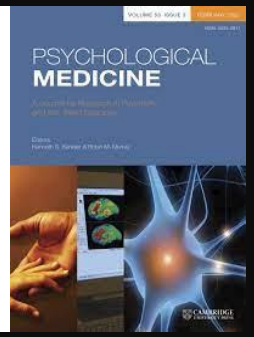

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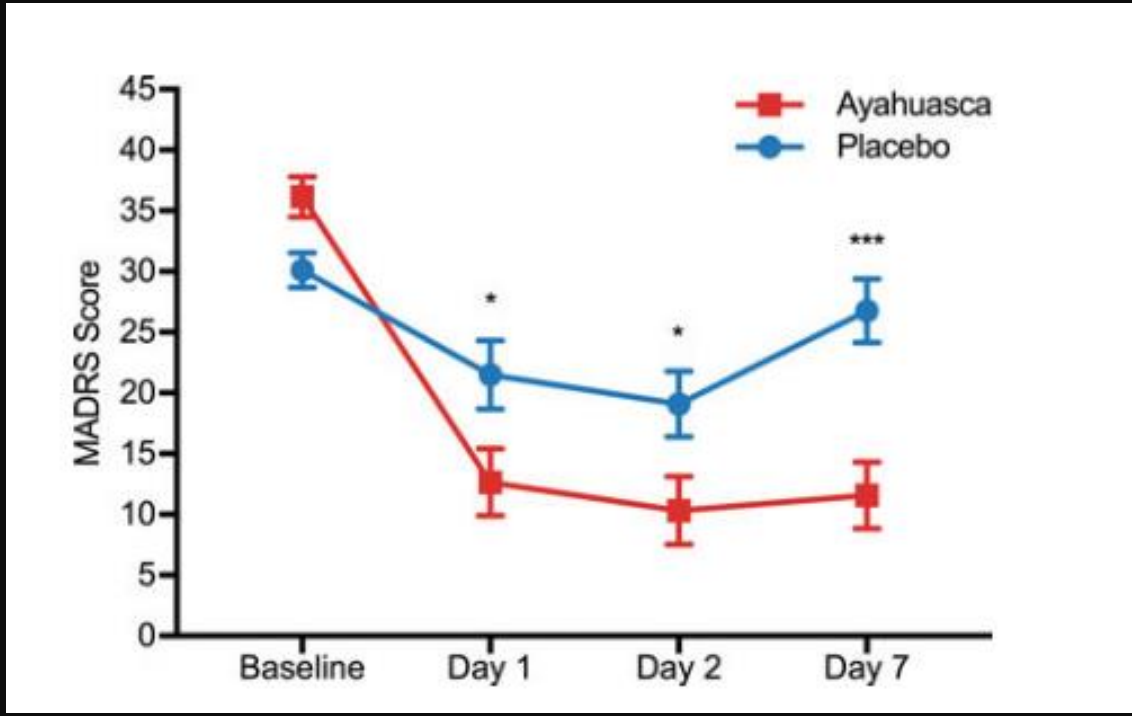

Rep (j7) : active = 57% ; placebo = 20%
Rem (j7) : active = 43% ; placebo = 13 %

Mais !
- Tbles perso et stresseurs externes ++
  → effet Cocooning
- Placebo non-psychédelique
- Harmaline = effet IMAO

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Johns Hopkins Psychedelic Research Unit

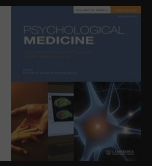
Roland R Griffiths[1,2], Matthew W Johnson[1], Michael A Carducci[3],

Essai randomisé, simple aveugle
N = 27(24)

2 doses de PCB (20 et 30mg/70Kg)
Intervalle = 1 sem

Pas de placebo (*delayed*)

Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial



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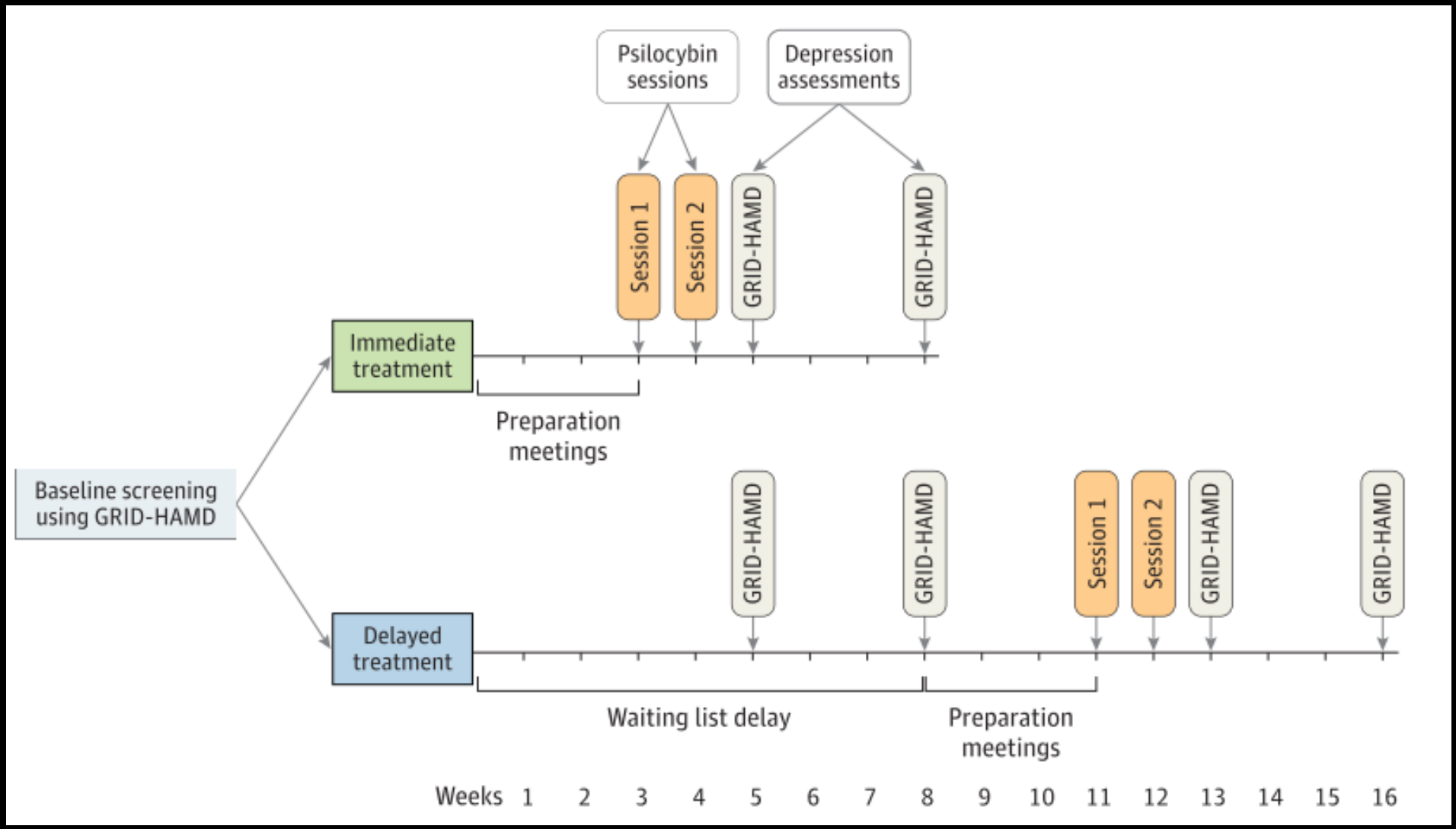

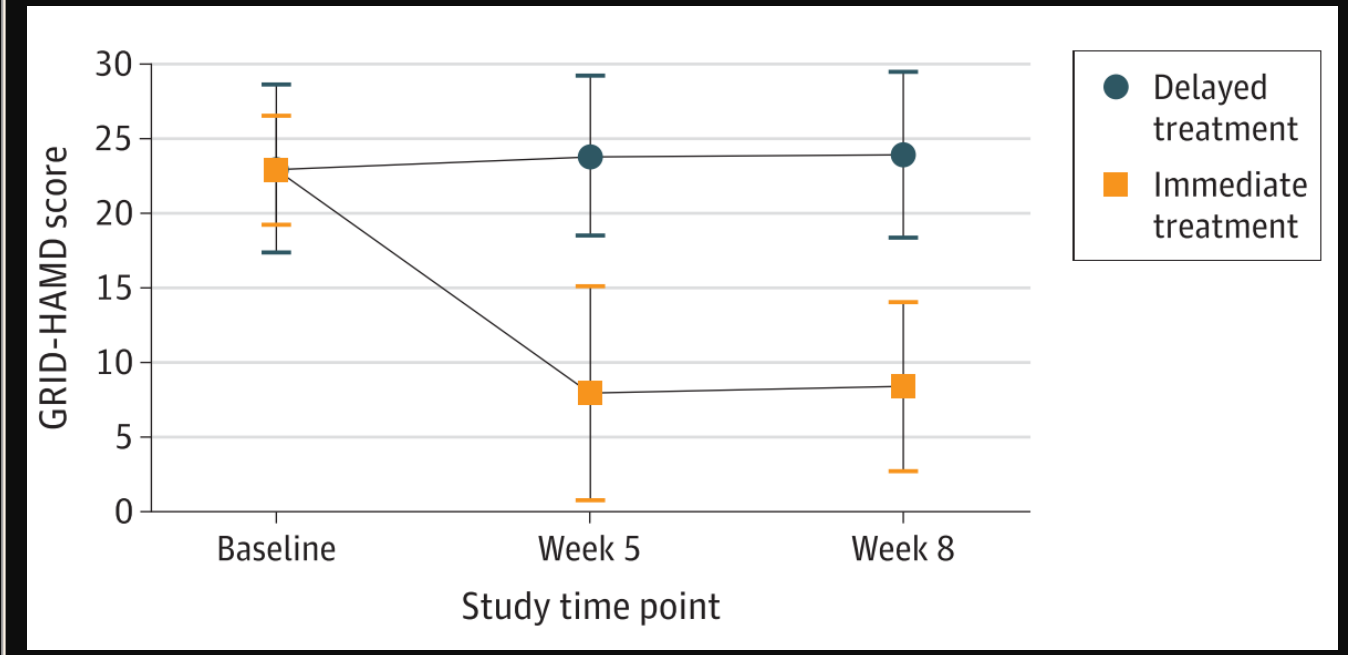

Réponse (sem1) : 71%
Rémission (sem1/sem4) : 58% / 54%

Essai randomisé, simple aveugle
N = 27(24)

2 doses de PCB (20 et 30mg/70Kg)
Intervalle = 1 sem

Pas de placebo (*delayed*)

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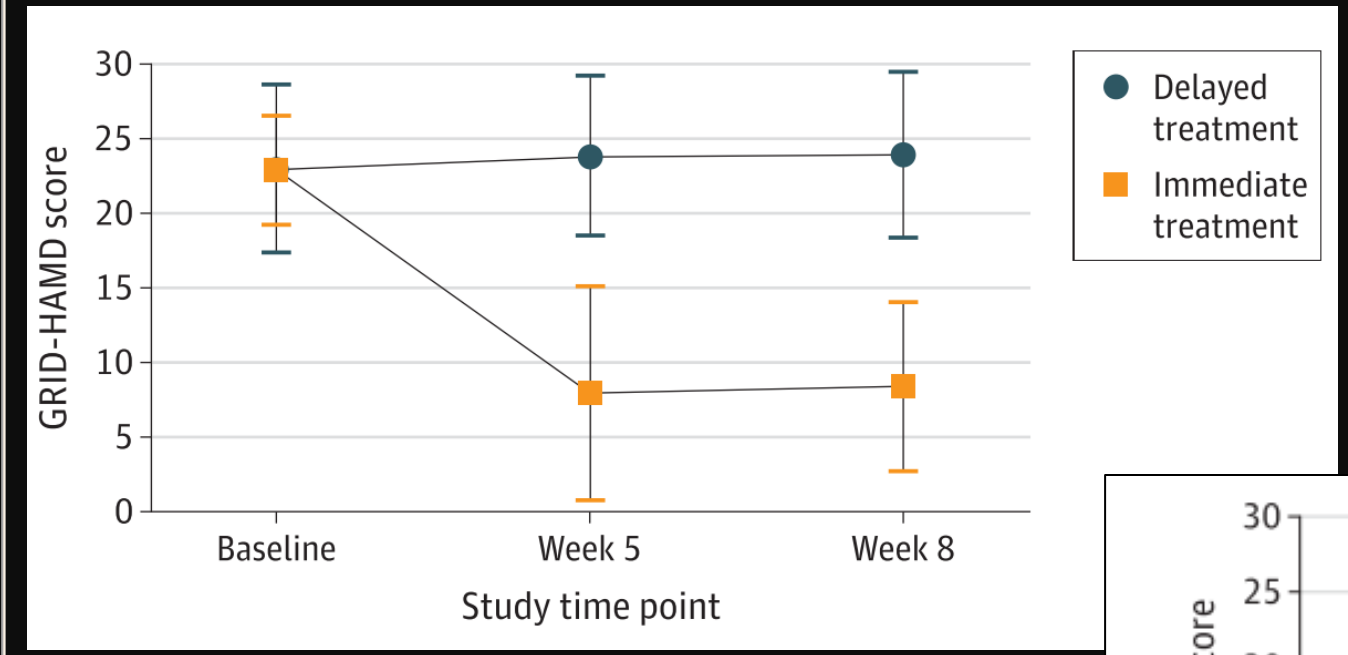

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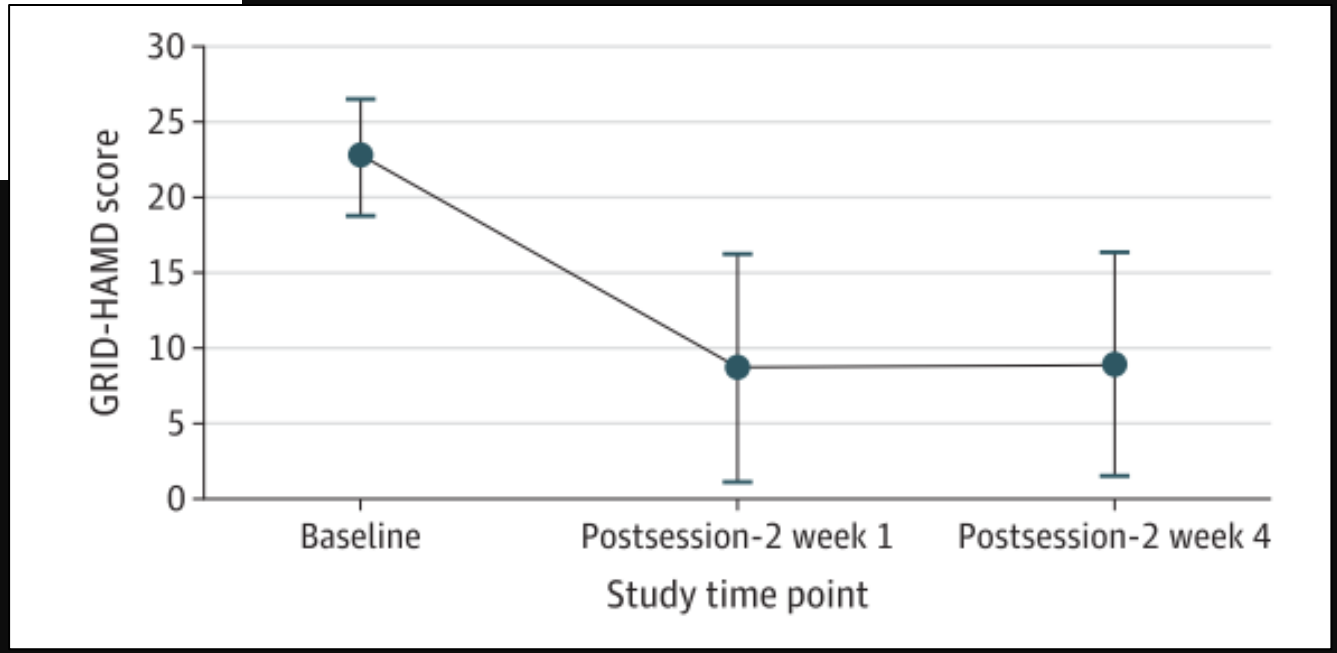

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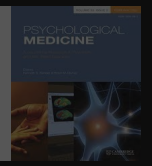

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Essai contrôlé en double aveugle vs placebo
N = 59 – MDE

- **Active** : 2 doses PCB (25mg) – interv. 1sem
- **Ct** : escitalopram 10 puis 25mg
  + 2 doses PCB (1mg) – interv. 1sem

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NEW ENGLAND JOURNAL OF MEDICINE 1812 1823 1828 1928

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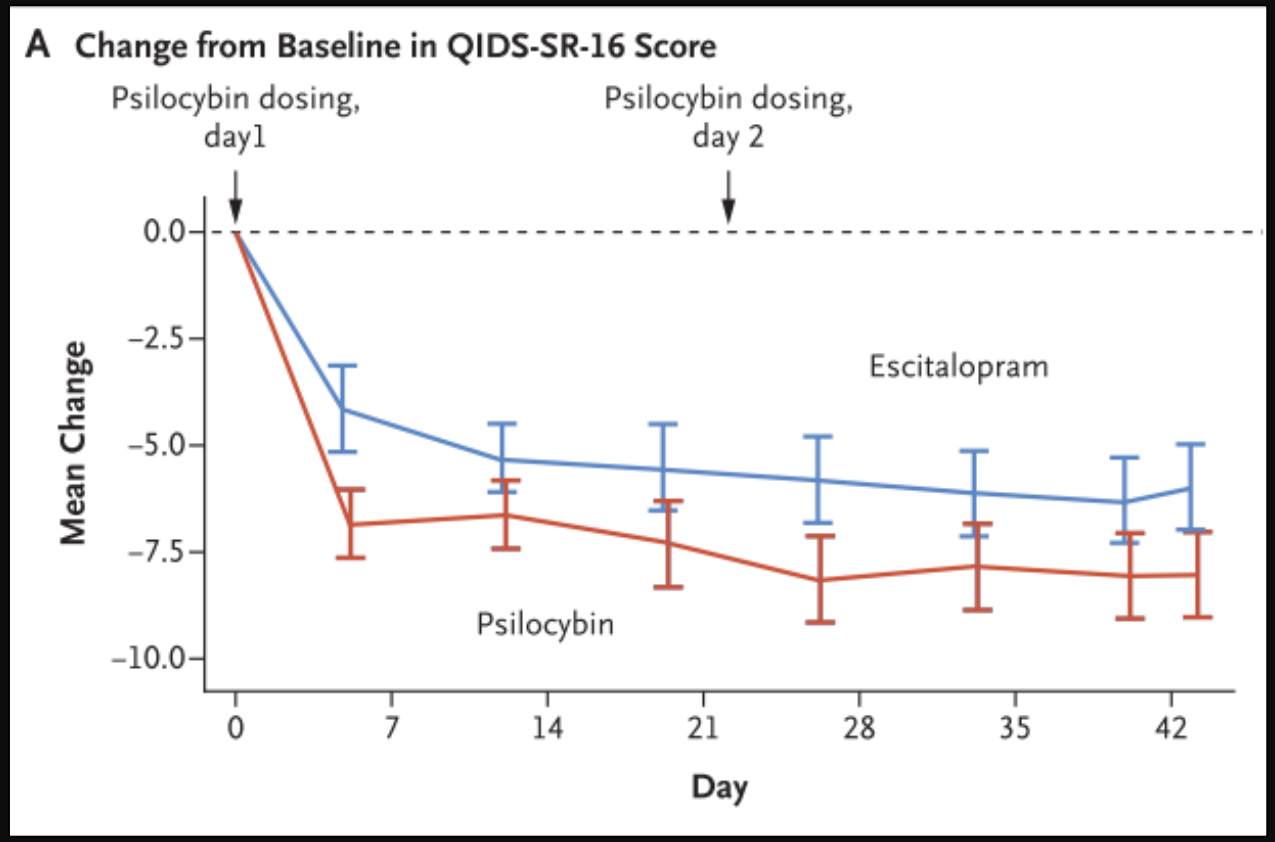

Différence non-sig

A 6 semaines

PSC : rep = 70% ; rem = 57%

ESC : rep = 48% ; rem = 28%

- 2 prises = efficacité similaire
- Potentiel effet du dosage placebo ?

Mais !

- Risque β = 0,2
- Temps d'observation limité pour ESC

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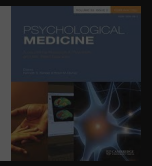

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COMPASSION
Navigating Mental Health Pathways

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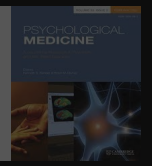

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Alan K. Davis, PhD; Frederick S. Barrett, PhD; Darrick G. May, MD; Mary P. Cosimano, MSW; Nathan D. Sepeda, BS; Matthew W. Johnson, PhD; Patrick H. Finan, PhD; Roland R. Griffiths, PhD

Trial of Psilocybin versus Escitalopram for Depression

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1er essai de grande ampleur : 233 patients TRD

Contrôlé, randomisé, double aveugle

3 groupes :

- PCB 25mg DU
- PCB 10mg DU
- PCB 1mg DU

COMPASSION
Navigating Mental Health Pathways

Guy Goodwin

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

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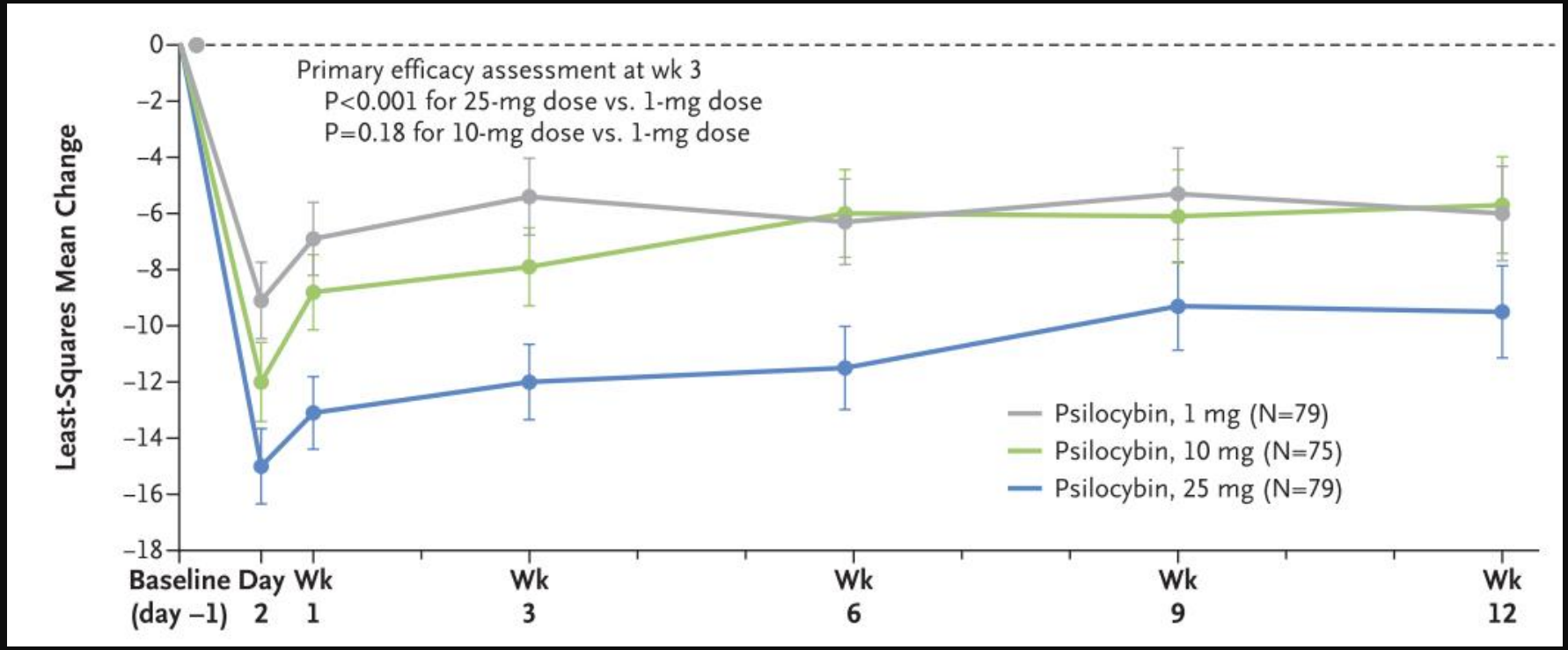

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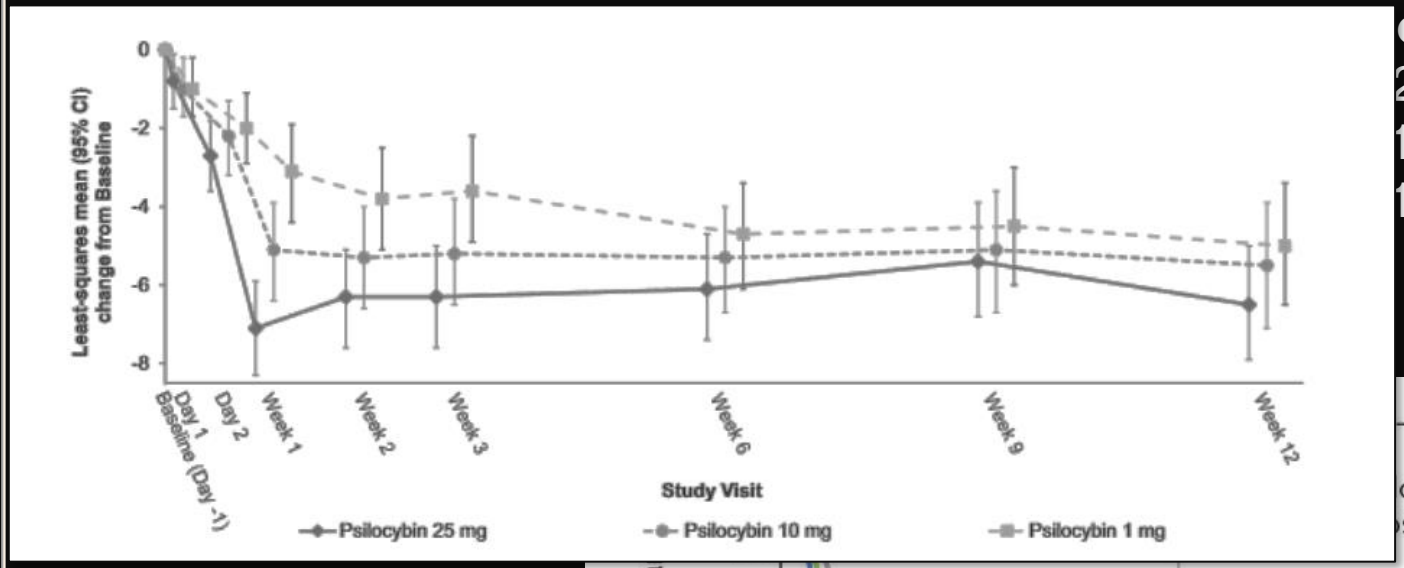

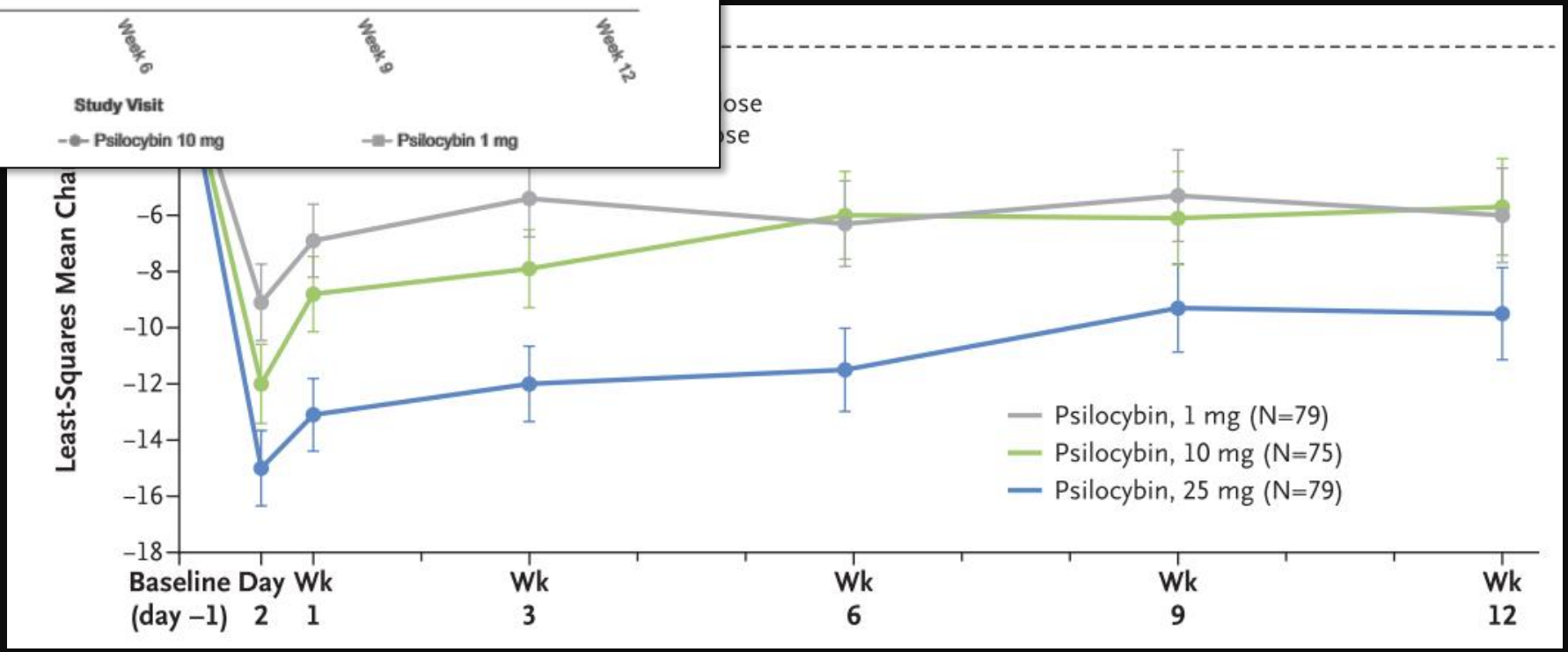

Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial

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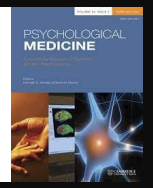

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Résultats clairement encourageants

Plusieurs observations répliquées

- Effet sur l'humeur et l'anxiété
- Rapidité d'action
- La persistance dans le temps

Données de sécurité rassurantes

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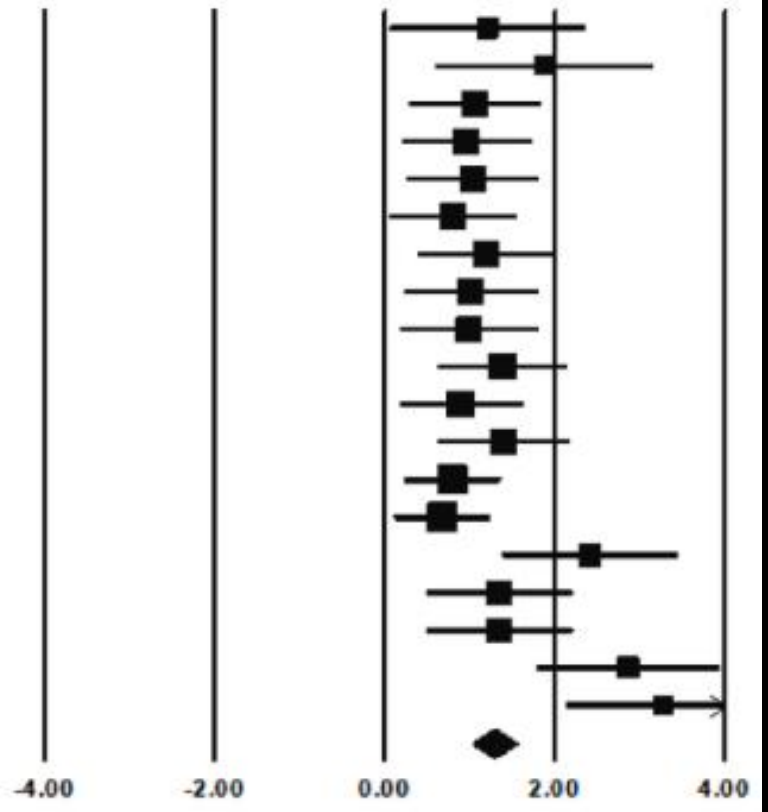
(a)

			Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Grob 2011 (a)	dosage1	duration1	1.209	0.587	0.345	0.058	2.360	2.059	0.040
Grob 2011 (b)	dosage1	duration1	1.883	0.657	0.432	0.595	3.171	2.866	0.004
Ross 2016 (a)	dosage2	duration1	1.068	0.394	0.155	0.296	1.840	2.712	0.007
Ross 2016 (b)	dosage2	duration1	0.961	0.389	0.151	0.199	1.723	2.472	0.013
Ross 2016 (c)	dosage2	duration2	1.039	0.392	0.154	0.270	1.808	2.648	0.008
Ross 2016 (d)	dosage2	duration2	0.796	0.382	0.146	0.047	1.545	2.084	0.037
Ross 2016 (e)	dosage2	duration1	1.201	0.416	0.173	0.386	2.016	2.888	0.004
Ross 2016 (f)	dosage2	duration2	1.017	0.406	0.165	0.221	1.813	2.503	0.012
Ross 2016 (g)	dosage2	duration2	0.996	0.414	0.172	0.184	1.808	2.404	0.016
Gabrielle 2020 (a)	dosage2	duration2	1.384	0.386	0.149	0.628	2.140	3.589	0.000
Gabrielle 2020 (b)	dosage2	duration2	0.896	0.368	0.135	0.175	1.617	2.434	0.015
Gabrielle 2020 (c)	dosage2	duration2	1.401	0.399	0.160	0.618	2.184	3.508	0.000
Griffiths 2016 (a)	dosage2	duration1	0.797	0.290	0.084	0.230	1.365	2.753	0.006
Griffiths 2016 (b)	dosage2	duration1	0.679	0.289	0.084	0.112	1.246	2.346	0.019
Carhart 2016 (a)	dosage3	duration1	2.414	0.526	0.277	1.383	3.445	4.588	0.000
Carhart 2016 (b)	dosage3	duration2	1.352	0.440	0.193	0.490	2.214	3.073	0.002
Carhart 2016 (c)	dosage3	duration2	1.352	0.440	0.193	0.490	2.214	3.073	0.002
Davis 2020 (a)	dosage4	duration1	2.867	0.550	0.302	1.789	3.944	5.214	0.000
Davis 2020 (b)	dosage4	duration1	3.283	0.593	0.352	2.121	4.445	5.537	0.000
			1.289	0.137	0.019	1.020	1.558	9.390	0.000



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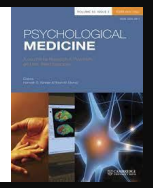

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Conclusion à ce stade :

Les psychédéliques soignent !

Absolument univoque ?

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Persistance de certains biais méthodologiques

- Des intérêts des investigateurs
- Un biais de sélection des patients
- Des difficultés d'élaboration des contrôles/placebo

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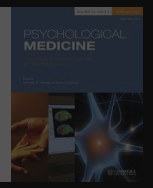

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Auteur majeur (premier ou dernier) lié :

- À un réseau militant
- A un laboratoire industriel

BECKLEY FOUNDATION

COMPASSION Navigating Mental Health Pathways

MAPS MULTIDISCIPLINARY ASSOCIATION FOR PSYCHEDELIC STUDIES

Et toujours un risque de méconduite scientifique...

Single-dose psilocybin-assisted therapy in major depressive disorder: A placebo-controlled, double-blind, randomised clinical trial

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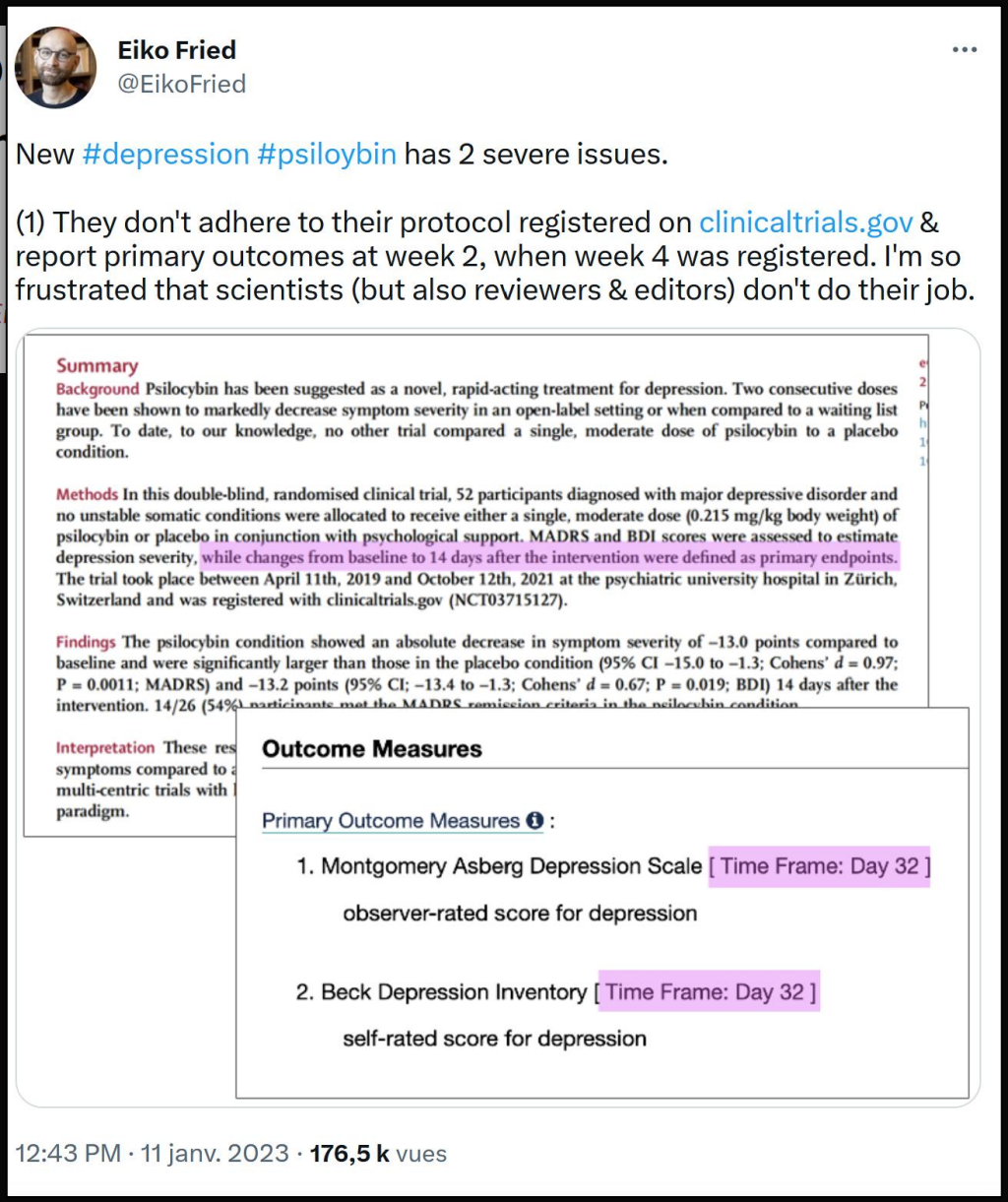
Plusieurs biais méthodologiques

Ne respectent pas la méthodologie planifiée
- Risque de p-hacking
- Puissance de l'étude inadaptée



Eiko Fried
@EikoFried

New #depression #psiloybin has 2 severe issues.

(1) They don't adhere to their protocol registered on clinicaltrials.gov & report primary outcomes at week 2, when week 4 was registered. I'm so frustrated that scientists (but also reviewers & editors) don't do their job.

Summary

Background Psilocybin has been suggested as a novel, rapid-acting treatment for depression. Two consecutive doses have been shown to markedly decrease symptom severity in an open-label setting or when compared to a waiting list group. To date, to our knowledge, no other trial compared a single, moderate dose of psilocybin to a placebo condition.

Methods In this double-blind, randomised clinical trial, 52 participants diagnosed with major depressive disorder and no unstable somatic conditions were allocated to receive either a single, moderate dose (0.215 mg/kg body weight) of psilocybin or placebo in conjunction with psychological support. MADRS and BDI scores were assessed to estimate depression severity, while changes from baseline to 14 days after the intervention were defined as primary endpoints. The trial took place between April 11th, 2019 and October 12th, 2021 at the psychiatric university hospital in Zürich, Switzerland and was registered with clinicaltrials.gov (NCT03715127).

Findings The psilocybin condition showed an absolute decrease in symptom severity of −13.0 points compared to baseline and were significantly larger than those in the placebo condition (95% CI −15.0 to −1.3; Cohens' $d = 0.97$; $P = 0.0011$; MADRS) and −13.2 points (95% CI; −13.4 to −1.3; Cohens' $d = 0.67$; $P = 0.019$; BDI) 14 days after the intervention. 14/26 (54%) participants met the MADRS remission criteria in the psilocybin condition

Interpretation These res
symptoms compared to
multi-centric trials with
paradigm.

Outcome Measures

Primary Outcome Measures :

1. Montgomery Asberg Depression Scale [Time Frame: Day 32]
   observer-rated score for depression

2. Beck Depression Inventory [Time Frame: Day 32]
   self-rated score for depression

12:43 PM · 11 janv. 2023 · **176,5 k** vues

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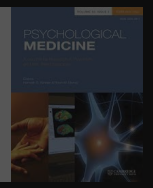

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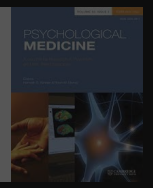

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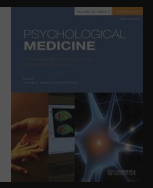

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- A priori positif
  Attentes

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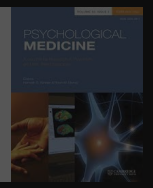

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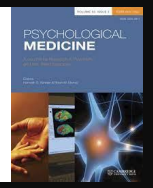

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G.M. Goodwin, S.T. Aaronson, O. Alvarez, P.C. Arden, A. Baker, J.C. Bennett, C. Bird, R.E. Blom, C. Brennan, D. Brusch,

Problématique du placebo demeure

- Effet psychédélique = thérapeutique
  Facilement repéré par patient / investigateur
- Dose minime = potentiellement efficace
- Pas de sédation possible

OR effet placebo probablement majeur

- Lié au biais de sélection
- Psychédéliques = hypersuggestibilité
  (Carhart-Harris, Kaelen et al. 2015)

Minimum méthodologique : évaluer la qualité de l'aveugle

Ça soigne *ou* *ça soigne ?*

Ce que ça ne soigne pas

- Symptômes psychotiques
- Troubles bipolaires

Clinical case	References
• 21-year-old woman • Depression and PTSD, unmedicated • Positive family history of bipolar disorder (father and paternal grandmother) • Psychotic mania 36 h after ingestion of psilocybin-containing mushrooms • Stabilized with lithium and aripiprazole, later lamotrigine	Hendin and Penn, 2021
• 40-year-old male psychiatrist • Known bipolar disorder (a single previous manic episode) • Hospitalized with psychotic mania after self-medicating for depression: 1 g daily of vaporized DMT for 6 months, then plus phenelzine (60 mg p.o.) 3 weeks before the episode • Stabilization with lithium 1200 mg/d, paliperidone 6 mg/d, and clonazepam 3.5 mg/d • No follow-up possible	Brown et al., 2017b
• 25-year-old male • Known bipolar disorder and history of cannabis abuse • Hospitalized with psychotic mania 2 days after ayahuasca ingestion • Remission with benperidole, olanzapine and lorazepam	Zellner et al., 2019
• 30-year-old male • Previous hypomanic episodes • Positive first-degree family history of bipolar disorder • Psychotic mania two days after a ayahuasca ritual • Stabilization with risperidone 2 mg/d and clonazepam 2 mg/d	Szmulewicz et al., 2015

(Bosch, Halm et al. 2022)

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

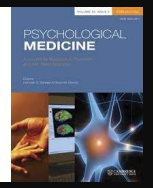
Stephen Ross[1,2,3,4,5,6], Anthony Bossis[1,2,4], Jeffrey Guss[1,2,4], Gabrielle Agin-Liebes[10], Tara Malone[1], Barry Cohen[7],

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial

Johns Hopkins Psychedelic Research Unit

Roland R Griffiths[1,2], Matthew W Johnson[1], Michael A Carducci[3],

Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial



Fernanda Palhano-Fontes[1,2], Dayanna Barreto[2,3], Heloisa Onias[1,2],

JAMA Psychiatry | Original Investigation

Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder
A Randomized Clinical Trial

Alan K. Davis, PhD; Frederick S. Barrett, PhD; Darrick G. May, MD; Mary P. Cosimano, MSW; Nathan D. Sepeda, BS; Matthew W. Johnson, PhD; Patrick H. Finan, PhD; Roland R. Griffiths, PhD

JAMA Psychiatry

Trial of Psilocybin versus Escitalopram for Depression

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Characteristic	Psilocybin (N=30)	Escitalopram (N=29)
Demographic		
Age (range) — yr	43.3±11.7 (21–64)	39.1±9.7 (22–60)
Female sex — no. (%)	11 (37)	9 (31)
White race — no. (%)†	28 (93)	24 (83)
Employment status — no. (%)		
Employed	21 (70)	21 (72)
Student	2 (7)	3 (10)
Unemployed	7 (23)	5 (17)
University level education — no. (%)	22 (73)	23 (79)
No previous psilocybin use — no. (%)	22 (73)	21 (72)
Weekly alcohol use (range) — g‡	36.8±43.1 (0–160)	67.7±66.6 (0–240)
Discontinued psychiatric medication for trial — no. (%)	11 (37)	12 (41)
Clinical		
Duration of illness (range) — yr	22.1±10.7 (3–44)	15.1±11.0 (2–46)
No. of psychiatric medications previously used (range)	2.2±1.6 (0–6)	1.8±1.5 (0–5)
Previous use of psychotherapy — no. (%)	28 (93)	26 (90)
QIDS-SR-16 score at pretreatment baseline (range)§	14.5±3.9 (7–23)	16.4±4.1 (6–22)

- Durée longue
- Intensité modérée
- Peu traitée

Ou

- Association tbles perso
- Stresseurs externes

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Max 35 % de dépression
MAIS >70% de rémission

Table 6. Percentage of participants with clinically significant response rate and symptom remission rate as assessed with the clinician-rated measures of depression and anxiety[+a].

Measure	Group	Assessment time-point					
		Post-session 1		Post-session 2		6 months[b]	
		Clinical response	Symptom remission	Clinical response	Symptom remission	Clinical response	Symptom remission
GRID-HAMD-17 (Depression)	Low-Dose-1st (High-Dose-2nd)	32%	16%	75%	58%	77%	59%
	High-Dose-1st (Low-Dose-2nd)	92%***	60%**	84%	68%	79%	71%
HAM-A (Anxiety)	Low-Dose-1st (High-Dose-2nd)	24%	12%	83%	42%	82%	50%
	High-Dose-1st (Low-Dose-2nd)	76%***	52%**	80%	60%	83%	63%

(Griffiths, Johnson et al. 2016)

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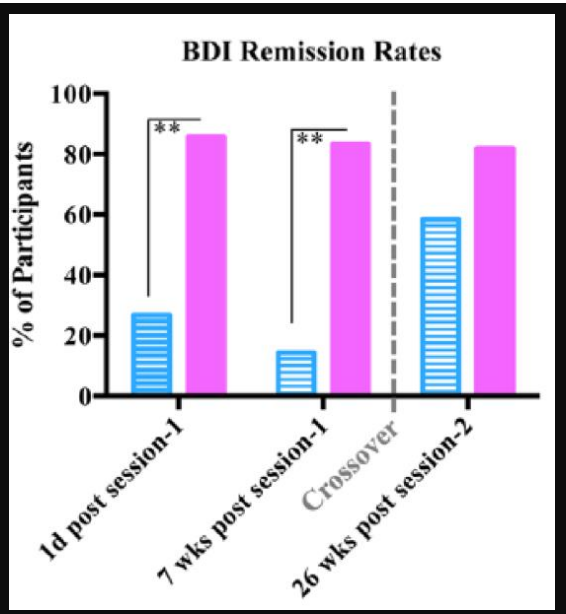

(Ross, Bossis et al. 2016)

Deux paradigmes différents

Modèle biomédical

"Les maladies sont dues à une étiologie ou une physiopathologie qu'il convient de traiter"

Essais cliniques : établir si TTT efficace pour la pathologie
→ indications

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"Les maladies sont dues à une étiologie ou une physiopathologie qu'il convient de traiter"

Essais cliniques : établir si TTT efficace pour la pathologie
→ indications

Modèle centré sur l'effet du produit

"Les psychotropes ont des effets généraux, parfois ils sont utiles pour améliorer la santé"

Ex : psychédéliques = bien être
ISRS = anesthésie affective
→ intérêt en cas de souffrance psychique

Essais cliniques : démontrer l'effet du TTT
Puis appliquer cet effet à des symptômes
→ champs d'application, dont le normal

Table 2 Study summary of clinical trials included in the meta-analysis

Study	Design	*N*	Subject	Psychedelic	Dose	Session[#]	Placebo
Gasser et al. 2014	CO	12	A and LT	LSD	200 µg	2	LSD 20 µg
Schmid et al. 2015	CO	16	Healthy	LSD	200 µg	1	Mannitol**
Dolder et al. 2016	CO	16	Healthy	LSD	100 µg	1	Mannitol**
Palhano-Fontes et al. 2019	P	29	TRD	Ayahuasca	360 µg/kg	1	Zinc sulfate
Hasler et al. 2004	CO	8	Healthy	Psilocybin	[&]115, 215 and 315 µg/k	4	Lactose
Wittmann et al. 2007	CO	12	Healthy	Psilocybin	115 and 250 µg/kg	2	Lactose
Griffiths et al. 2006	CO	30	Healthy	Psilocybin	429 µg/kg	1	Methylphenidate
Kometer et al. 2012	CO	17	Healthy	Psilocybin	215 µg/kg	1	Not specified
Kraehenmann et al. 2015	CO	25	Healthy	Psilocybin	160 µg/kg	1	Lactose
Griffiths et al. 2016	CO	51	A, D and LT	Psilocybin	314 and 429 µg/kg	1	P* 43 and 14 µg/kg
Ross et al. 2016	CO	29	A and LT	Psilocybin	300 µg/kg	1	Niacin
Grob et al. 2011	CO	12	A and LT	Psilocybin	200 µg/kg	1	Niacin

(Galvão-Coelho, Marx et al. 2021)

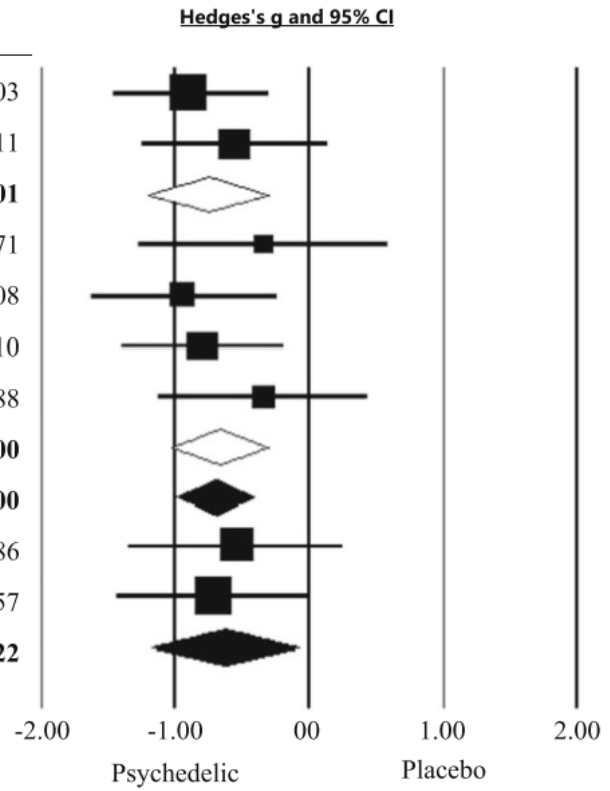
Table 2 Study summary of clinical trials included in the meta-analysis

Study

Gasser
Schmid
Dolder
Palhan
Hasler
Wittma
Griffith
Komet
Kraehe
Griffith
Ross et
Grob et

Acute Effects of Psychedelics for Negative Mood State

Study	Psychedelic	Subject	Outcome	Statistic for each study						
				SMD	SE	I^2	ℓ-CI	u-CI	Z	p
Dolder et al. (2016)	LSD	H	AMRS (1d)	-0.898	0.298	8.9	-1.482	-0.313	-3.009	0.003
Schmid et al. (2015)	LSD	H	AMRS (1d)	-0.561	0.352	12.4	-1.251	0.128	-1.596	0.111
	LSD	**H**		**-0.757**	**0.228**	**5.2**	**-1.203**	**-0.311**	**-3.327**	**0.001**
Hasler et al. (2004)	Psilocybin	H	AMRS (c)	-0.344	0.477	22.7	-1.278	0.590	-0.721	0.471
Kometer et al. (2012)	Psilocybin	H	PANAS (3h)	-0.945	0.354	12.5	-1.639	-0.251	-2.669	0.008
Kraehenmann et al. (2015)	Psilocybin	H	PANAS (3.5h)	-0.799	0.308	9.5	-1.403	-0.195	-2.593	0.010
Wittmann et al. (2007)	Psilocybin	H	AMRS (4.5h)	-0.343	0.397	15.8	-1.121	0.436	-0.863	0.388
	Psilocybin	**H**		**-0.671**	**0.185**	**3.4**	**-1.034**	**-0.309**	**-3.632**	**0.000**
	Combined	**H**		**-0.705**	**0.143**	**2.1**	**-0.987**	**-0.424**	**-4.916**	**0.000**
Grob et al. (2011)	Psilocybin	P	POMS (c)	-0.539	0.408	16.6	-1.338	0.260	-1.322	0.186
Ross et al. (2016)	Psilocybin	P	POMS (1d)	-0.709	0.373	13.9	-1.440	0.022	-1.901	0.057
	Psilocybin	**P**		**-0.632**	**0.275**	**7.6**	**-1.171**	**-0.092**	**-2.295**	**0.022**



(Galvão-Coelho, Marx et al. 2021)

Table 2 Study summary

Study

Gasser
Schmid
Dolder
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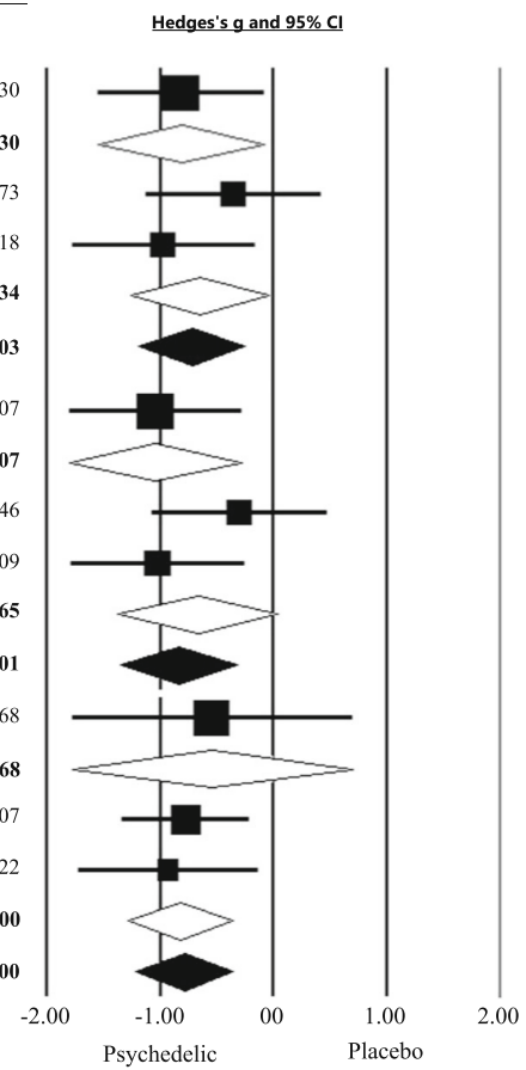
Griffith
Ross et
Grob et

Study

Dolder et al. (2
Schmid et al. (2
Hasler et al. (20
Kometer et al. (
Kraehenmann e
Wittmann et al.
Grob et al. (201
Ross et al. (201

Effects of Psychedelics on Depressive Symptoms

Study	Psychedelic	Subject	Outcome	Statistic for each study						
				SMD	SE	I^2	ℓ-CI	u-CI	Z	p
Acute Effects										
Palhano-Fontes et al. (2018)	Ayahuasca	P	MADRS (1d)	-0.816	0.377	14.2	-1.555	-0.078	-2.167	0.030
	Ayahuasca	**P**		**-0.816**	**0.377**	**14.2**	**-1.555**	**-0.078**	**-2.167**	**0.030**
Grob et al. (2011)	Psilocybin	P	BDI (1d)	-0.354	0.397	15.8	-1.133	0.425	-0.891	0.373
Ross et al. (2016)	Psilocybin	P	C (1d)	-0.974	0.411	16.9	-1.779	-0.168	-2.370	0.018
	Psilocybin	**P**		**-0.655**	**0.310**	**9.6**	**-1.262**	**-0.048**	**-2.115**	**0.034**
	Combined	P		**-0.720**	**0.239**	**5.7**	**-1.189**	**-0.251**	**-3.010**	**0.003**
Medium-term Effects										
Palhano-Fontes et al. (2018)	Ayahuasca	P	C (2,7d)	-1.042	0.388	15	-1.802	-0.283	-2.690	0.007
	Ayahuasca	**P**		**-1.042**	**0.388**	**15**	**-1.802**	**-0.283**	**-2.690**	**0.007**
Grob et al. (2011)	Psilocybin	P	BDI (15d)	-0.302	0.397	15.7	-1.079	0.475	-0.762	0.446
Ross et al. (2016)	Psilocybin	P	C (15d)	-1.024	0.392	15.3	-1.792	-0.256	-2.615	0.009
	Psilocybin	**P**		**-0.666**	**0.361**	**13**	**-1.374**	**0.042**	**-1.844**	**0.065**
	Combined	**P**		**-0.841**	**0.264**	**7**	**-1.359**	**-0.323**	**-3.183**	**0.001**
Long-term Effects										
Gasser et al. (2014)	LSD	P	HADS (60d)	-0.546	0.630	3.97	-1.780	0.698	-0.867	0.368
	LSD	**P**		**-0.546**	**0.630**	**3.97**	**-1.780**	**0.698**	**-0.867**	**0.368**
Griffiths et al. (2016)	Psilocybin	P	C (35d)	-0774	0.287	8.2	-1.336	-0.212	-2.701	0.007
Ross et al. (2016)	Psilocybin	P	C (42,49d)	-0.930	0.406	16.5	-1.725	-0.135	-2.292	0.022
	Psilocybin	**P**		**-0.826**	**0.234**	**5.5**	**-1.285**	**-0.367**	**-3.528**	**0.000**
	Combined*	**P**		**-0.792**	**0.219**	**4.8**	**-1.222**	**-0.362**	**-3.609**	**0.000**



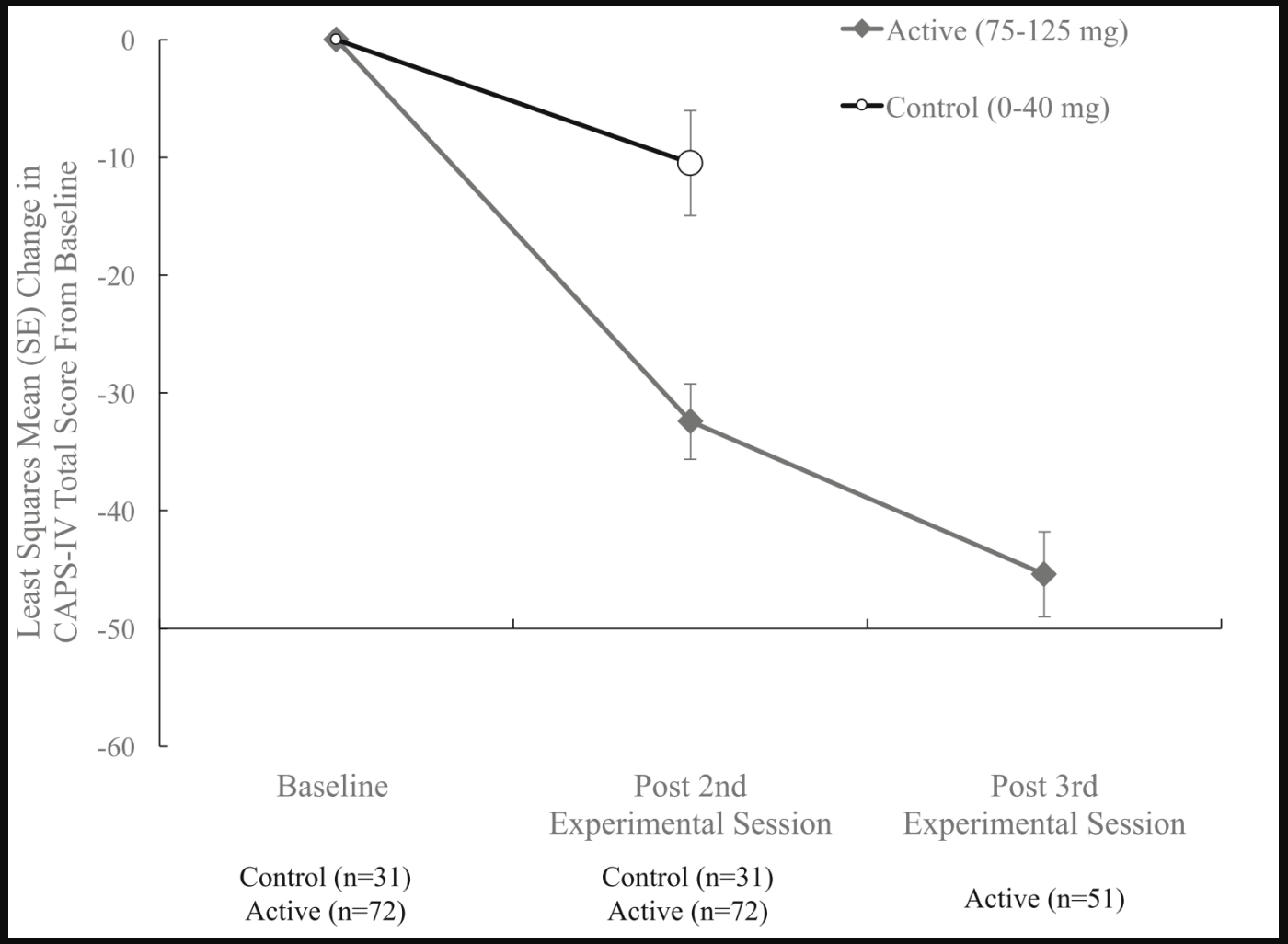
(Galvão-Coelho, Marx et al. 2021)

Autre utilisation : MDMA et PTSD

Plusieurs essais de phase 2
Phase 3 en cours

Psychothérapie augmentée
Résultats encourageants

Limites idem



Le progrès de la littérature

Période "héroïque"

- Large diffusion, pas de contrôles méthodo
- Politisation / mouvement culturel

Le progrès de la littérature

Le retour

- Études open modestes, population et chercheurs avec a-priori (+)
- Obj : démonstration physio / psycho → modèle centré sur le produit
- Recherche du placebo idéal

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La phase scientifique / médicale
- Contrôle / rando /aveugle = norme ↑ N, attention portée aux biais
- Obj : prouver l'effet thérapeutique, → modèle psy "médical"
- Travail sur placebo

Période "héroïque"
- Large diffusion, pas de contrôles méthodo
- Politisation / mouvement culturel

Take home messages

- L'effet thérapeutique des psychédéliques est régulièrement illustré par des essais dont la qualité augmente
- Certaines propriétés sont reproductibles : rapidité, taille d'effet, dosing...

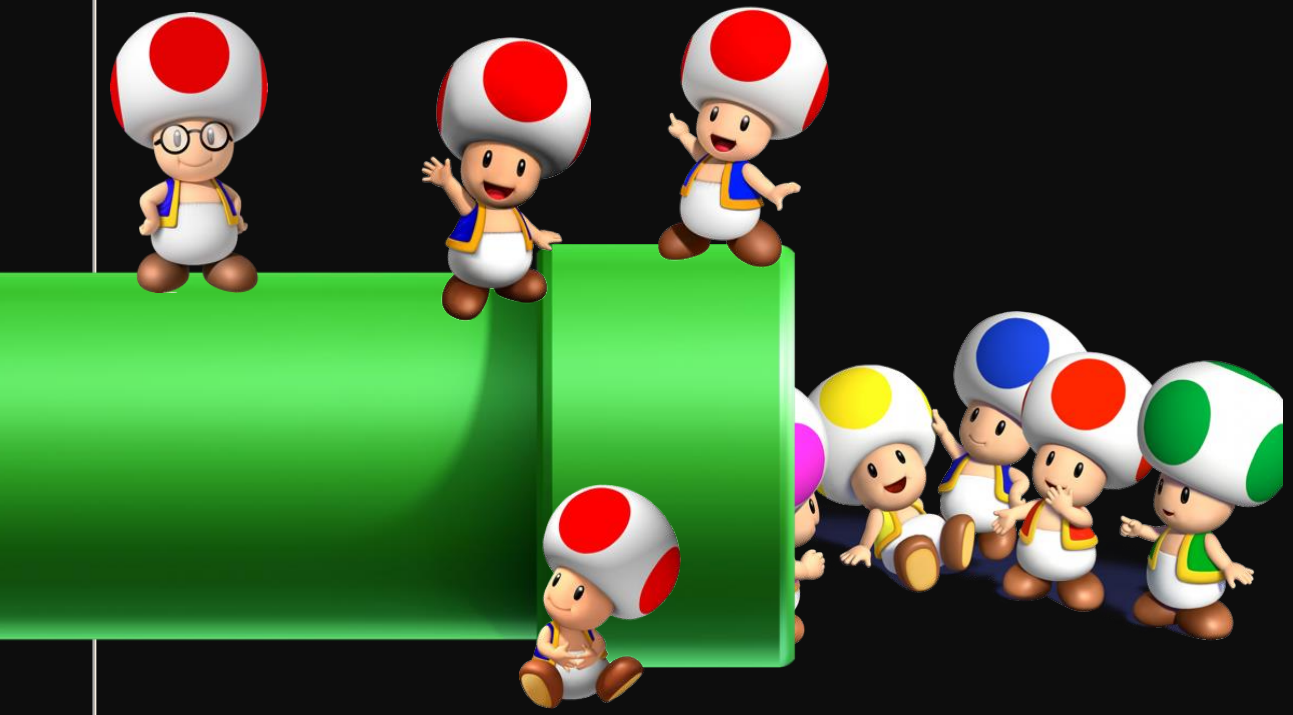
Take home messages

- L'effet thérapeutique des psychédéliques est régulièrement illustré par des essais dont la qualité augmente
- Certaines propriétés sont reproductibles : rapidité, taille d'effet, dosing...

Mais

- Les erreurs du passé ont la vie dure : biais de sélection, conflits d'intérêt
- La littérature est issue d'un milieu bercé par un paradigme différent : centré sur le produit (et son effet) ≠ du paradigme médical habituel
- La mise au point d'un placebo est difficile ++ → besoin de revoir le modèle de l'EBM ?

Merci pour votre attention



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l.jeanjean@unistra.fr