Common Threads: Session 9

Psychedelics in the Treatment of

HEADACHE AND PAIN DISORDERS

Dr. Emmanuelle Schindler

Disclosures

- **Current research funding:** Wallace Research Foundation
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*** Dr. Schindler is an employee of the US Department of Veterans Affairs. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the presenter and do not necessarily reflect the views of the US Department of Veterans Affairs ***

Session Learning Objectives

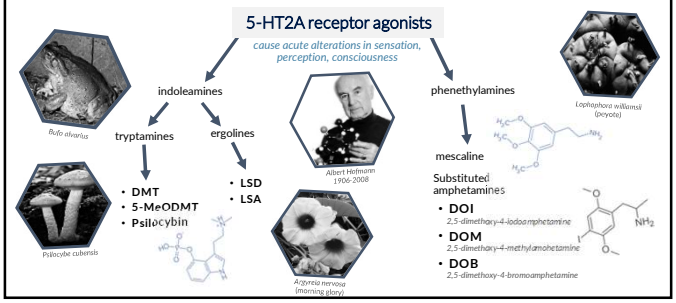
01 | Brief overview of psychedelics and clinical research in the field.

02 | Reports and investigations related to headache and pain disorders.

03 | Pathophysiological overlap with potential mechanism of action.

04 | Considerations for future headache and pain studies with psychedelics.

Classic Psychedelics



Clinical Research with Psychedelics

- Depression
- Anxiety
- End of life
- Smoking cessation
- Alcohol Use Disorder
- Cocaine Use Disorder
- OCD
- PTSD
- Eating Disorders
- Migraine
- Cluster headache
- Post-Traumatic Headache
- Phantom Limb Syndrome
- Fibromyalgia
- Cancer-related Pain
- Post-Lyme Infection Pain
- …

Table 2 Clinical Trials Involving Psychedelics Published During the Present 'Second Wave' of Psychedelic Research

Study	Population/indication and sample size	Drug and design	Main efficacy outcome
Moreno *et al* (2006)	Obsessive compulsive disorder; $n = 9$	Psilocybin: single-arm, within subjects, variable doses. Up to four doses of psilocybin	All patients showed improvements within 24 h of a treatment but no effect of dose
Grob *et al* (2011)	Anxiety and depression in end-stage cancer; $n = 12$	Psilocybin: DB-RCT, crossover; inert placebo	Significant reductions in trait anxiety at 3 months
Johnson *et al* (2014)	Long-term chronic tobacco smoking, $n = 15$	Psilocybin: open-label. Up to three doses of psilocybin after four CBT sessions	80% of sample abstinent at 6 month follow-up
Gasser *et al* (2014)	Anxiety related to life-threatening disease, $n = 12$	LSD: DB-RCT, crossover; very low dose (VLD) LSD = control. Single dose of LSD	Significant decreases in state and trait anxiety *vs* VLD at 2 months and sustained for 12 months
Bogenschutz *et al* (2015)	Alcohol dependence, $n = 10$	Psilocybin: open-label. Up to two doses after seven motivational therapy sessions	Significant decrease in drinking behaviors for up to 9 months
Osorio Fde *et al* (2015) and Sanches *et al* (2016)	Major depressive disorder (MDD), $n = 6$ +study extension to $n = 17$	Ayahuasca: open-label. Single dose of ayahuasca	Significant decreases in depressive symptoms for up to 21 days
Carhart-Harris *et al* (2016a,b)	Treatment-resistant MDD, $n = 12$ +study extension to $n = 20$	Psilocybin: open-label. Two doses of psilocybin	Significant decreases in depressive symptoms for up to 6 months
Ross *et al* (2016)	Anxiety and depression related to life-threatening cancer, $n = 29$	Psilocybin: DB-RCT, crossover; niacin = active placebo. Single dose of psilocybin	Significant decreases in anxiety and depression *vs* niacin at 7 weeks (pre crossover) and sustained for 6.5 months
Griffiths *et al* (2016)	Anxiety and depression related to life-threatening cancer; $n = 51$	Psilocybin: DB-RCT, crossover; VLD psilocybin = control. Single dose of psilocybin	Significant decreases in anxiety and depression *vs* VLD at 5 weeks (pre crossover). Effects sustained for 6 months

Karst et al., 2010 | Cluster headache; n = 5 case series | BOL 30µg/kg, three doses five days apart each | Attack frequency reduced out to 12 weeks after completion of three doses

Abbreviations: DB-RCT, double-blind randomised controlled trial; VLD, very low dose; MDD, major depressive disorder; TRD, treatment-resistant depression.

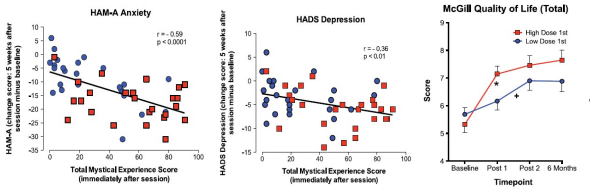
Carhart-Harris and Goodwin. *Neuropsychopharmacology*. 2017 Oct;42(11):2105-2113

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

Journal of Psychopharmacology. 2016, Vol. 30(12) 1181–1197

Roland R Griffiths[1,2], Matthew W Johnson[1], Michael A Carducci[3], Annie Umbricht[1], William A Richards[1], Brian D Richards[1], Mary P Cosimano[1] and Margaret A Klinedinst[1]

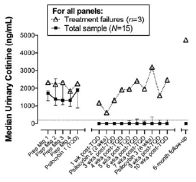
- Patients with life-threatening cancer dx + anxiety or depression; N = 51
- Randomized, double-blind, cross-over design
- 2 drug sessions about 5 weeks apart
- Low (1 or 3 mg/70 kg), high (22 or 30 mg/70 kg) dose
- Preparatory, inter-dosing, and post-dosing sessions with monitors (6 sessions, ~14 hours)
- HAM-A and GRID-HAMD at 5 weeks post dosing



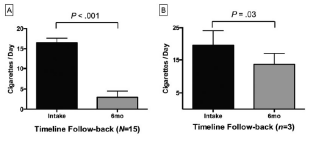
Pilot study of the 5-HT$_{2A}$R agonist psilocybin in the treatment of tobacco addiction

Journal of Psychopharmacology. 2014, Vol. 28(11) 983–992

Matthew W Johnson[1], Albert Garcia-Romeu[1], Mary P Cosimano[1] and Roland R Griffiths[1,2]



- Patients who smoke ≥10 cigarettes daily, past quit attempts, desire to quit; N = 15
- Open label design
- Three drug sessions at weeks 5, 7, and 13
- Moderate dose (20 mg/70 kg) in first session, high dose (30 mg/70 kg) in sessions 2 and 3
- 15-week smoking cessation program: weekly meetings, cognitive behavioral therapy
- Biomarkers (breath CO, urine cotinine), mean number of cigarettes per day



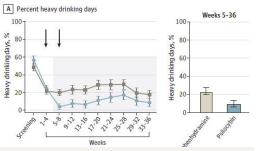
JAMA Psychiatry | Original Investigation

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

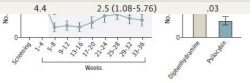
Michael P. Bogenschutz, MD; Stephen Ross, MD; Snehal Bhatt, MD; Tara Baron, MA; Alyssa A. Forcehimes, PhD; Eugene Laska, PhD; Sarah E. Meisenenga, PhD; Kelley O'Donnell, MD, PhD; Lindsay T. Owens, MA; Samantha Podosbarac, MA; John Rotrosen, MD; J. Scott Tonigan, PhD; Lindsay Worth, MA

JAMA Psychiatry. 2022;79(10):953-962



- Patients with alcohol dependence, ≥4 heavy drinking days in the past month; N = 93
- diphenhydramine (50 or 100 mg)
- Psychotherapy: 12 sessions, motivational enhancement therapy, cognitive behavioral therapy
- % heavy drinking days during weeks 5 to 32

	Follow-up period	No. (%)[a] Diphenhydramine (n = 45)	Psilocybin (n = 48)	NNT	OR (95% CI)[b]	P value[b,c]
Abstinence	Weeks 5-36	4 (8.9)	11 (22.9)	7.1	3.05 (0.89-10.40)	.06
	Weeks 33-36	11 (24.4)	23 (47.9)	4.3	2.84 (1.17-6.89)	.02
No heavy drinking	Weeks 5-36	5 (11.1)	16 (33.3)	4.5	4 (1.32-12.10)	.01
	Weeks 33-36	18 (40.0)	30 (62.5)	4.4	2.5 (1.08-5.76)	.03



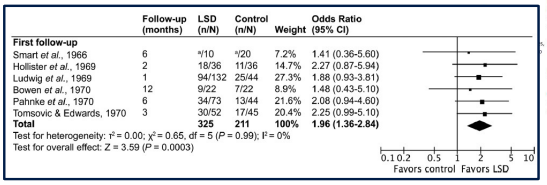
Lysergic acid diethylamide (LSD) for alcoholism: meta-analysis of randomized controlled trials

J. Psychopharmacol. 2012. 26, 994–1002

Teri S Krebs[1,2] and Pål-Ørjan Johansen[1,2]

Table 2. Details of treatment programs in included trials of LSD for alcoholism.

	Treatment program (approximate length in days)	Preparation for LSD session	Treatment during experimental session	Setting of experimental session room	Aftercare related to experimental session
Smart et al., 1966	Individual and group therapy within a therapeutic community	Brief orientation; not told name of LSD nor that an active control drug was used	3 h interview, followed by occasional observation	No music or visual stimuli; all patients strapped to bed by wrist belt	One follow-up review session with interviewer
Hollister et al., 1969	Brief counselling on alcohol misuse; focus on alcohol withdrawal (7)	Brief orientation; not told name of LSD nor that an active control drug was used	Brief supportive reassurance; emphasis on self-examination	Basic, comfortable furniture	None mentioned; discharged within 48 hours; overall: 'little or no specific psychotherapy' No follow-up with experimental session therapist
					None mentioned
					Multiple follow-up review sessions
					One follow-up review session in group therapy



ATTENUATION OF ANTICIPATION: A THERAPEUTIC USE OF LYSERGIC ACID DIETHYLAMIDE*

BY ERIC KAST, M. D.

Psychiatr. Q. 41, 646–657

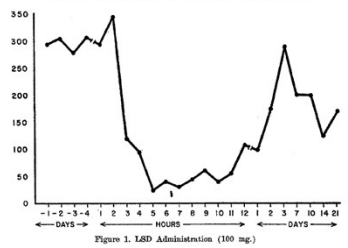
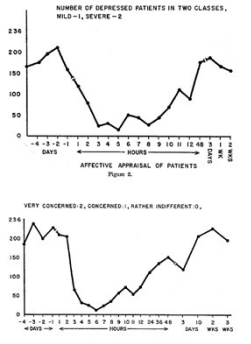
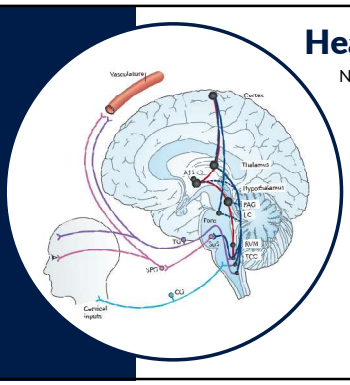


Figure 1. LSD Administration (100 mg.)



Pain Reference	Study Type	N	Drug, Oral Dose, And Regimen	Preventive Effects
Terminal Cancer Pain				
Kast, 1967	Case series	128	LSD 100µg once (subjects told "potent medicine")	Acute: Reduced pain score by ~80% for 12 hrs
Pahnke et al., 1970 Grof et al., 1973	Case series	50	LSD 100µg, dihydro-morphinone (D) 2mg, meperidine (M) 100mg, once each	Acute: Between the first and third hours, LSD reduced pain by ~80%, D and M each reduced pain by ~30%
Kurland, 1985	Case series	4	LSD 200 to 600µg once (some doses IM or IV; sessions repeated up to 4 times; overlap with Pahnke et al., 1969)	Acute: 2 subjects had relief, 1 subject initially had pain increase but after 50µg IV had relief
Phantom Limb Syndrome				
Fanciullacci et al., 1977	Case series	7	LSD 25µg daily x 1 week, then 50µg daily x 2 weeks	Pain and analgesic consumption were reduced in 5 subjects; residual pain reduction for several weeks
Ramachandran et al., 2018	Case report	1	Psilocybin (0.2 - 3gm dried mushroom) & mirror therapy	Acute: Psi alone = pain relief; Psi + MT = longer lasting acute relief pain relief
Low Back Pain				
Johnson and Black, 2020	Case report	1	LSA (single ingestion of 6 HBWR seeds)	Acute: "abated completely"
Lyes et al., 2022	Case report (from series)	1	Psilocybin mushroom 1 gram every 6-8 weeks + PT exercises	Pain freedom for 2 weeks Baseline MSK pain reduced from 9→7/10 x 3 months Neuropathic pain resolved after 3rd dose
Other				Acute: 2-5 grams, pain relief 8 to 20 hours
Lyes et al., 2022	Case series (Spinal injury, CPRS)	2	Psilocybin 50 to 500mg daily *	Pain relief for 3-8 hours *

Headache Reference	Study Type	N	Drug, Oral Dose, And Regimen	Preventive Effects
Cluster Headache				
Matharu et al., 2005	Case report	1	Psilocybin 1gm dried mushroom every 1-2 months	Pain free for 2-6 weeks
Sewell et al., 2006	Survey	53	LSD, psilocybin mushrooms (varied regimens)	Acute: Psilocybin (n=26) 85%; LSD (n=2) 50% [redacted] as effective in
Karst et al., 2010	Case series	5	BOL 30µg/kg, three doses five days apart each	Attack frequency reduced out to 12 weeks after completion of three doses
Post, 2014	Case series	2	5-MeO-DALT 15mg, 30mg	Single administration prevents attacks out to two weeks, regular use (15mg every 5 days) prevented attacks entirely
Schindler et al., 2015	Survey	496	Psilocybin mushrooms, LSD, LSA (seeds), BOL, DMT (varied regimens, every few weeks to annually)	In those who tried the drug, efficacy was as follows: psilocybin (n=181, 71%); LSD (n=74, 78%); LSA (n=108, 59%; DMT (n=18, [redacted] Acute: Psilocybin (n=146) 26% [redacted] 77.5% who used any of the drugs had a response ("fully or in part")
Di Lorenzo et al., 2016	Survey	54	Psilocybin mushrooms, LSD, LSA (seeds) (varied regimens, some only 1-3 times/year, sub-psychedelic doses)	
de Coo et al., 2019	Survey	643	Psilocybin mushrooms, LSD (unclear regimen)	In those who used psilocybin (n=39) and LSD (n=5) to treat, attack frequency was reduced in 56% and 60%, respectively
Johnson and Black, 2020	Case report	1	LSA (single ingestion of 6 HBWR seeds)	Relief for two weeks
Schindler et al., 2022	Randomized, double-blind, placebo-controlled clinical trial	14	Psilocybin (0.143 mg/70 kg) pulse of 3 doses, 5 days apart each vs. Placebo (microcrystalline cellulose); chronic and episodic subjects	Acute: "abated completely" [redacted] e 3 weeks
Madsen et al., 2022	Open label clinical trial	10	Psilocybin (0.143 mg/70 kg) pulse of 3 doses, 7 days apart each; chronic subjects only	Approximate 30% reduction in weekly attacks over the 4 weeks after completion of pulse (p=0.008)
Migraine				
Sicuteri, 1963	Case series	390	LSD 50 to100µg; BOL 2 to 4mg (unclear regimen)	LSD had moderate effect; BOL a mild effect compared to methysergide
Schindler et al., 2021	Double-blind, placebo-controlled, cross-over trial	10	Psilocybin 10mg/70kg vs. placebo, one dose each	Approximate 50% reduction in weekly migraine days in the 2 weeks after a single administration



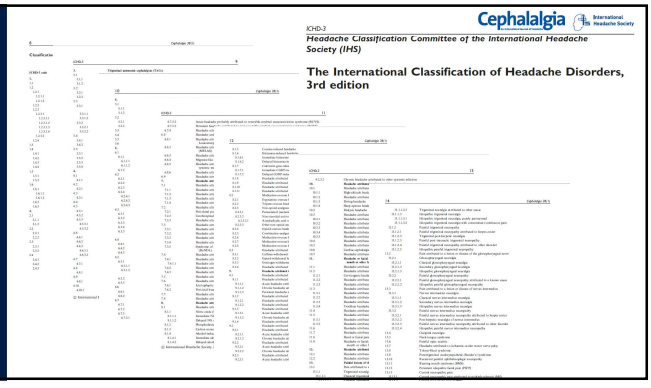
Headache Disorders

Neurological disorders characterized by recurrent paroxysms of head, neck, and/or face pain

Hallmark of a particular disorder is the headache attack:

- Pain quality, severity
- Location
- Duration
- Frequency
- Associated symptoms

SOURCE: Akerman et al., 2011



Cephalalgia — International Headache Society

ICHD-3

Headache Classification Committee of the International Headache Society (IHS)

The International Classification of Headache Disorders, 3rd edition

Headache Disorders

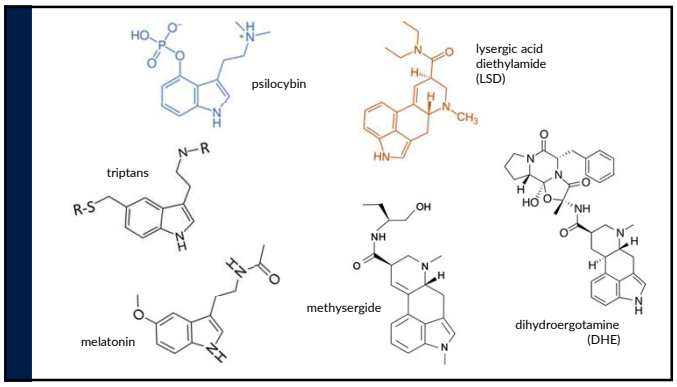
Migraine

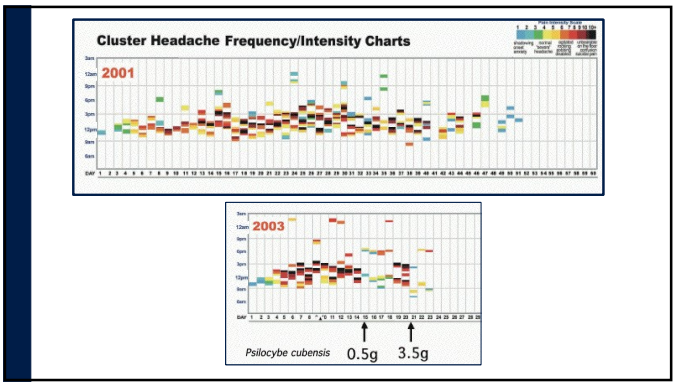
- 15% prevalence; F > M
- Year-round
- Migraine attacks
  - Moderate to severe unilateral or bilateral throbbing pain
  - Light/sound sensitivity, nausea/vomiting
  - Worsened by activity
  - Lasts 4 to 72 hours
  - Typically, no more than one/day
- Top worldwide disability rating
- US FDA-approved/cleared treatments ≈ two dozen

Cluster

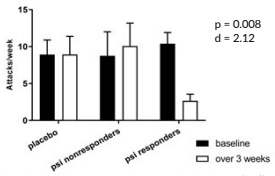
- 0.05 – 0.1% prevalence; M > F
- Annual cycles or year-round
- Cluster attacks
  - Severe or very severe unilateral, periorbital stabbing pain
  - Autonomic activation
  - Restlessness, self-injury
  - Lasts 15 min to 3 hours
  - Occurs up to 8 times daily
- AKA "suicide headache"
- US FDA-approved/cleared treatments = 3

SOURCE: Horton, 1952





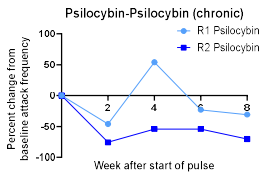
The psilocybin 'busting' regimen reduced attack frequency in some subjects. Responders (≥25% reduction) had a clear clinical effect.



- Patients with cluster headache per *ICHD-3b*, episodic with cycles ≥6 weeks or chronic, ≥1 attack/day; N = 14
- Randomized, double-blind, placebo-controlled design
- Three drug sessions 5 day apart each
- Psilocybin (10 mg/70 kg) or microcrystalline cellulose
- Attacks per week over 3 weeks compared to baseline

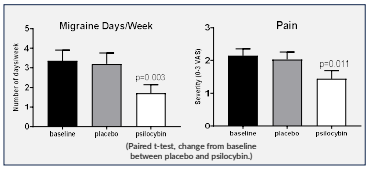
Schindler et al., *Headache*, in press

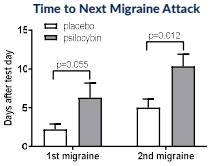
Round 2 (≥6 months later) will inform on repeating the pulse.



Exploratory Controlled Study of the Migraine-Suppressing Effects of Psilocybin

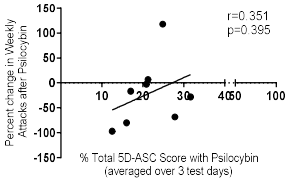
- Patients with migraine per ICHD-3b, ≥2 attacks/week; N = 10
- Double-blind, placebo-controlled, crossover design
- Two drug sessions 14 days apart
- Psilocybin (10 mg/70 kg) or microcrystalline cellulose
- Migraine days/week over 2 weeks compared to baseline



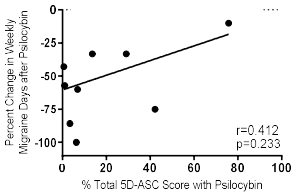


Mild psychedelic effects were reported on psilocybin test days; ratings did not correlate with changes in headache frequency.

Cluster Study

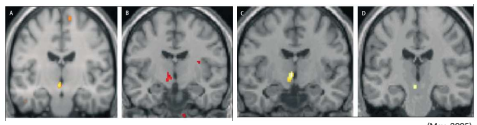


Migraine Study



Cluster Headache Pathophysiology

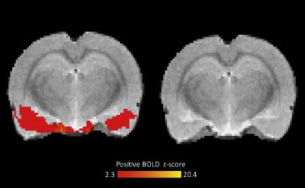
- Hypothalamus: posterior region
  (Bartsch et al., 2009; Cohen and Goadsby, 2006; May and Goadsby, 2001)



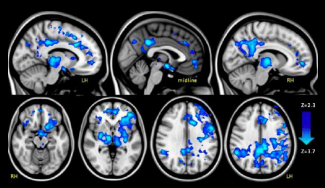
(May, 2005)

- Hormones: cortisol, prolactin, testosterone, melatonin, hypocretin
  (Barloese et al., 2015; Chazot et al., 1984; Ferrari et al., 1983; Romiti et al., 1983)
- Genetics: hypocretin R2, PACAP R, neprilysin
  (Bacchelli et al., 2016; Rainero et al., 2007)
- Inflammation: CGRP, TNFα, IL2, IL6
  (Goadsby and Edvinsson, 1994; Rozen and Swidan, 2007; Steinberg et al., 2011; Sarchielli et al., 2006)

The Hypothalamus as a Target for Psychedelics



2mg/kg psilocin



0.03 mg/kg psilocin

(Spain et al., 2015)

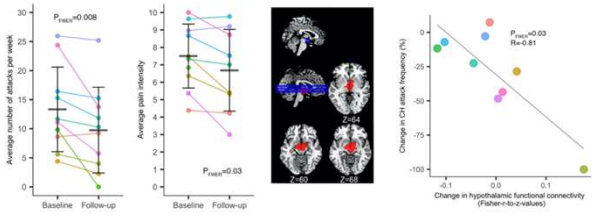
2mg intravenous psilocybin vs. placebo

(Carhart-Harris et al., 2012)

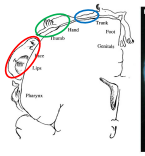
Psilocybin-induced reduction in chronic cluster headache attack frequency correlates with changes in hypothalamic functional connectivity

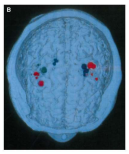
Martin K. Madsen,[1,2] Anja Sofie Petersen,[3] Dea S. Stenbæk,[1,4] Inger Marie Sørensen,[1] Harald Schiønning,[1] Tobias Fjeld,[1] Charlotte H. Nykjær,[1] Sara Marie Ulv Larsen,[1] Maria Grzywacz,[1] Tobias Mathiesen,[1] Ida L. Klausen,[1] Oliver Overgaard-Hansen,[1] Kristoffer Brendstrup-Brix,[1] Kristian Linnet,[5] Sys S. Johansen,[5] Patrick M. Fisher,[1] Rigmor H. Jensen,[1,6] Gitte M. Knudsen,[1,6]

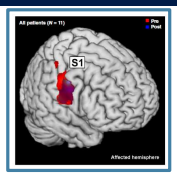
https://www.medrxiv.org/content/10.1101/2022.07.30.22277414v1



Aberrant neural reorganization in phantom limb syndrome



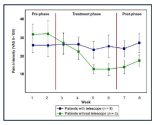




Combined MEG and 3D surface-rendered MRI of patient F.A. The unaffected right hemisphere shows three spots corresponding to the left face (red), hand (green) and upper arm region (blue).

Neuronal activity in somatosensory cortex during lip pursing task before (red) and after (blue) mirror therapy.

(Foell et al., 2014)



"...the adult mammalian brain has the latent capacity for a much more rapid functional reorganization and over a much greater spatial extent than previously suspected, a ***capacity that could conceivably be exploited for therapeutic purposes.****"*

(Ramachandran and Hirstein, 1998)

Phantom Limb Syndrome and Psychedelics

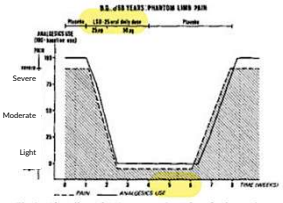


Fig 1.—The effect of LSD-25 on pain and analgesic use in a patient with phantom limb pain.

(Fanciullacci et al, 1977)

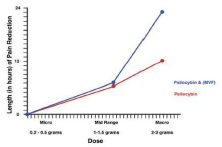


Figure 4. Length of pain reduction for psilocybin and (MVF) with psilocybin.

"...the psilocybin might both make the brain ***more receptive to mirror therapy*** *and make the pain reduction last longer or even disappear."*

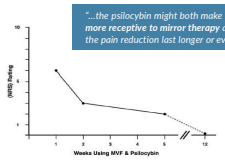


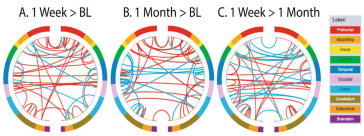
Figure 5. Pain ratings (Numeric Pain Rating Scale) across 12 weeks.

(Ramachandran et al, 2018)

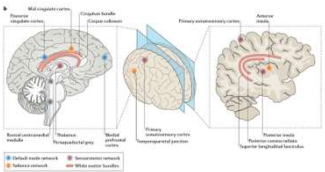
Neuroimaging Techniques With Potential Utility

- Functional MRI
  - Resting state functional connectivity (RSFC)
- Positron Emission Tomography (PET)
- Electroencephalo-graphy (EEG)
  - Lempel-Ziv complexity (LZc)
- Magnetoencephalo-graphy (MEG)

Key brain areas, resting state functional networks and white matter in which activity is often found to be abnormal in chronic pain.
(Davis et al., 2017)

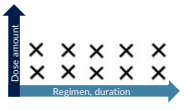


Longitudinal effects of a single high dose of psilocybin on the strength of static functional brain connectivity. Static functional connections (edges) that significantly increase (red lines) or decrease (blue lines) in strength. (Barrett et al., 2020)



Microdosing psilocybin for chronic pain: a case series

Microdosing psilocybin for chronic pain: a case series
Pain. 2022 Sept 5



Patient	Pain Source / Sx	Tx Type	Drug/Regimen	Outcomes	Other
DC 37 M	**Spinal injury** (T4 plegic) Thoracic, abdominal, leg searing, electrical pain	Acute	Psilocybin mushroom 5 grams	Near total pain relief for 8-10 hours	• Stopped tramadol, diazepam, cannabis
		Preventive	Psilocybin mushroom 50mg daily (6 months)	Pain reduced from 90-95% pain relief for 6 to 8 hours	• Denies withdrawal, rebound, tolerance • No change in baseline pain
ES 69 F	**CRPS** (left leg) Burning, cramp, spasms, weakness, allodynia, hyperalgesia, spread to right leg, depressive sx	Acute	Psilocybin mushroom 2 grams	Pain freedom for 18-20 hours	• Denies withdrawal, rebound, tolerance • No change in baseline pain
		Preventive	Psilocybin mushroom 500mg daily for 7-10 days, 2-3 day break for GI relief(1 year)	80% pain relief for 3-4 hours	
JP 40 F	**Low back pain** Stiff MSK pain and bilateral radicular pain	Acute	Psilocybin mushroom 1 gram + PT exercises	Pain freedom (for 2 weeks)	• Denies withdrawal, rebound, tolerance • Psilocybin alone produced some relief, but addition of PT sustained the effect
		Preventive	Psilocybin mushroom 1 gram every 6-8 weeks + PT exercises	As above - Baseline MSK pain reduced from 9→7 x 3 months Neuropathic pain resolved after 3rd dose	

Ongoing / Upcoming Clinical Trials in Chronic Pain

Condition	Design	Drug, dose, regimen	Primary Outcome(s) *	Location	NCT #
Cancer (and MDD)	OL	Psilocybin 25 mg Single session			
Cancer (hospice)	OL	Psilocybin 25 mg Single session, ps			
Cancer (demoralization, chronic pain)	OL	Psilocybin 25 mg Single session, ps multidisciplinary support			
Non-cancer Chronic Pain (on opioids)	OL	Psilocybin 25 mg Two sessions 2 w psychotherapy			
Fibromyalgia	R, DB, PC	Psilocybin 0.36 m dextromethorphe Single session			
Fibromyalgia	OL	Psilocybin (TRP-8 mg 2 wks later, p			
Fibromyalgia	CO	Psilocybin up to 2 (4 weeks apart); physical therapy			
Phantom limb pain	R, TB, PC	Psilocybin 25 mg Single session			
Lyme disease (post-treatment)	OL	Psilocybin 15 mg, Two sessions 2 w			
Low Back Pain	R, QB, PC	Psilocybin 1-25 m modafinil, placeb Single session, prep/monitor/int			

Ongoing / Completed / Upcoming Headache Clinical Trials

Condition	Design	Drug, dose, regimen	Primary Outcome(s) *	Location	NCT #
Cluster headache	R, DB, PC	Psilocybin 0.0143 mg/kg, 0.143 mg/kg, microcrystalline cellulose Three sessions about 5 days apart each	Change in cluster attack frequency over 2 months	VACHS / Yale University	02981173
Chronic cluster headache	R, DB, PC, CO	LSD 100 µg, Placebo Three sessions within 3 weeks, then CO at 8 wks	Change in cluster attack frequency over 8 wks	University Hospital, Basel	03781128
Chronic cluster headache	OL	Psilocybin 0.14 mg/kg Three doses 1 wk apart each	Change in cluster attack frequency over 4 wks; resting state functional MRI	Copenhagen University Hospital	04280055
Chronic cluster headache	R, DB, PC	LSD base 25 µg or placebo Q3 days for 3 weeks	Change in cluster attack frequency in week 3	Canisius-Wilhelmina Hospital, Netherlands	05477459
SUNHA *WITHDRAWN*	OL	Psilocybin, 3 ascending doses	Change in headache attack frequency out to 39 days	Kings College London	04905121
Chronic post-traumatic (concussion) headache *COMPLETED*	R, DB, PC, CO	Psilocybin 0.0143 mg/kg, 0.143 mg/kg, microcrystalline cellulose Two different doses, given 2 wks apart	Change in headache attack frequency over 2 wks	VACHS / Yale University	03806985
Migraine *COMPLETED*	R, DB, PC	Psilocybin 10mg, diphenhydramine 25mg Two sessions 1 wk apart, randomized to receive psilocybin 0, 1, or 2 times	Change in migraine attack frequency over 2 months	VACHS / Yale University	04218539

Summary

1. Clinical psychedelic research in numerous psychiatric and neurological conditions has spanned decades and includes headache and pain disorders.
2. The preventive and transitional effects of psychedelics are what make the drug class unique and where research has been focused.
3. Drug doses, regimens, and protocols vary among different headache and pain disorders to best target the disorder.
4. The mechanisms of action of psychedelics in headache and pain disorders remain unknown but might involve neurobiological processes relevant to those conditions.

Knowledge Check

Classic psychedelics include which of the following compounds?

A. LSD, psilocybin, mescaline, MDMA (ecstasy), ketamine

B. LSD, psilocybin, mescaline, MDMA (ecstasy), cannabis

C. LSD, psilocybin, mescaline

D. LSD, psilocybin, ketamine

Knowledge Check

Classic psychedelics include which of the following compounds?

A. LSD, psilocybin, mescaline, MDMA (ecstasy), ketamine ✗

B. LSD, psilocybin, mescaline, MDMA (ecstasy), cannabis ✗

C. LSD, psilocybin, mescaline ✓

D. LSD, psilocybin, ketamine ✗

Knowledge Check

The clinical effects of classic psychedelics in cluster headache are reported for:

A. Abortive use only

B. Preventive/transitional use only

C. Both abortive and preventive/transitional use

D. A negative study showed there are no clinical effects

Knowledge Check

The clinical effects of classic psychedelics in cluster headache are reported for:

A. Abortive use only ✗

B. Preventive/transitional use only ✗

C. Both abortive and preventive/transitional use ✓

D. A negative study showed there are no clinical effects ✗

Knowledge Check

Reports of self-administration of classic psychedelics in chronic pain conditions reveal what sort of dosing regimen(s)?

A. Chronic daily dosing

B. A few large doses

C. Intermittent dosing

D. All of the above

Knowledge Check

Reports of self-administration of classic psychedelics in chronic pain conditions reveal what sort of dosing regimen(s)?

A. Chronic daily dosing ✗

B. A few large doses ✗

C. Intermittent dosing ✗

D. All of the above ✓

Knowledge Check

In designing future clinical trials in headache and pain disorders, which of the following should be considered?

A. Drug doses and protocols should be relevant for the specific condition being studied.

B. Psychotherapy should be included in all studies.

C. High doses are required for clinical efficacy.

D. B and C

Knowledge Check

In designing future clinical trials in headache and pain disorders, which of the following should be considered?

A. Drug doses and protocols should be relevant for the specific condition being studied. ✔

B. Psychotherapy should be included in all studies ✗

C. High doses are required for clinical efficacy. ✗

D. B and C ✗

Thank You!

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Course Wrap Up
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