

Psychedelika-assistierte Therapie mit Ayahuasca und DMT

Potenziale und Herausforderungen

Psychiatrisches Kolloquium PUK | Freitag, 5. April 2024



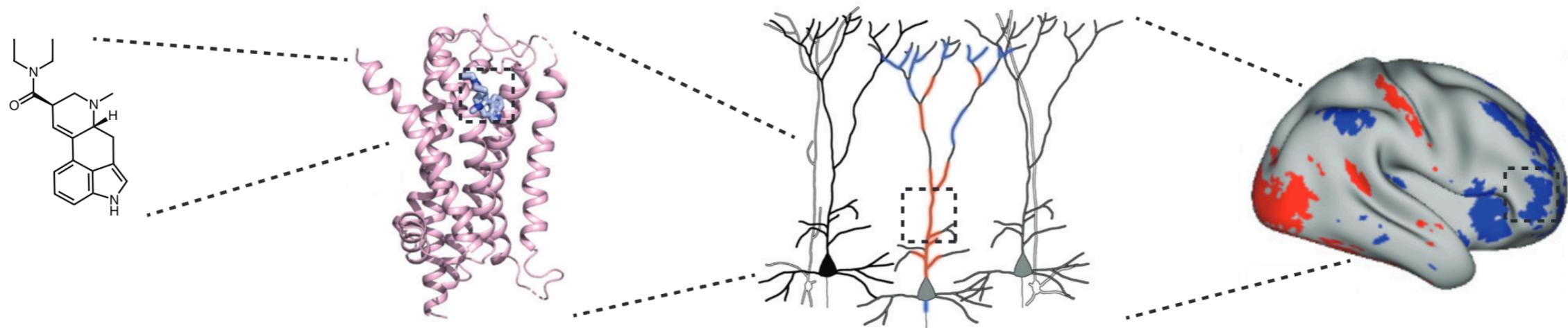
Dr. sc. Dr. med. Milan Scheidegger, MA HPK

Psychedelic Research & Therapy Development

Klinik für Psychiatrie, Psychotherapie und Psychosomatik, PUK Zürich

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Psychedelika - Potential für Psychiatrie



Psychedelic

Molecular

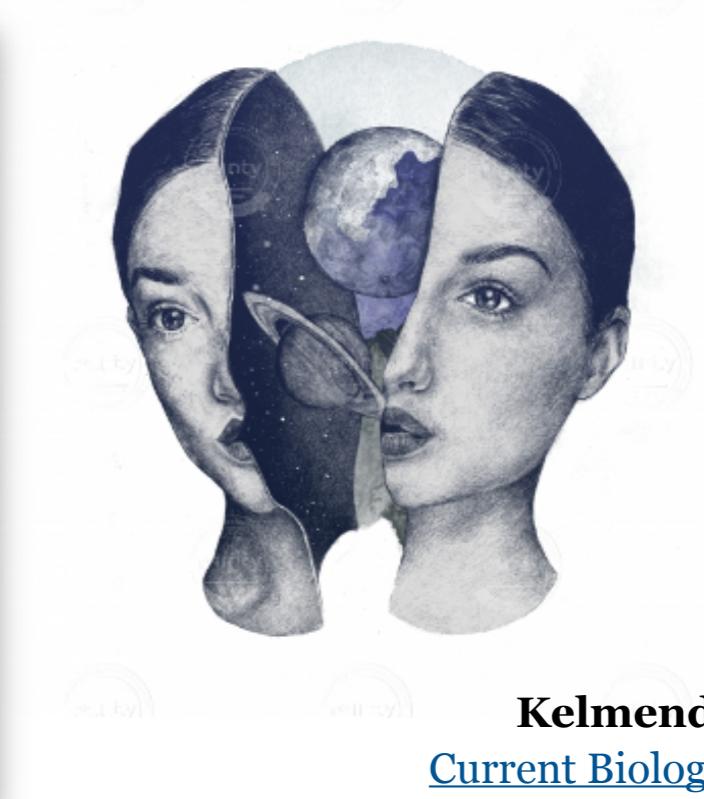
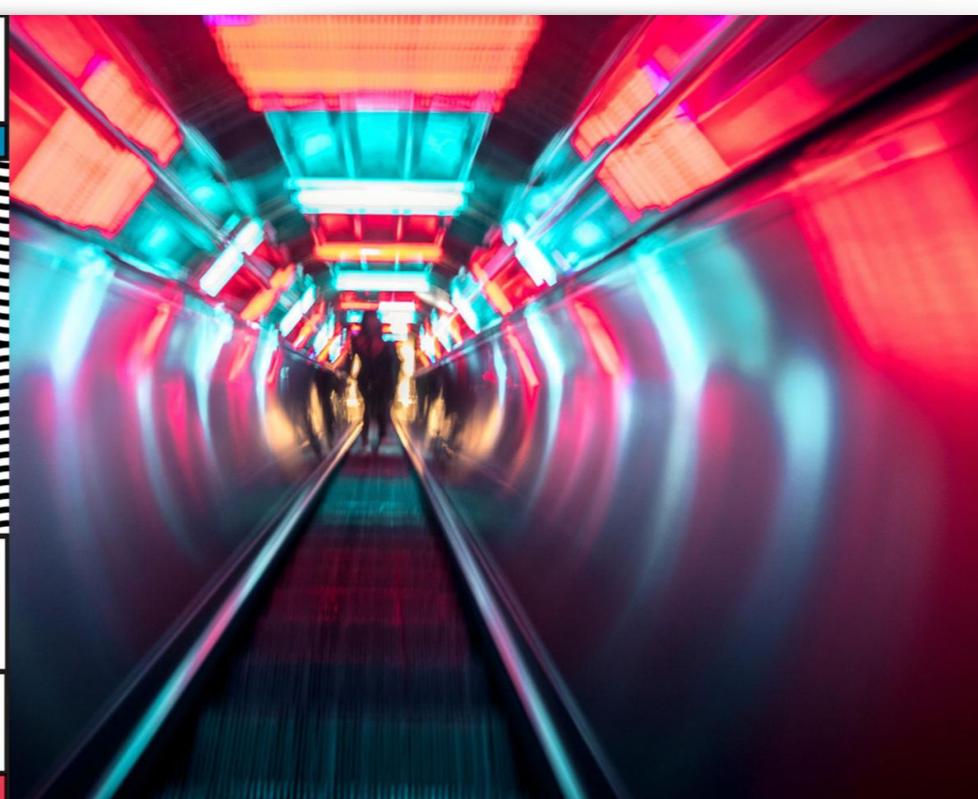
Serotonin receptors
(5-HT_{2A}, 5-HT_{2C}, 5-HT_{1A}, ...)
Signal transduction pathways

Cellular and circuit

Neural plasticity
(structural remodeling,
gene expression, ...)
Spiking activity dynamics

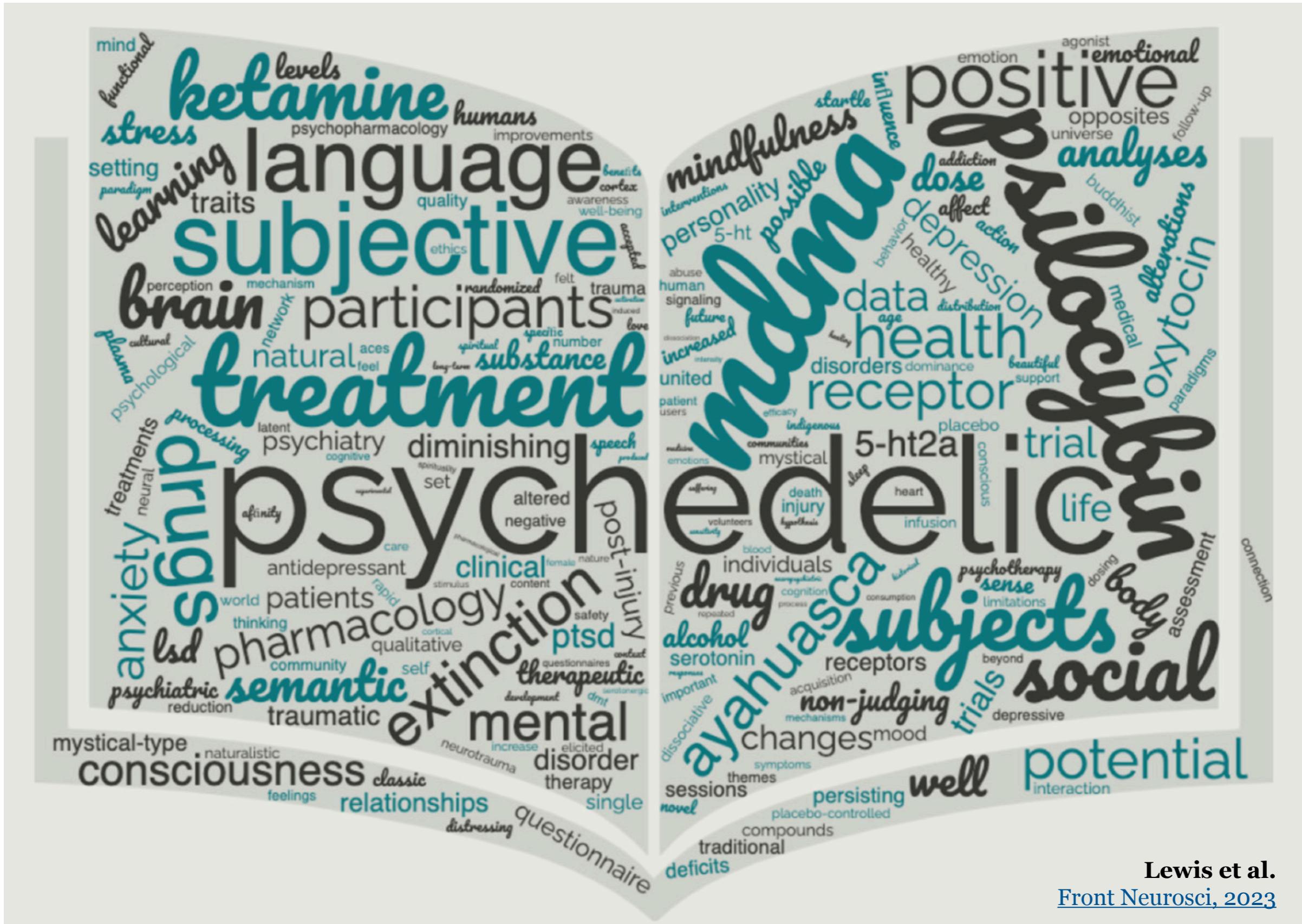
Network

Regional suppression
(default mode network)
Functional connectivity



Kelmendi et al.
[Current Biology, 2022](#)

Psychedelika - Potential für Psychiatrie



Psychedelics Research

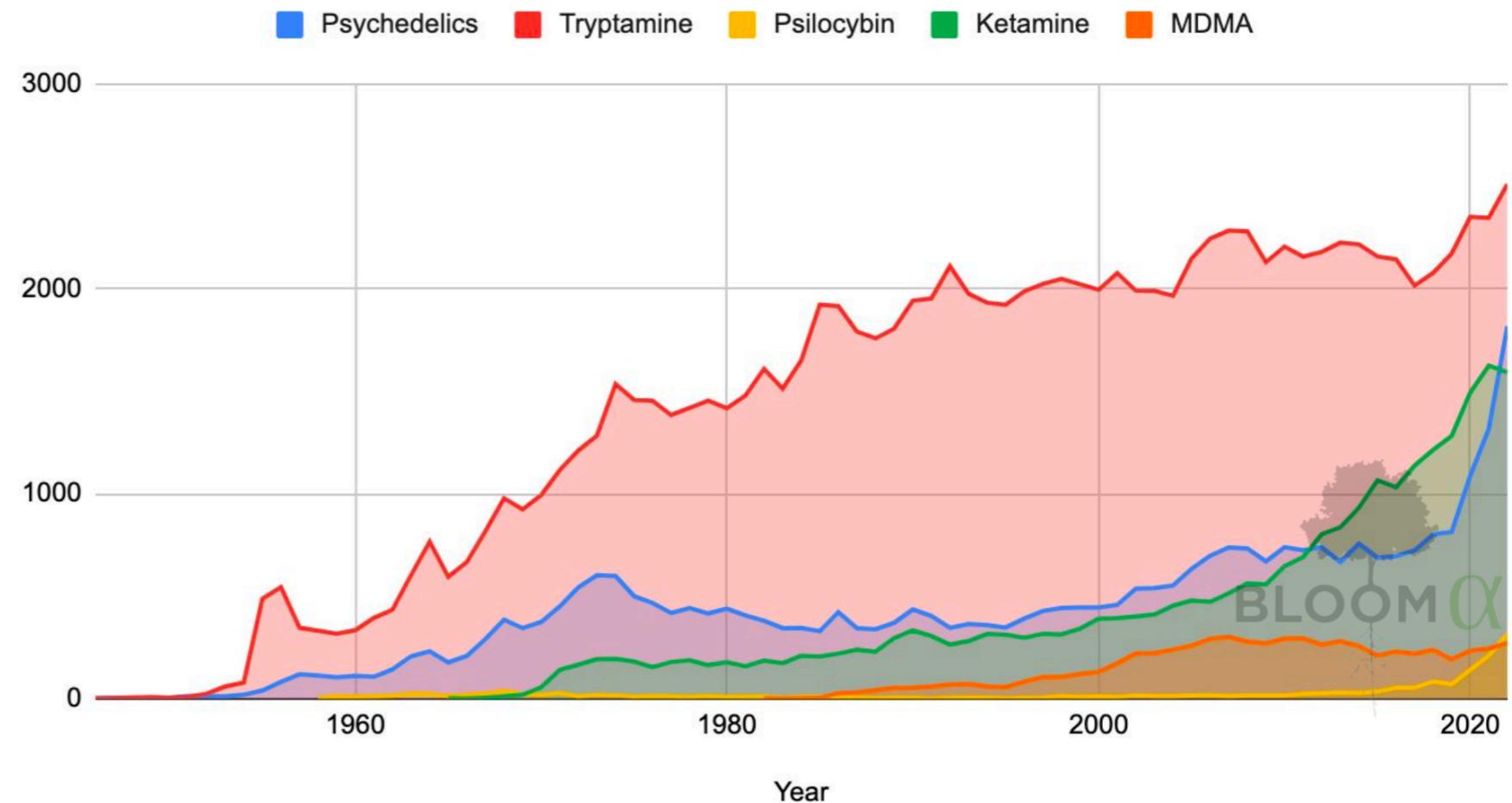


High hopes

Psychedelic drugs fell from grace in the 1960s. Now, scientists are rediscovering them as potential treatments for a range of illnesses

By Kai Kupferschmidt

Number of Medical Psychedelics Publications



Psychedelics Research

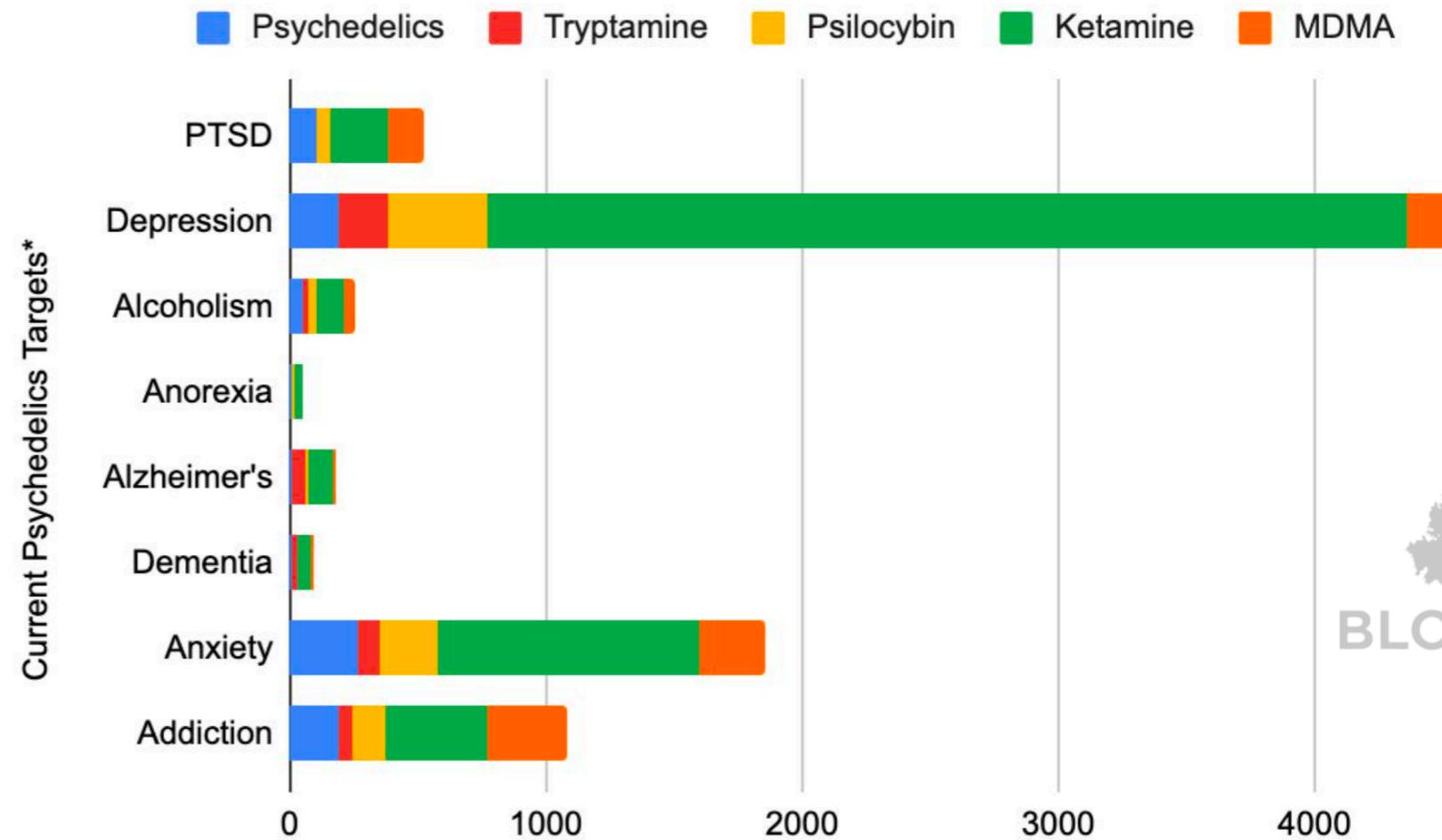


High hopes

Psychedelic drugs fell from grace in the 1960s. Now, scientists are rediscovering them as potential treatments for a range of illnesses

By Kai Kupferschmidt

Total Research Volumes by Main Psychedelics Targets



Psychedelika - Wirksamkeitsstudien

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NEWS FEATURE | 19 April 2023

US could soon approve MDMA therapy – opening an era of psychedelic medicine

Perceptions have shifted dramatically in the past few years on the therapeutic value of illicit drugs such as ecstasy. But questions still linger about what FDA approval might look like.

Sara Reardon

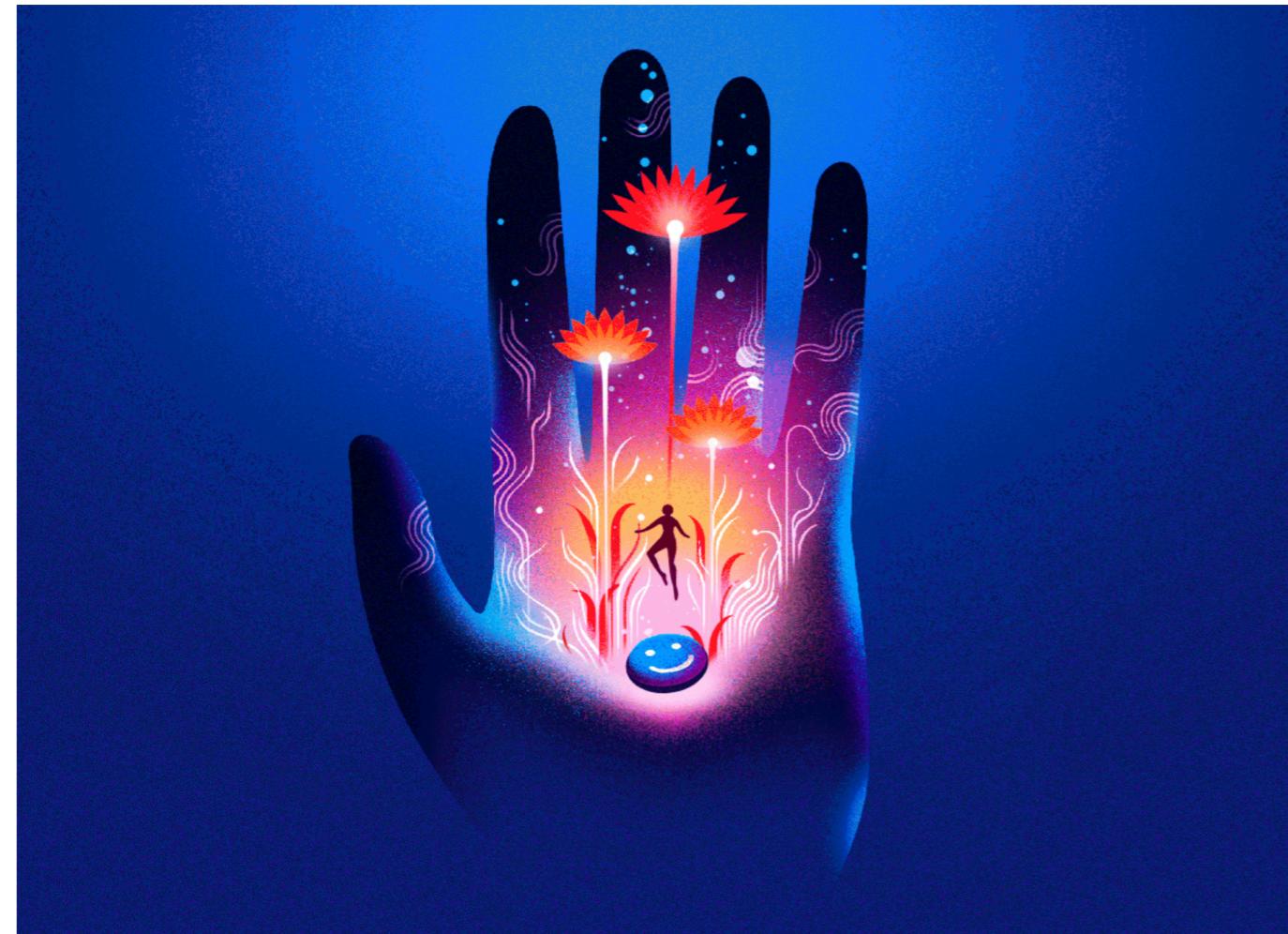


Illustration by Adrià Voltà

RESPONSE TO MDMA THERAPY

Results from a phase III clinical trial for MDMA therapy for post-traumatic stress disorder in 90 adults found that approximately twice the number of participants who received the drug with therapy experienced a loss of clinical diagnosis or remission, compared with those who received a placebo with therapy.

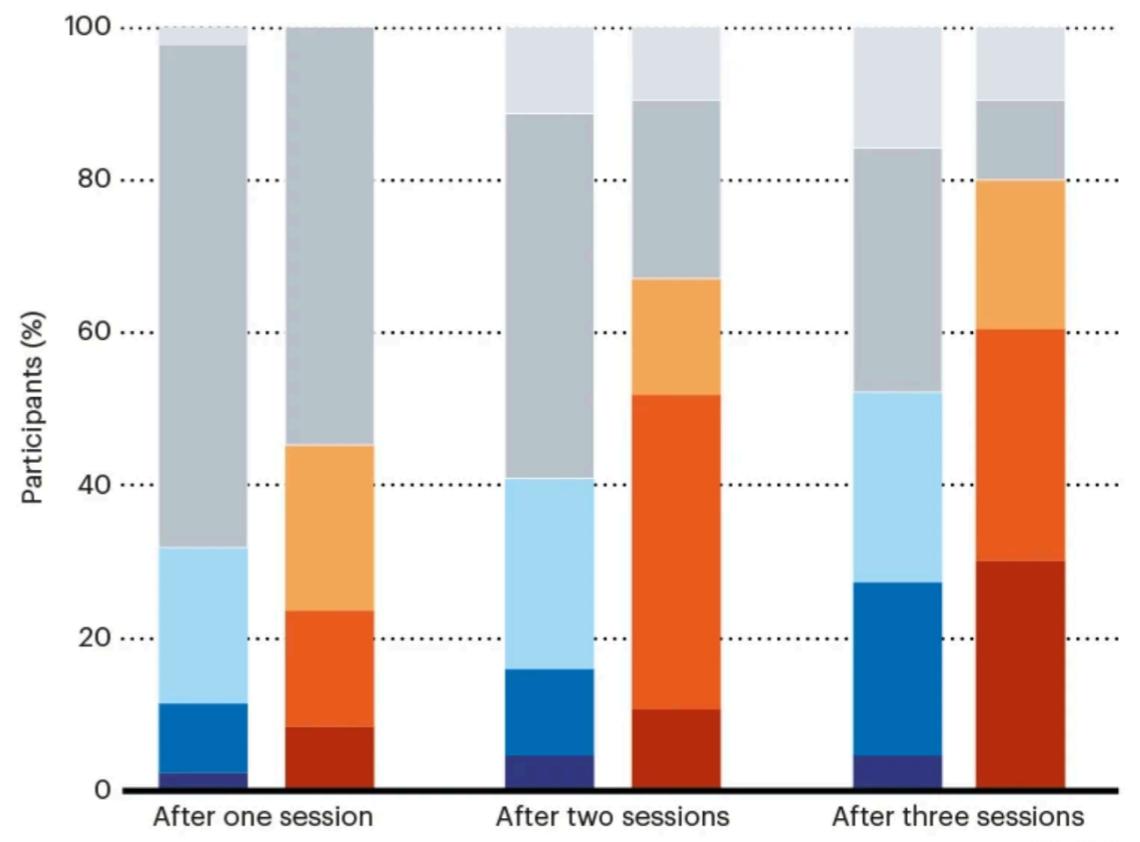
Placebo with therapy

■ Responders ■ Loss of diagnosis ■ Remission

MDMA-assisted therapy

■ Responders ■ Loss of diagnosis ■ Remission

■ Withdrawals ■ Non-responders



©nature

Mitchell et al.
[Nature Med, 2021](#)

Psychedelika - Wirksamkeitsstudien

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812

NOVEMBER 3, 2022

VOL. 387 NO. 18

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

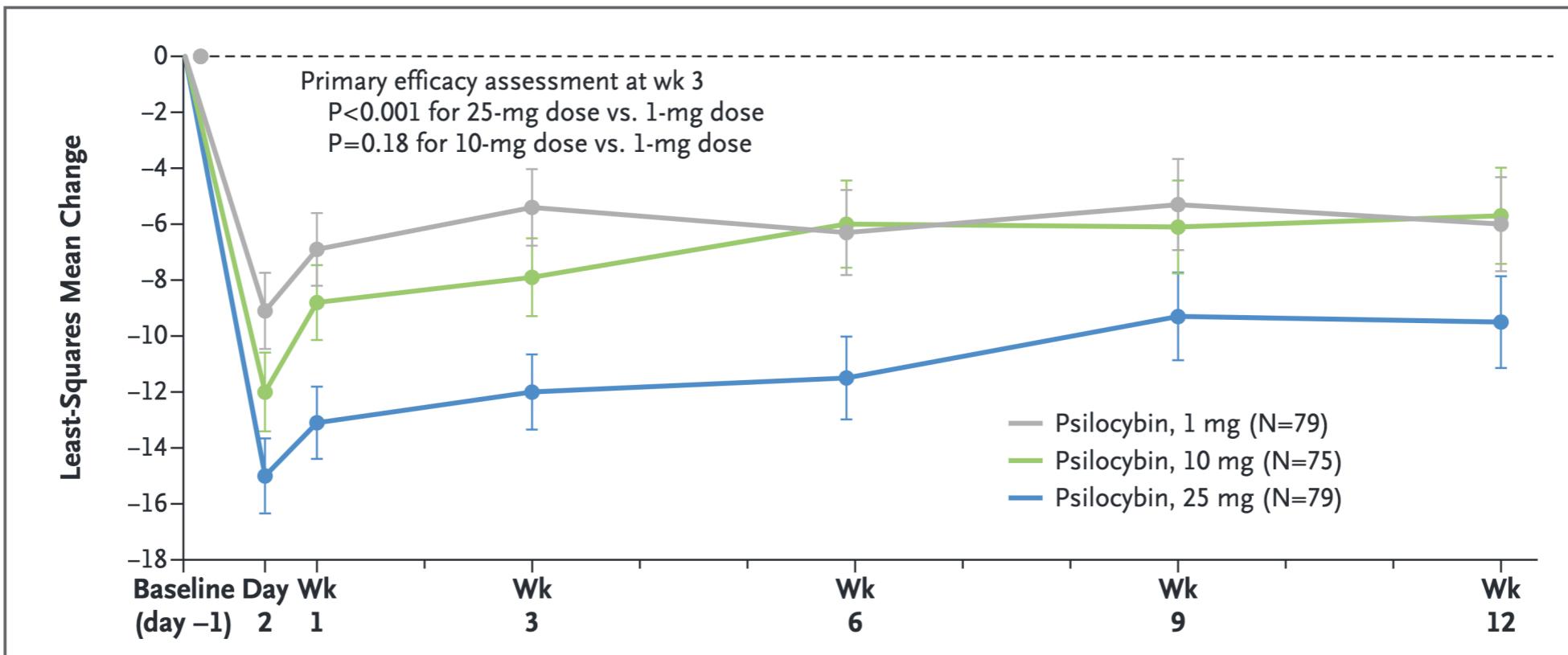


Figure 2. Change from Baseline in MADRS Total Score (Modified Intention-to-Treat Population).

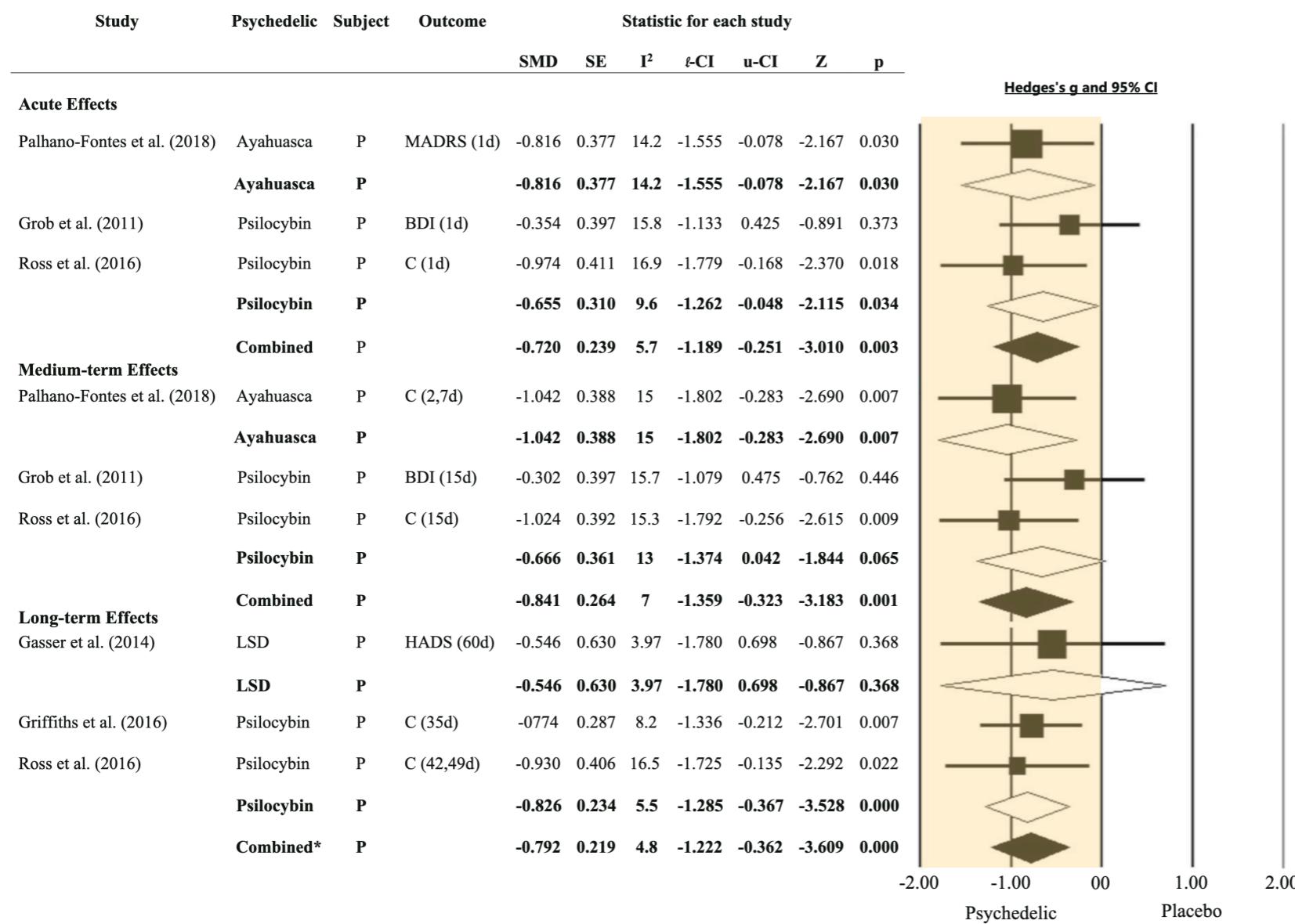
Total scores on the Montgomery–Åsberg Depression Rating Scale (MADRS) range from 0 to 60, with higher scores indicating greater severity of depression. I bars represent standard errors.

Psychedelika - Wirksamkeitsstudien

Classic serotonergic psychedelics for mood and depressive symptoms: a meta-analysis of mood disorder patients and healthy participants

Nicole L. Galvão-Coelho^{1,2,3,4,5}  · Wolfgang Marx⁶ · Maria Gonzalez⁴ · Justin Sinclair⁴ · Michael de Manincor⁴ · Daniel Perkins⁷ · Jerome Sarris^{4,8}

Effects of Psychedelics on Depressive Symptoms

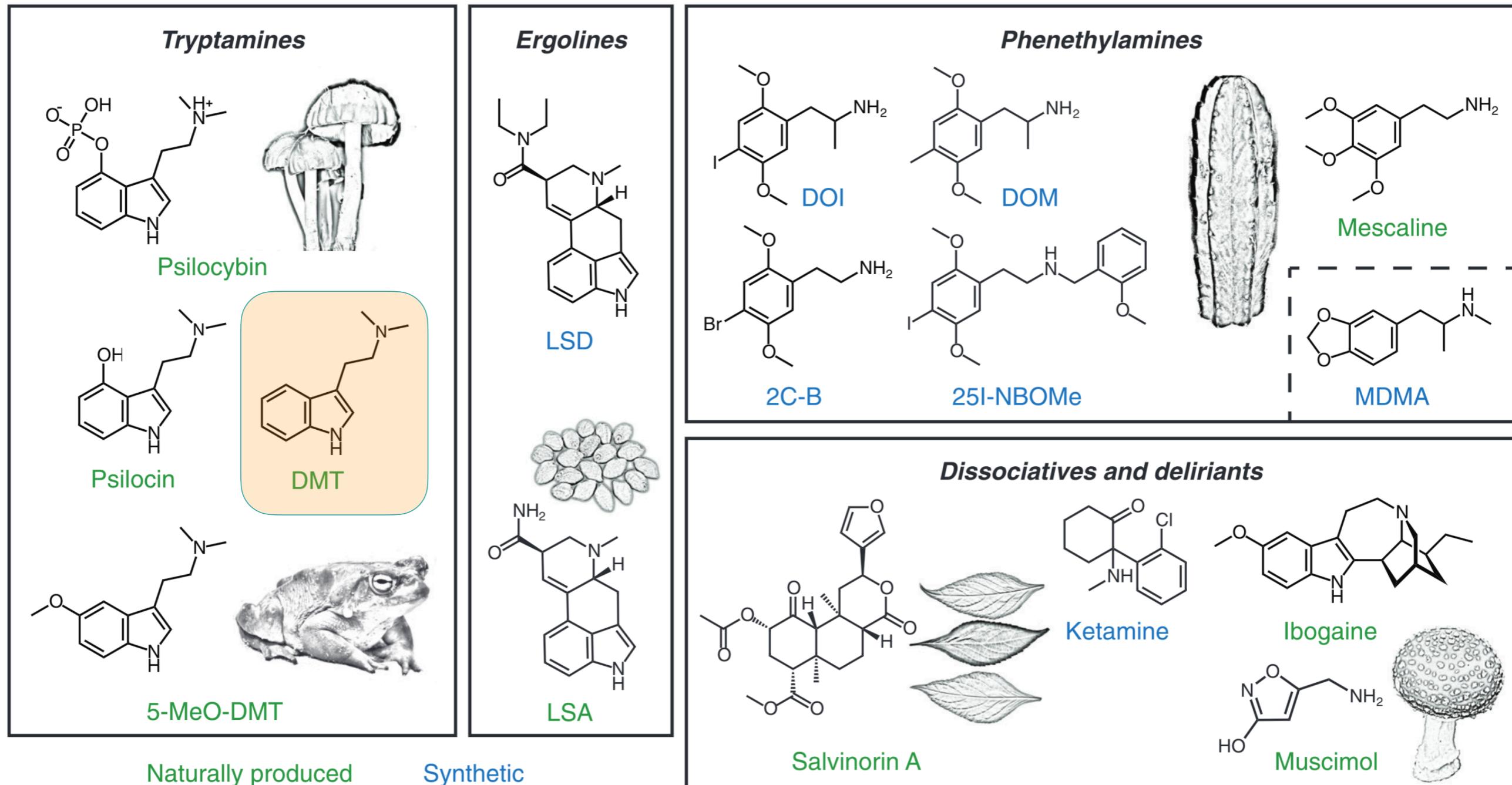


Some meta-analyses suggest that psychedelics might actually be more effective in reducing symptoms of depression and anxiety compared to conventional antidepressants in terms of their effect size.

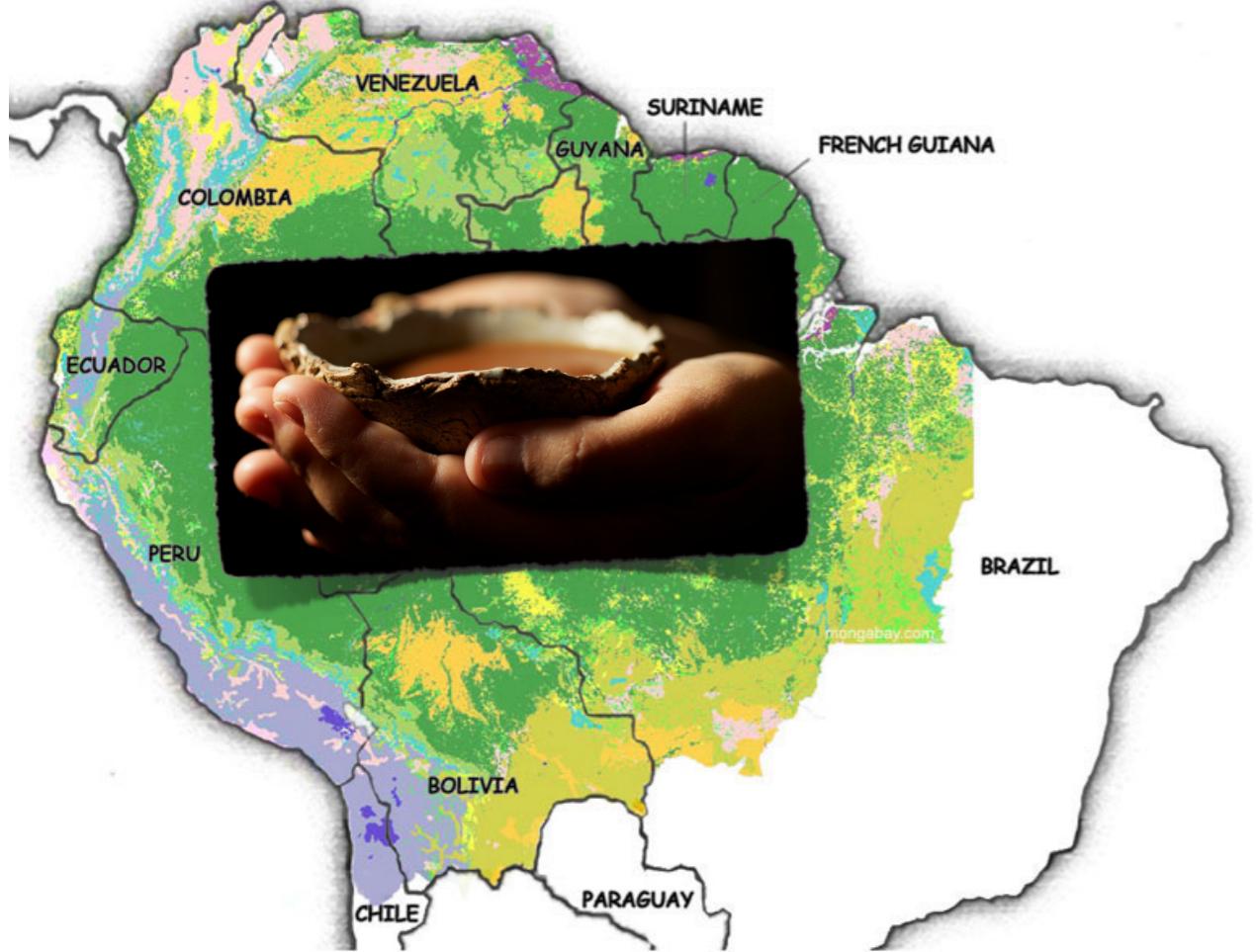
It is plausible that the reported effectiveness of psychedelics in clinical trials might undergo revisions as more comprehensive, diverse, and long-term studies in larger sample sizes are conducted.

Galvão-Coelho et al.
Psychopharmacology, 2021

Psychedelika - Wirkstoffklassen



Ayahuasca - Indigene Pflanzenmedizin



- Ritueller Gebrauch von Ayahuasca als Pflanzenmedizin im Amazonas
- Induktion veränderter Bewusstseinszustände (Grob, McKenna et al. 1996)



JOSH COCHRAN

Ayahuasca, used for centuries in South American jungles, is booming in the U.S.

Illustration by Bjørn Lie



Ayahuasca - Ethnobotanik

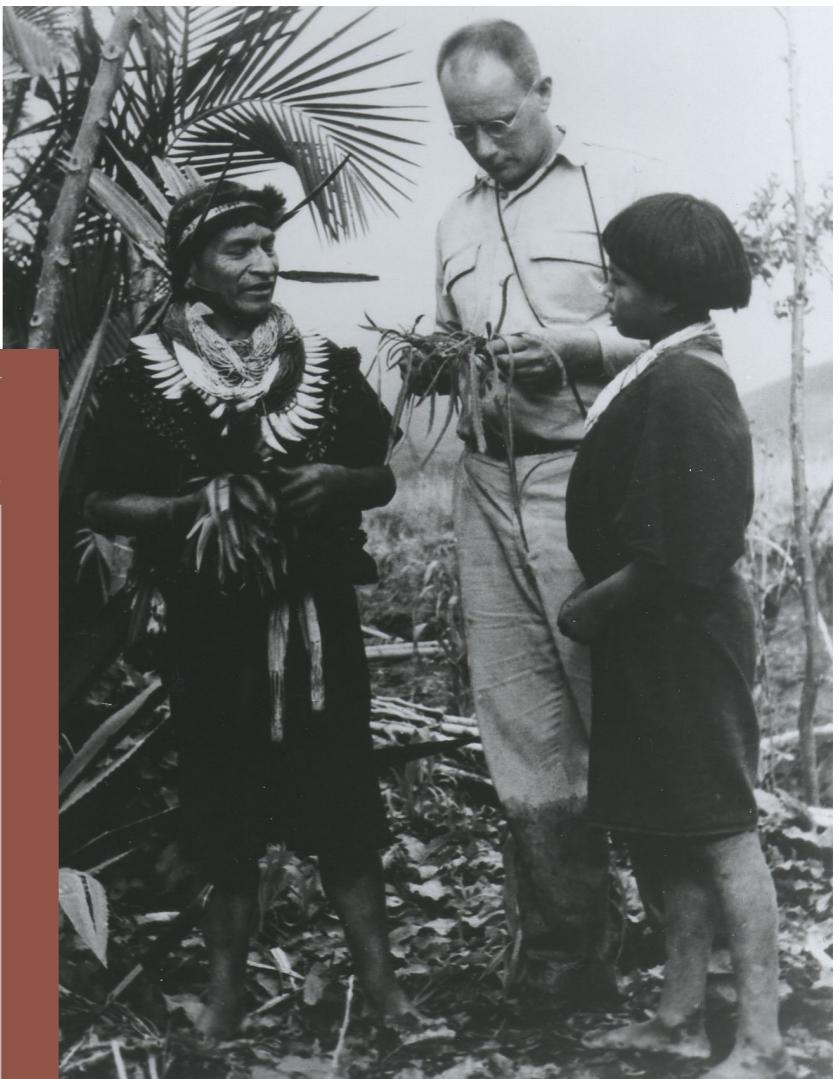
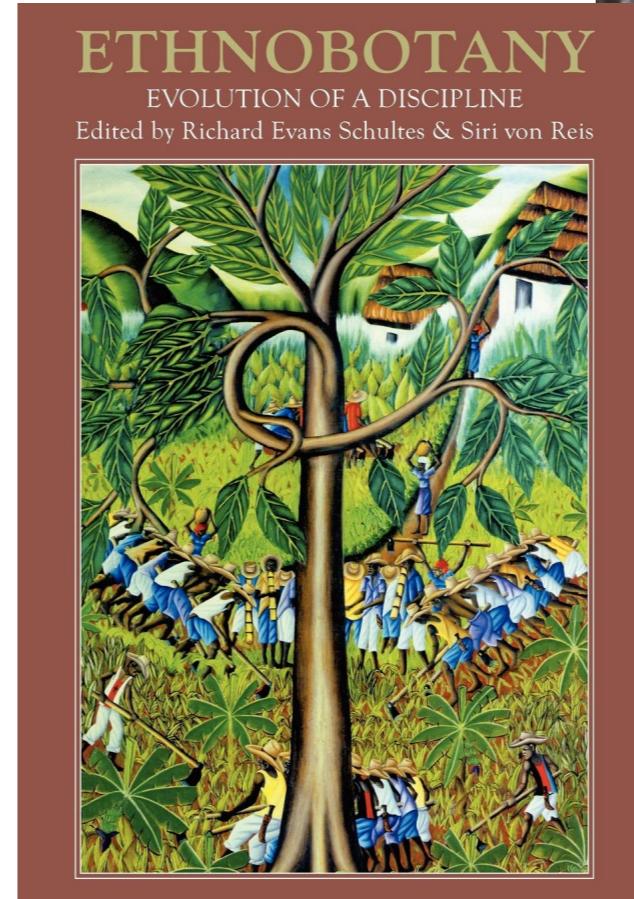
Hallucinogens of Plant Origin

Interdisciplinary studies of plants sacred in primitive cultures yield results of academic and practical interest.

Richard Evans Schultes



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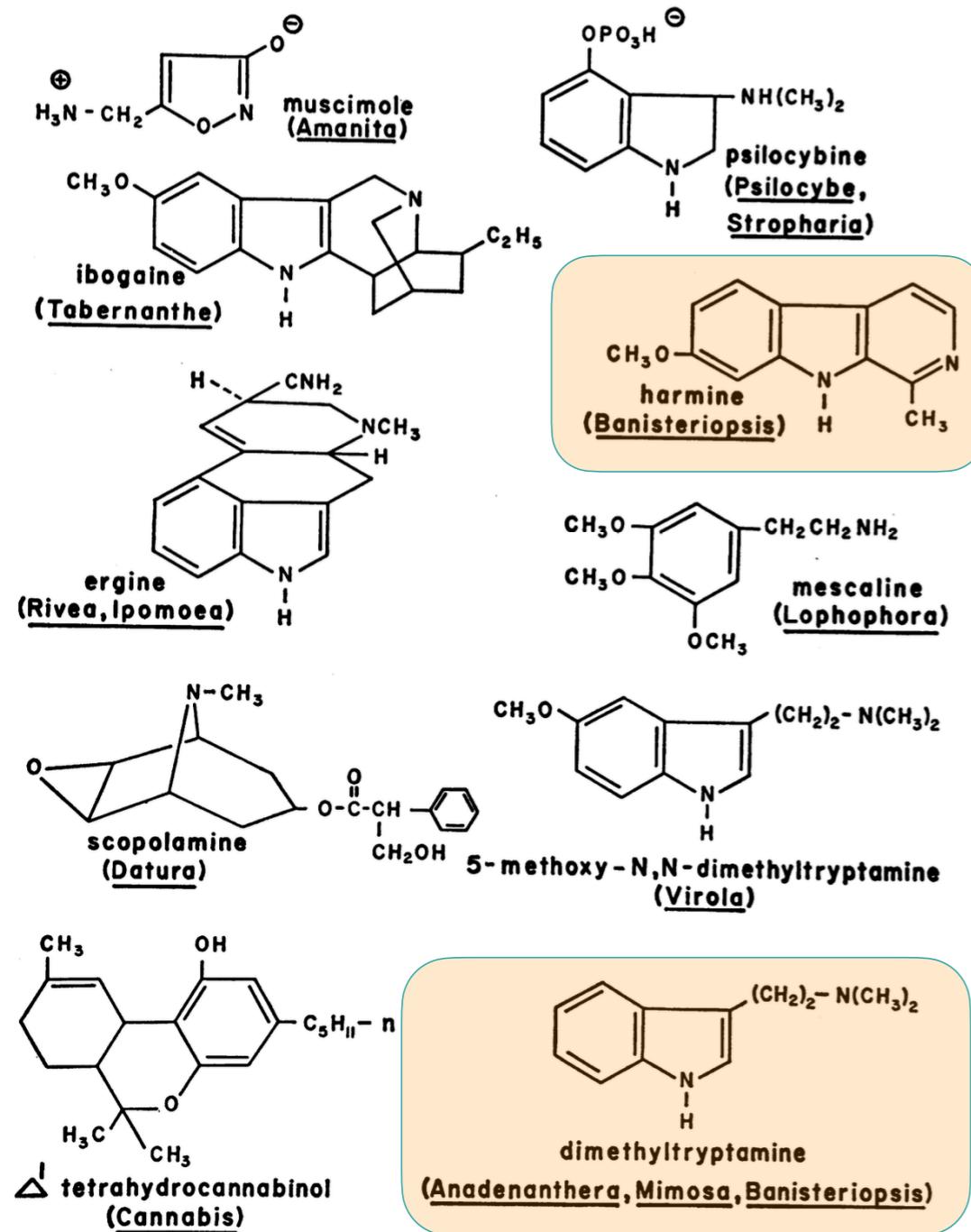


Science
AAAS

Schultes
[Science, 1969](#)

Fig. 5. A witch doctor of the Noanama tribe holding trunk and leaves of the dapá plant (*Banisteriopsis* sp.) from which an hallucinogenic drink is prepared. Near mouth of Calima River, San Juan drainage area, Pacific Coast, Colombia. [Photograph by G. Reichel-Dolmatoff]

Ayahuasca - Ethnobotanik



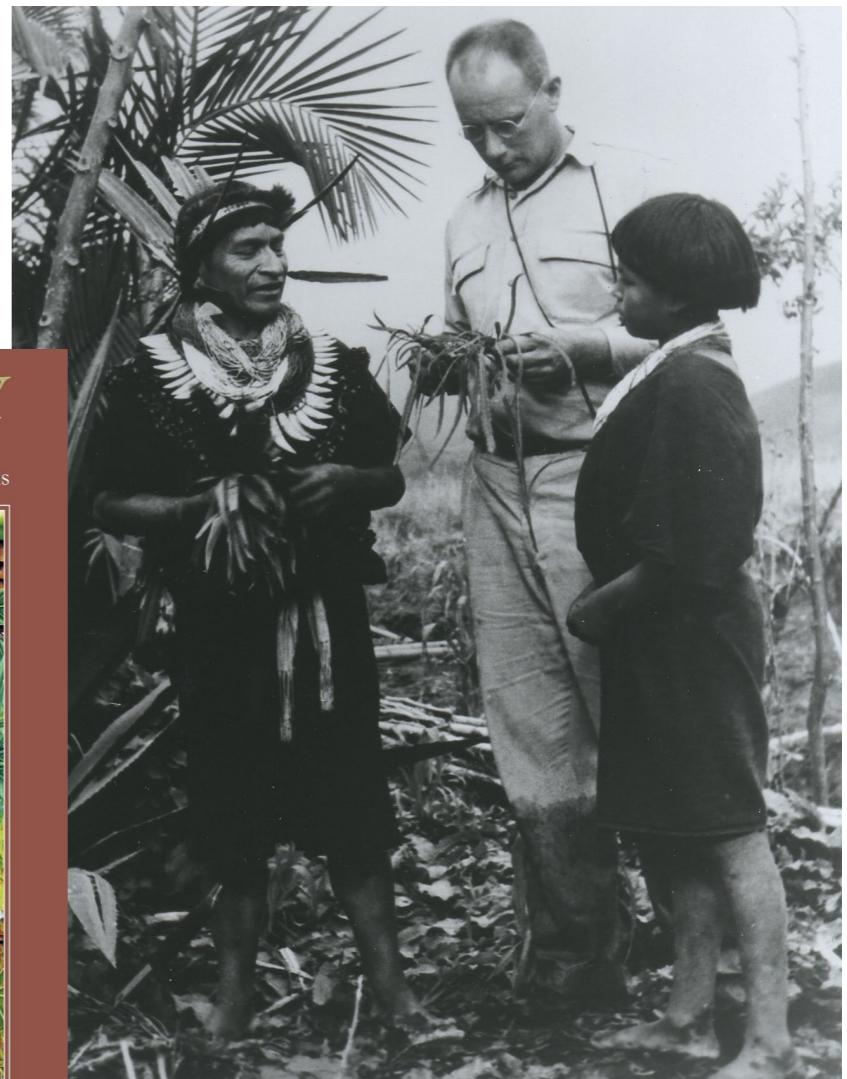
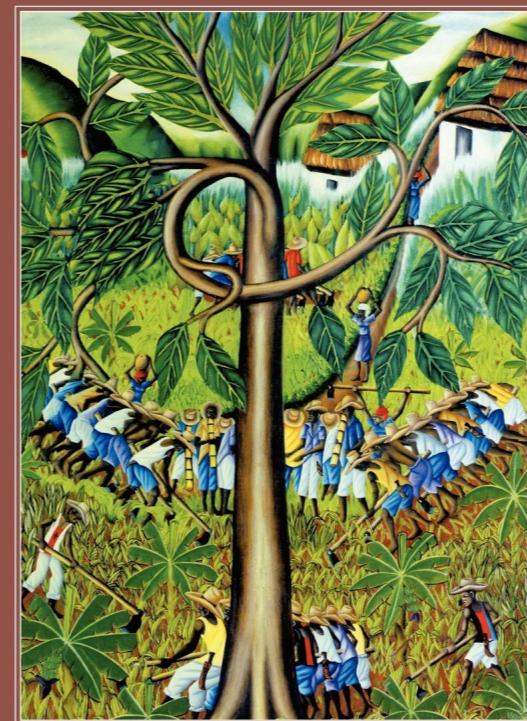
Hallucinogens of Plant Origin

Interdisciplinary studies of plants sacred in primitive cultures yield results of academic and practical interest.

Richard Evans Schultes

ETHNOBOTANY

EVOLUTION OF A DISCIPLINE
Edited by Richard Evans Schultes & Siri von Reis



Science
AAAS

Schultes
[Science, 1969](#)

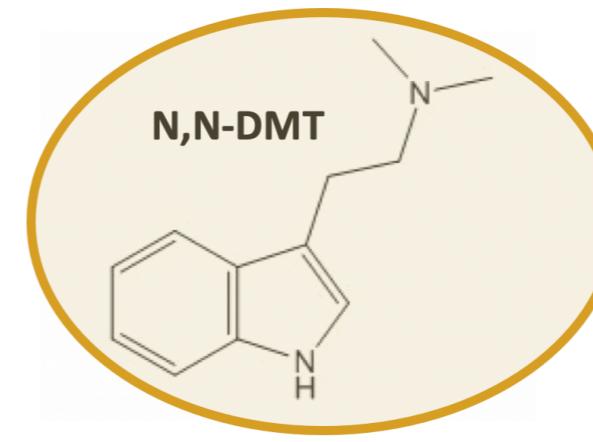
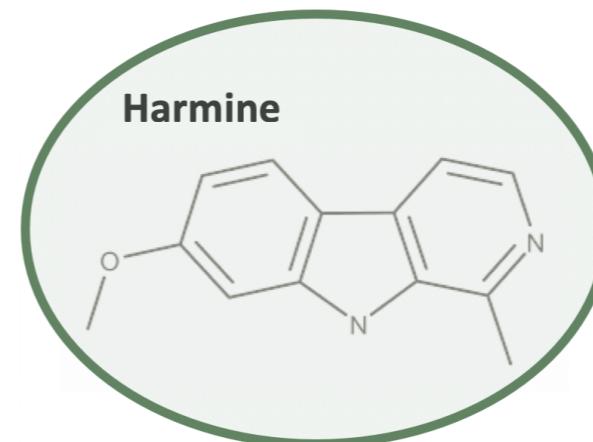
Fig. 1. Main hallucinating constituents of psychotomimetic plants.

Ayahuasca - Ethnobotanik



Beta-Carboline (z.B. Harmin, Harmalin, THH, etc.)

- MAO-A Hemmer (reversibel)
- hemmen Abbau von N,N-DMT sowie 5-HT und NA

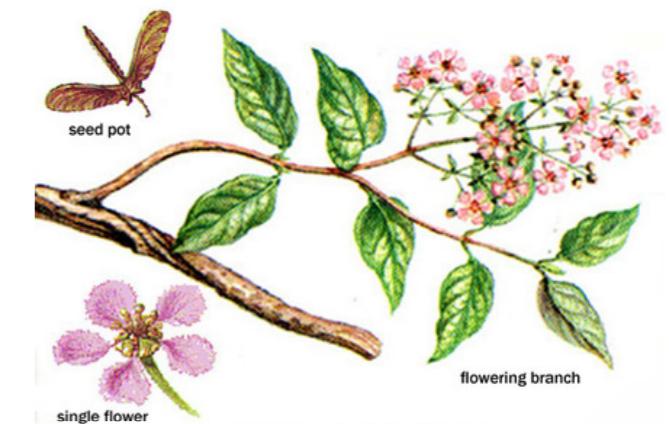


N,N-Dimethyltryptamin (N,N-DMT)

- oral inaktiv (Abbau durch GI-MAO-A)
- oral aktiv in Kombination mit MAO-A Hemmern
- Affinität an 5-HT_{1A}/2A/2C, D₁₋₃, alpha_{1A}/2A, TAAR1, H₁, SERT, DAT, NET

Carbonaro et al.
[Brain Res Bull](#), 2016

Banisteriopsis Caapi



Psychotria Viridis



Ayahuasca - Indigener Gebrauch

Chemical evidence for the use of multiple psychotropic plants in a 1,000-year-old ritual bundle from South America

Melanie J. Miller^{a,b,1}, Juan Albarracín-Jordan^c, Christine Moore^d, and José M. Capriles^{e,1}

^aDepartment of Anatomy, University of Otago, Dunedin 9016, New Zealand; ^bArchaeological Research Facility, University of California, Berkeley, CA 94720;

^cInstituto de Investigaciones Antropológicas y Arqueológicas, Universidad Mayor de San Andrés, La Paz, Bolivia; ^dImmunalysis Corporation, Pomona, CA 91767; and ^eDepartment of Anthropology, The Pennsylvania State University, University Park, PA 16802

Edited by Linda R. Manzanilla, Universidad Nacional Autónoma de México, Mexico, D.F., Mexico, and approved April 9, 2019 (received for review February 6, 2019)

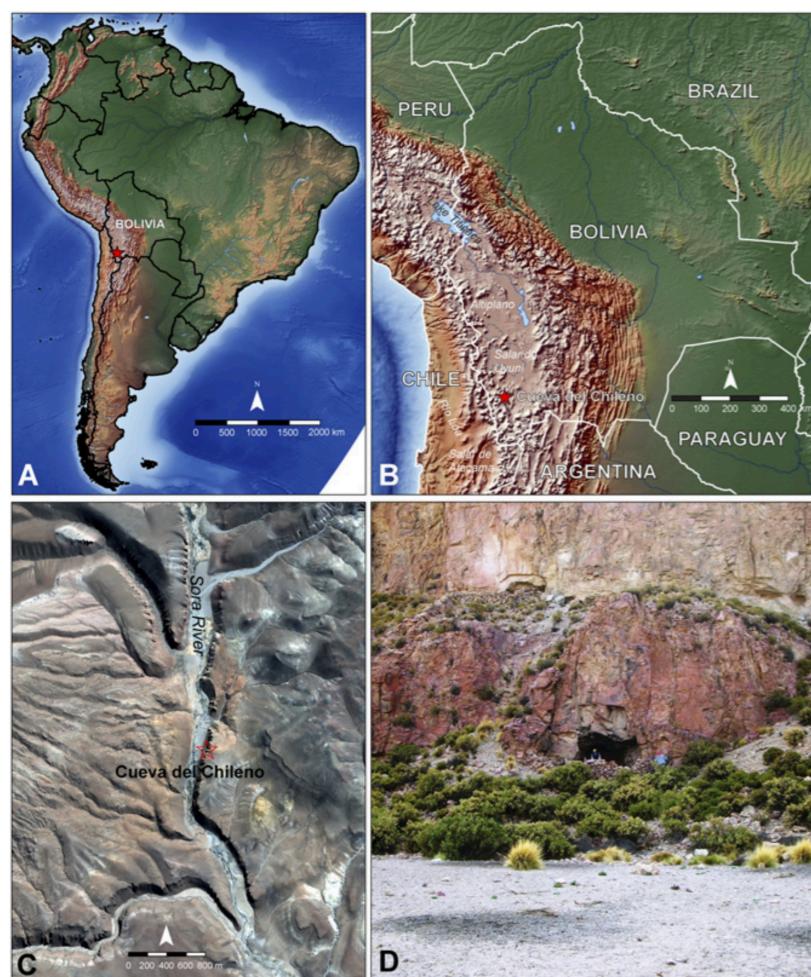


Fig. 1. The study area is located in the south-central Andes (A), in the Lipez highlands of southwestern Bolivia (B). An aerial view of the Sora River Valley (C) shows Cueva del Chileno on its eastern side (c/o GeoEye Foundation), and a photograph (D) of the exterior of the rock shelter during excavation.

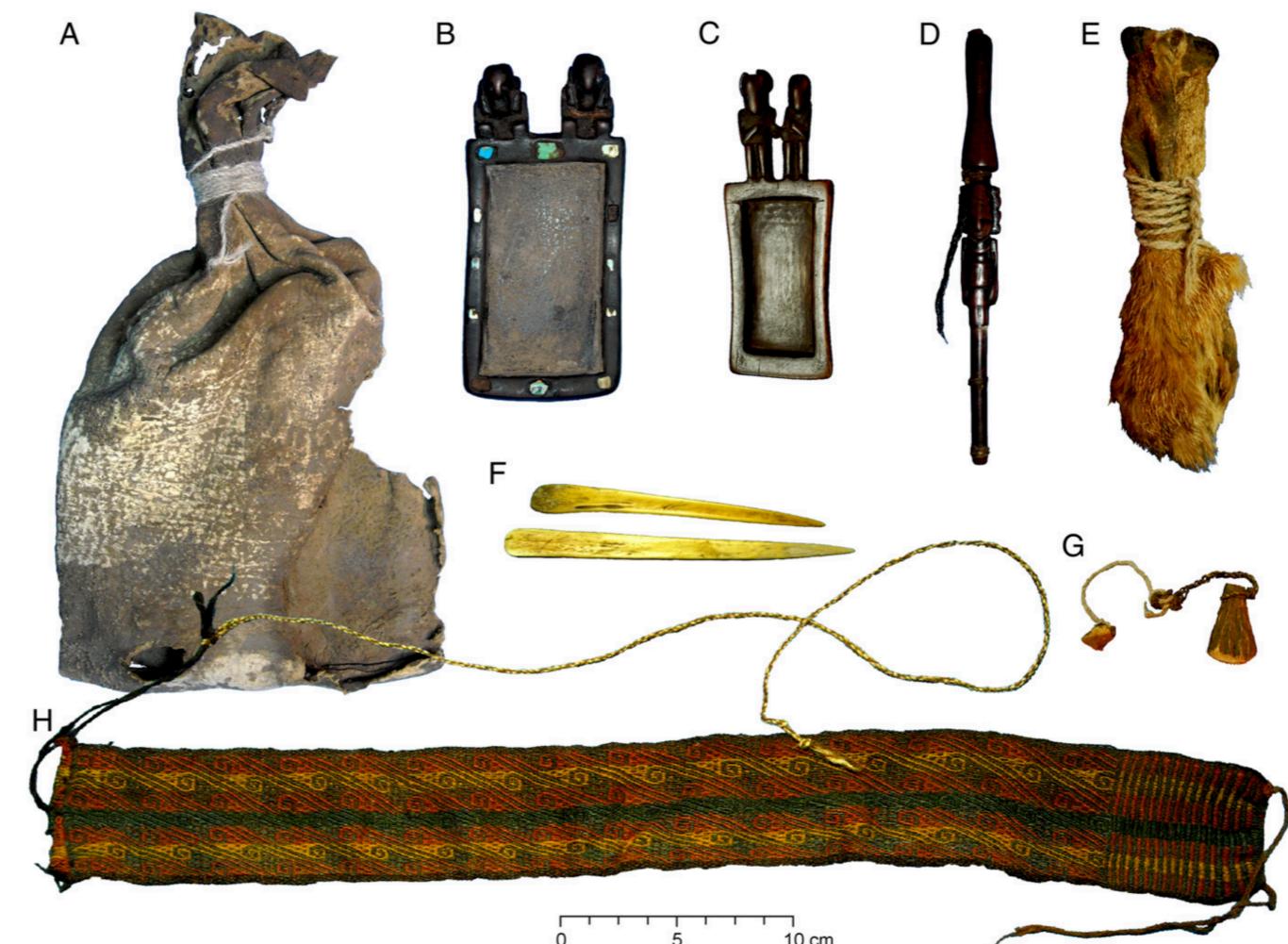


Fig. 2. The Cueva del Chileno ritual bundle consisting of: outer leather bag (A), expertly carved and decorated wooden snuffing tablets with anthropomorphic figurines (B and C), intricate anthropomorphic snuffing tube with two human hair braids attached to it (D), animal-skin pouch constructed of three fox snouts (*L. culpeus*) stitched together (E), two camelid (*L. glama*) bone spatulas (F), two small pieces of dried plant material attached to wool and fiber strings (G), and a polychrome woven textile headband (H). Artifacts (E and G) were tested using LC-MS/MS analysis.

Ayahuasca - Indigener Gebrauch

Chemical evidence for the use of multiple psychotropic plants in a 1,000-year-old ritual bundle from South America

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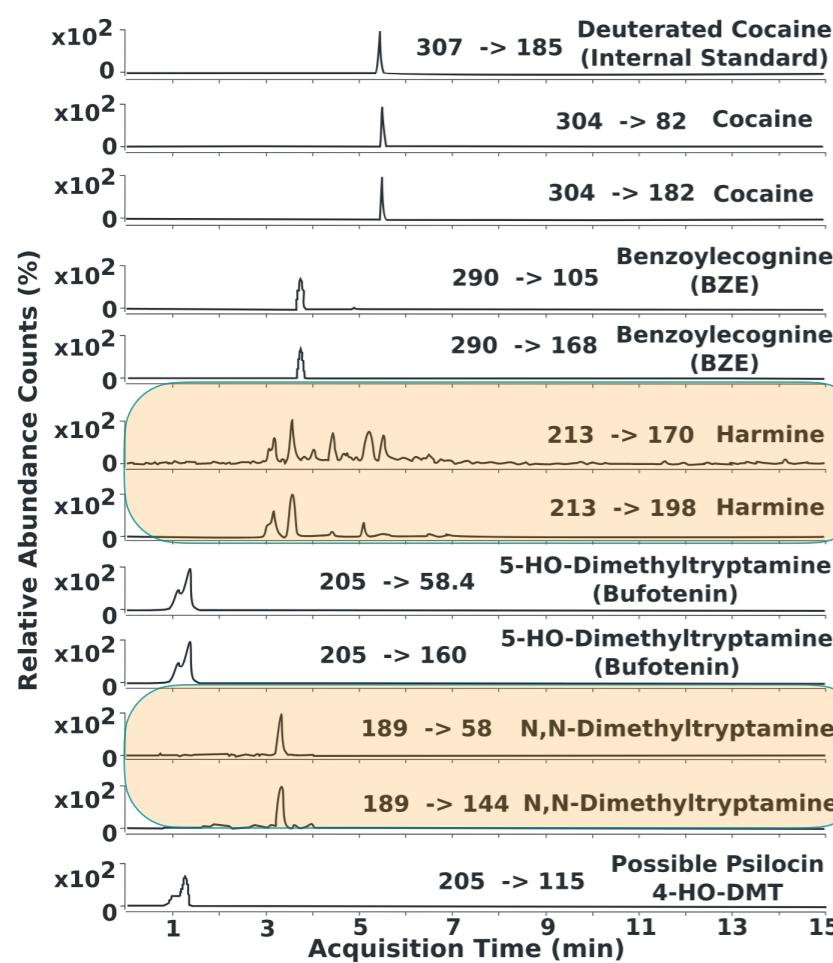


Fig. 3. LC-MS/MS results from the fox-snout pouch indicating the presence of cocaine, BZE, harmine, bufotenine, DMT, and peak potentially corresponding to psilocin.

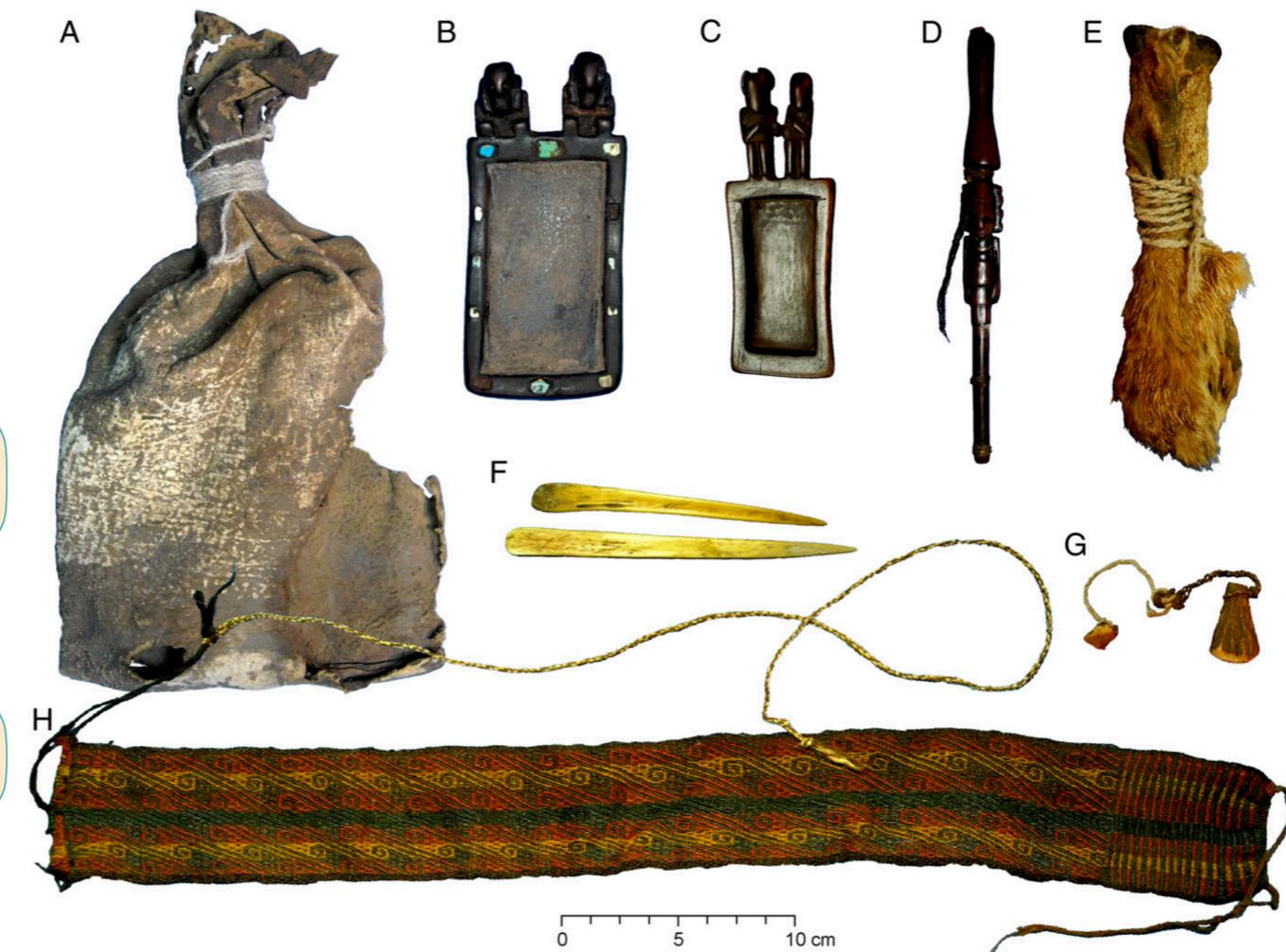
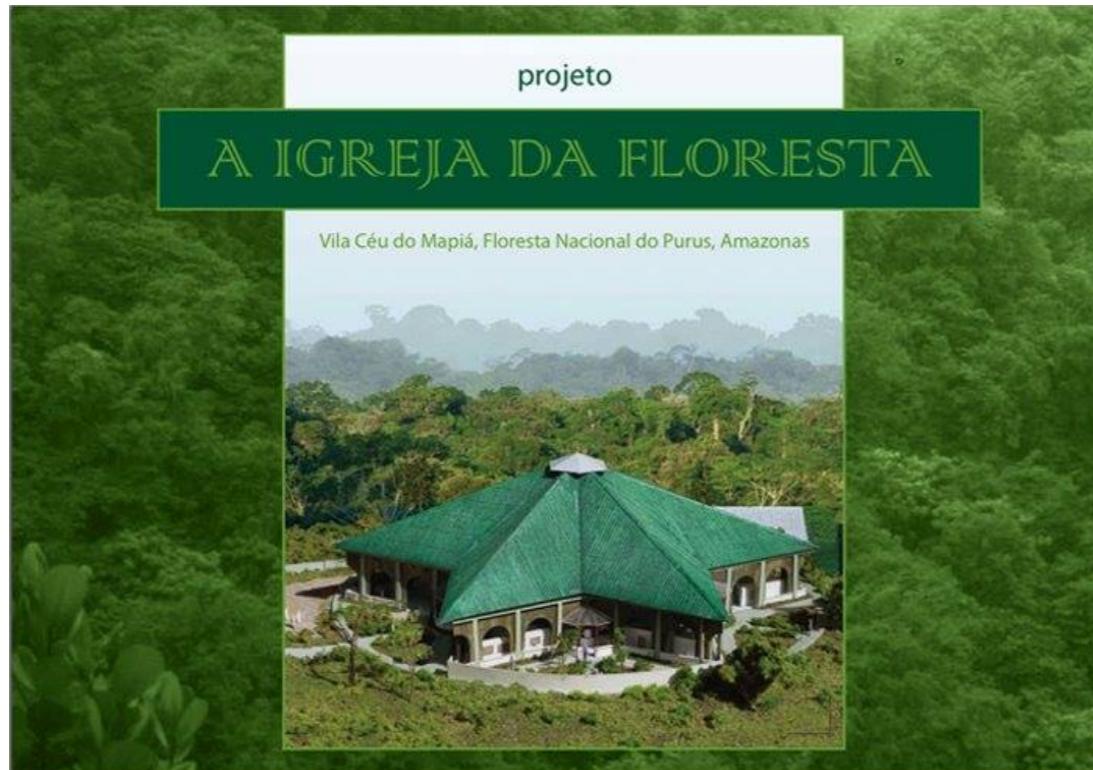


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Ayahuasca - Religiöser Gebrauch



Ayahuasca - Trendmedizin des Westens



The New York Times

Ayahuasca: A Strong Cup of Tea



JOSH COCHRAN

Ayahuasca, used for centuries in South American jungles, is booming in the U.S.

Illustration by Bjørn Lie



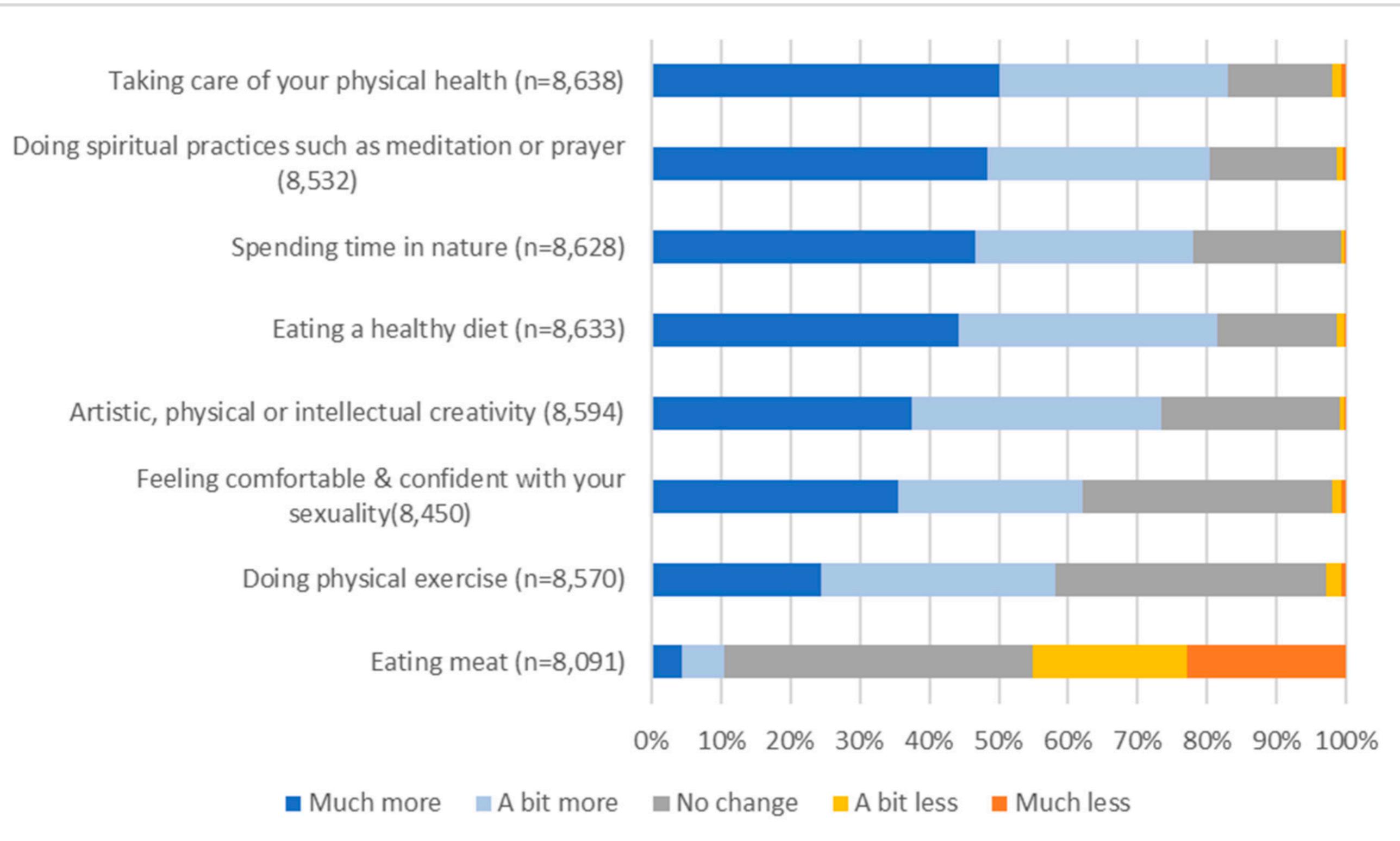
Four Million People Have Taken Ayahuasca Worldwide

Only 10% of these four million people belong to Indigenous groups where ayahuasca has traditionally been an integral part of their knowledge systems, which highlights the significant impact of the globalization of this plant medicine.



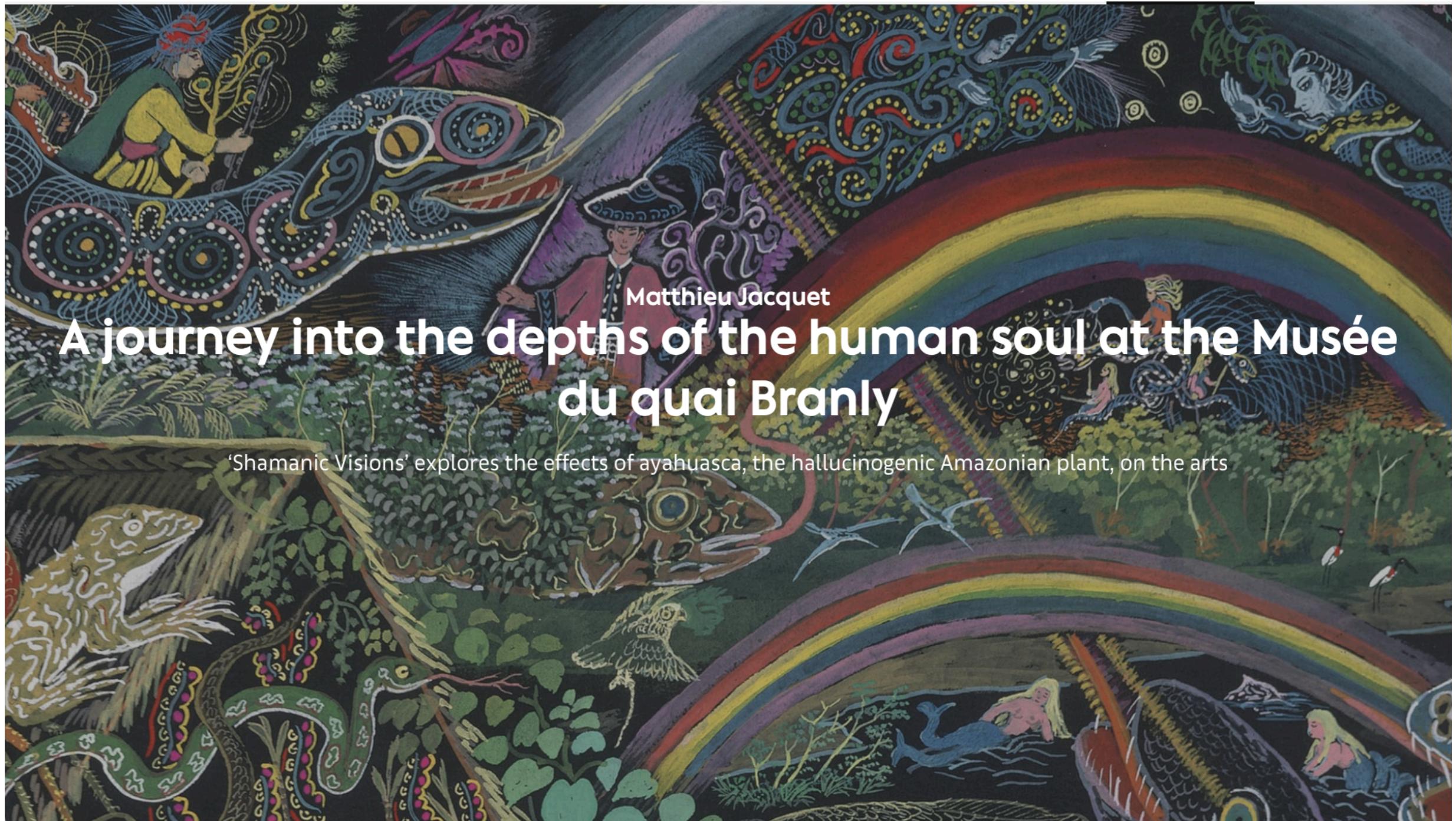
Insights and subsequent life and lifestyle changes appear to have a central role in the transformative effects reported by individuals consuming ayahuasca, with these occurring across contexts of use and demographic groups.

Ayahuasca - Trendmedizin des Westens

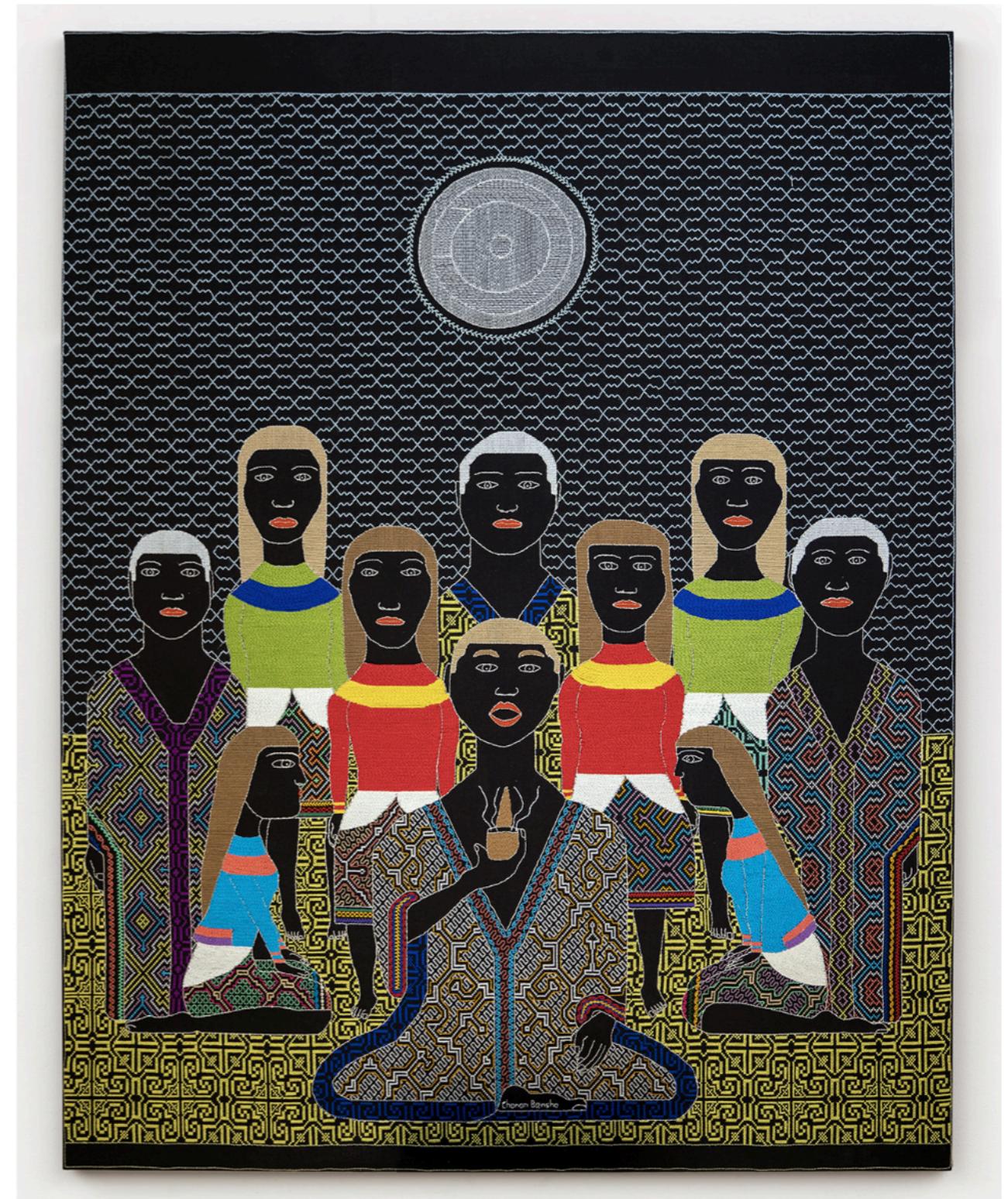
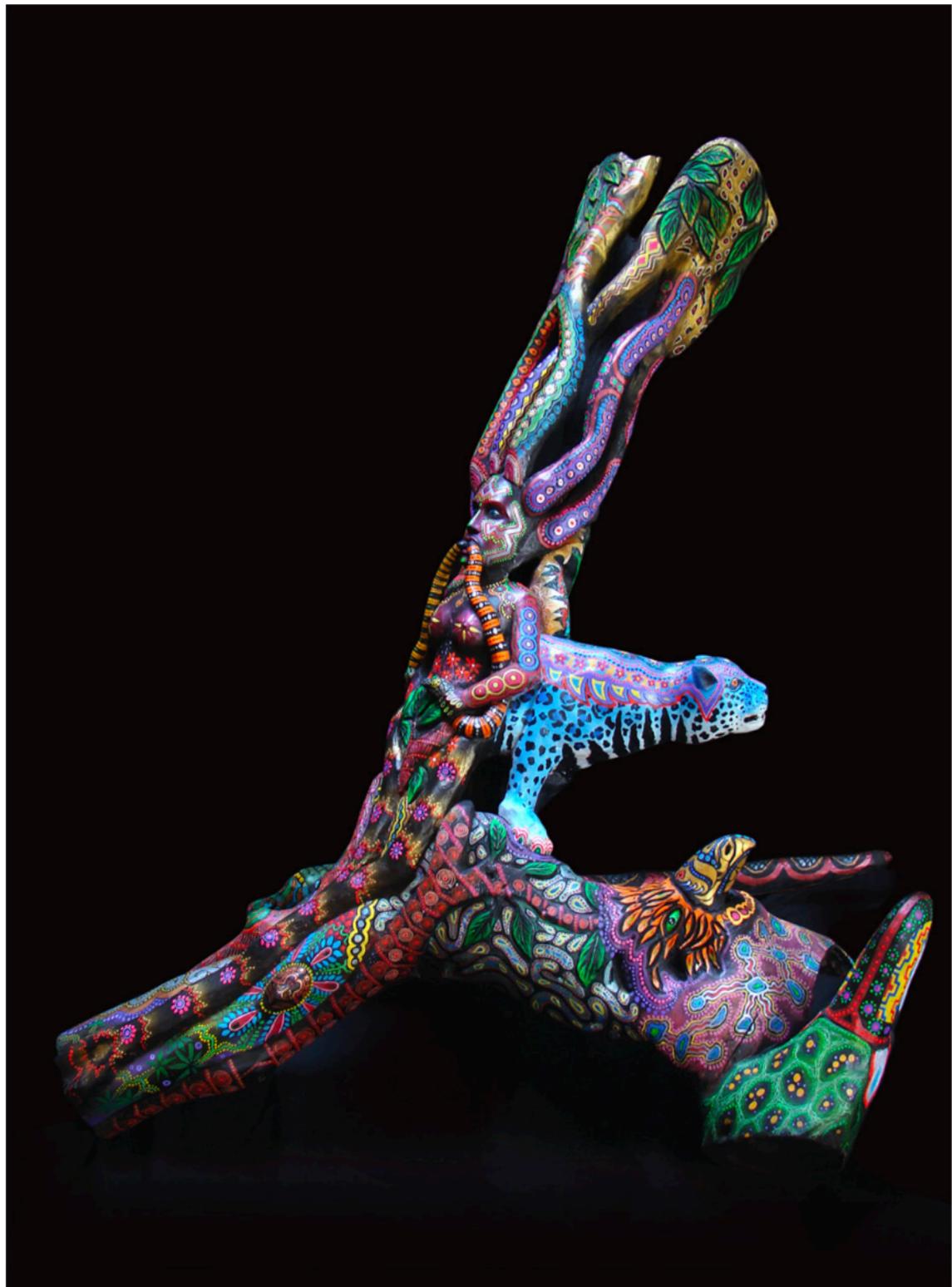


Ayahuasca - Subjektive Wirkung

Übersicht Fokus auf Hong Kong Künstler*innen Kunstmarkt Sammeln Reisen Lifestyle **Ausstellungen** Kunst & Umwelt



Ayahuasca - Subjektive Wirkung



Left: José Tamani and Jheferson Saldaña, *El espíritu de la ayahuasca*, 2002. Collection Jean-Michel Gassend. Right: Chonon Bensho, *Moatian jonibo*, 2022. Courtesy of the artist. © The Shipibo-Conibo Center and © W-Galería.

Ayahuasca - Subjektive Wirkung

The mental effects of ayahuasca are described as comparably more sober and clear-headed in style (compared to other psychedelics such as LSD or psilocybin):

- **Psychological Insights & Meaning Enhancement**

- existential self-realization through perceived exposure to inner mechanics of consciousness (e.g. behaviors, motivations, decision-making, character traits, beliefs, etc.)

- **Mindfulness & Embodied Presence**

- increased recognition of external and mental events with curiosity, openness, and acceptance

- **Empathy, Affection, and Sociability Enhancement**

- feelings of positive mood, compassion, and connection with others

- **Language Suppression**

- pre-verbal, intuitive, pre-reflective, symbolic experiences

- **Personality Regression**

- autobiographical memory enhancement, insights into life trajectory, trauma processing

- **Regenerative & Afterglow Phenomena**

- mental clarity, emotional stability, calmness, increased focus, cognitive refreshment

Ayahuasca - Therapeutisches Potenzial

Scientific Evidence



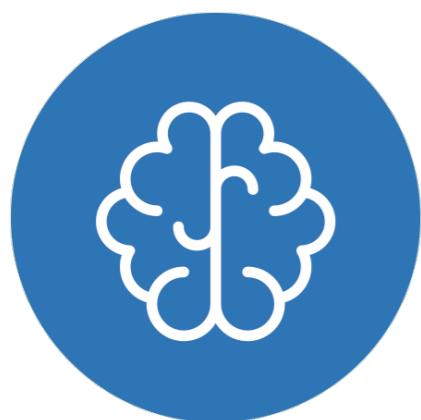
- **antidepressant effect** in treatment-resistant depression
- decrease in **suicidal ideation**
- positive outcomes in **substance use, eating disorders, PTSD, grief therapy**

Health Benefits



- promotes **mindfulness, decentering, and cognitive flexibility**
- **confronting difficult emotions** or psychological content can be experienced as therapeutic

Brain Health



- activates brain areas related to **episodic memory** and the **awareness of emotions** and internal sensations
- DMT promotes **neurogenesis** and **neuroprotection** (in vitro and in vivo)
- Harmala alkaloids stimulate **adult neurogenesis** (in vitro)

Mental Health



- used to support **psychological well-being**, personal development, social cohesion, and spiritual experiences
- most people who take ayahuasca are **well-adapted and integrated** in their social, working, and family environments

Online: <https://www.iceers.org/ayahuasca-technical-report/the-therapeutic-potential-of-ayahuasca/>

Ayahuasca - Risiken & Nebenwirkungen

Adverse Effects



- **nausea, vomiting, and diarrhea** are the main physical adverse effects
- „la purga“ (purging ritual) in traditional Amazonian medicine is an **intended therapeutic effect**

Risk Factors



- risks could be related to **unknown source or composition** of the brew
- beta-carbolines (MAOI) can **interact with tyramine-rich foods**
- combination of **MAOIs with SSRIs** or similar drugs is **counterindicated** (risk of serotonin syndrome)

Adverse Reactions



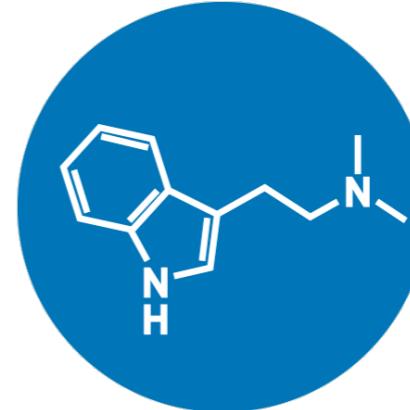
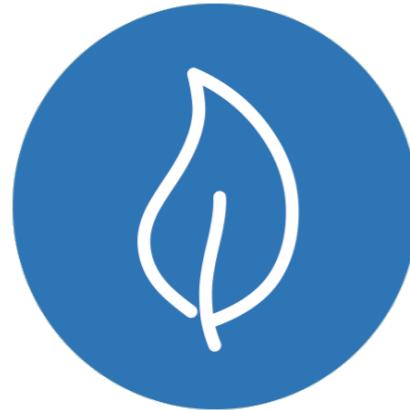
- psychedelic effects can be transiently **very intense and challenging**
- difficult **psychological adverse reactions** are the primary risk
- with **appropriate support**, also challenging experiences can have positive, long-lasting effects

Toxicity & Abuse



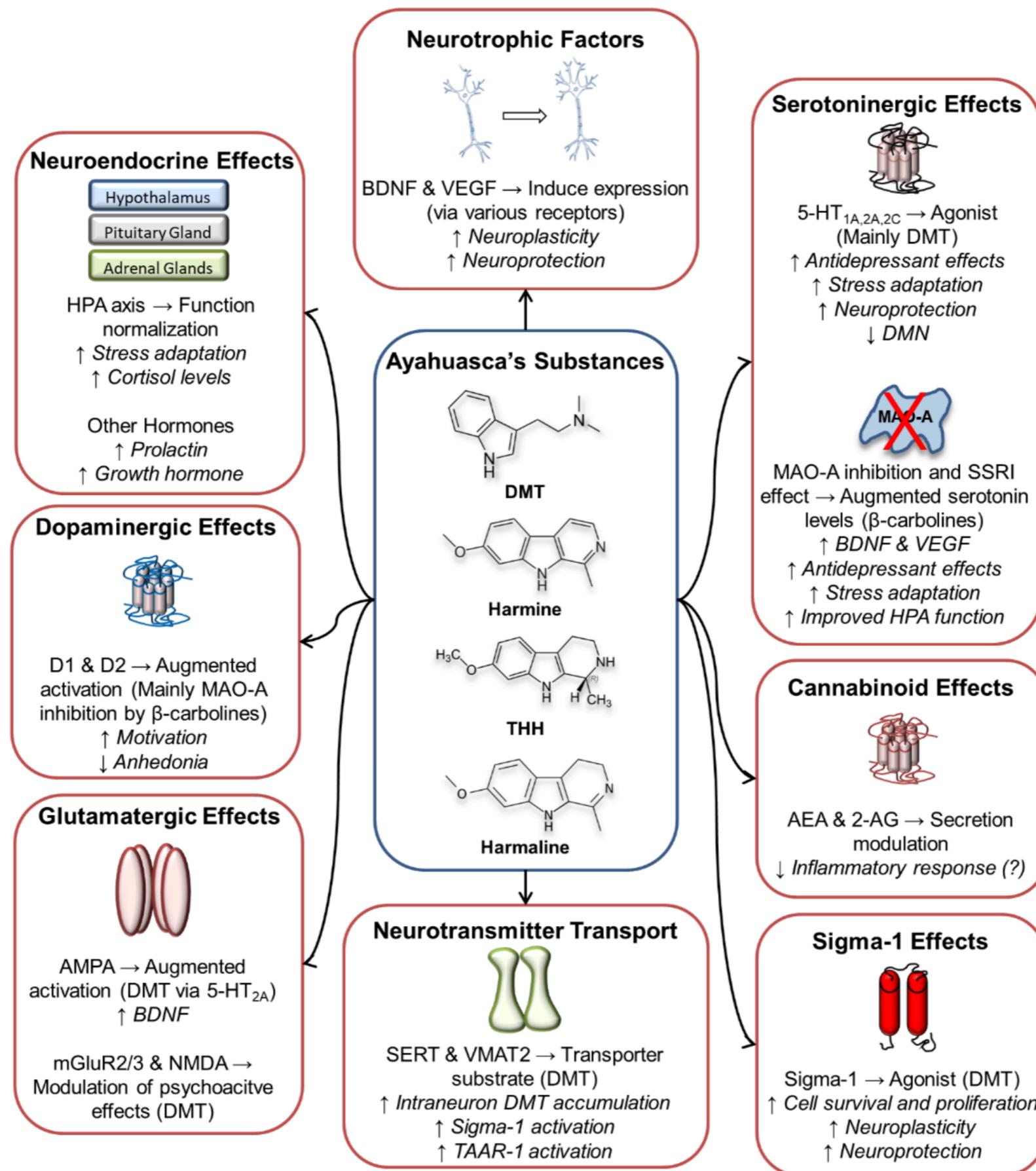
- **no signs of toxicity** in the body or brain after chronic use
- **low risk of abuse** and no signs of physical dependence
- **protective antiaddictive effect** regarding harmful drugs and alcohol consumption

Ayahuasca vs. DMT

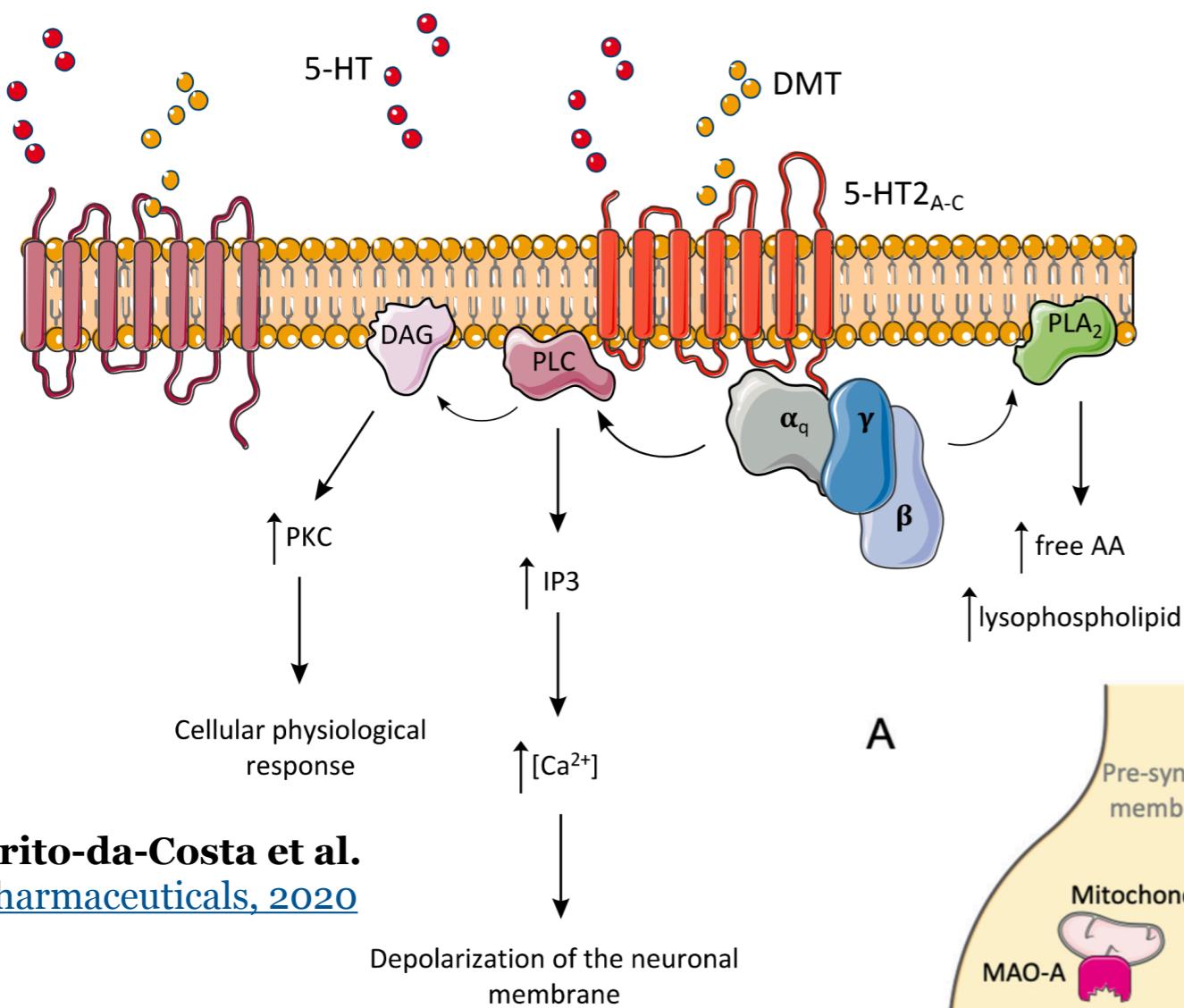


- Ayahuasca is a natural decoction with about **2,000 plant components**
- The amounts of **DMT vary depending on the batch**, in clinical trials between 0.5-1mg/kg of DMT
- 45-60 minutes to onset and **2-6 hours duration**, usually **repeated servings** per session
- Regulations are different by country, the **DMT-containing plants are not regulated** in most places.
- The **ritual use of ayahuasca** is rooted in Indigenous cosmologies and syncretic religious beliefs.
- **Modern ayahuasca practices** and ceremonial designs are adapted for Western participants.
- DMT (N,N-dimethyltryptamine) is a **ubiquitous tryptamine** found in some plants, animal species, and human body fluids.
- The acute effects of DMT are **more intense and last for 10-20 mins** when inhaled or injected.
- Synthetic or extracted DMT is listed in **Schedule 1**, in the 1971 Convention on Psychotropic Substances, and is **illegal in most jurisdictions**.
- **Amazonian tribes** also use **DMT-containing snuffs** such as Yopo (*Anadenanthera peregrina*)
- **Western recreational use** of DMT is rooted in the cultural history of the psychedelic movement.

Ayahuasca - Wirkmechanismen

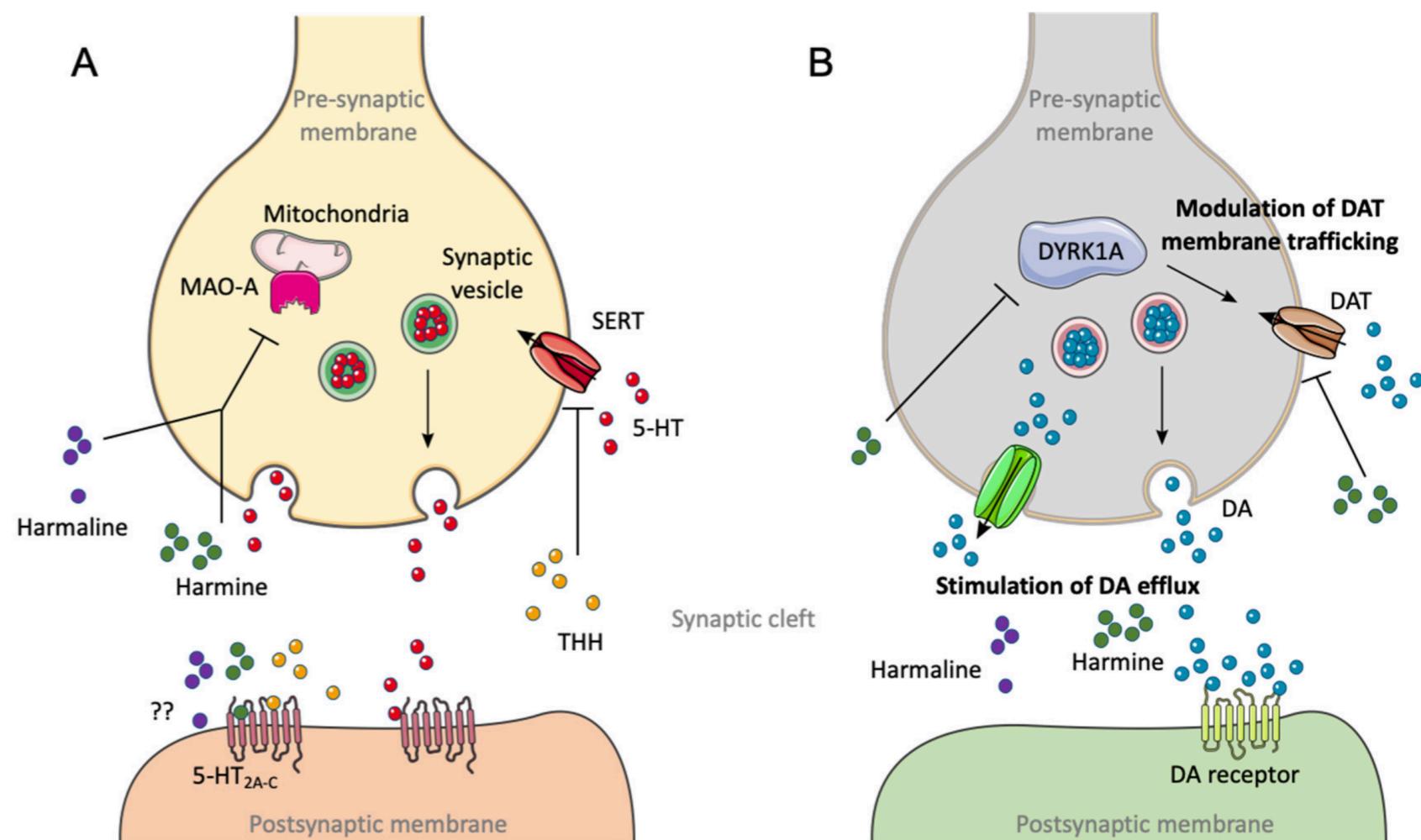


Ayahuasca - Wirkmechanismen

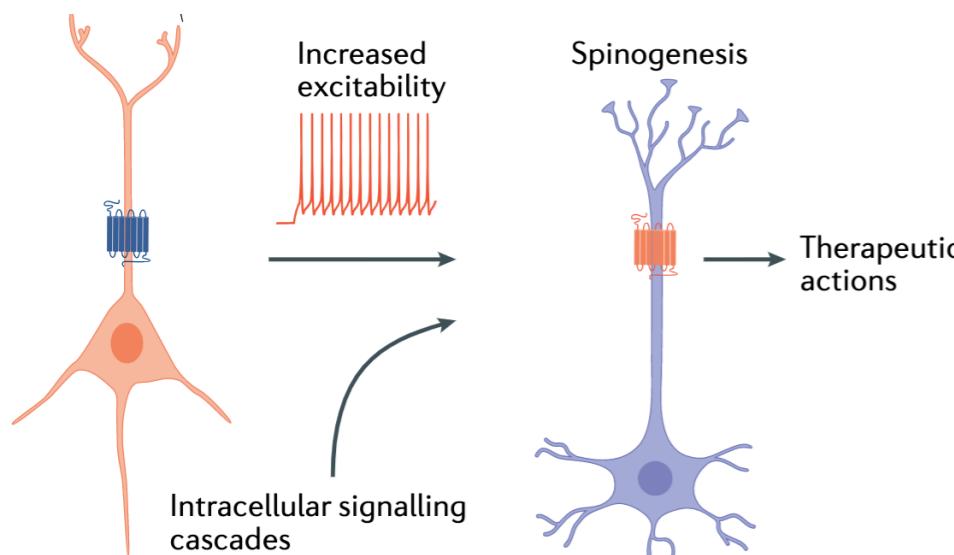


Brito-da-Costa et al.
[Pharmaceuticals, 2020](#)

The **β-carbolines harmine and harmaline** act as **selective and reversible MAO-AI**, while **THH** acts as **an inhibitor of the 5-HT reuptake**. Harmine seems to cause increased **DA release and inhibition of the DA transporter (DAT)**, resulting in tonic elevations of DA in the synaptic cleft.

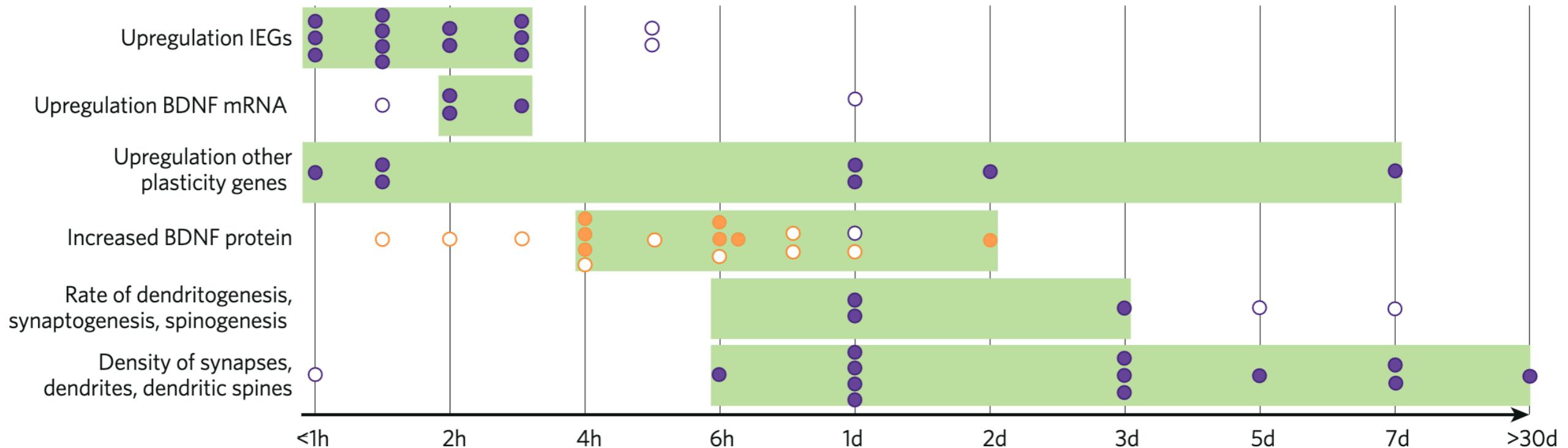
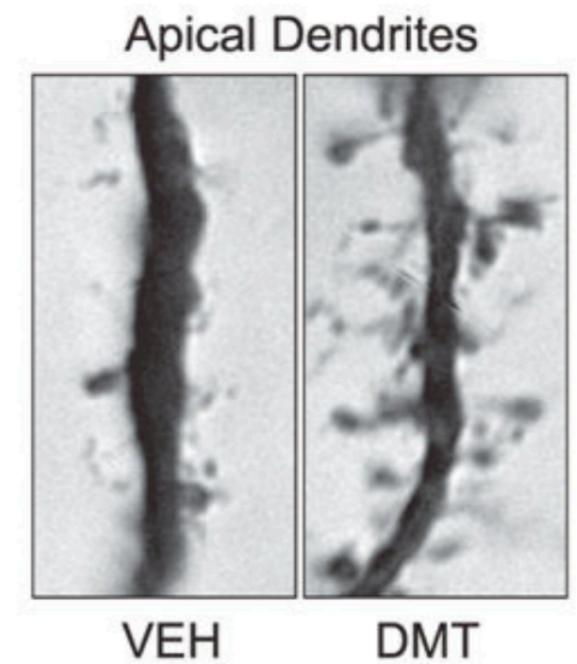
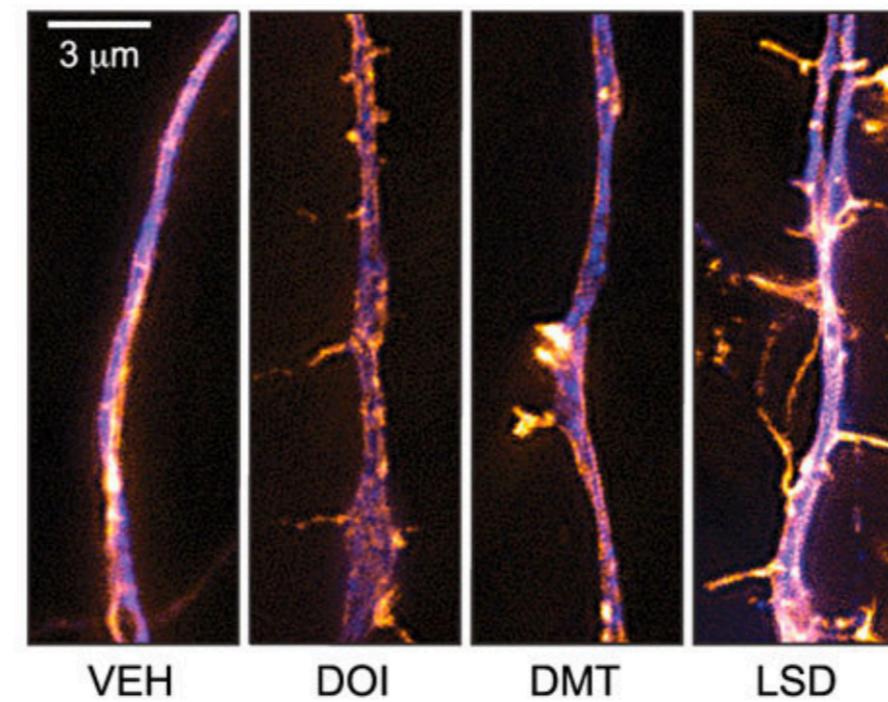


Psychedelika steigern die Neuroplastizität



McClure-Begley & Roth
[Nat Rev Drug Discovery, 2022](#)

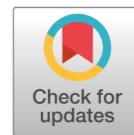
Ly et al.
[Cell Rep, 2018](#)



Calder & Hasler
[Neuropsychopharmacology, 2022](#)

● Significant increase
○ No change
● Human study

[Increase observed in this time period]



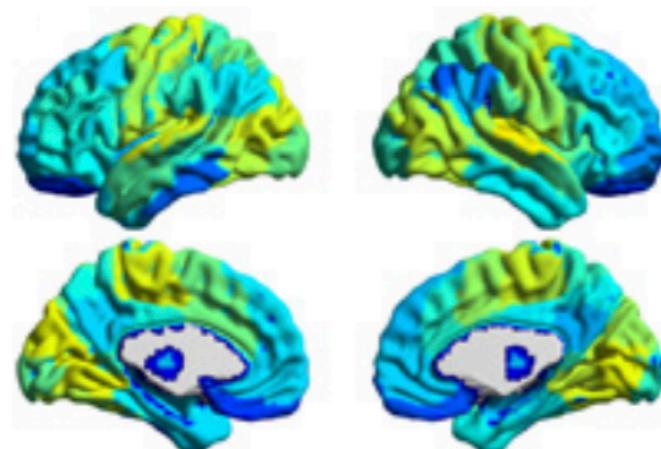
Human brain effects of DMT assessed via EEG-fMRI

Christopher Timmermann^{a,1} , Leor Roseman^a, Sharad Haridas^a, Fernando E. Rosas^{a,b,c,d} , Lisa Luan^a, Hannes Kettner^a, Jonny Martell^a , David Erritzoe^a , Enzo Tagliazucchi^{e,f}, Carla Pallavicini^f, Manesh Girn^g, Andrea Alamia^h , Robert Leechⁱ , David J. Nutt^a , and Robin L. Carhart-Harris^{a,j}

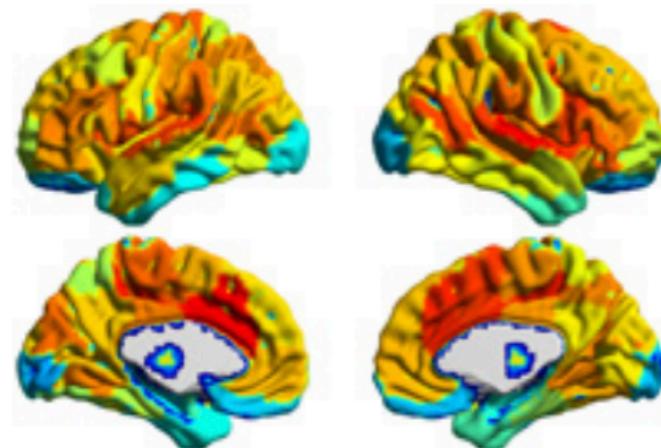
Edited by Marcus Raichle, Washington University in St Louis School of Medicine, St. Louis, MO; received November 12, 2022;
accepted December 14, 2022

GFC

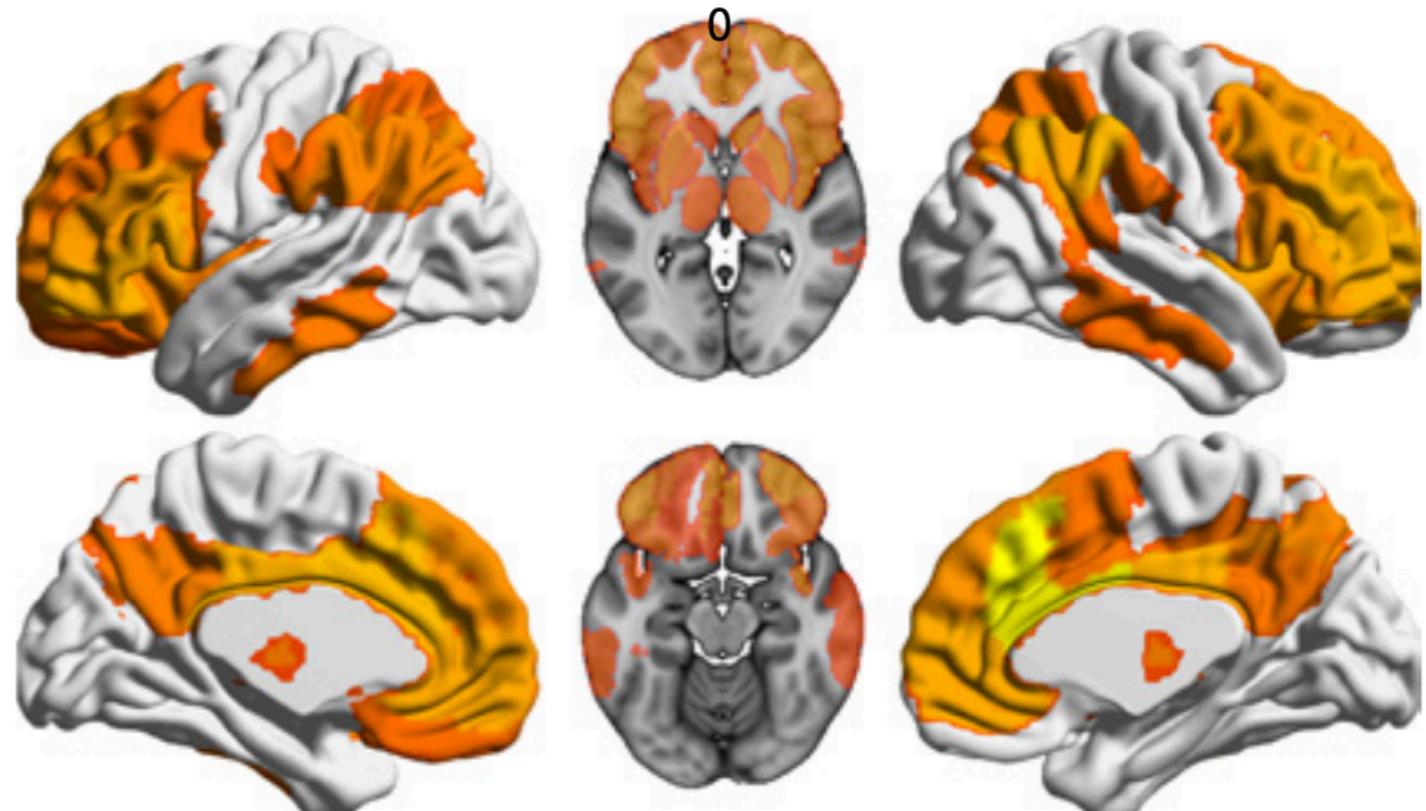
PCB



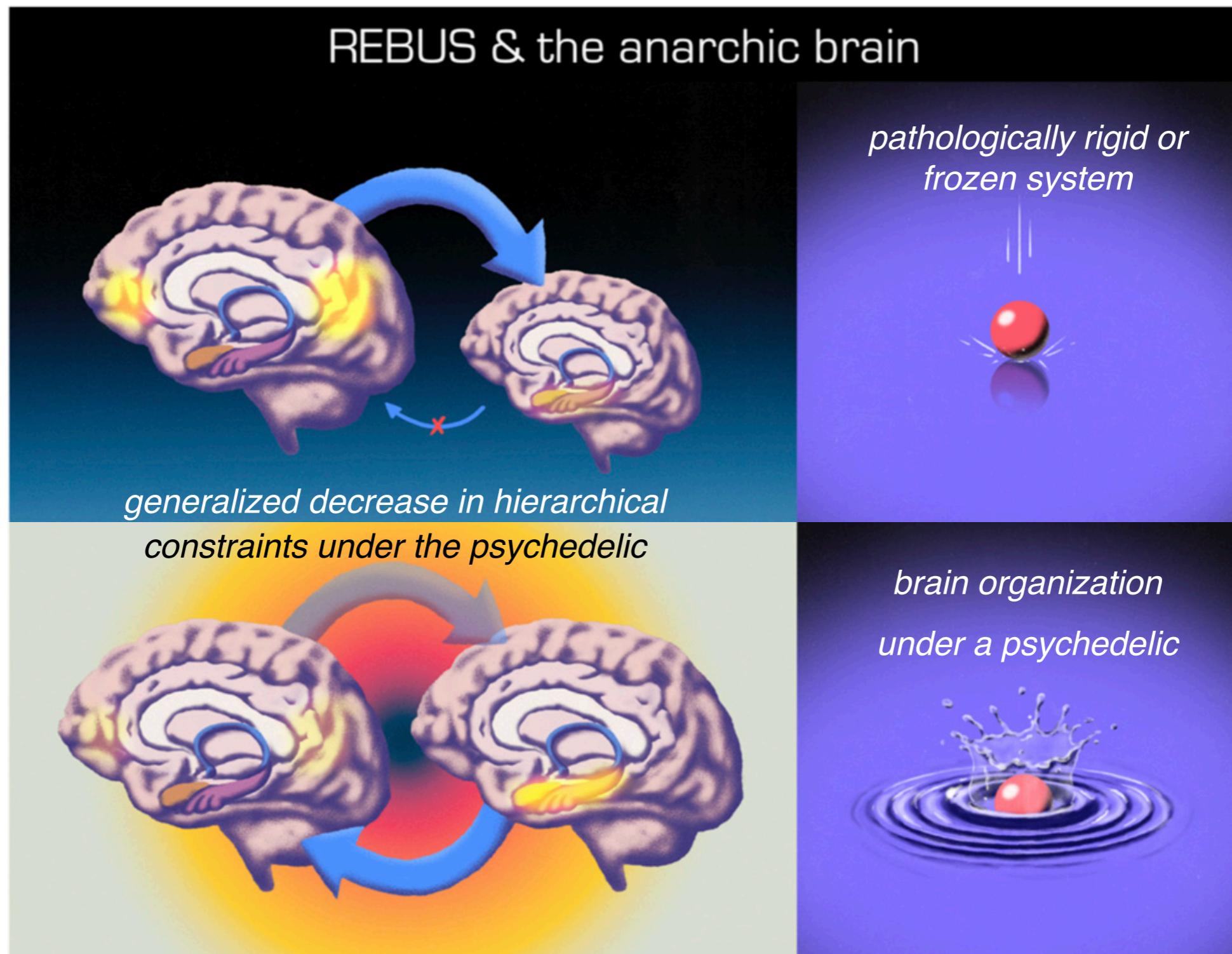
DMT



DMT vs PCB

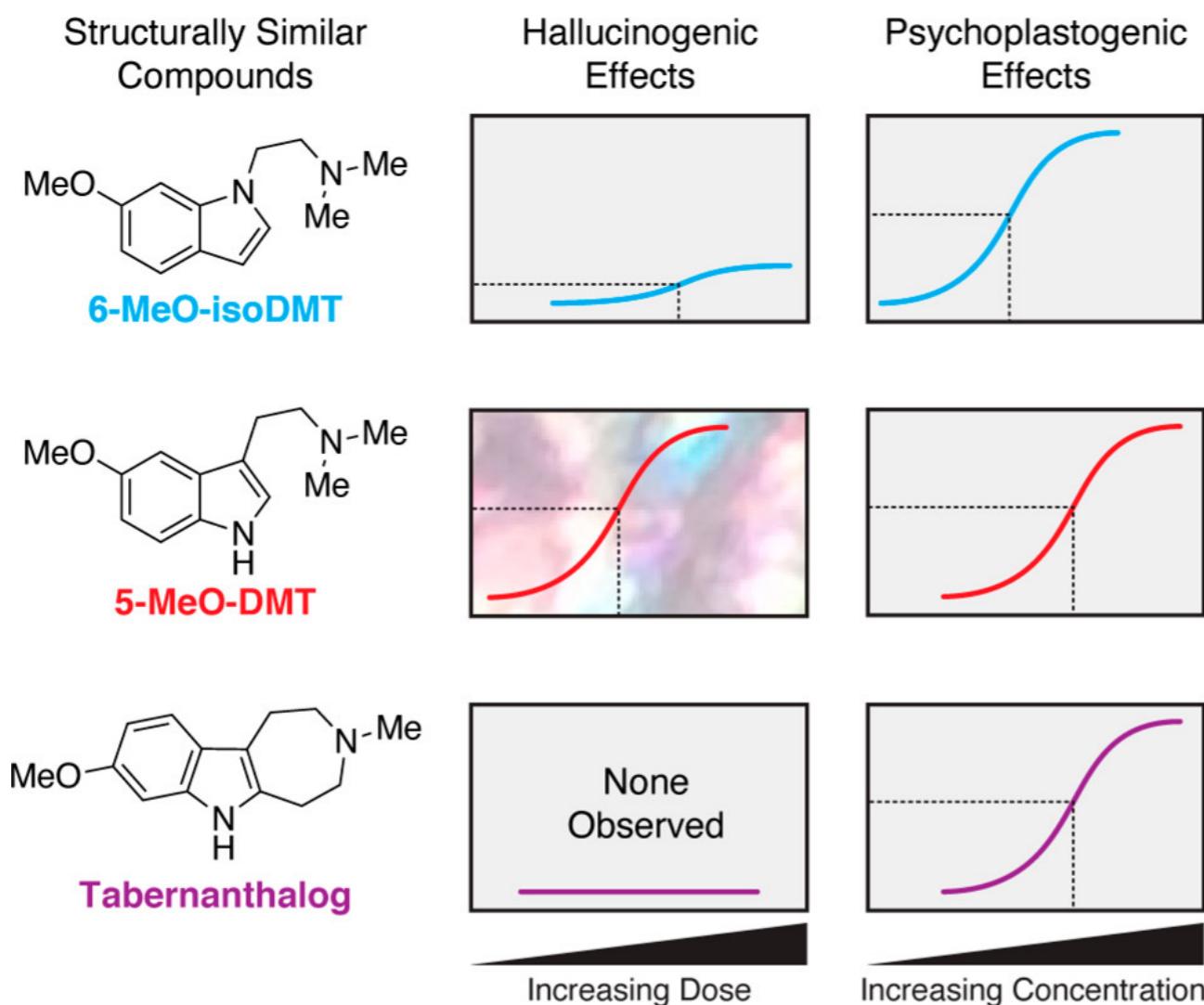
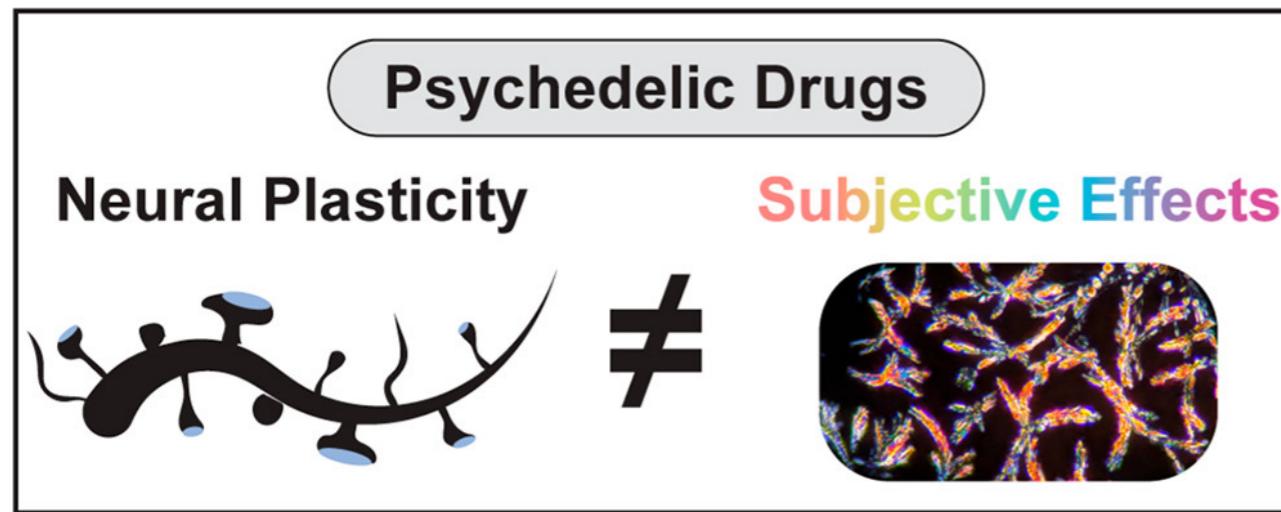


Psychedelika steigern die neuronale Flexibilität



Carhart-Harris and Friston
[Pharmacological Reviews, 2019](#)

Neue psychoplastogene Substanzen...?



Psychoplastogens are compounds that can induce changes in perception, mood, and cognitive processes without causing hallucinogenic effects.

These substances potentially offer the benefits of psychedelics without the trip, making them suitable for use in a wider range of therapeutic contexts.

Olson

ACS Pharmacol. Transl. Sci. 2020

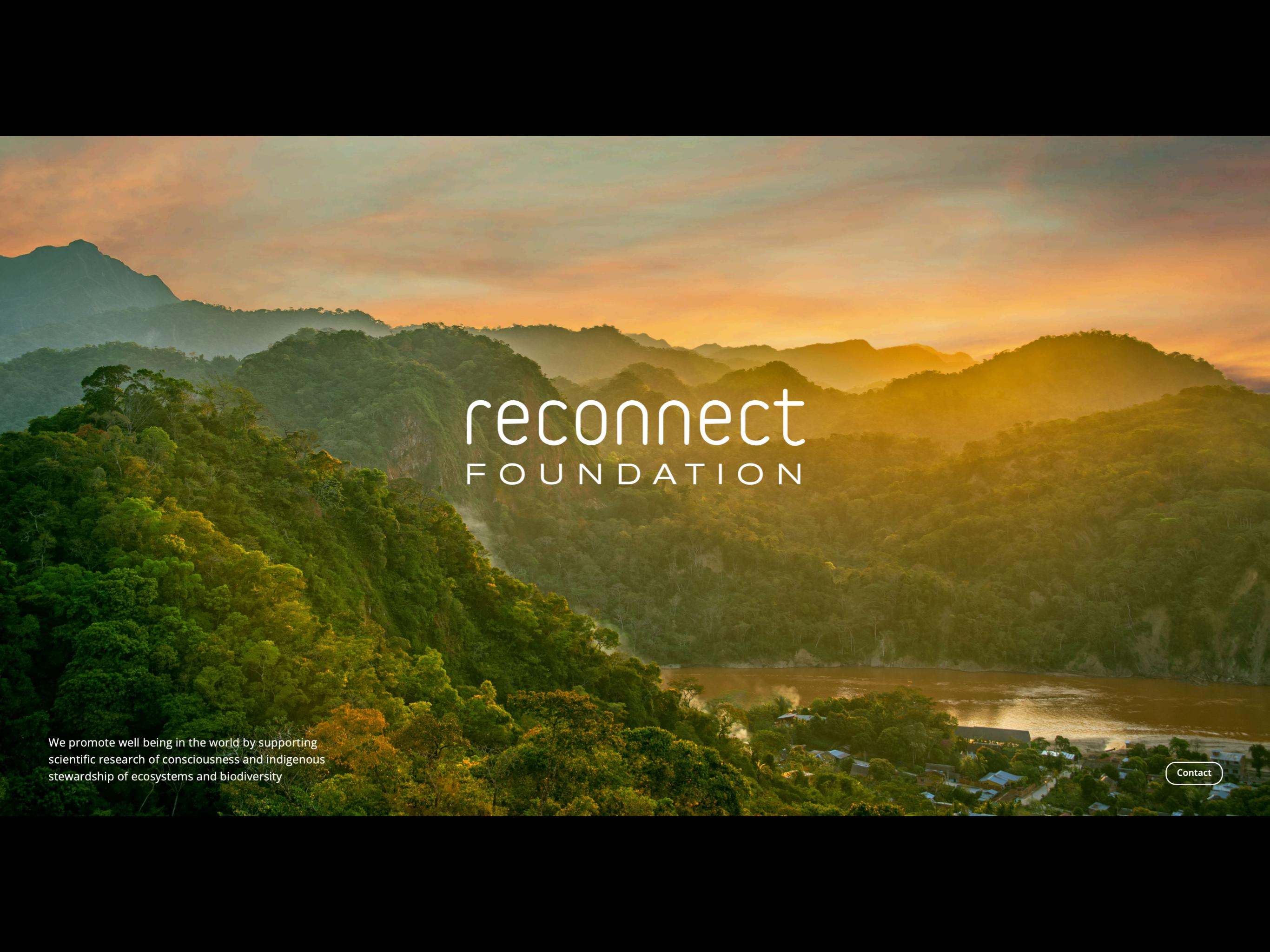
Ayahuasca - Interkultureller Wissenstransfer



- Die **Integration von Ayahuasca in westliche Gesundheitssysteme** setzt interkulturellen Respekt und Bereitschaft für Dialog voraus.
- Die **biomedizinische Forschung mit Ayahuasca-Wirkstoffen** wirft Fragen der kulturellen Aneignung auf, die es zu reflektieren gilt.
- Die **Nutzung synthetisierter Moleküle** könnte eine ökologisch nachhaltige Lösung für die steigende Nachfrage nach Ayahuasca im Westen sein.
- Im Westen existieren **polarisierende Ansichten** über den Gebrauch von Ayahuasca, während die indigenen Traditionen sich durch **Globalisierung** stetig wandeln.
- Es sollte ein **transkulturelles ethisches Anliegen** sein, sichere Erfahrungsräume zu ermöglichen, die auf die jeweilige Kultur abgestimmt sind.

**Intercultural Health
From Theory to Practice**

Executive Summary
December 2023

The background image shows a vast landscape during a golden sunset. In the foreground, there's a dense forest of green and yellow trees. A river flows through the middle ground, reflecting the warm light. On the right side, a small village with several houses and a few people is visible. The background features a range of mountains, their peaks partially obscured by mist and the setting sun.

reconnect FOUNDATION

We promote well being in the world by supporting scientific research of consciousness and indigenous stewardship of ecosystems and biodiversity

[Contact](#)



Hypokinese und Rigor

bei postencephalitischem Parkinsonismus und Paralysis agitans.

Fertige Gebrauchsformen:

Kapseln zu 0.02 g Packungen mit 20 und 50 Stück
(Kapseln zu 0.04 g auf bes. Bestellung)

Ampullen mit 0.02 g in 1 ccm und 0.04 g in 2 ccm
Schachteln mit 5 und 10 Stück

(Suppositorien müssen in den Apotheken hergestellt werden:

Rp. Harmin 0.04
Oil, Cacao 2.0
M. f. supposit.
S. Je nach Lage des Falles 1-2-3 mal täglich 1 Zäpfchen.)

LITERATUR DURCH
E. MERCK
DARMSTADT

Chemisch und pharmakologisch
identisch mit Banisterin

HARMIN »MERCK«

INDIKATIONEN:

Folgezustände von Encephalitis

Rigor bei Parkinsonismus u. Paralysis agitans

ANWENDUNG:

Innen: Pulver und Suppositorien 0.02–0.04
(Rezeptverschreibung)

Gebrauchsfertige Kapseln zu 0.02 g
Packungen mit 20 und 50 Stück

Subkutan: Harmin-Ampullen 0.02 und 0.04 g
Schachteln mit 5 und 10 Stück

Dem Banisterin chemisch, pharmakologisch
und klinisch identisches Alkaloid.

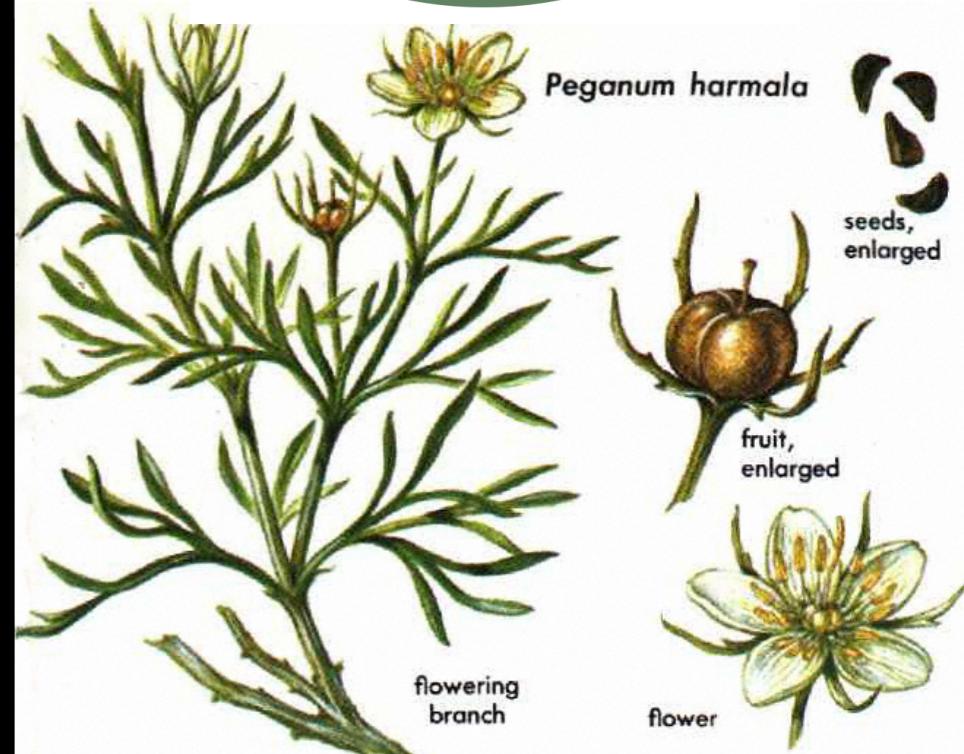
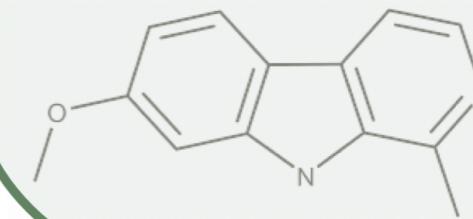
E. MERCK-DARMSTADT



Banisteriopsis Caapi



Harmine



Klinische Forschung mit Ayahuasca- und DMT-Präparaten

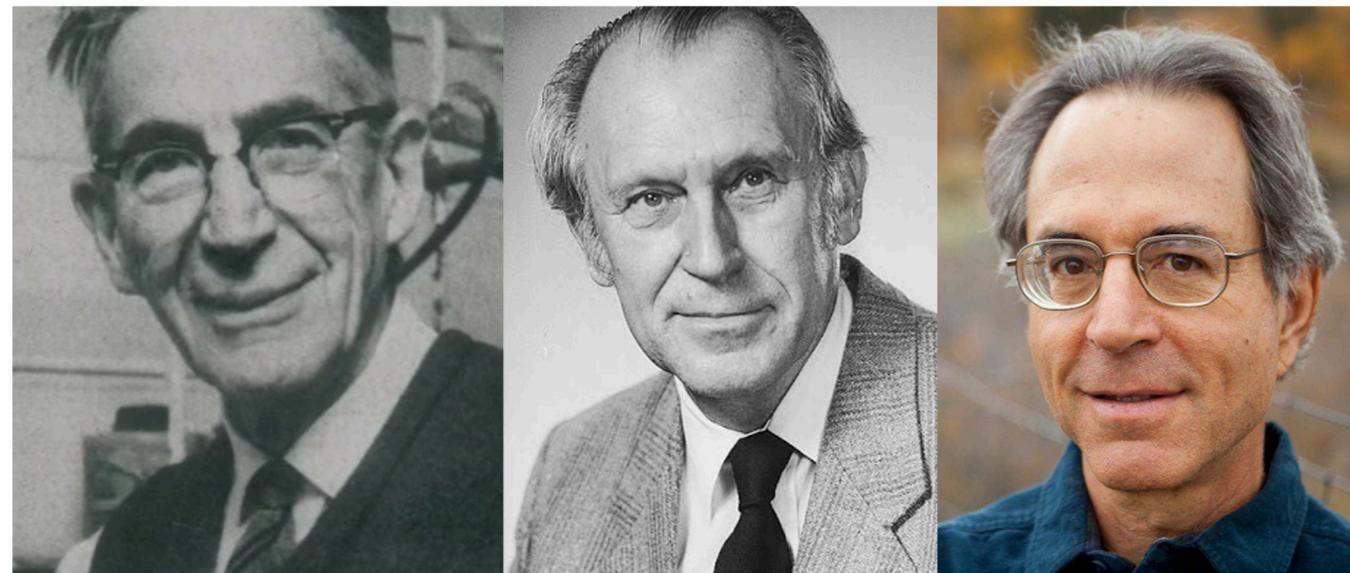
Arch. Psychiat. Nervenkr. 223, 77—87 (1976)

Archiv für Psychiatrie
und Nervenkrankheiten
Archives of Psychiatry
and Neurological Sciences
© by Springer-Verlag 1976

Vergleich veränderter Bewußtseinszustände unter den Halluzinogenen **(–)- Δ^9 -trans-Tetrahydrocannabinol (Δ^9 -THC) und N,N-Dimethyltryptamin (DMT)**

A. Dittrich, P. Bickel, J. Schöpf und D. Zimmer

Psychiatrische Universitätsklinik Burghölzli, Forschungsdirektion, Postfach 68,
CH-8029 Zürich, Schweiz



Dr Richard Manske

Dr Stephen Szára

Dr Rick Strassman

1931: DMT-Synthese (Richard Manske)

**1956: Entdeckung der psychotropen Effekte
von DMT** (Stephen Szára)

1976: Erste DMT-Studien an der PUK Zürich
(Dittrich, Angst, Scharfetter)

**1990 - 1994: Pharmakokinetik & -dynamik
von DMT** (Rick Strassman)

**1984 - 2003: Pharmakokinetik & -dynamik
von Ayahuasca** (McKenna, Callaway, Riba)

**2015 - 2018: Erste klinische Studien mit
Ayahuasca in MDD** (Osorio, Palhano-Fontes)

**2018 - heute: Entwicklung von DMT-
Präparaten für Psychiatrie** (Reconnect Labs,
Small Pharma, ATAI, MindMed)

Ayahuasca - Pharmakokinetik/-dynamik

Table 1. Chemical composition and alkaloid content of ayahuasca preparations.

Ayahuasca Preparations	DMT (mg/mL)	Harmine (mg/mL)	Harmaline (mg/mL)	THH (mg/mL)	Total Alkaloids (mg/mL)	Reference
Rio Purús ¹	0.13	0.15	n.a.	0.05	0.33	[26]
UDV	0.24	1.70	0.20	1.07	3.21	[13]
Pucallpa ²	0.60	4.67	0.41	1.60	7.28	[16]

¹ A river that flows through the countries of Brazil and Peru. ² A city from Peru. DMT: N,N-Dimethyltryptamine; THH: Tetrahydroharmine; UDV: União do Vegetal; n.a.: Information not available.

MONOAMINE OXIDASE INHIBITORS IN SOUTH AMERICAN HALLUCINOGENIC PLANTS: TRYPTAMINE AND β -CARBOLINE CONSTITUENTS OF AYAHUASCA

DENNIS J. MCKENNA^a, G.H.N. TOWERS^a and F. ABBOTT^b

^aDepartment of Botany and ^bFaculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, B.C. (Canada)

(Accepted November 26, 1983)

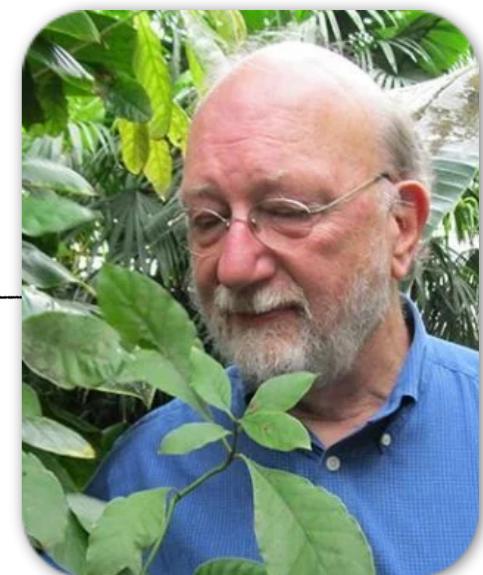
PERUVIAN AYAHUASCA – HPLC QUANTITATION OF UNDILUTED SAMPLES

Name of sample	Alkaloid concentration (mg/ml) ^a									
	Harmol	Harmine	%	THH	%	Harmaline	%	DMT	%	Total
Don Fidel no. 1	tr	3.85 (0.01)	66	1.06 (0.05)	18	0.3 (0.1)	5	0.61 (0.01)	10	5.85 (0.19)
Don Fidel no. 2	tr	4.64 (0.3)	62	1.77 (0.1)	24	0.45 (0.1)	6	0.6 (0.1)	8	7.48 (0.16)
Don Fidel no. 3	tr	3.4 (0.2)	58	1.94 (0.06)	30	0.34 (0.2)	5	0.7 (0.2)	11	6.38 (0.1)
Don Juan no. 1	tr	5.3 (0.36)	66	1.73 (0.1)	21	0.51 (0.16)	6	0.51 (0.16)	6	8.05 (0.36)
Don Juan no. 2	tr	5.51 (0.26)	67	1.67 (0.07)	20	0.41 (0.14)	5	0.6 (0.2)	7	8.19 (0.28)
Average alkaloid content ^b		4.67 (0.2)	65	1.60 (0.08)	22	0.41 (0.06)	6	0.6 (0.06)	8	7.28 (0.28)

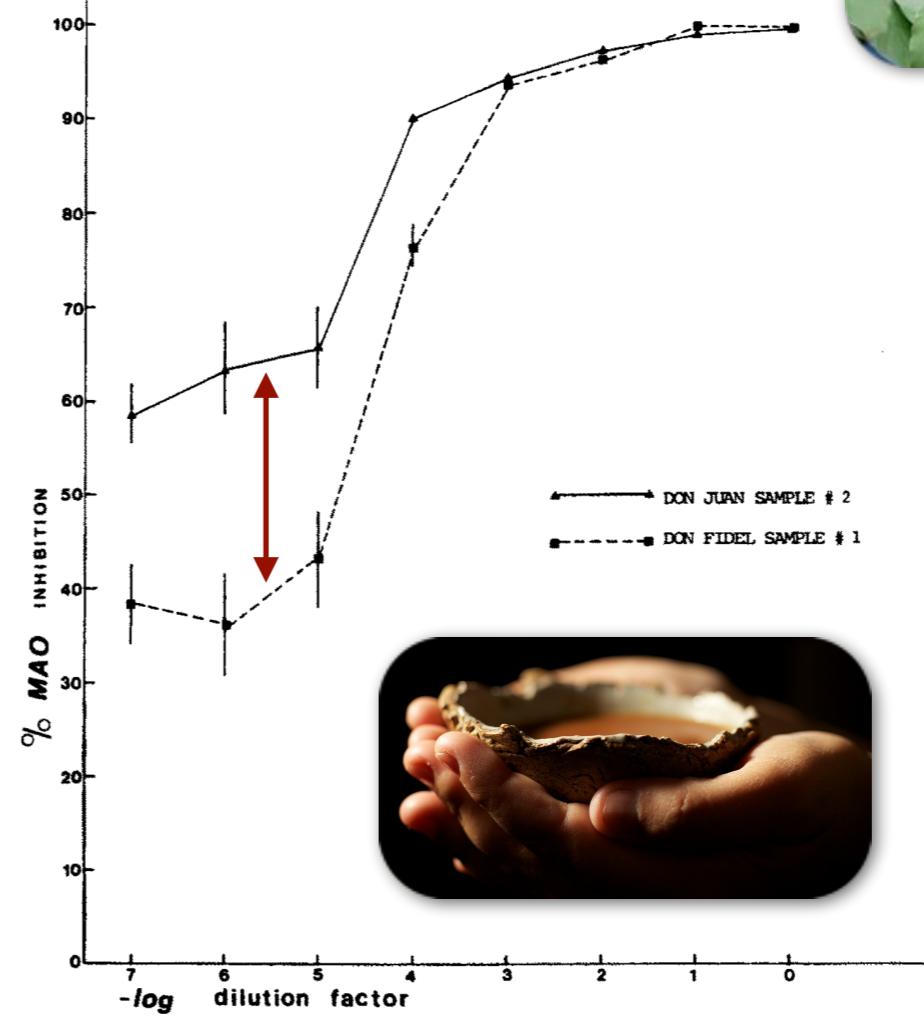
^aFigures given are mg alkaloid/ml of undiluted sample, \pm S.E., shown in parentheses; percentages are % total alkaloid.

^bAverage based on $n = 18$ replicate injections.

**Brito-da-Costa et al.
Pharmaceutics, 2020**



- large PKPD variability
- challenge for standardization



**McKenna et al.
J Ethnopharm, 1984**



Fig. 3. In vitro inhibition of rat-liver MAO by ayahuasca samples. See text for details.

0022-3565/03/3061-73-83\$7.00
THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS
Copyright © 2003 by The American Society for Pharmacology and Experimental Therapeutics
JPET 306:73-83, 2003

Vol. 306, No. 1
49882/1069698
Printed in U.S.A.

Human Pharmacology of Ayahuasca: Subjective and Cardiovascular Effects, Monoamine Metabolite Excretion, and Pharmacokinetics

JORDI RIBA, MARTA VALLE, GLORIA URBANO, MERCEDES YRITIA, ADELAIDA MORTE, and MANEL J. BARBANOJ

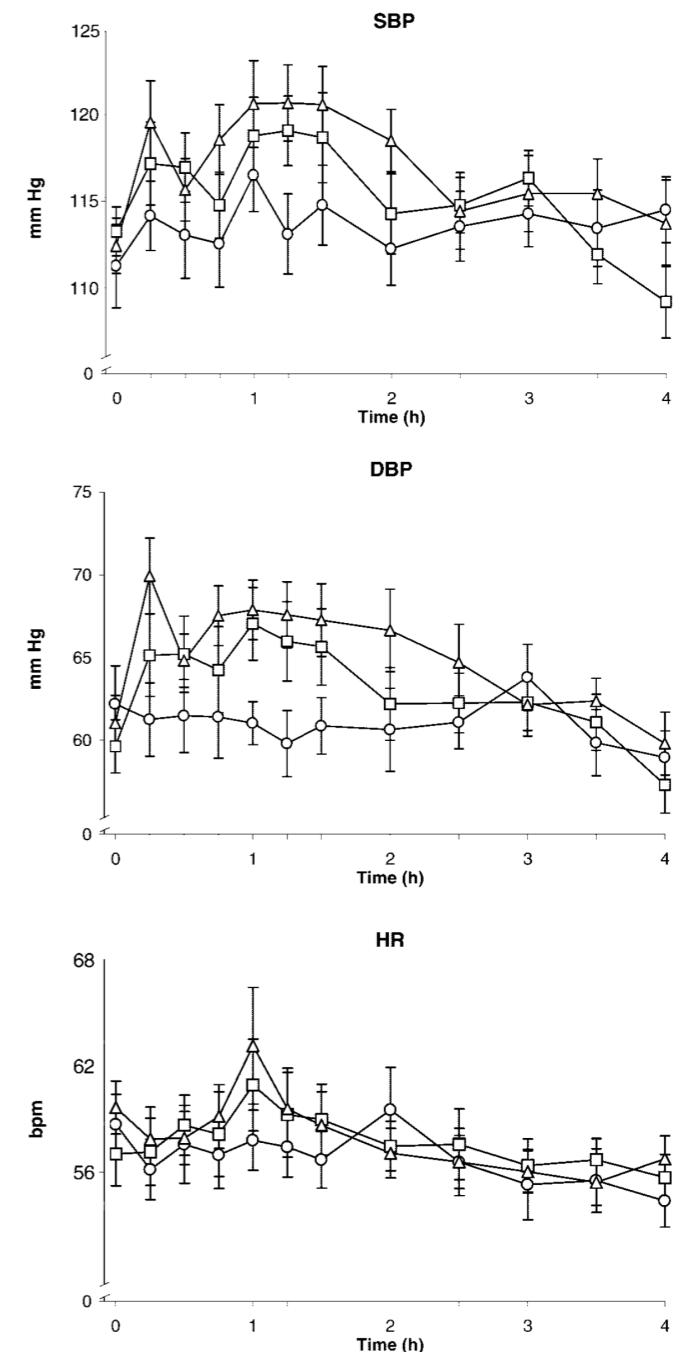
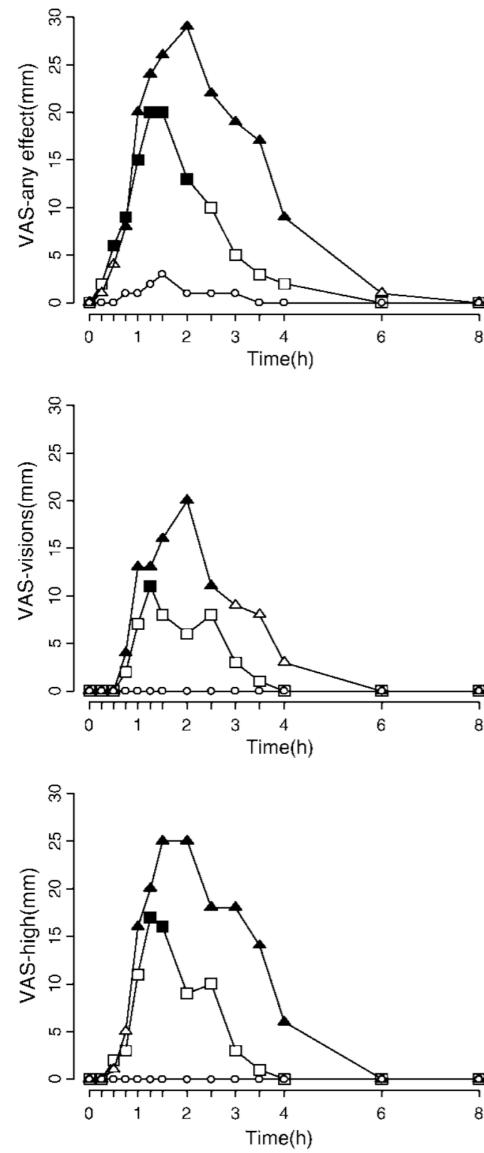


Fig. 2. Time curves of scores on the seven VAS items (means from 18 volunteers) after administration of placebo (circle), 0.6 mg of DMT/kg of body weight ayahuasca (square), and 0.85 mg of DMT/kg of body weight ayahuasca (triangle). Filled symbols indicate a significant difference from placebo.

Riba et al.

[J Pharm Exp Ther, 2003](#)

DMT - Pharmakokinetik/-dynamik

ORIGINAL ARTICLE

Dose-Response Study of N,N-Dimethyltryptamine in Humans

I. Neuroendocrine, Autonomic, and Cardiovascular Effects

Rick J. Strassman, MD, Clifford R. Qualls, PhD

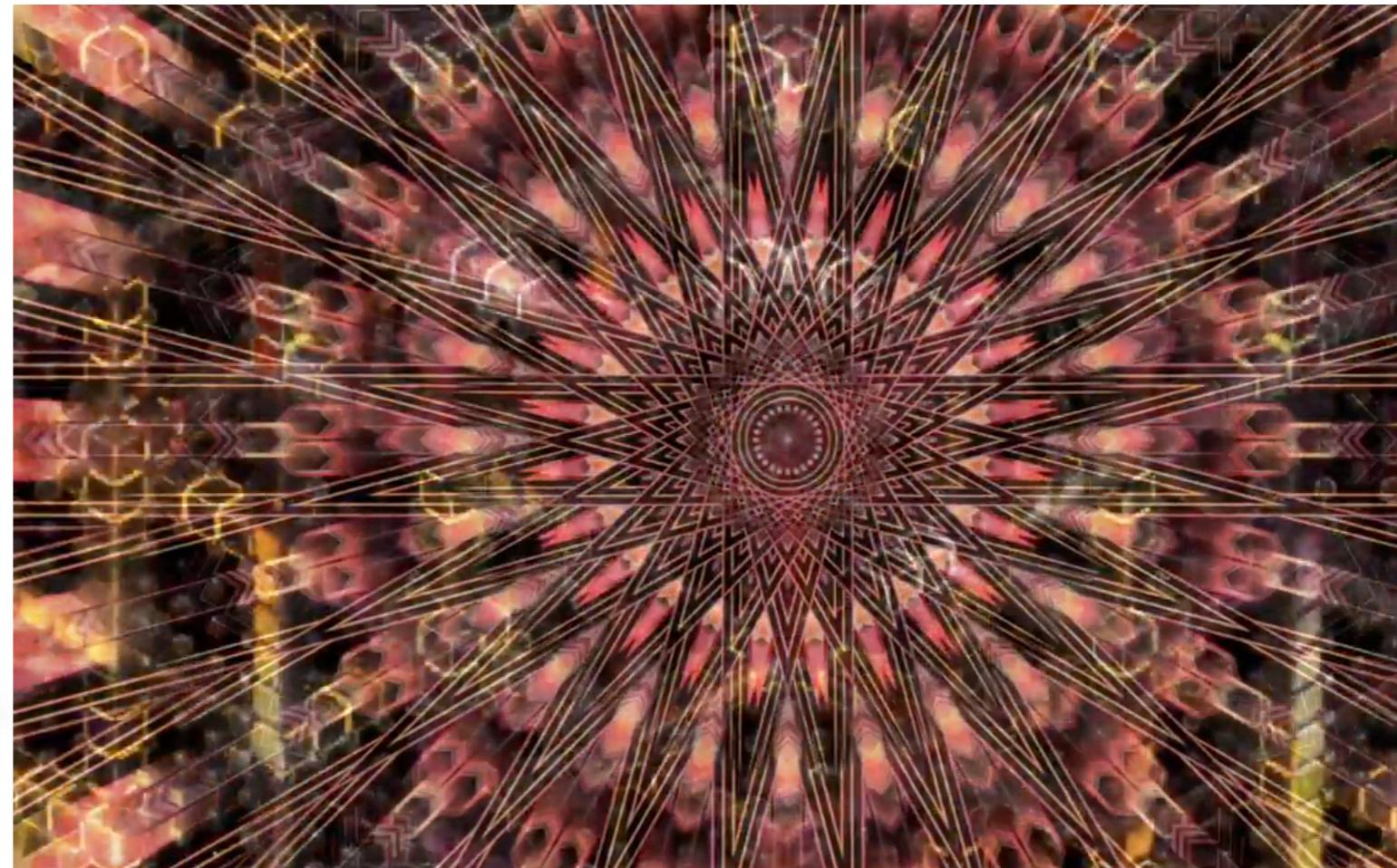
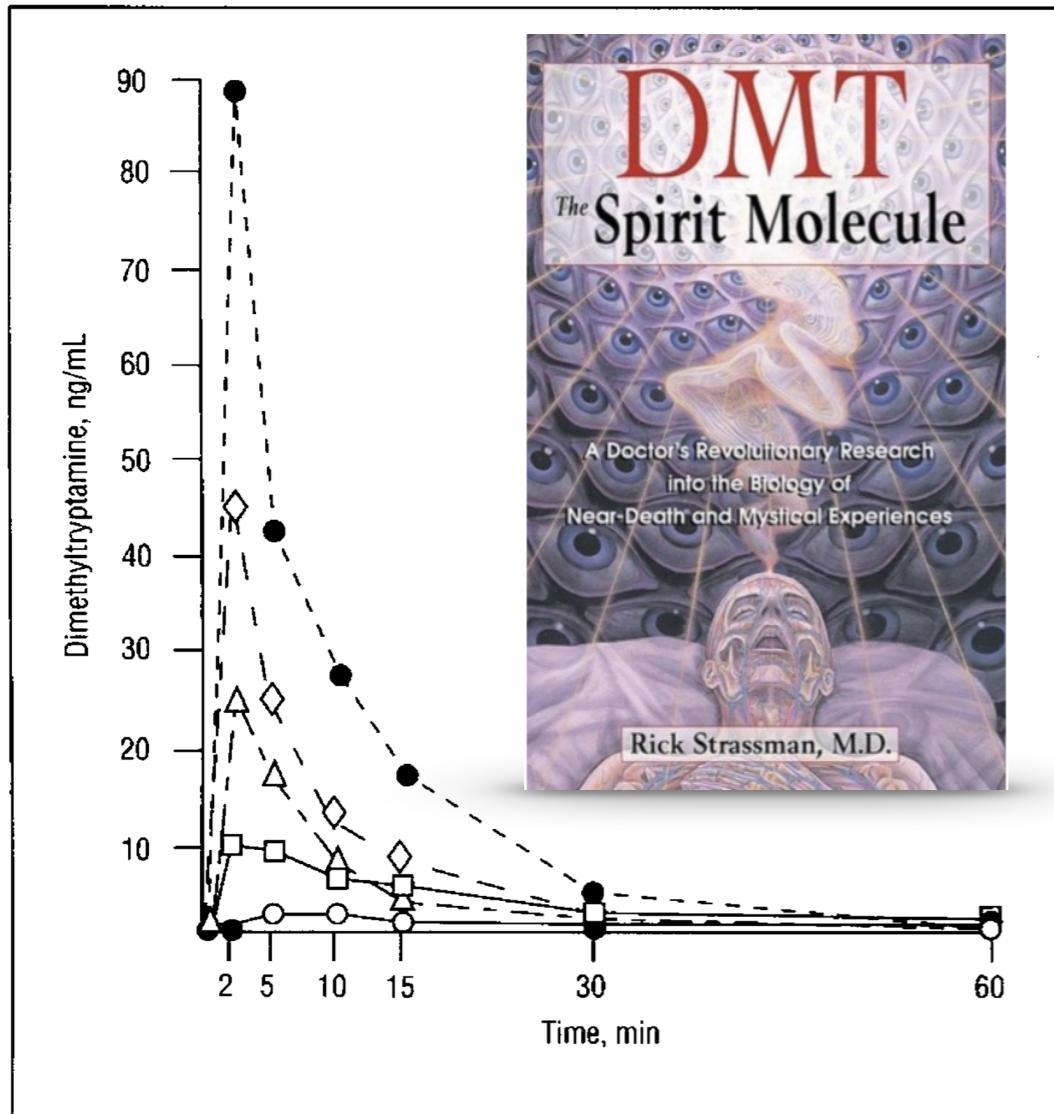


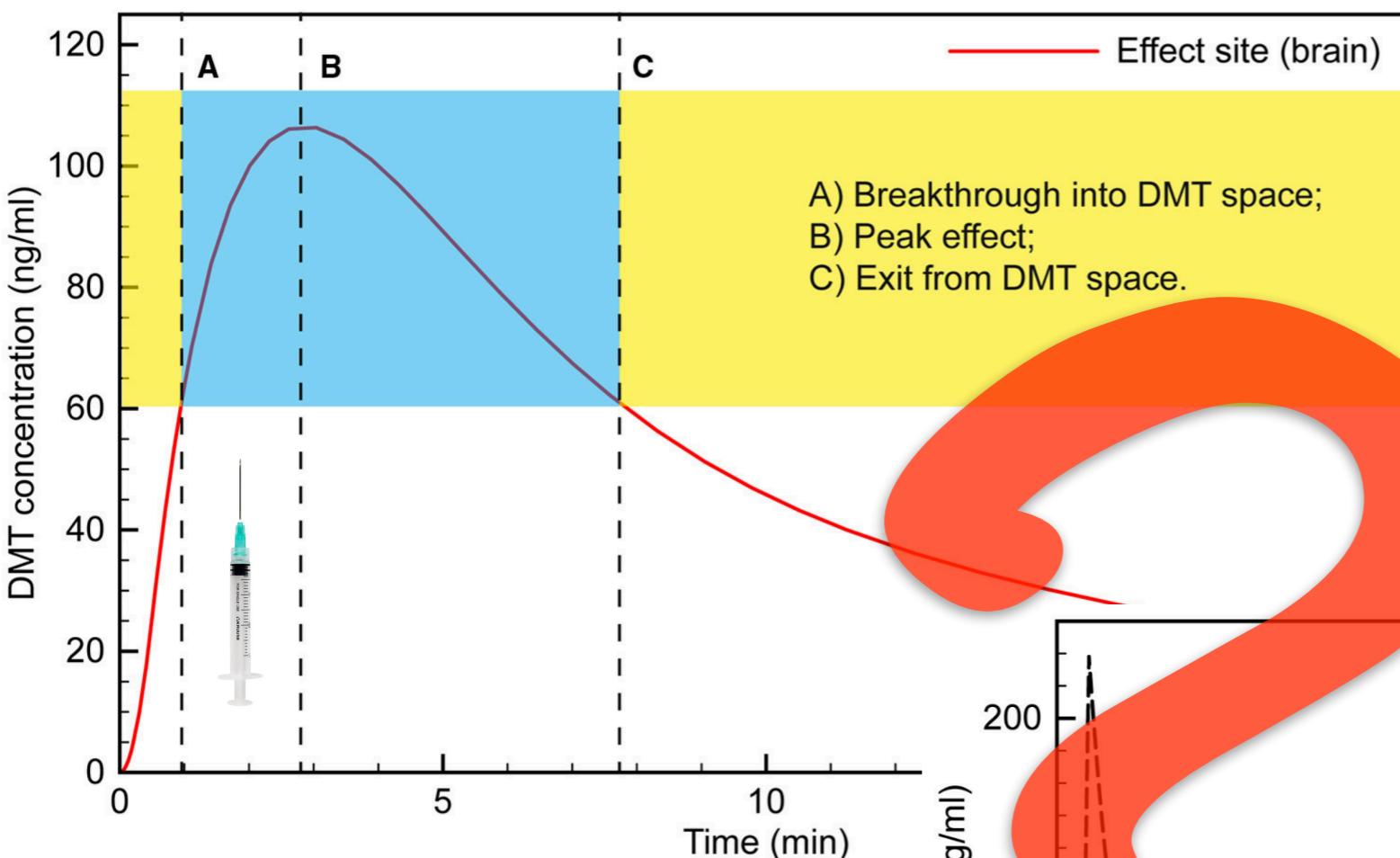
Figure 1. Mean dimethyltryptamine (free base) values in 10 subjects after four doses of intravenous dimethyltryptamine fumarate (0.05 mg/kg [squares], 0.1 mg/kg [triangles], 0.2 mg/kg [diamonds], and 0.4 mg/kg [closed circles]) and saline placebo (open circles).

Strassman et al.
[Arch Gen Psych, 1994](#)

DMT - Pharmakokinetik/-dynamik

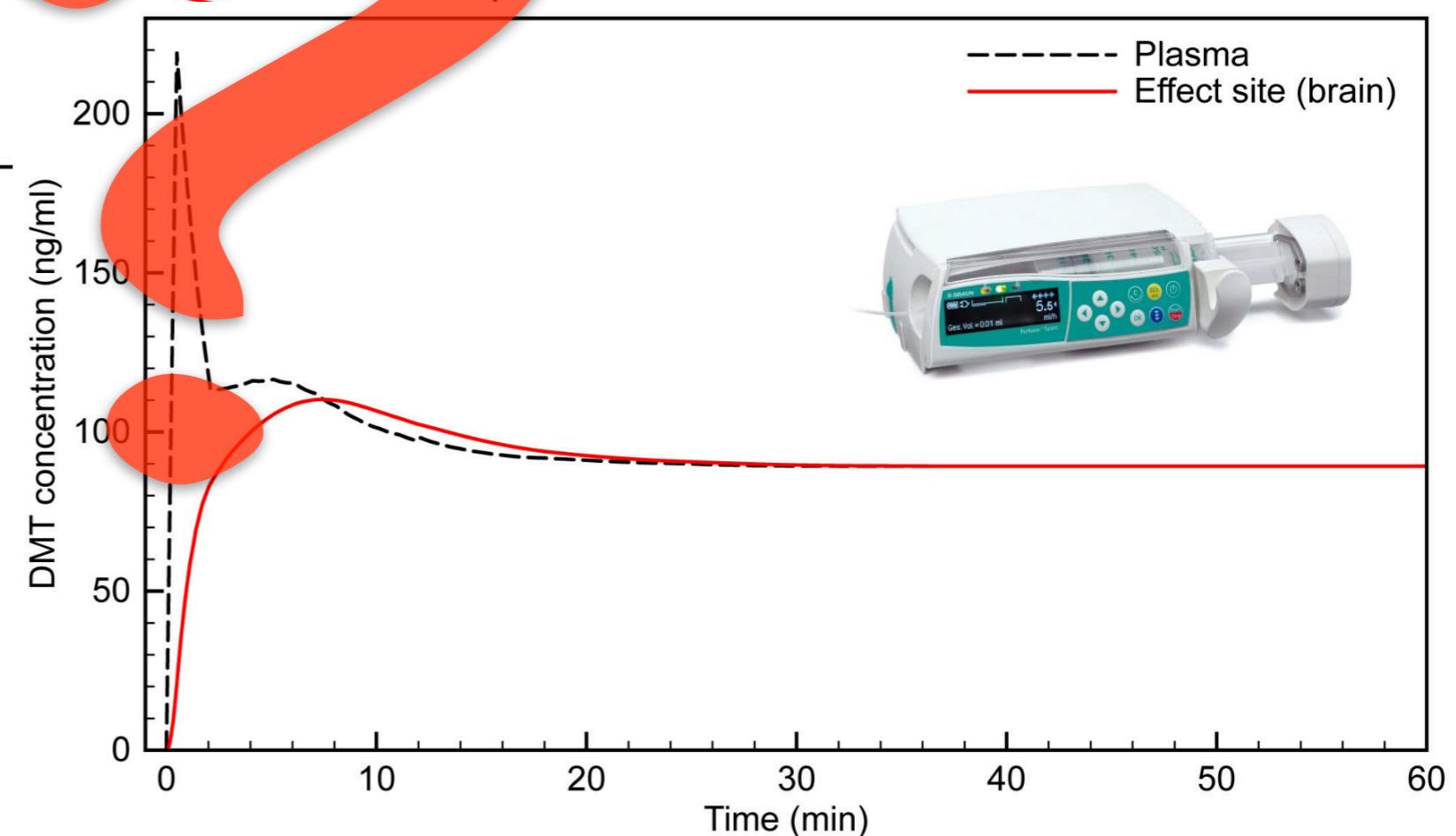
Gallimore and Strassman

Target-Controlled IV DMT Infusion



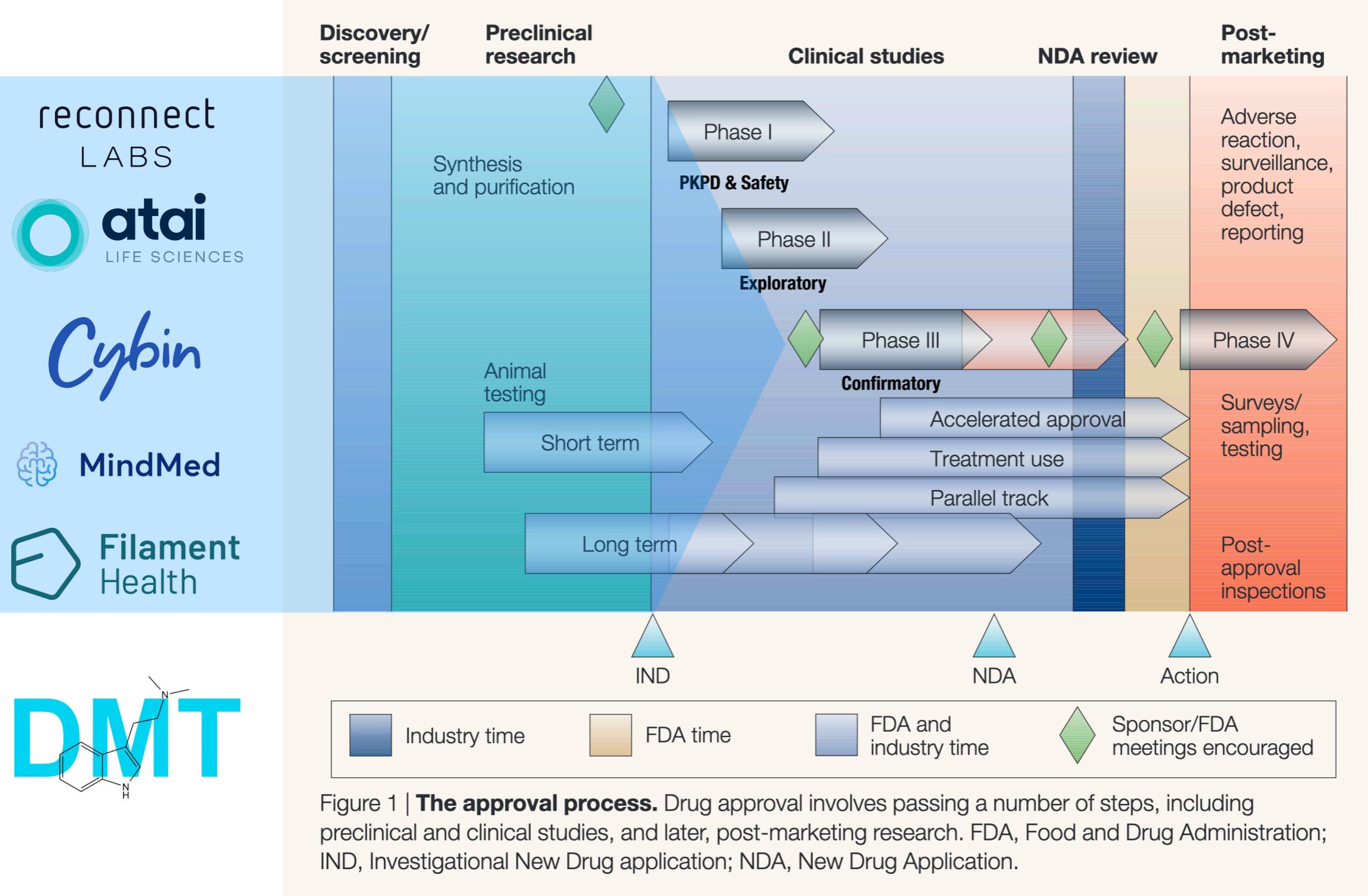
Phase 2a safety and efficacy for SPL026 (IV DMT) in 34 participants with MDD, demonstrating a clinically relevant and statistically significant reduction in depression symptoms at two weeks after dosing (-7.4 point difference in MADRS between SPL026 and placebo).

<https://cybin.com/development-pipeline/>



Translationale Arzneimittelentwicklung

von DMT-Präparaten





SPÄTER SCHAUEN

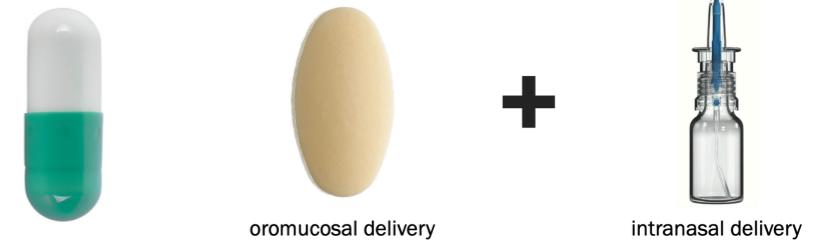
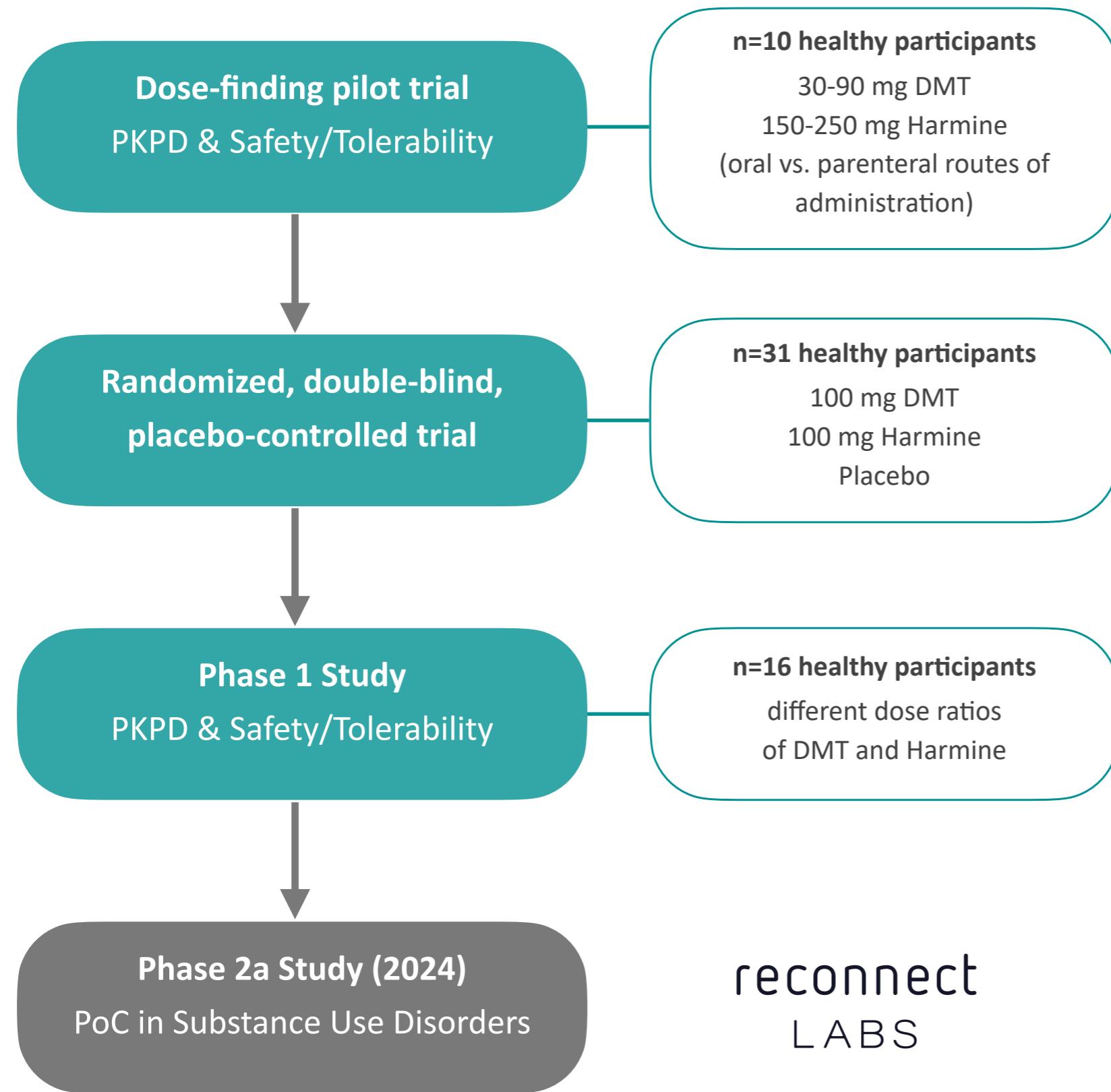
Psychedelika in der Therapie – Die Forschung holt auf

[Startseite](#) > [Dok & Reportagen](#) > [NZZ Format](#) > [UT](#) 14.09.2023 · 30 Min

Sie wurden verfeindet, verbannt und verboten: Psychedelische Substanzen wurden lange Zeit als Drogen abgetan. Doch in der Schweiz war es dank einer Ausnahmebewilligung des Bundesamts für Gesundheit immer möglich, mit ihnen zu forschen. Seit 15 Jahren blüht die Psychedelika-Forschung wieder auf.

Sie wurden verfeindet, verbannt und verboten: Psychedelische Substanzen wurden lange Zeit als Drogen abgetan. Zu schnell gerieten Psychedelika in den 1960er-Jahren unkontrolliert aus dem Labor in den Massenkonsum und wurden daraufhin weltweit verboten. Das psychotherapeutische Potenzial der Substanz... [MEHR INFOS](#)

[MEHR VON NZZ FORMAT](#) >



Dornbierer et al.
[Frontiers Pharmacology, 2023](#)



Müller & Aicher & Dornbierer et al.
under review

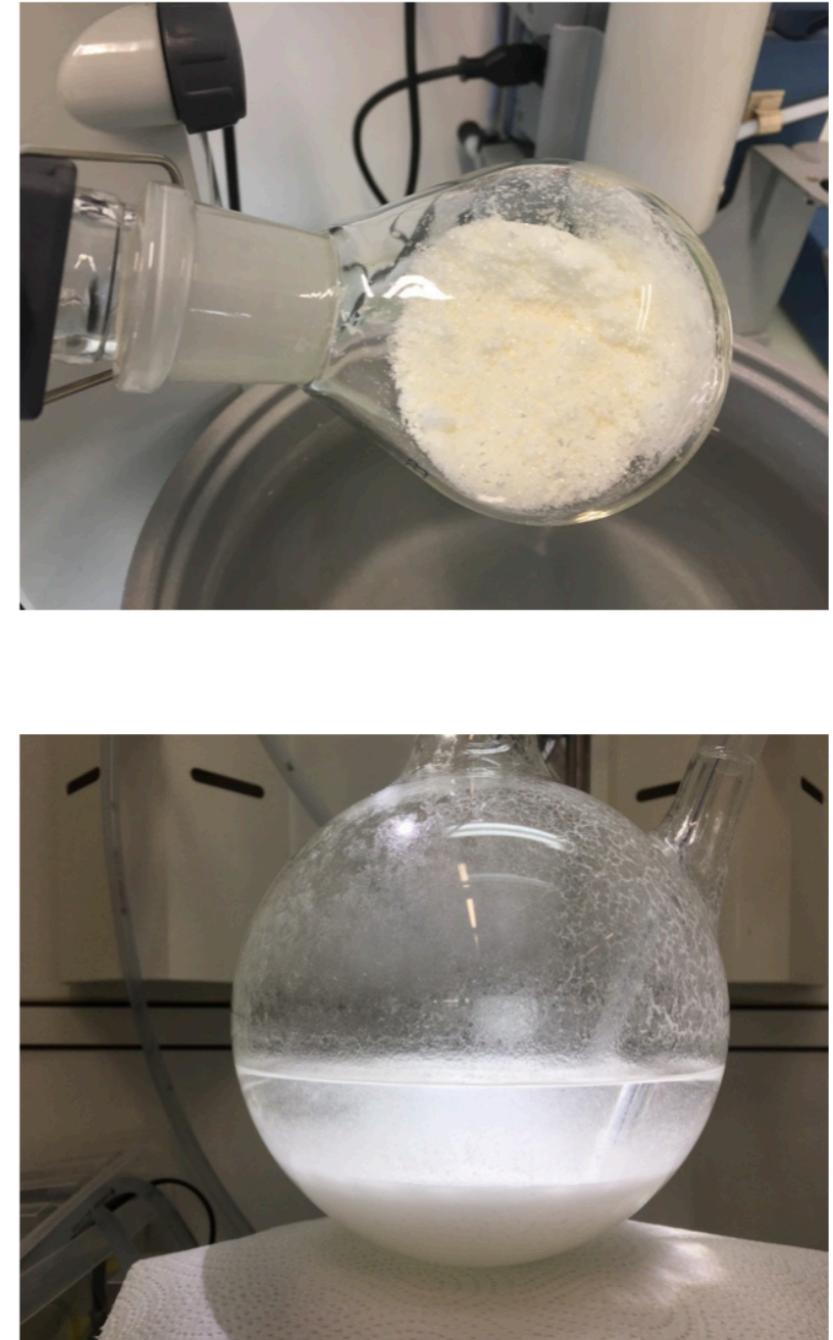
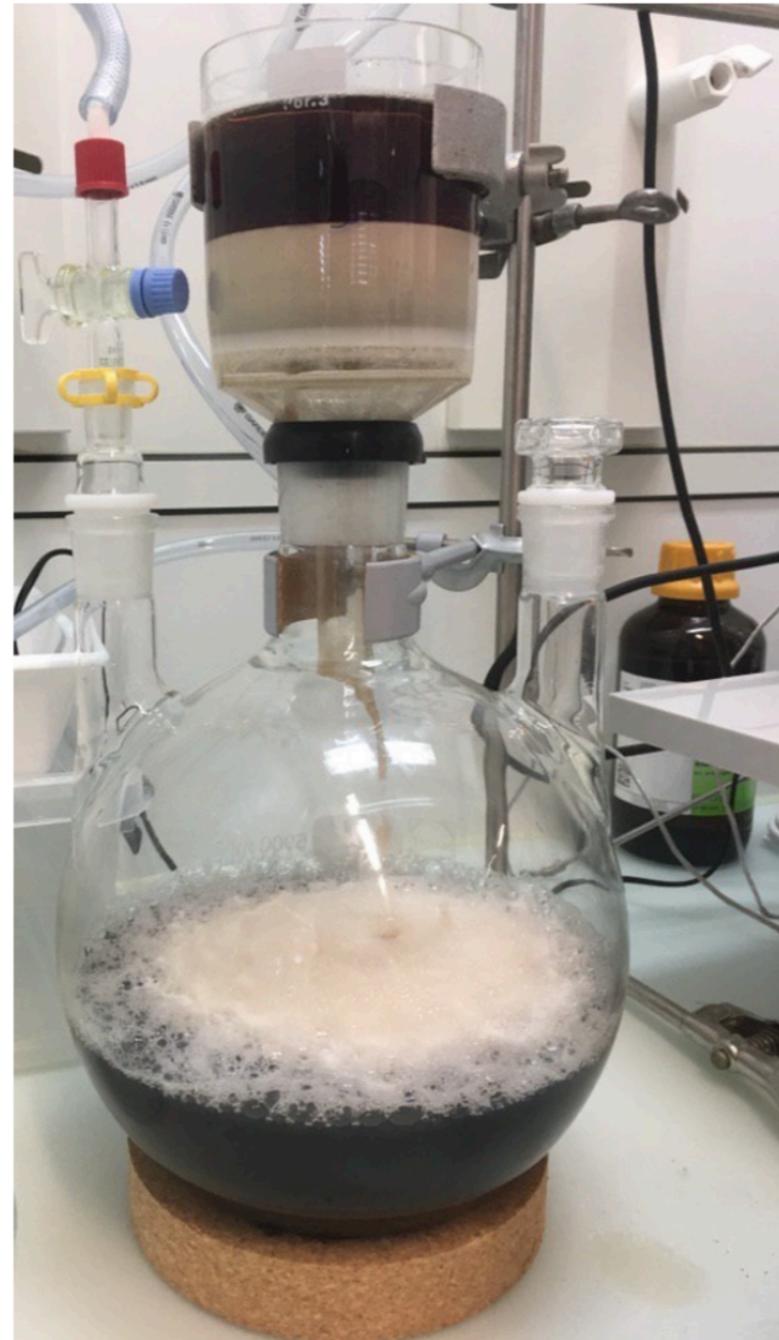
Aicher & Müller et al.
[Frontiers Psychiatry, 2024](#)

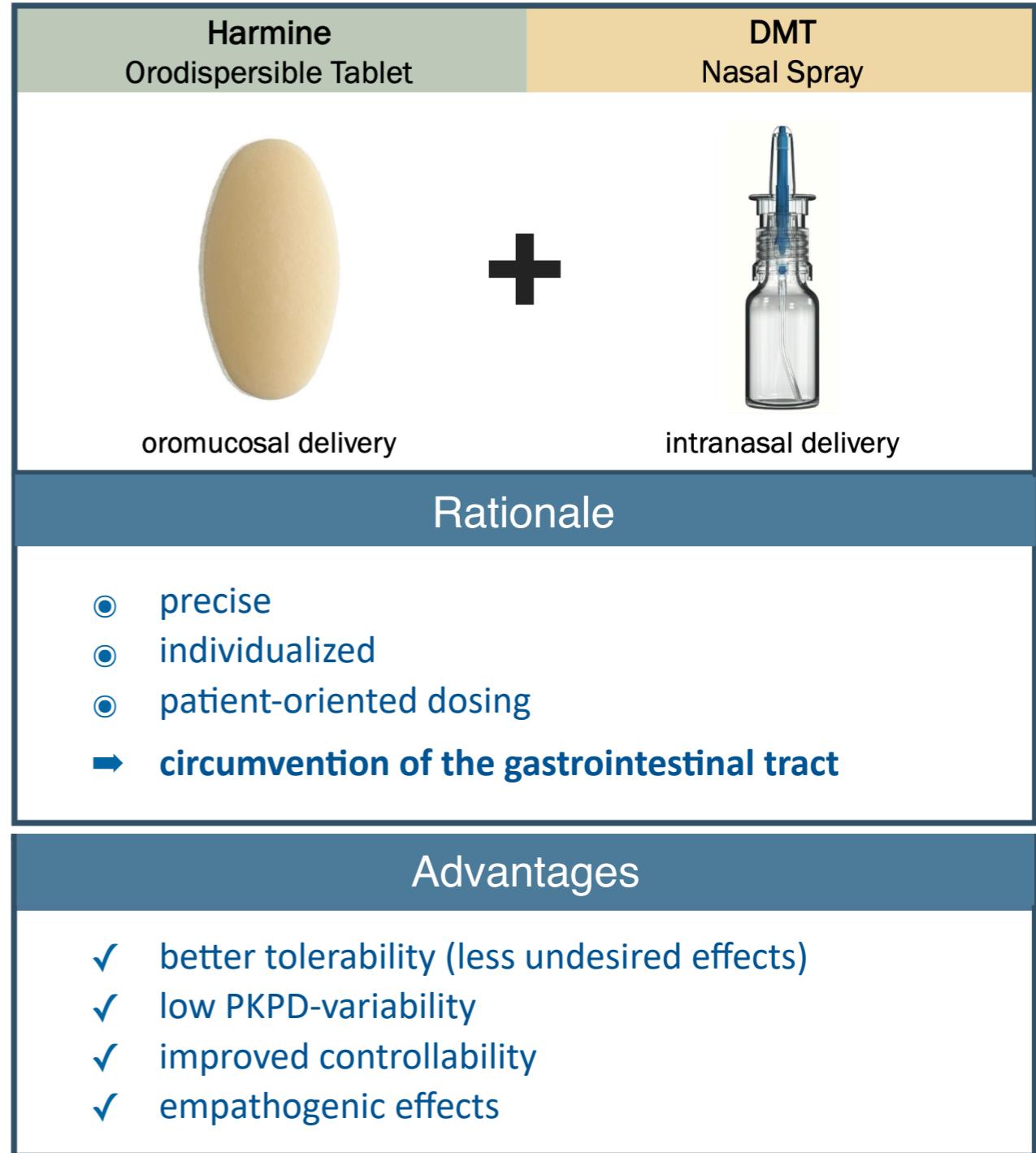


Egger & Jareño et al.
in preparation

reconnect
LABS

Isolation von N,N-DMT aus der Wurzelrinde von *Mimosa hostilis* (Incubator Lab, IREM UZH)





Overcoming the clinical challenges of traditional ayahuasca: a first-in-human trial exploring novel routes of administration of N,N-Dimethyltryptamine and harmine

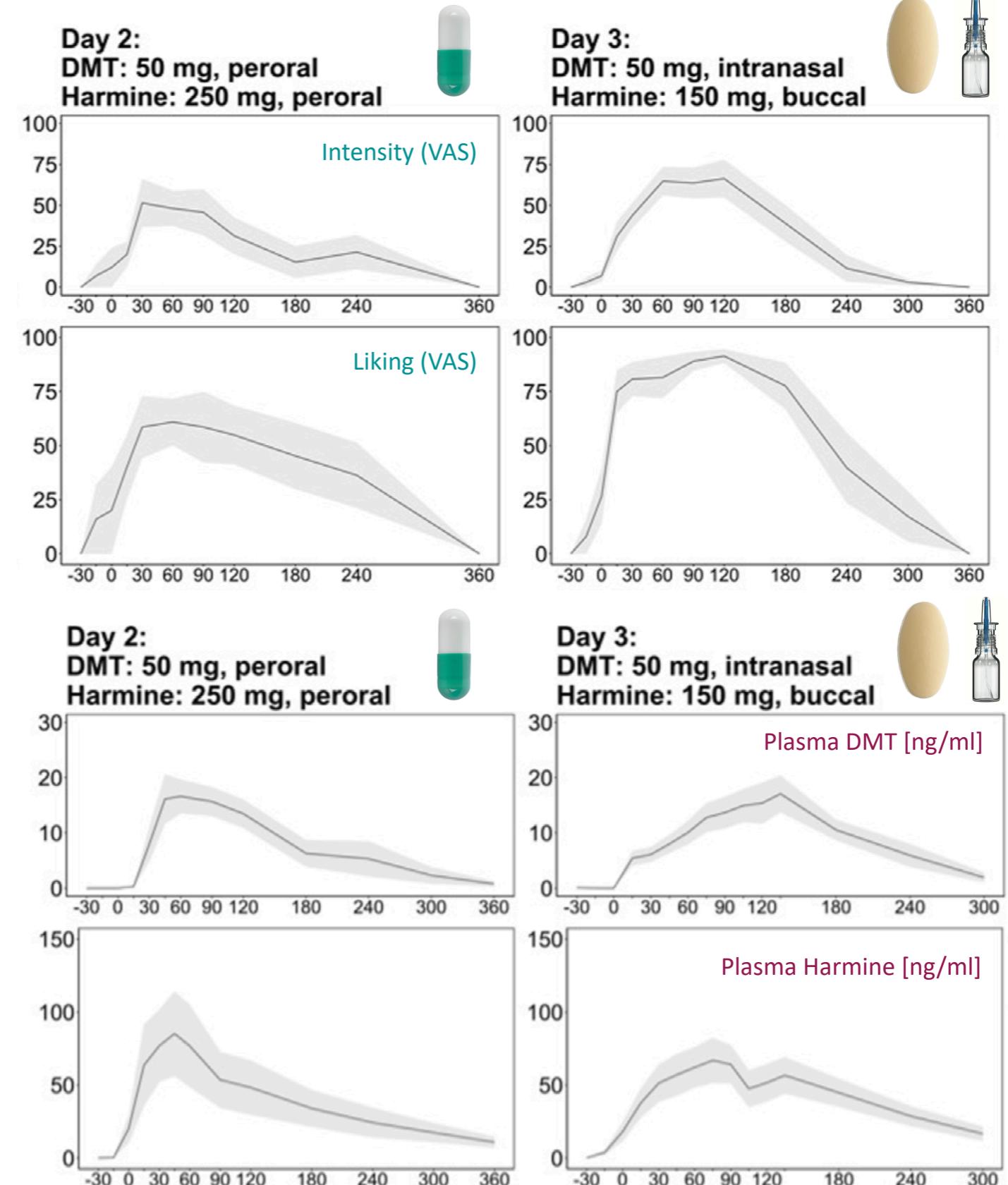
Dario A. Dornbierer^{1,2,3*}, Laurenz Marten^{3,4}, Jovin Mueller³, Helena D. Aicher^{3,5,6}, Michael J. Mueller^{3,6,7}, Martina Boxler², Michael Kometer⁸, Davor Kosanic⁸, Robin von Rotz³, Maxim Puchkov⁹, Thomas Kraemer², Hans-Peter Landolt^{1,6}, Erich Seifritz^{3,6} and Milan Scheidegger^{3,6}

 open-label, within-subject, dose-escalation study

 10 healthy male participants (30.7 ± 5.4 y; BMI 18.5–25)

 Harmine: 150–250 mg (oral vs. buccal)
DMT: 30–90 mg (oral vs. intranasal)

Dornbierer et al.
Frontiers Pharmacology, 2023



Studiensetting (RCT)

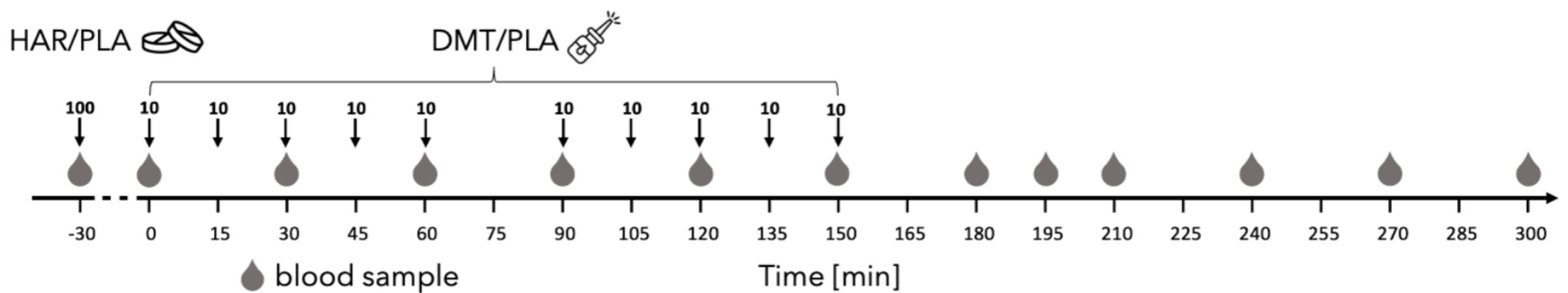
Psychedelic Lab Space @ University of Zurich



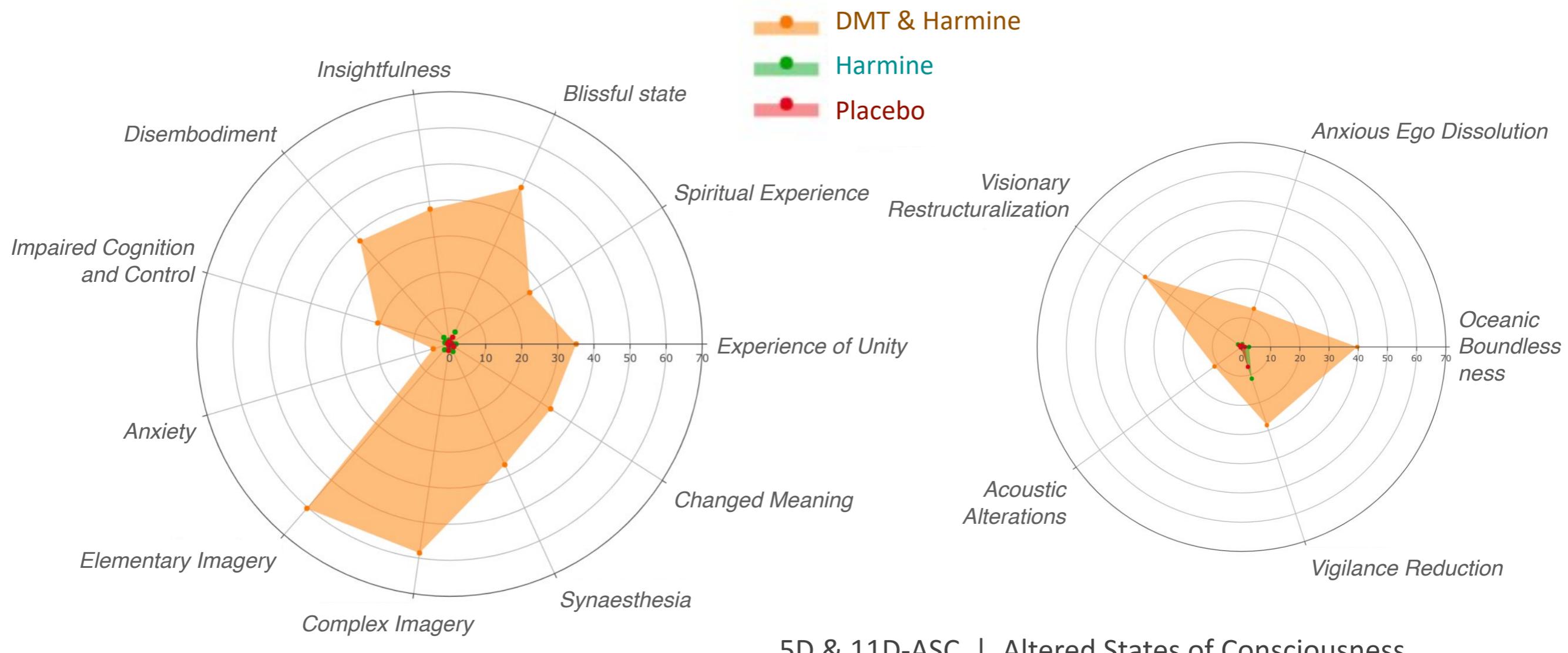
Studiendesign (RCT)

Psychedelic Lab Space @ University of Zurich

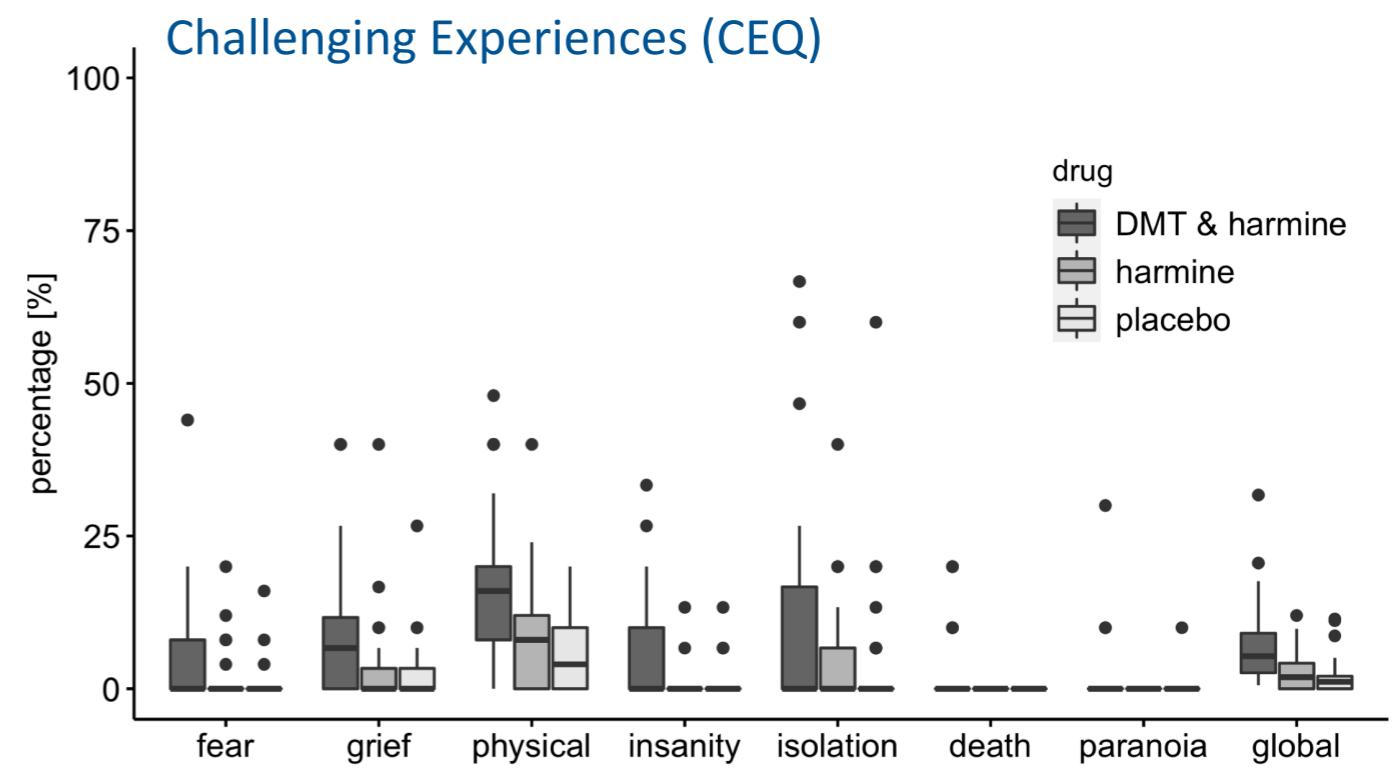
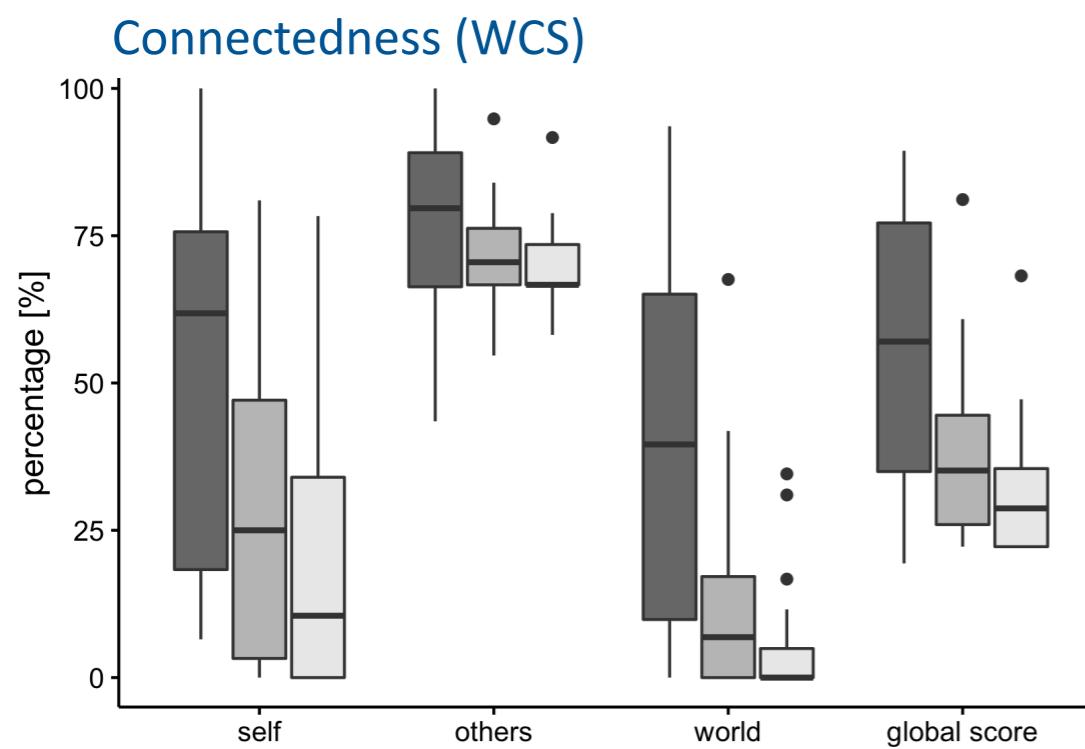
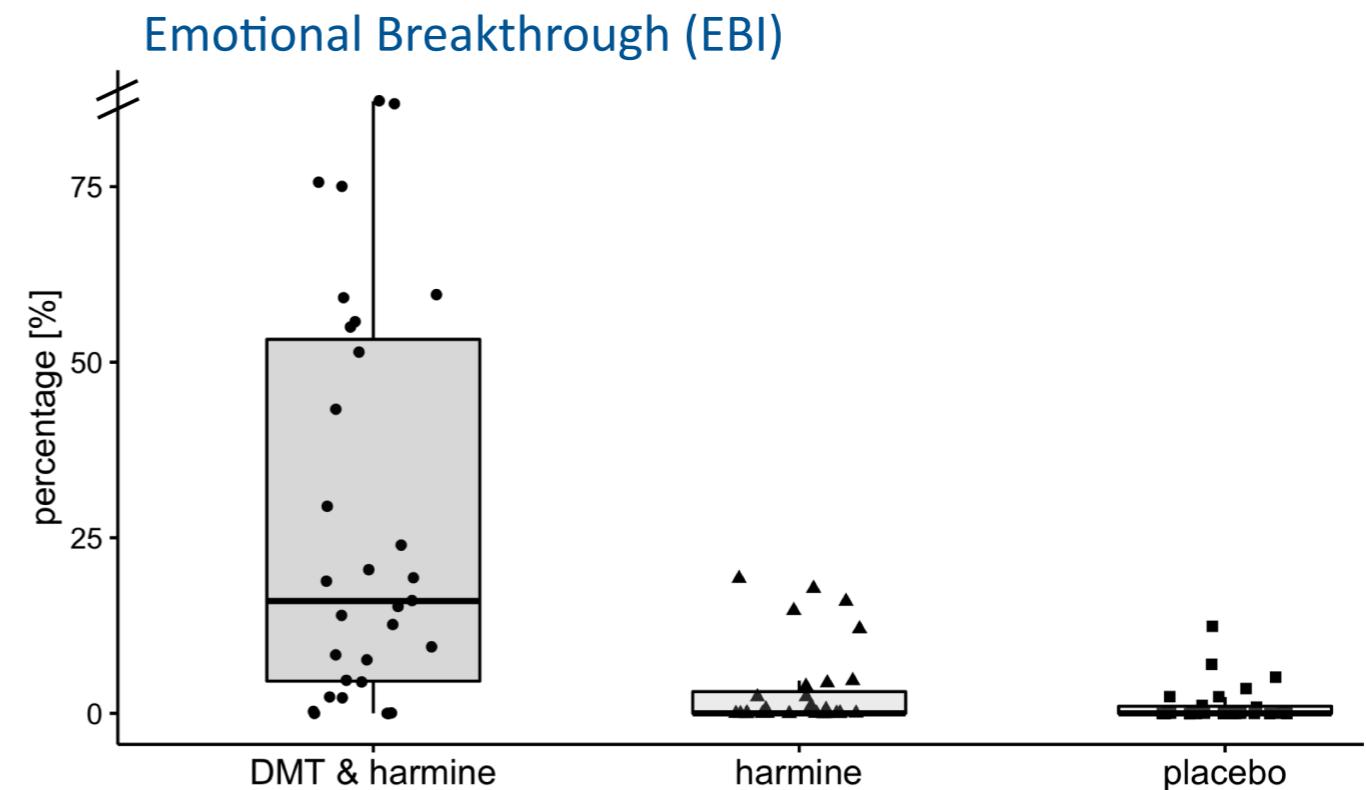
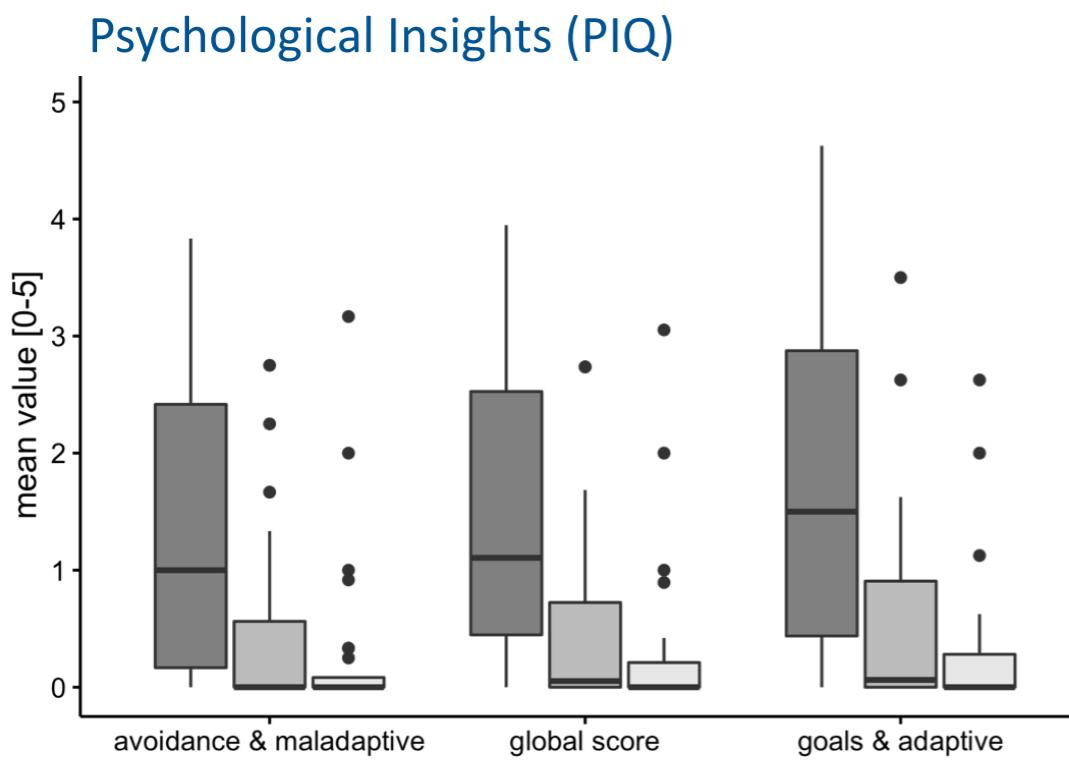
- double-blind, randomized, placebo-controlled, within-subject study
- 31 healthy male participants (25 ± 4 years | BMI 18.5–25)
- 100 mg Harmine (buccal) + 100 mg DMT (intranasal)
- 100 mg Harmine (buccal) + Placebo (intranasal)
- Placebo (intranasal) + Placebo (intranasal)



DMT & Harmin - Erlebnisprofil



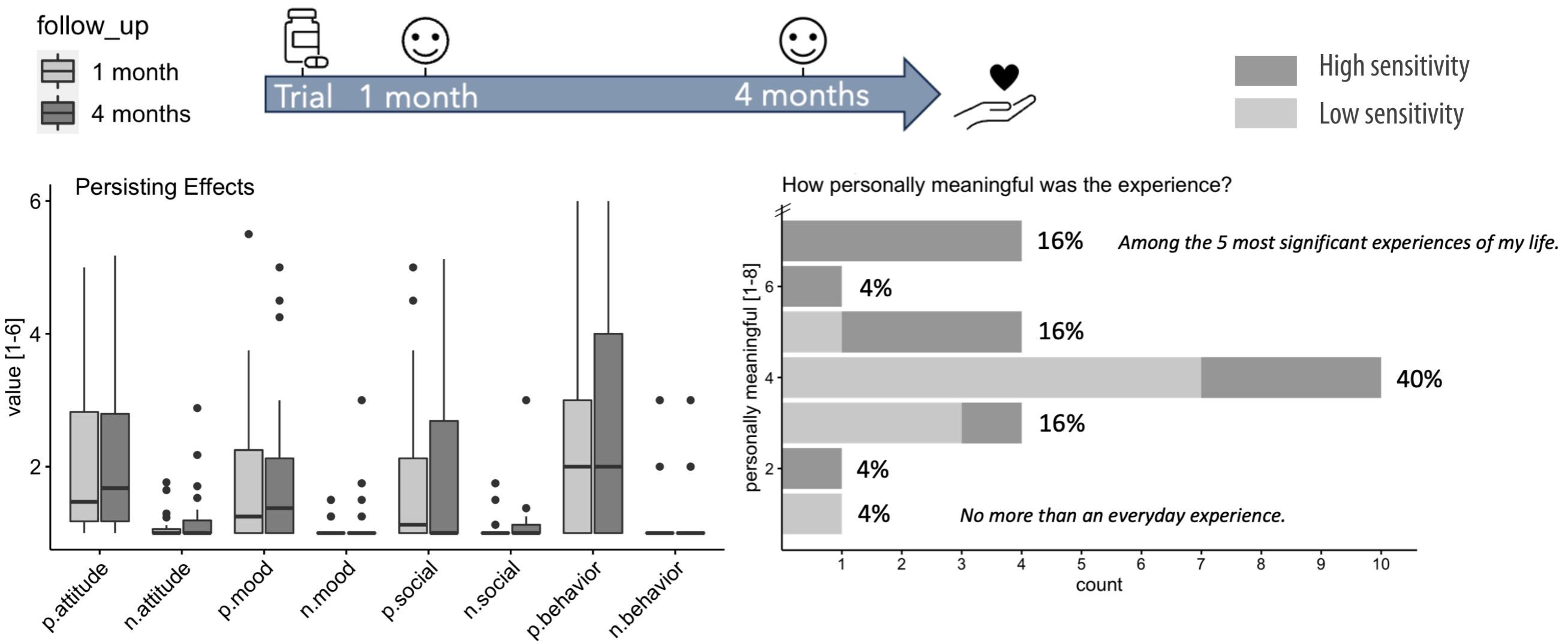
DMT & Harmin - Psychologische Effekte



DMT & Harmin - Psychologische Effekte

Pre- vs. Post-Session Ratings | Ecological Momentary Assessments (EMA)

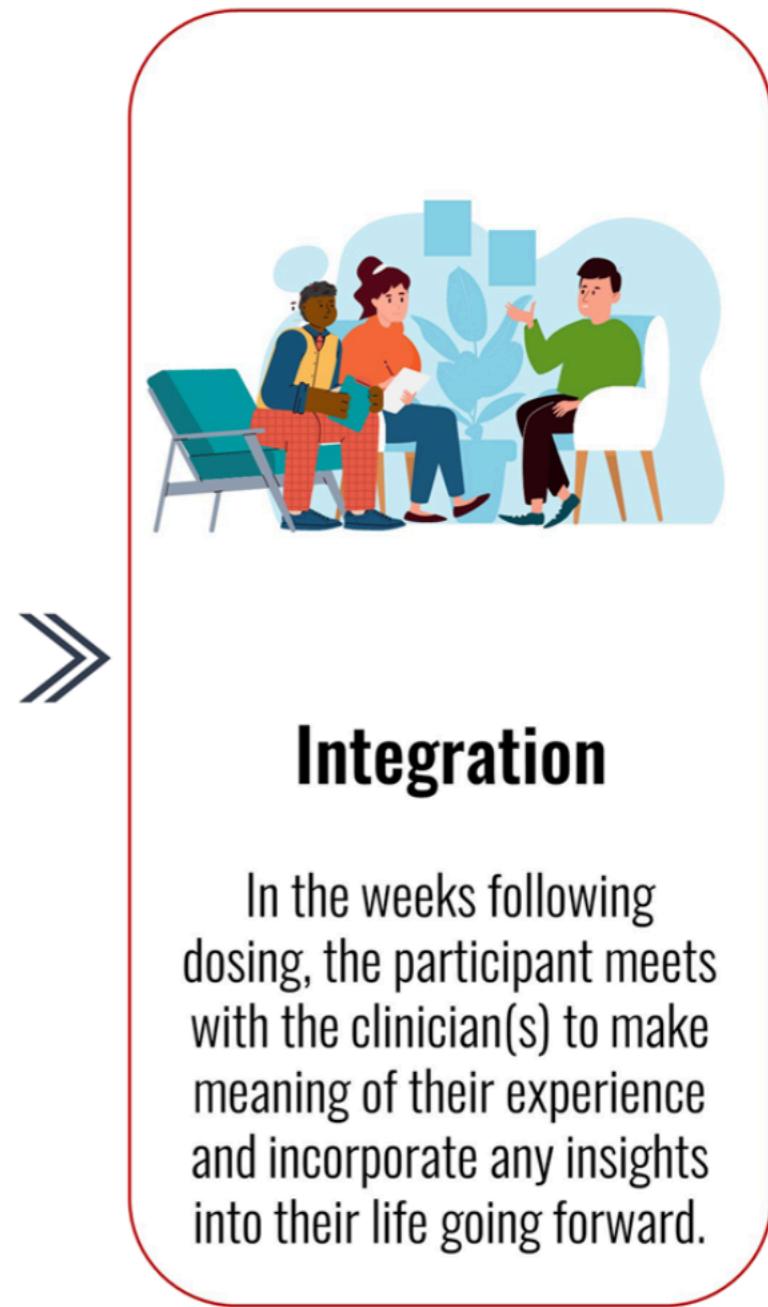
- **shift from negative to positive emotions after DMT/harmine**
- **increase in emotional acceptance, empathy, connection and optimism after DMT/harmine**
- **decrease in self-criticism, fear of failure, dissociation and pessimism in high sensitivity subgroup**



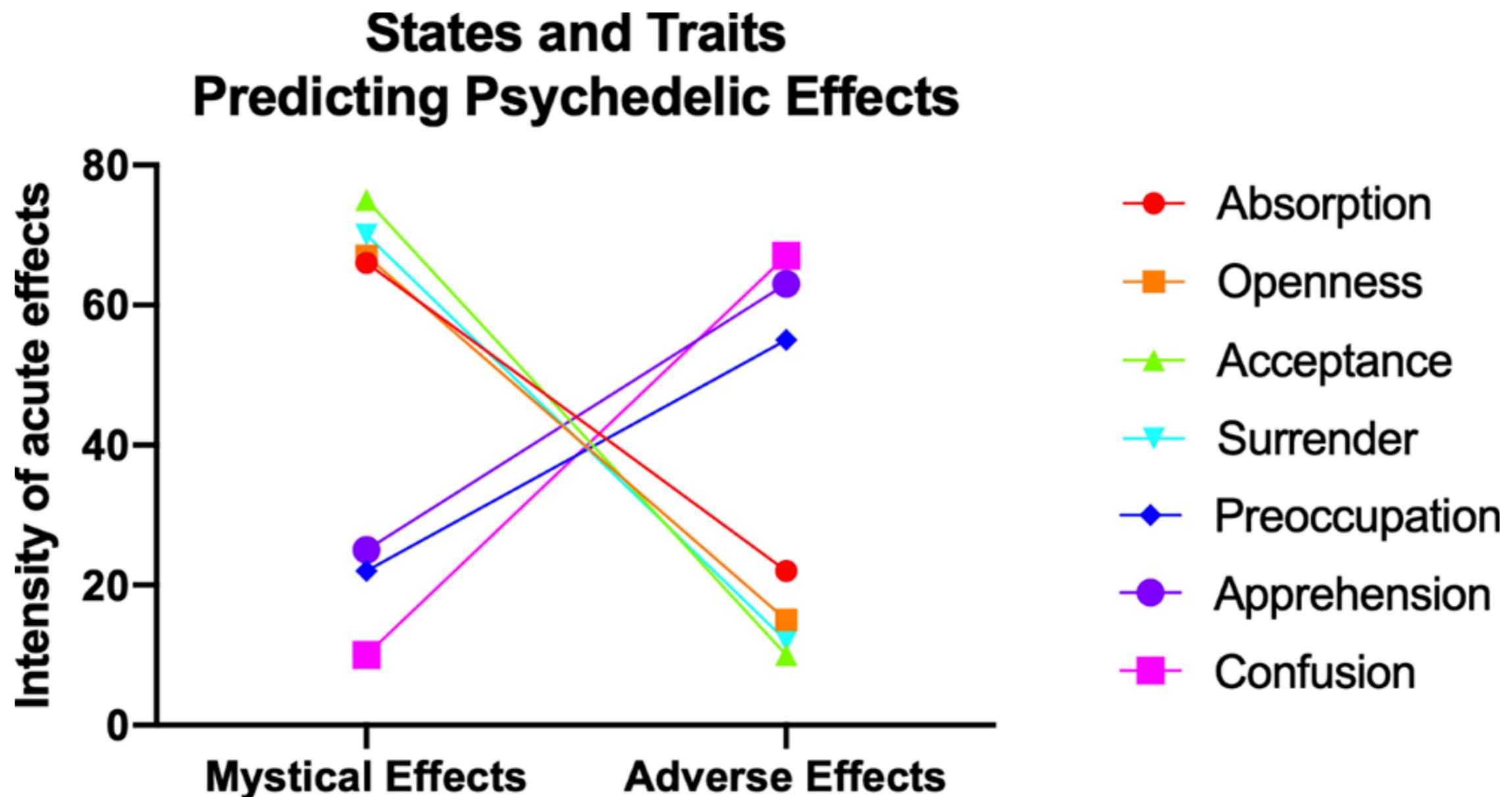
The subjective experience (11D-ASC, PIQ, EBI) **strongly correlated** with positive persisting effects and significance measures.

Aicher & Müller et al.
[Frontiers Psychiatry, 2024](#)

Ablauf einer Psychedelischen Therapie



Einfluss von Set und Setting





NZZ
format

SRF 1

Deconstructed, parsed, and diagnosed.

A hypothetical example illustrates how precision medicine might deconstruct traditional symptom-based categories. Patients with a range of mood disorders are studied across several analytical platforms to parse current heterogeneous syndromes into homogeneous clusters.

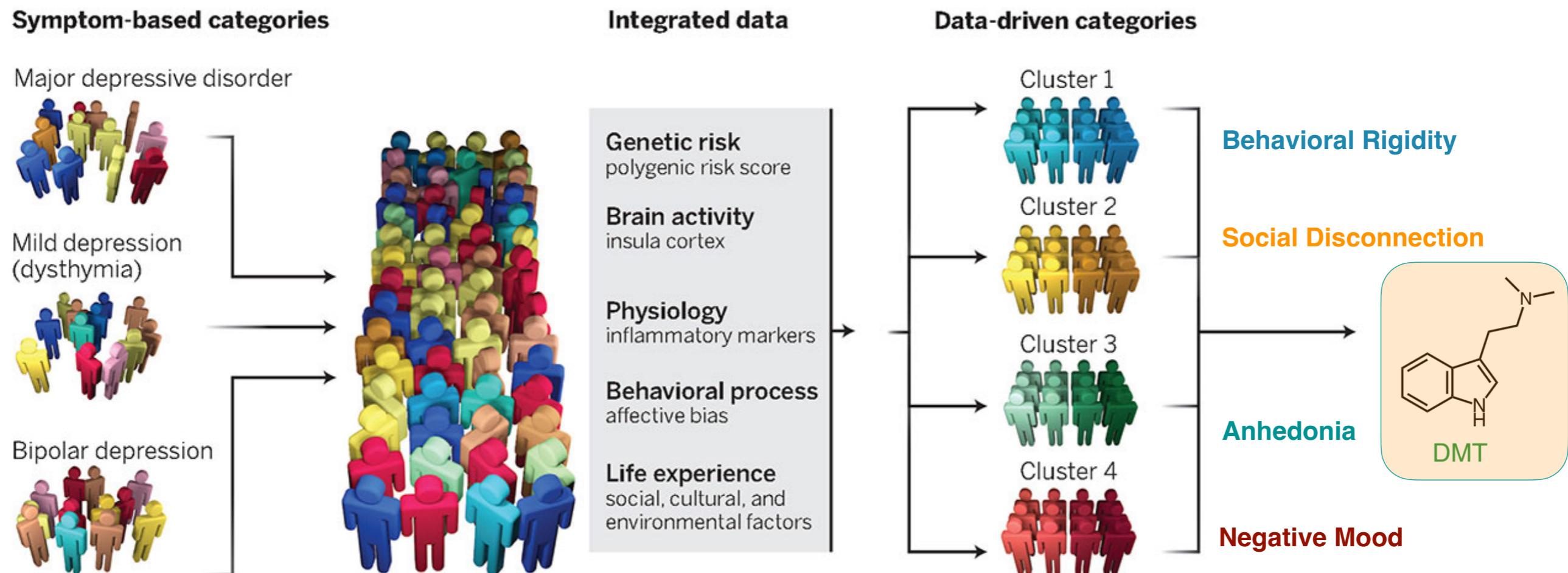


Fig. adapted from Insel & Cuthbert
[Science, 2015](#)

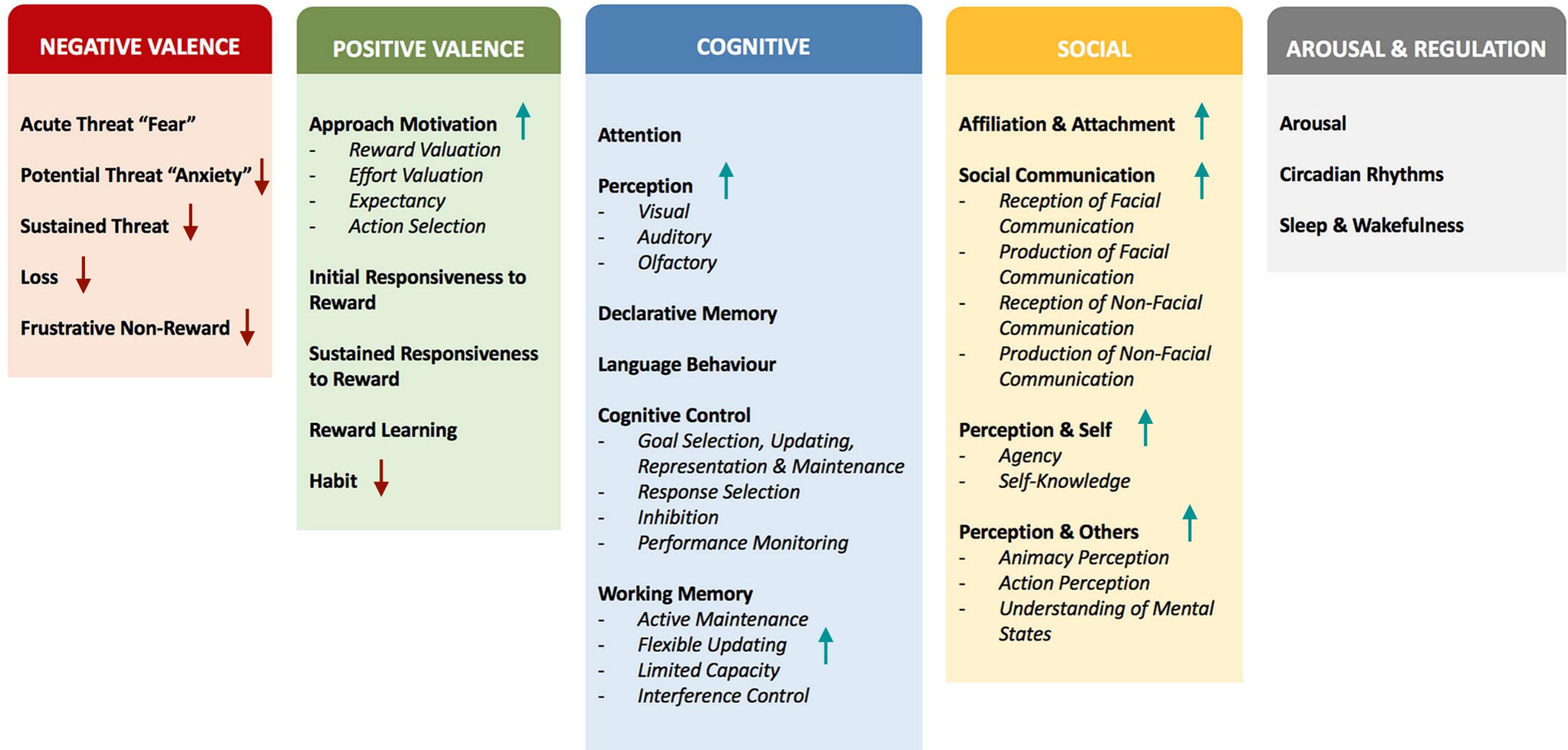


Fig. adapted from Yücel et al.
[Addiction, 2018](#)



Emotional processing

- Reduction of processing of negative stimuli
- Alterations in amygdala activity and connectivity

Potential therapeutic effect

- Normalization of negative bias
- Reduction of rumination
- Improvement of patient–therapist relationship
- Reduced social withdrawal
- Reinstatement of reward processing

Self-processing

- Decreased self–other differentiation
- Positive self-dissolution
- Unity

Social processing

- Increased empathy
- Reduced rejection sensitivity

Vollenweider & Preller
[Nat Rev Neurosci, 2020](#)

Take Home Messages

- Psychedelika erfahren ein wissenschaftliches Revival, das neue Möglichkeiten für die Behandlung von psychischen Störungen bietet, insbesondere für Depressionen, Angststörungen, Abhängigkeitserkrankungen, und Traumafolgestörungen.
- Aufgrund ihrer psychoplastogenen Wirkung dienen Psychedelika vorwiegend als Verstärker der neuronalen Plastizität, auf deren Grundlage sich salutogenetische Veränderungsprozesse anbahnen können.
- Durch Emotionsaktivierung und Flexibilisierung des Denkens werden psychedelische Erfahrungen auch als transdiagnostische Verstärker zur Vertiefung von psychotherapeutischen Interventionen genutzt.
- Psychedelika zeigen in einem kontrollierten Setting ein relativ gutes Sicherheitsprofil und eine gute Verträglichkeit, es braucht noch grössere Vergleichsstudien zu Langzeitwirkungen und -verträglichkeit im Rahmen von klinischen Anwendungen.
- Aufgrund der kürzeren Wirkdauer und besseren Steuerbarkeit könnten innovative DMT-Präparate eine Alternative zu klassischen Psychedelika wie LSD, Psilocybin oder Meskalin darstellen, es sind jedoch weitere klinische Studien notwendig.

Psychedelic Research & Therapy Development (DPPP, PUK/UZH Zürich)

Dr. Dr. med. Milan Scheidegger (Junior Group Leader, Senior Physician)



Jasmine Ho
PostDoc Psychology



Helena Aicher
PostDoc Psychology



Dila Suay
cand. PhD Cogn. Sci.



Joëlle Dornbierer
cand. PhD Pharmacy



Michael Müller
cand. PhD Health Sci.



Daniel Meling
cand. PhD Cogn. Sci.



Klemens Egger
cand. PhD Neuroscience



Jonas Schlamberg
cand. PhD Digital Health



Emilia Vasella
Scientific Assistant



Jovin Müller
Study Physician



Javier Jareno
Study Physician



Ilhui Wicki
Study Physician



Claudius Elsner, MD
Study Physician



Laurenz Marten
Natural Sciences Student



Luzia Caflisch
Psychology Student



Alexandra Hempe
Psychology Student



Dominic Lanz
Medical Student



Nora Müller
Medical Student



Simon Selden
Medical Student



Per Müller
Medical Student



Anja Schiffmann
Medical Student



Paula Iversen
Psychology Student



Can Tekin
Psychology Student



Sebastian Penz
Psychology Student

Reconnect Labs

University of Zurich Spin-Off



Davor Kosanic, PhD
Chief Executive Officer



Emma Chaffin, PhD
Product Strategy
Otsuka, Jazz & other CNS



Milan Scheidegger, PhD
Chief Medical Officer



Andy Page
Commercialization
CEO Otsuka EU &
COO Beckley Psytech



Dario Dornbierer, PhD
Chief Scientific Officer



Mike Emanuel, PhD
Clinical Ops
J&J, Compass, Gilgamesh



Robin von Rotz, MS
Chief Clinical Officer



Nick Draeger, PhD
BD & Strategy
Roche, NHS, Innosuisse



Daniel Claussen, MBA
Chief Business Officer



Sascha Fritzsche, CFA
Finance & Operations
Optotune, USZ



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BoD: CureVac, Paion,
Cosmo Pharmaceuticals



Manfred Schneider, PhD
Consultant
Tox & Preclinical
AUC Consulting



Claire Gillis, PhD
Market Access Advisor
CEO, VLMYR Health



Eduardo Vianna, PhD
Clinical Strategy Advisor
Global Program Head,
MERCK



Peter Gasser, MD
Advisor,
Psychedelic Therapy
President, SAPT



Erich Seifritz, MD PhD
Clinical Advisor
Director, Psychiatric
University Clinic, Zurich

Scientific Advisors & Collaborators



Prof. Erich Seifritz
Director DPPP



Prof. H.-P. Landolt
Psychopharmacology



Prof. Thomas Krämer
Analytic Chemistry



Prof. Boris Quednow
Pharmacopsychology



Prof. Birgit Kleim
Psychotherapy



PD Maxim Puchkov
Pharmaceutical Science



Roch Ogier, MD PhD
Therapy Development Accelerator

TDA (UZH)

Vielen Dank für Ihre Aufmerksamkeit



Dr. sc. Dr. med. Milan Scheidegger, MA HPK

Psychedelic Research & Therapy Development

Klinik für Psychiatrie, Psychotherapie und Psychosomatik, PUK Zürich

milan.scheidegger@bli.uzh.ch