Augmentationsstrategien der Therapie depressiver Störungen – von Psychedelika bis Transkranielle Magnetstimulation

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OBG, online Weiter-/Fortbildung; Andreaas Wahl-Kordon / Matthias Müller; Online Zoom, 26. Oktober 2022

Universität Zürich[UZH]

Inhalt

- Allgemeine Prinzipien
- Leilinien Therapieresistenz
  - Kombination
  - Augmentation
  - Switch
  - Neuromodulation / Ketamin
- Psychedelika
  - glutamaterg
  - serotonerg
  - N_2O
  - Mechanismen
- Diskussion

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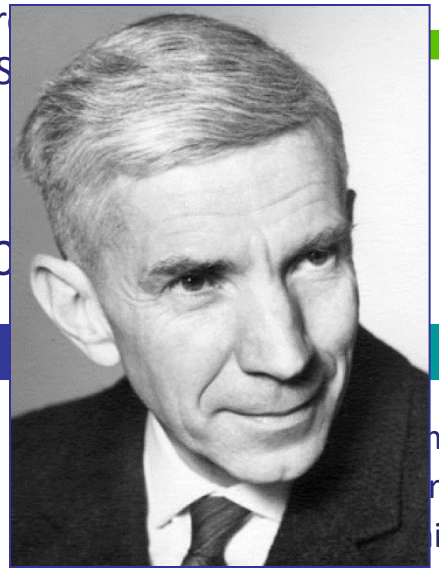
Monoamin-Hypothese der Depression seit 60 Jahren



Über die Behandlung depressiver Zustände mit einem Iminodibenzylderivat (G 22355)

Von R. Kuhn

Roland Kuhn, Schweiz. Med. Wochenschr., 1957 (35/36, 1135-1140)

Br… S…

Selektivere Substanzen

Neue Substanzen mit mehreren spezifischen Ansatzpunkten

1950 | 1970s | 1980s | 1990s | 2000+

…mipramin
…rtriptylin
…itriptylin
Desipramin
Phenelzin
Isocarboxazid
Tranylcypromin

Maprotilin
Amoxapin
Trazodon

Fluoxetin
Sertralin
Paroxetin
Fluvoxamin
Citalopram

Bupropion

Nefazodon
Mirtazapin
Venlafaxin
Milnacipran

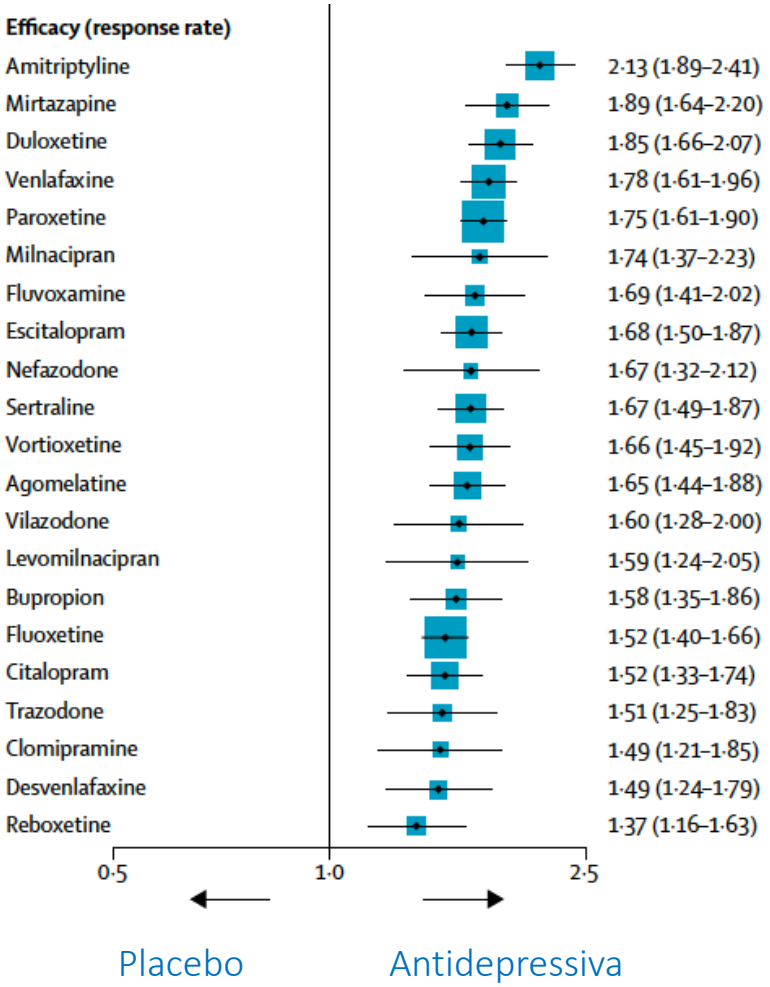
Duloxetin
Escitalopram
Agomelatin
Vortioxetin
(aNL)

➔ serotonin || noradrenalin

Kuhn 1957

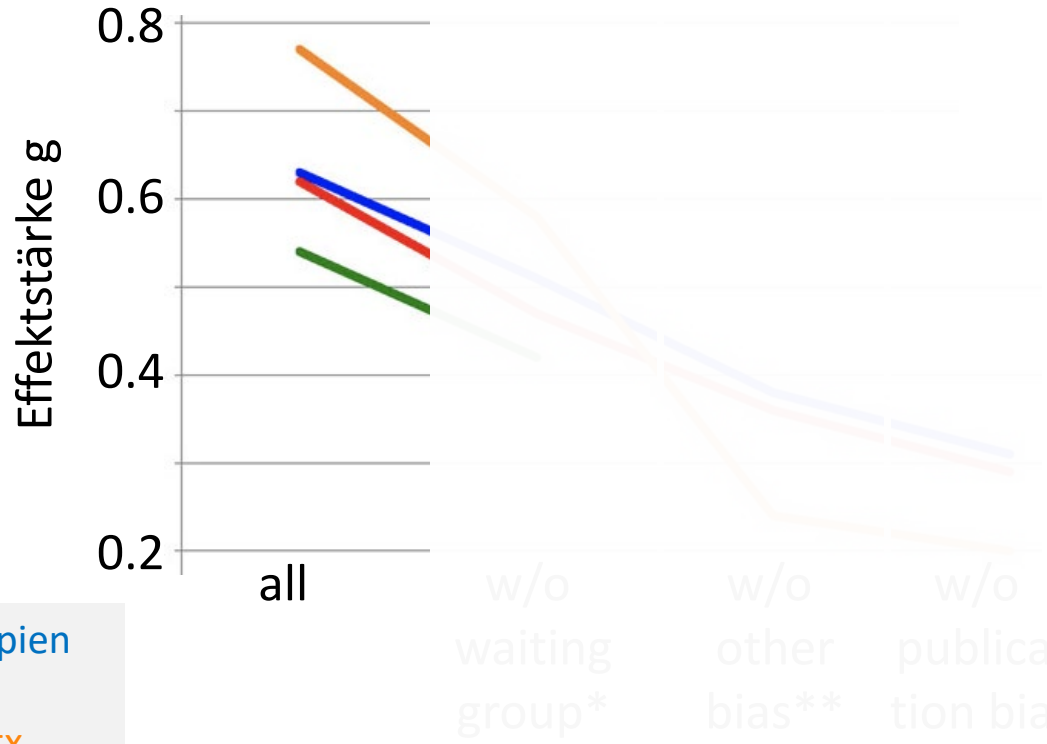
Wirksamkeit der Antidepressiva

- 522 RCT
- 116.477 patients



Cipriani et al, The Lancet. 2018, 391:135766

Wirksamkeit der Psychotherapie



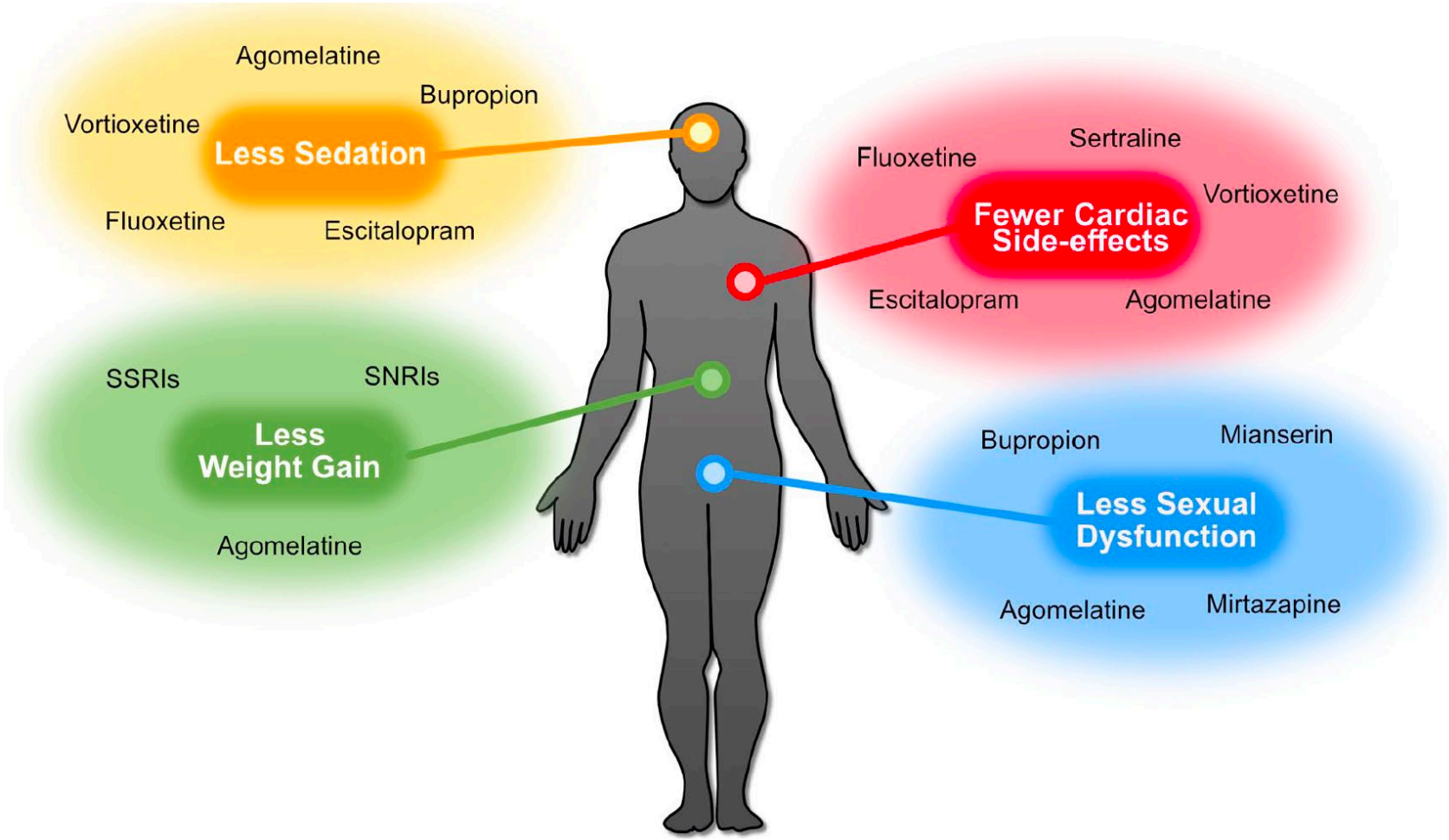
alle Psychotherapien
CBT
Problemsolving tx
IPT

*waiting group: nocebo | **garbage in - garbage out

➔ only 23% of published studies apply strict methods

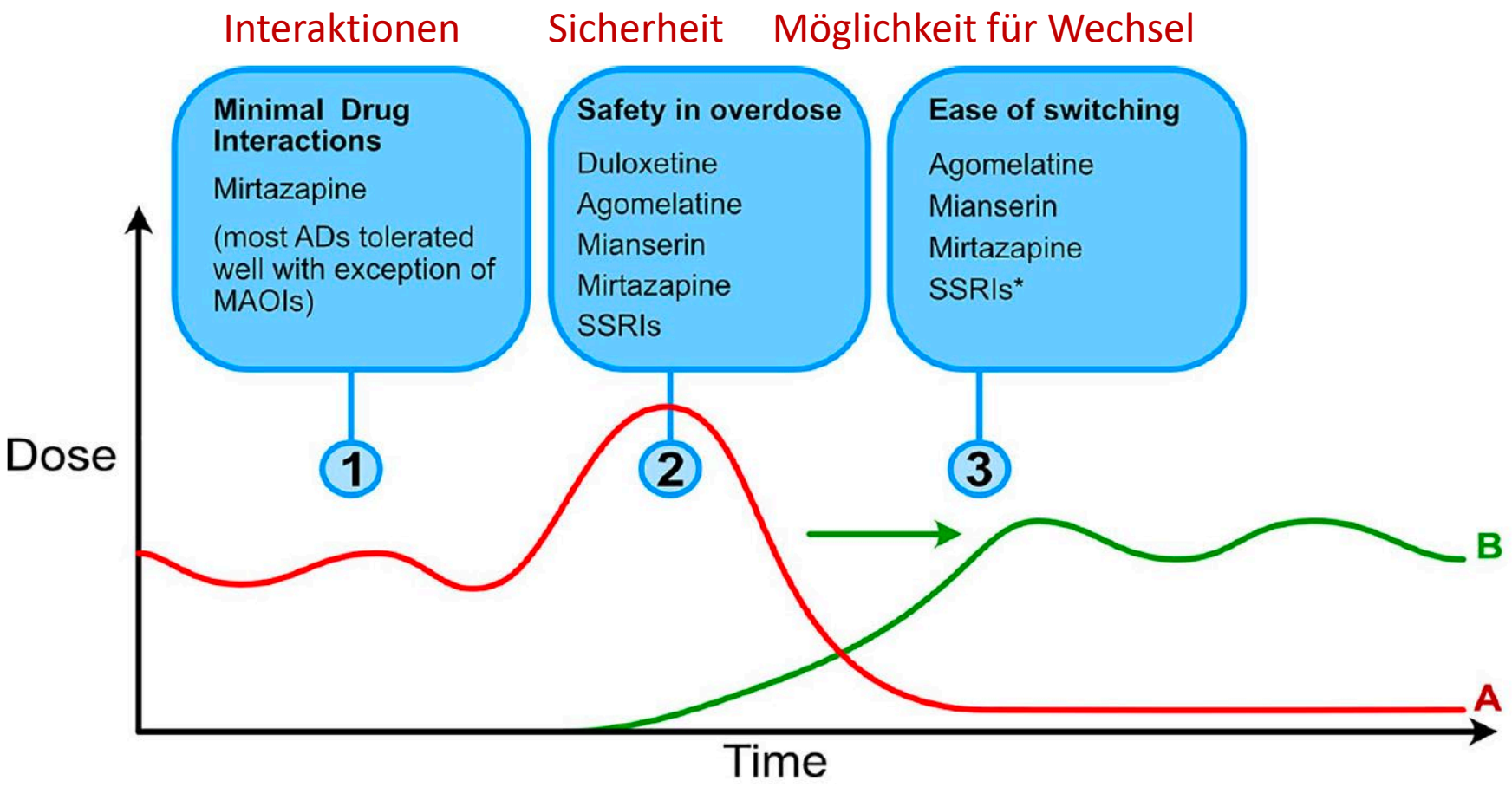
Cuijpers et al., Epidemiol Psychiatr Sci. 2019, 28:21–30

Individuelle Antidepressiva Auswahl: nach Nebenwirkungen



aus: Australische/Neuseeländische Behandlungsleitlinien:
Malhi GS et al. Aust N Z J Psychiatry 2021, 55:7-117, doi:10.1177/0004867420979353
Malhi GS et al. Bipolar Disord 2020, 22:788-804, doi:10.1111/bdi.13035

Individuelle Antidepressiva Auswahl: weitere Kriterien



Malhi GS et al. Aust N Z J Psychiatry 2021, 55:7-117, doi:10.1177/0004867420979353
Malhi GS et al. Bipolar Disord 2020, 22:788-804, doi:10.1111/bdi.13035

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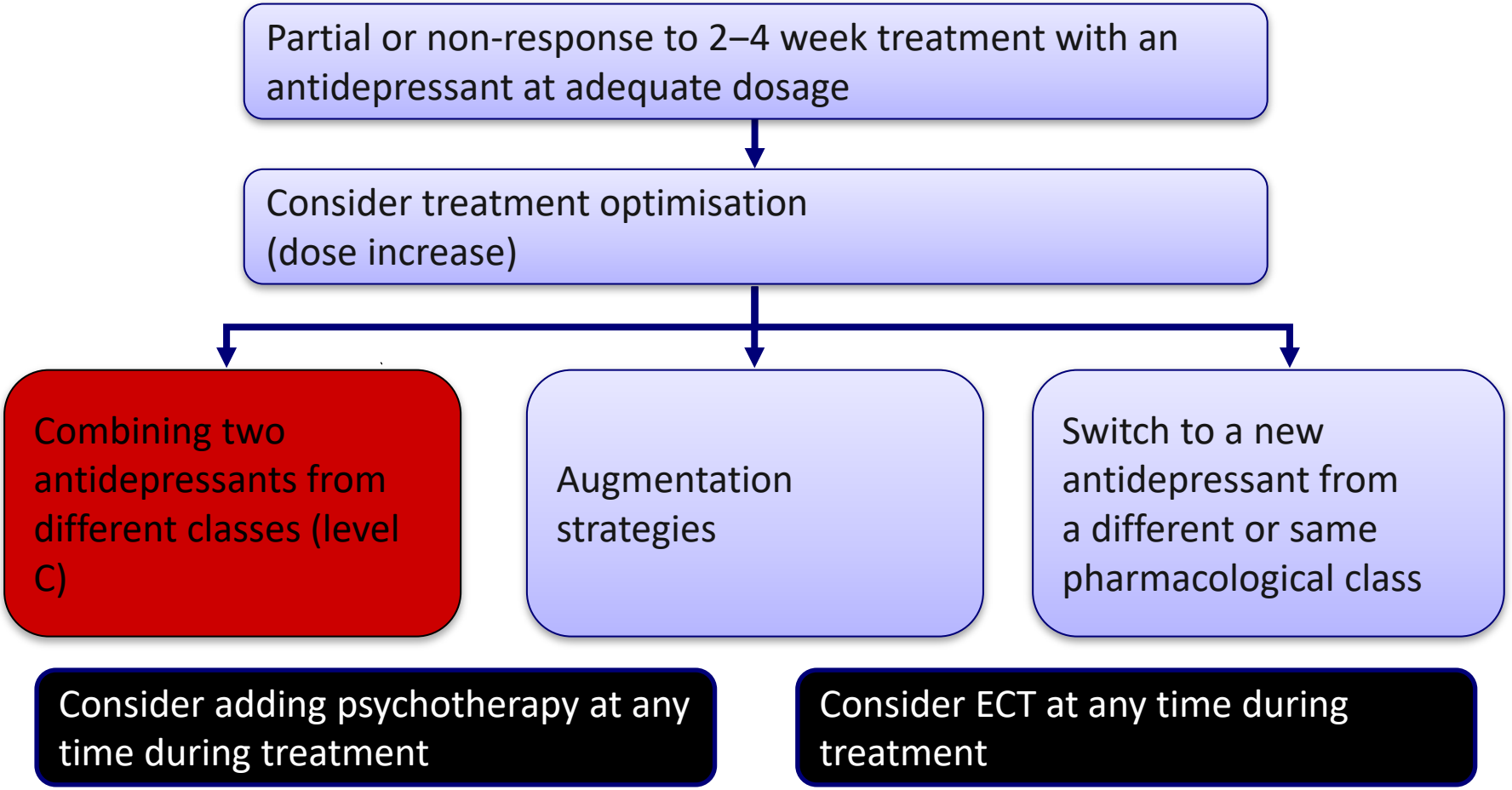
Teil-/Non-Response – Abklärungen

1. Stimmt primäre psychiatrische Dg?
2. Vorbehandlung adäquat (AD, Dosis, Dauer)?
3. Adhärenz/Compliance bei Vorbehandlung?
4. Pharmakogenetik oder Blutspiegel sinnvoll?
5. Psychiatrische Komorbidität mit zusätzlicher Therapieindikation?
6. Somatische Komorbidität mit zusätzlicher Therapieindikation?
7. Somatische Erkrankung, die sekundäre Depression verursacht?
8. Umgebungs Stressfaktoren

   (soziale/familiäre/berufliche/wirtschaftliche/schulische/...)?

Rush AJ et al. Aust N Z J Psychiatry 2019, 53:109-18

WFSBP: Teil-/Non-Response



Bauer et al, World Journal of Biological Psychiatry 2013, 14, 334-385
Bauer et al The World Journal of Biological Psychiatry 2007;8:67-104
Bauer et al The World Journal of Biological Psychiatry 2002;3:69-86
Bauer et al The World Journal of Biological Psychiatry 2002;3:5-43

WFSBP: Teil-/Non-Response: Mirtazapine + Venlafaxine

WFSBP recommendation:

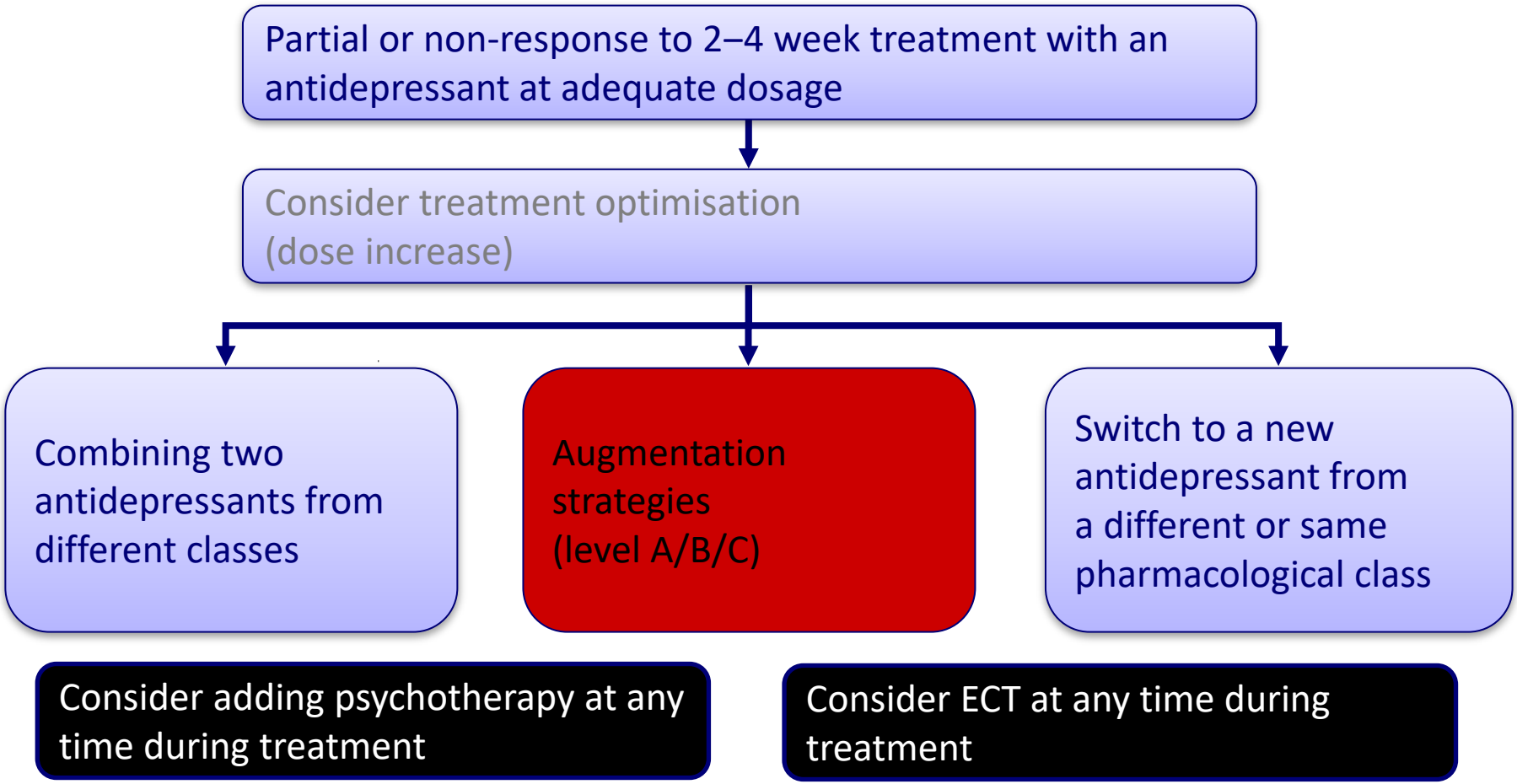
Combination of an SSRI with an inhibitor of presynaptic autoreceptors (e.g., mirtazapine) is an evidence-based choice in cases where monotherapy failed. The combination of venlafaxine with mirtazapine may be accompanied by worsening side effects.

CE A, RG 2

Steve Stahl: "Rocket Fuel"

Bauer et al, World Journal of Biological Psychiatry 2013, 14, 334-385

WFSBP: Teil-/Non-Response



Bauer et al, World Journal of Biological Psychiatry 2013, 14, 334-385
Bauer et al The World Journal of Biological Psychiatry 2007;8:67-104
Bauer et al The World Journal of Biological Psychiatry 2002;3:69-86
Bauer et al The World Journal of Biological Psychiatry 2002;3:5-43

WFSBP: Teil-/Non-Response: Augmentation

	Evidenz-Level
• **Lithium**	**A**
• **Atyp. Antipsychotika**	**A/B/C**
• Schilddrüsenhormon (Triiodthyronin T3)	B
• Schilddrüsenhormon (L-Thyroxin)	C
• Antikonvulsiva (Lamotrigin, Valproat)	C
• MAO-Inhibitor Hochdosistherapie	C
• Östrogen (F) – Testosteron (M)	C
• Dopaminagonisten (Pramipexol)	C
• Psychostimulanzien (Methylphenidat)	C
• Pindolol	C

Bauer et al The World Journal of Biological Psychiatry 2007/2013

WFSBP: Teil-/Non-Response: Lithium Augmentation

WFSBP recommendation:

Adding lithium to ongoing antidepressant treatment is recommended in case monotherapy failed.

CE A, RG 2

Lithium augmentation should be administered for 2–4 weeks in order to allow assessment of the patient's response. The recommended lithium serum target levels are 0.6 to 0.8 mmol/L.[1] In case of response, lithium augmentation should be continued for at least 12 months.[2,3]

CE A, RG 2

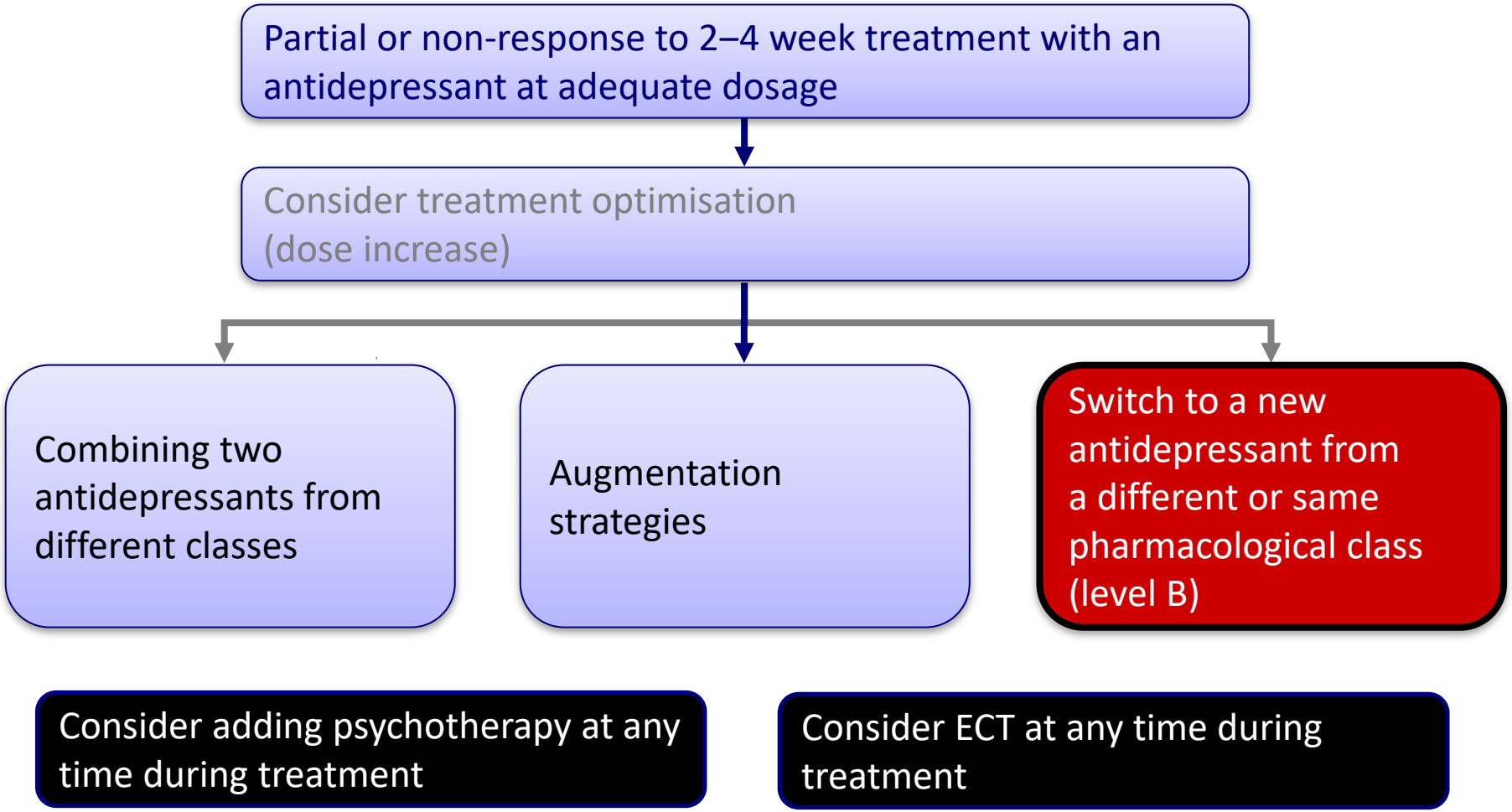
[1]Bschor et al. (2003), [2]Bauer et al. (2000), [3]Bschor et al. (2002).

2 – 4 Wochen

> 12 Monate

Bauer et al, World Journal of Biological Psychiatry 2013, 14, 334-385

WFSBP: Teil-/Non-Response



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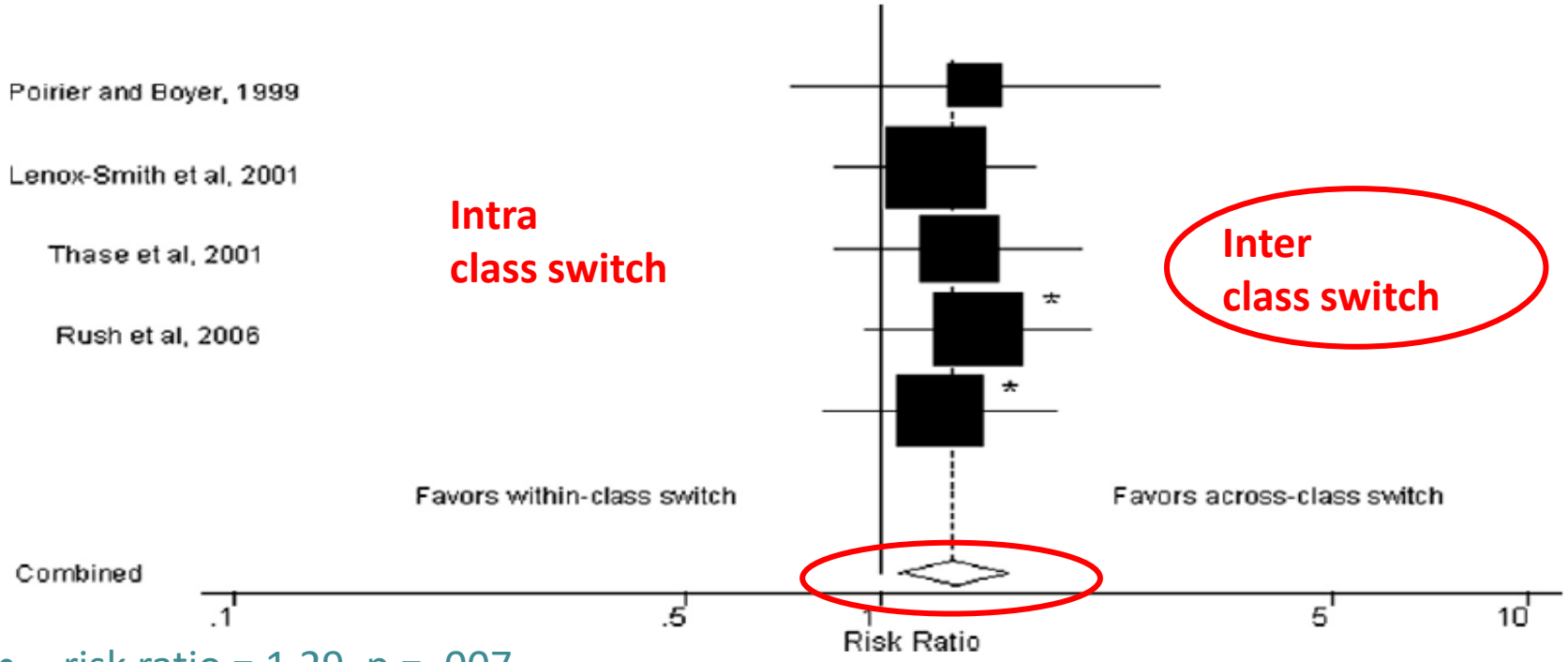
Bauer et al The World Journal of Biological Psychiatry 2007;8:67-104
Bauer et al The World Journal of Biological Psychiatry 2002;3:69-86
Bauer et al The World Journal of Biological Psychiatry 2002;3:5-43

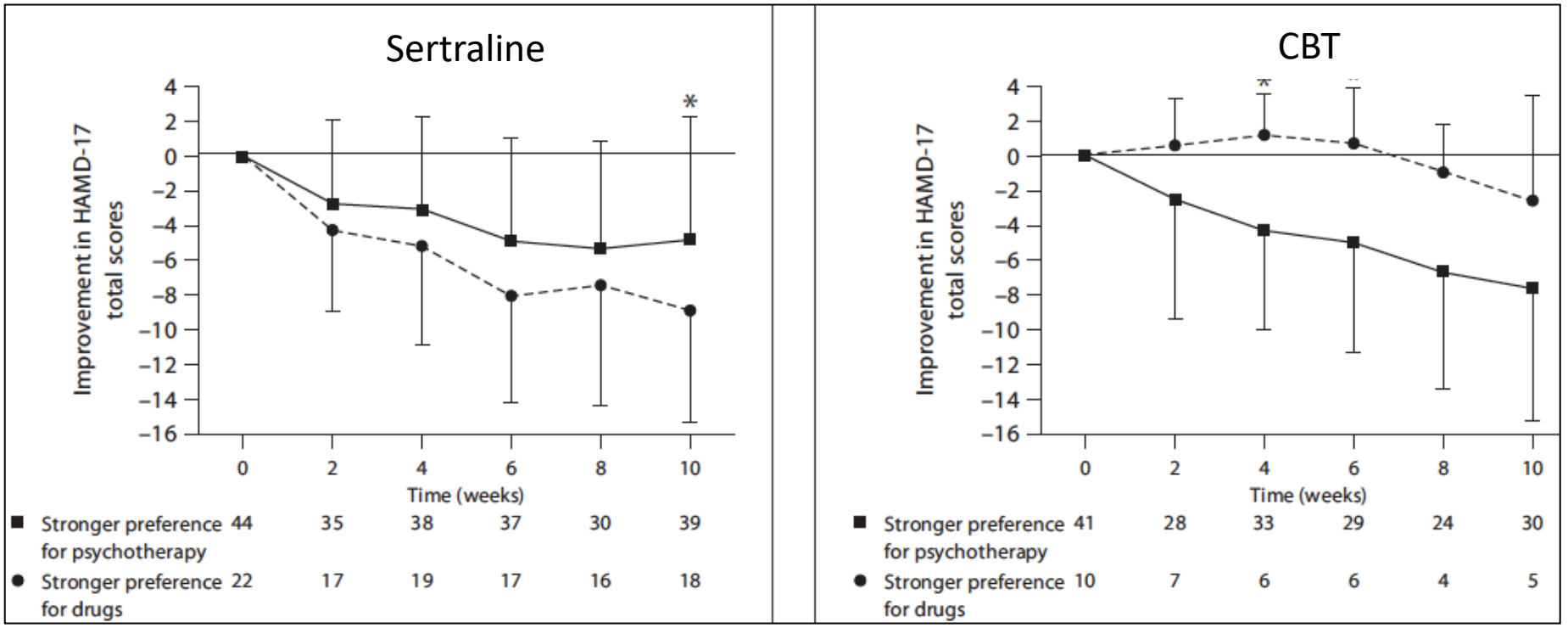
WFSBP: Teil-/Non-Response: Switch, intra- vs. inter-Klasse?



- risk ratio = 1.29, p = .007
- Pooled remission rates:
- **28%** (inter class switch) und
- **23.5%** (intra class switch SSRI to SSRI)

Papakostas et al Biol Psychiatry 2008;63:699-704

PatientInnen Präferenz



➔ *preferred treatment more efficient*

➔ *if non preferred treatment given, AMD more efficient than PT*

Mergl et al, Psychother Psychosom 2011;80:39-47

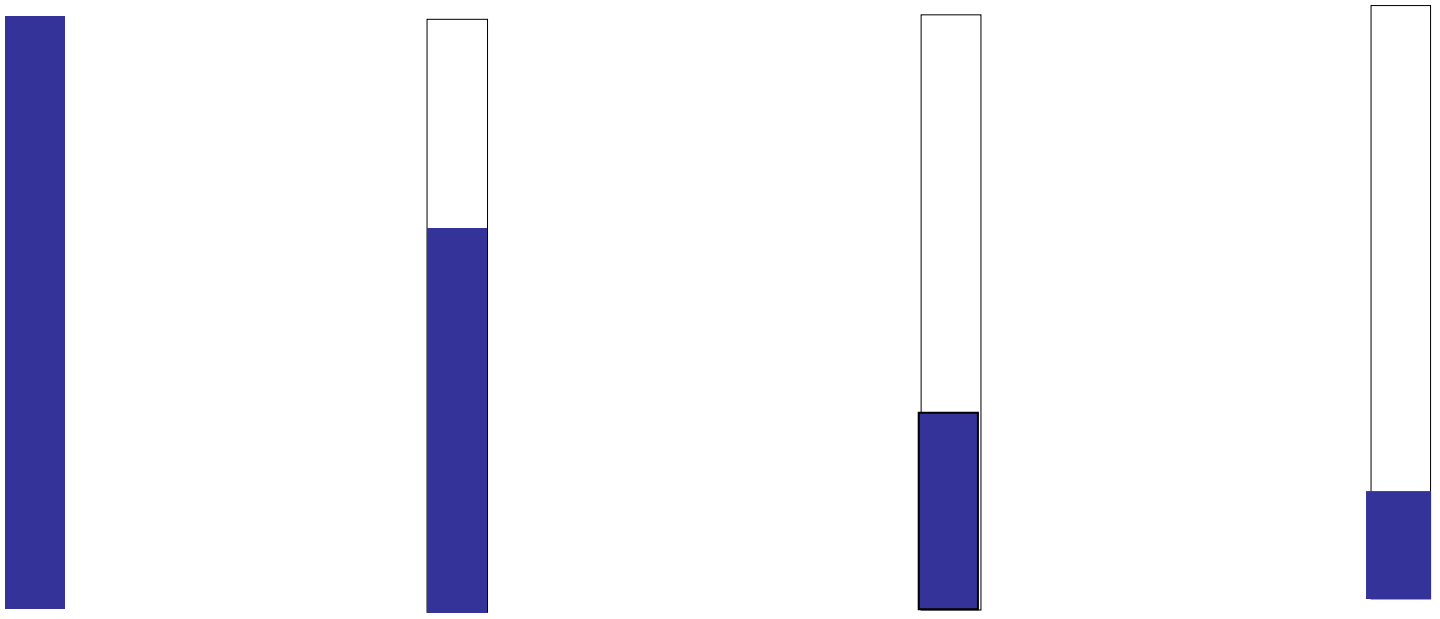
Klinische Realität

Affected pts.
in G: 4 Mio

Treated by GP
2,4 - 2,8 Mio

Correct
diagnosis
1,2 - 1,4 Mio.

Appropriate
therapy
400.000



60-70%

30-35%

10%

Elektrokonvulsionstherapie EKT

- Notfallindikationen
  - Akute Suizidalität oder andere vital bedrohliche Zustände (z.B. Nahrungsverweigerung) bei schweren affektiven erkrankungen
  - Schwere affektive Syndrome in Schwanger- schaft und Postpartalzeit

- Weitere indikationen
  - Schwere wahnhafte depression, depressiver Stupor
  - Therapieresistente depression
  - Gutes Ansprechen auf eKt in der Anamnese
  - Kontraindikationen für andere Behandlungen (höheres risiko, Nebenwirkungen)
  - Expliziter Wunsch PatientIn

Zavortonyy et al, Behandlungsoptionen bei schwer behandelbarer Depression und Therapieresistenz, Swiss Arch Neurol Psychiatr Psychother. 2022;173:w10075. doi: 10.4414/sanp.2022.w10075

rTMS

- Hochfrequente repetitive transkranielle Magnetstimulation (rTMS) des linken dorsolateralen präfrontalen Kortex (dlPFc) kann bei PatientInnen eingesetzt werden, die primär nicht auf eine antidepressive Pharmakotherapie angesprochen haben.

Zavortonyy et al, Behandlungsoptionen bei schwer behandelbarer Depression und Therapieresistenz, Swiss Arch Neurol Psychiatr Psychother. 2022;173:w10075. doi: 10.4414/sanp.2022.w10075

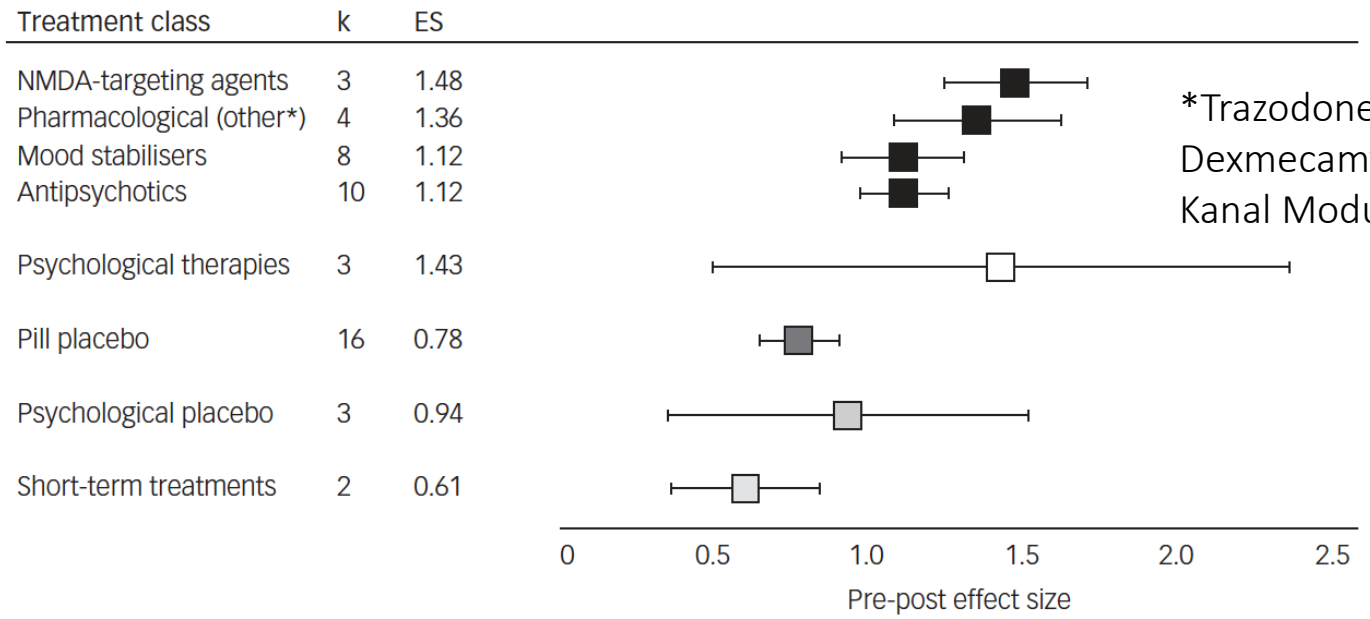
Esketamin

- PatientInnen mit TRD /DTD, gegenwärtig mittel-gradige oder schwerere Episode und fehlendes Ansprechen, in Kombination mit einem oralen Antidepressivum.

Zavortonyy et al, Behandlungsoptionen bei schwer behandelbarer Depression und Therapieresistenz, Swiss Arch Neurol Psychiatr Psychother. 2022;173:w10075. doi: 10.4414/sanp.2022.w10075

Augmentation bei TRD – Metaanalyse

- schwache Studienlage (Metaanalyse: 23 von rd 1600 Studien einbezogen)
- **keine klare Präferenz Psychotherapie vs. Pharmakotherapie**
- solideste Datenlage für **Aripiprazol** und **Lithium**
- grösste Effektstärken für **Ketamin**
- es bleibt **klinische Entscheidung**: UAW, Präferenz Patient, Nachhaltigkeit, ...



*Trazodone, Buspirone, Dexmecamylamine (Nicotin-Kanal Modulator), T3/T4

Strawbridge R et al. Br J Psychiatry 2019, 214:42-51

TRD vs DTD: Konzept

	Treatment resistant depression	Difficult to treat depression
Standpunkt	➔ Gegensatz zu behandelbar	➔ kollaboratives Konzept
KH Modell	➔ akute KH	➔ chron. KH
Therapie Ansatz	➔ biomedizinisch: Heilung	➔ bio-psycho-sozial/recovery
Therapie Ziel	➔ kategorial	➔ dimensional

Rush AJ et al. Aust N Z J Psychiatry 2019, 53:109-18

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  - **serotonerg**
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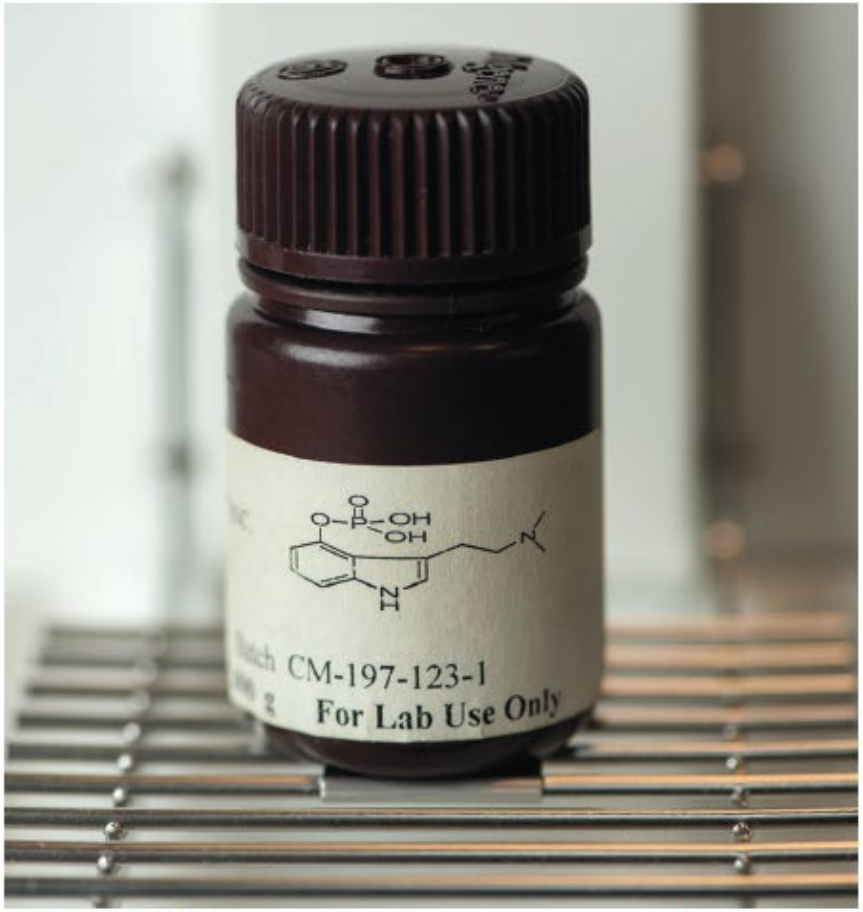
Stephen Ross holding a chalice with a psilocybin capsule.



A bottle of psilocybin in Ross's lab is weighed every day to prevent theft.

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**

Science
AAAS

Nature Outlook - September 2022

OUTLOOK | 28 September 2022

Research round-up: psychedelic medicine

Predicting bad trips, treating depression without hallucinations, and other highlights from studies of psychedelics.

Michael Eisenstein

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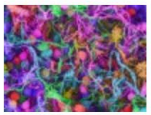
Psychedelic medicine faces the acid test

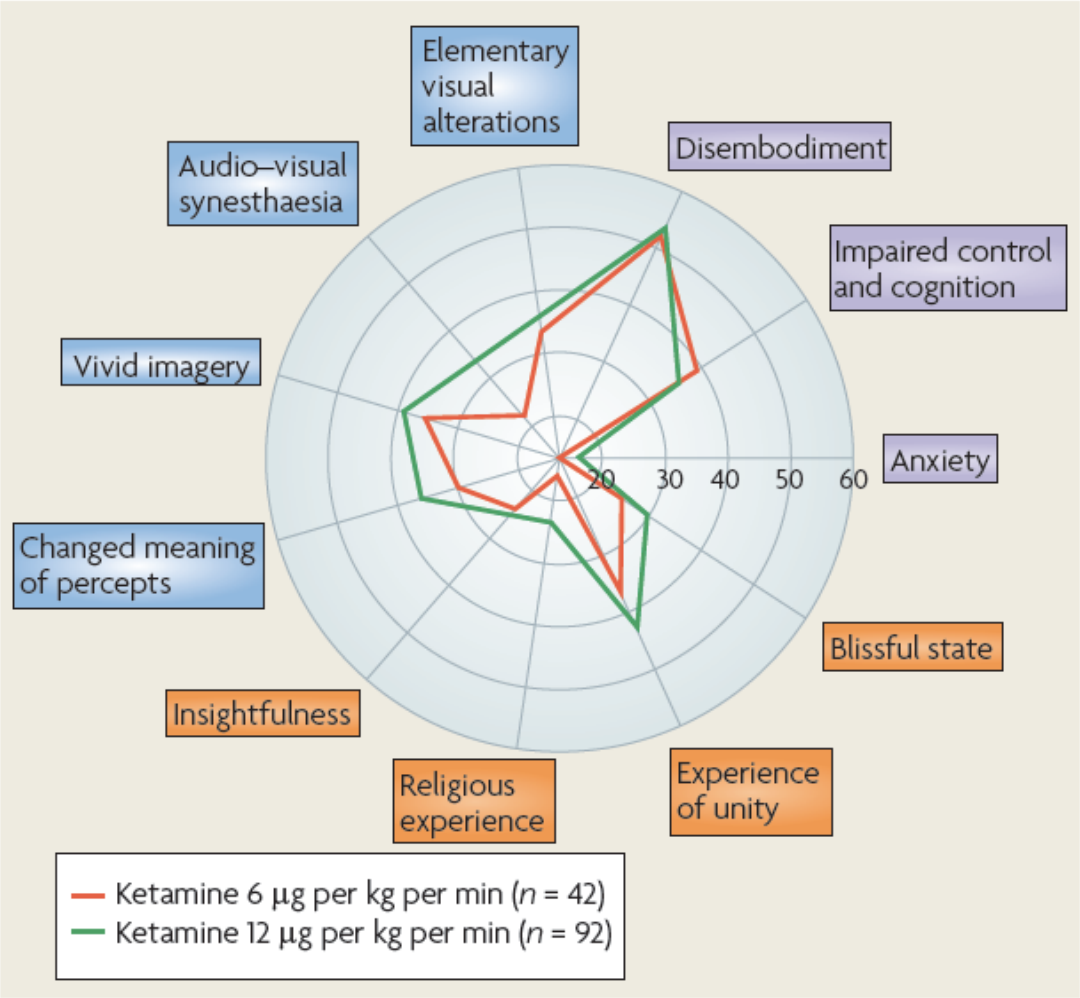
Taking the tripping out of psychedelic medicine



Ketamin - NMDA-R-Antagonist

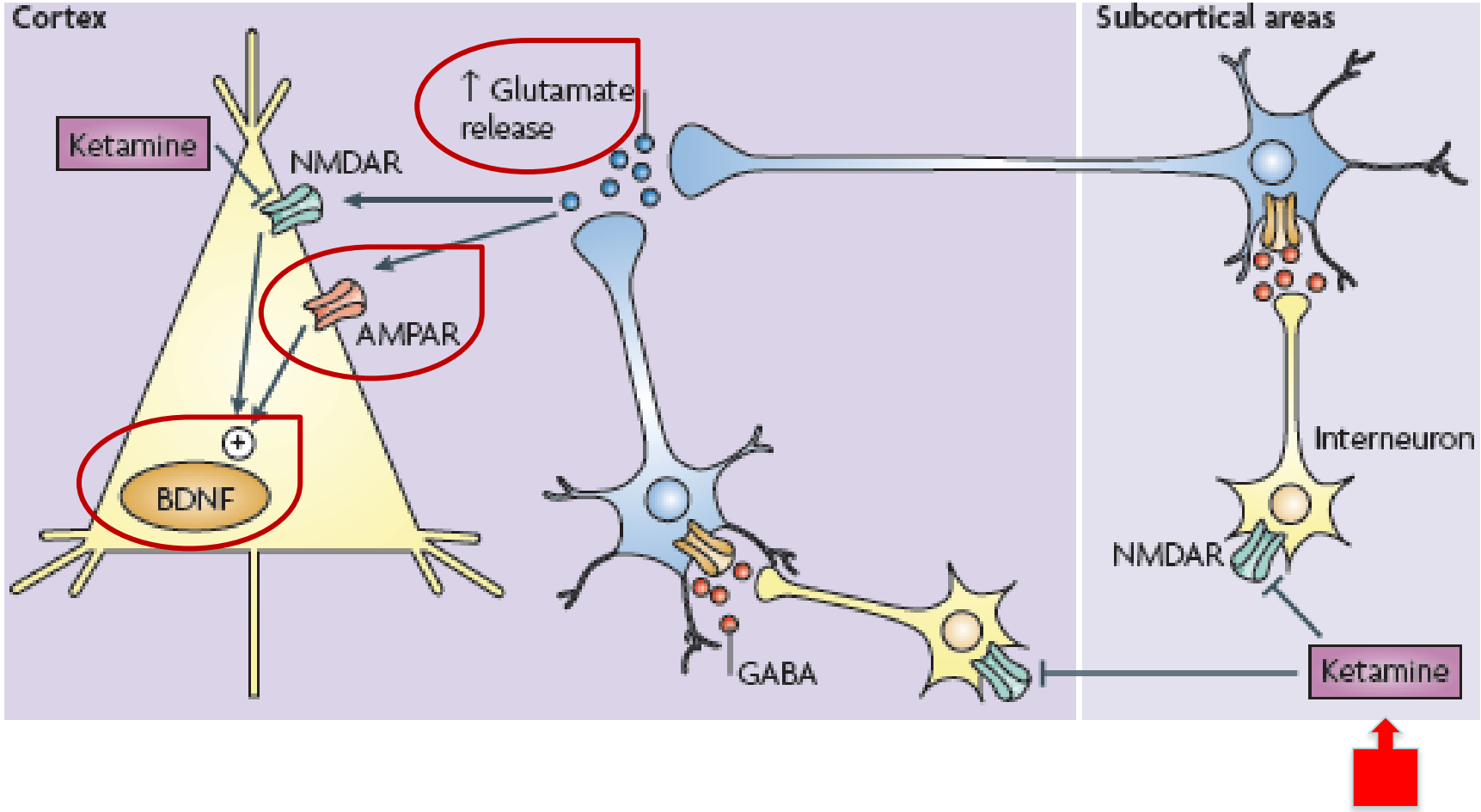
(RS)-2-(2-Chlorophenyl)-2-(methylamino)cyclohexanone

Psychologische Effekte von Ketamin



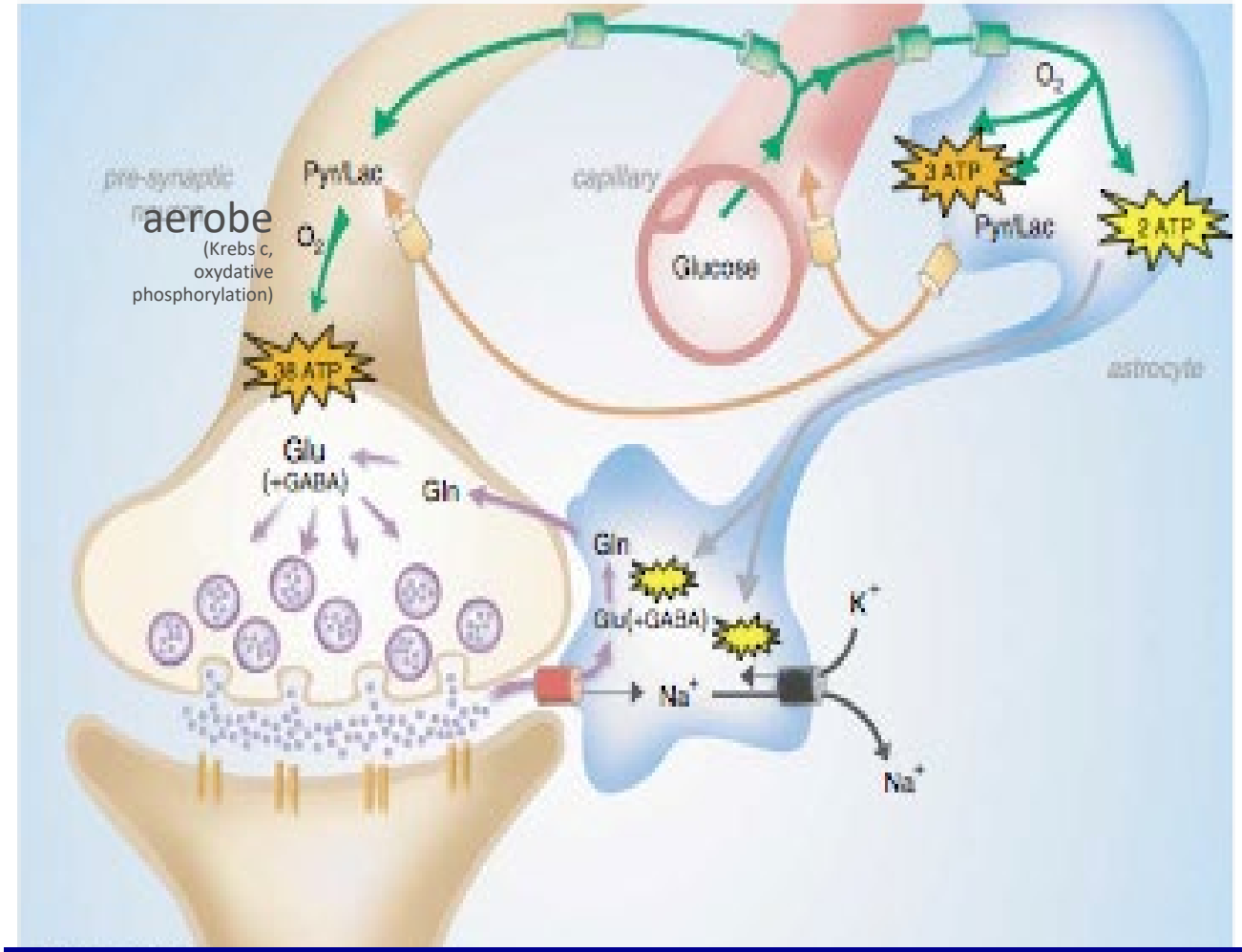
Vollenweider and Kometer, Nat Rev Neurosci, 2010

Ketamin: NMDA-R-Antagonist



Vollenweider & Kometer. Nat Rev Neurosci. 2010, 11:642–51

Glutamat – wichtigster Neurotransmitter im menschlichen Gehirn



Glutamate
GABA] 90% (80/20%of total signalling in the brain)

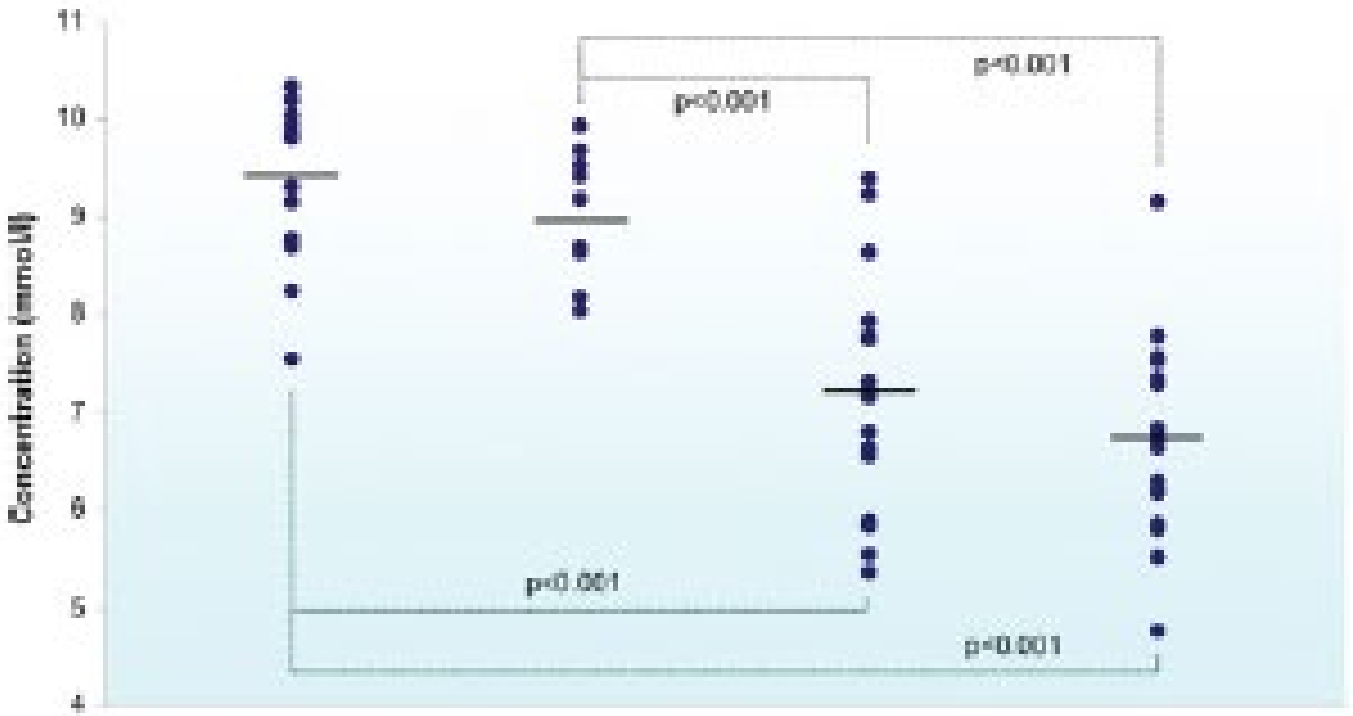
1 Glu : 3 Na^+ ~ 1 Glc : 2 ATP

1 glutamate reuptate needs 1 glucose molecule = 2 ATP

Hyder et al., J Cereb Blood Flow & Metabolism, 2006

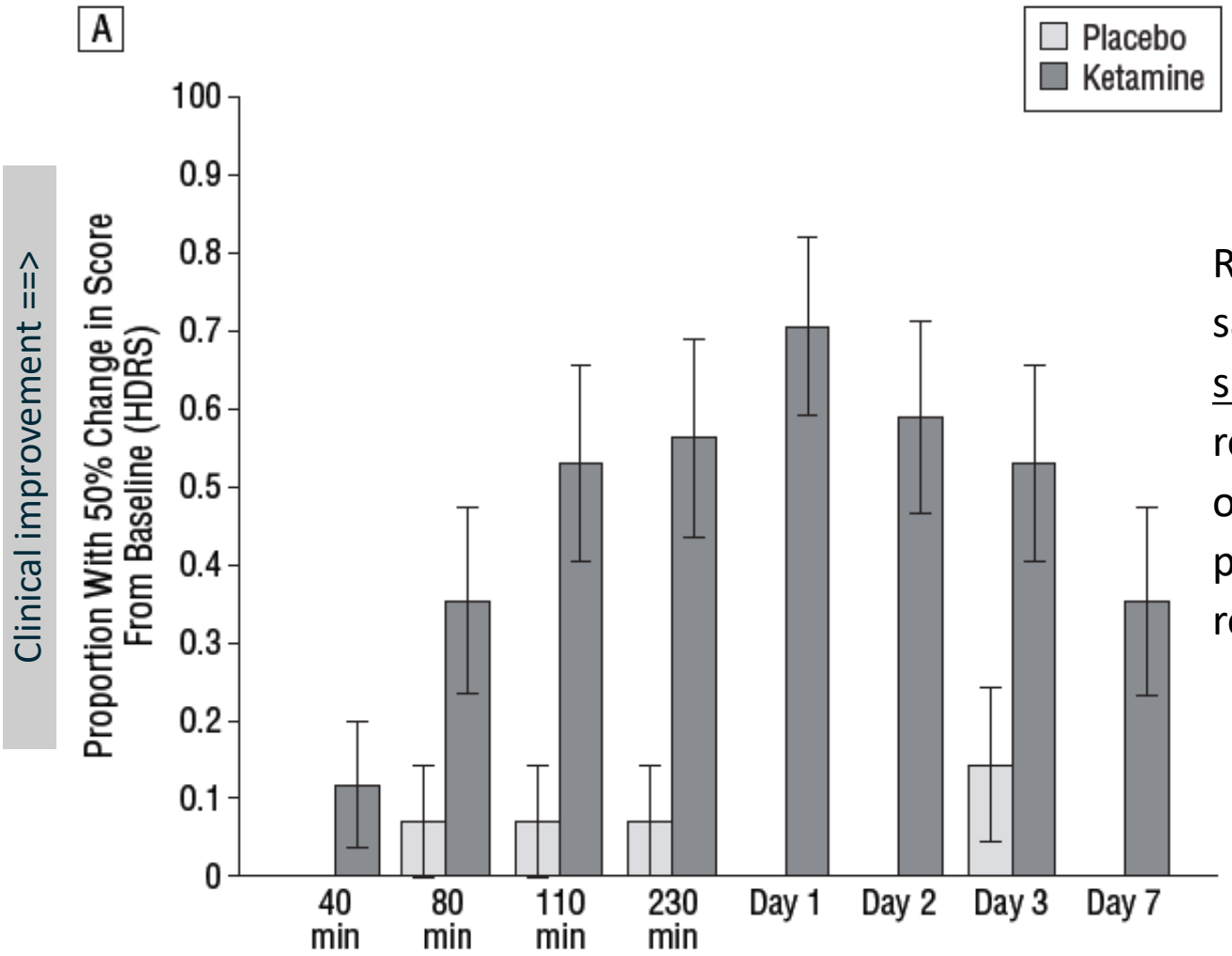
Präfontaler Kortex: Glutamat und Stadium der Majoren Depression

Glutamat (Glu)



Portella et al, J Psychiat Res, 2011

NMDA-R Antagonist Ketamin

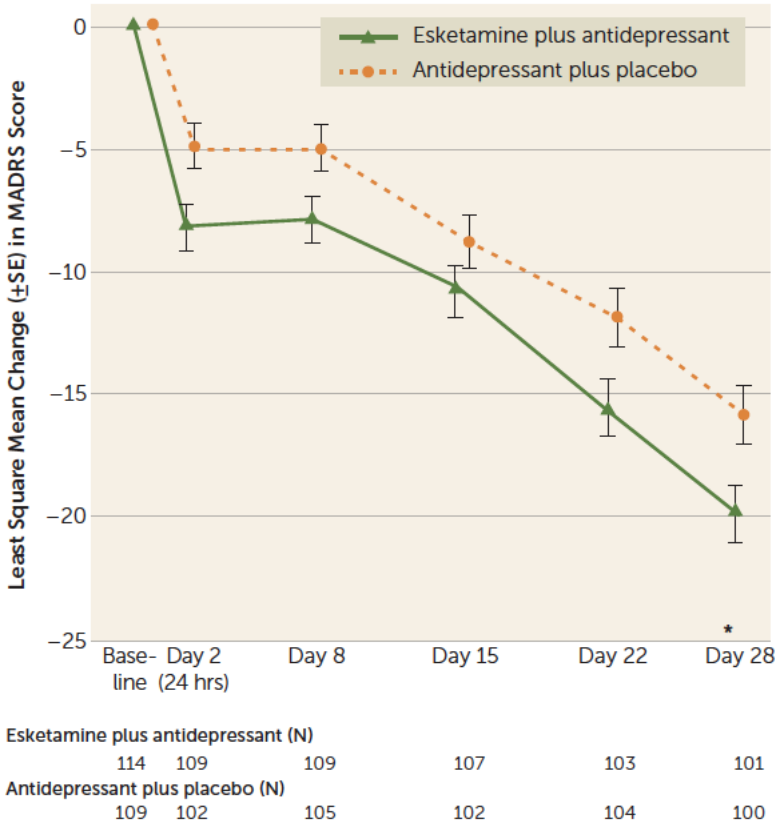


Robust and rapid antidepressant effect resulted from a single i.v. dose of the NMDA receptor antagonist ketamine; onset occurred within 2 hours postinfusion and continued to remain significant for 1 week.

Zarate et al, Arch Gen Psychiat 2006

Add-on Esketamin i.n. – randomisierte kontrollierte Studie

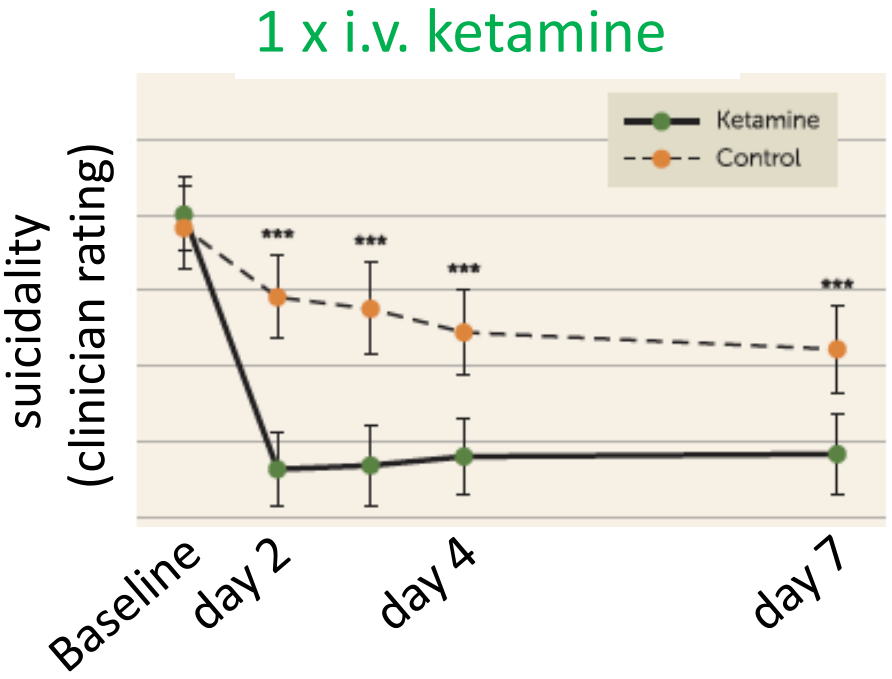
- RCT, double blind w/ active control, multicenter (N = 227); 28 days, MADRS
- moderate to severeMDE, TRD (> 2 x non-response)
- 56 or 84 mg 2 x / w ketamine i.n. + ADM vs PLAC



Adverse Event	Esketamine Plus Antidepressant (N=114)		Antidepressant Plus Placebo (N=109)	
	N	%	N	%
Dissociation	30	26.1	4	3.7
Nausea	30	26.1	7	6.4
Vertigo	30	26.1	3	2.8
Dysgeusia	28	24.3	13	11.9
Dizziness	24	20.9	5	4.6
Headache	23	20.0	19	17.4
Somnolence	15	13.0	7	6.4
Blurred vision	14	12.2	3	2.8
Paresthesia	13	11.3	1	0.9
Anxiety	12	10.4	5	4.6
Increased blood pressure	11	9.6	0	0.0
Insomnia	11	9.6	5	4.6
Vomiting	11	9.6	2	1.8
Diarrhea	10	8.7	10	9.2
Dry mouth	9	7.8	3	2.8
Feeling drunk	9	7.8	1	0.9
Oral hypoesthesia	9	7.8	1	0.9
Oral paresthesia	9	7.8	1	0.9
Throat irritation	9	7.8	5	4.6
Postural dizziness	8	7.0	1	0.9
Hypoesthesia	8	7.0	1	0.9
Nasal discomfort	8	7.0	2	1.8
Fatigue	5	4.3	6	5.5

Popova V et al. Efficacy and safety of flexibly dosed esketamine nasal spray combined with a newly initiated oral antidepressant in treatment-resistant depression: A randomized double-blind active-controlled study. Am J Psychiatry. 2019; 176: 428-38

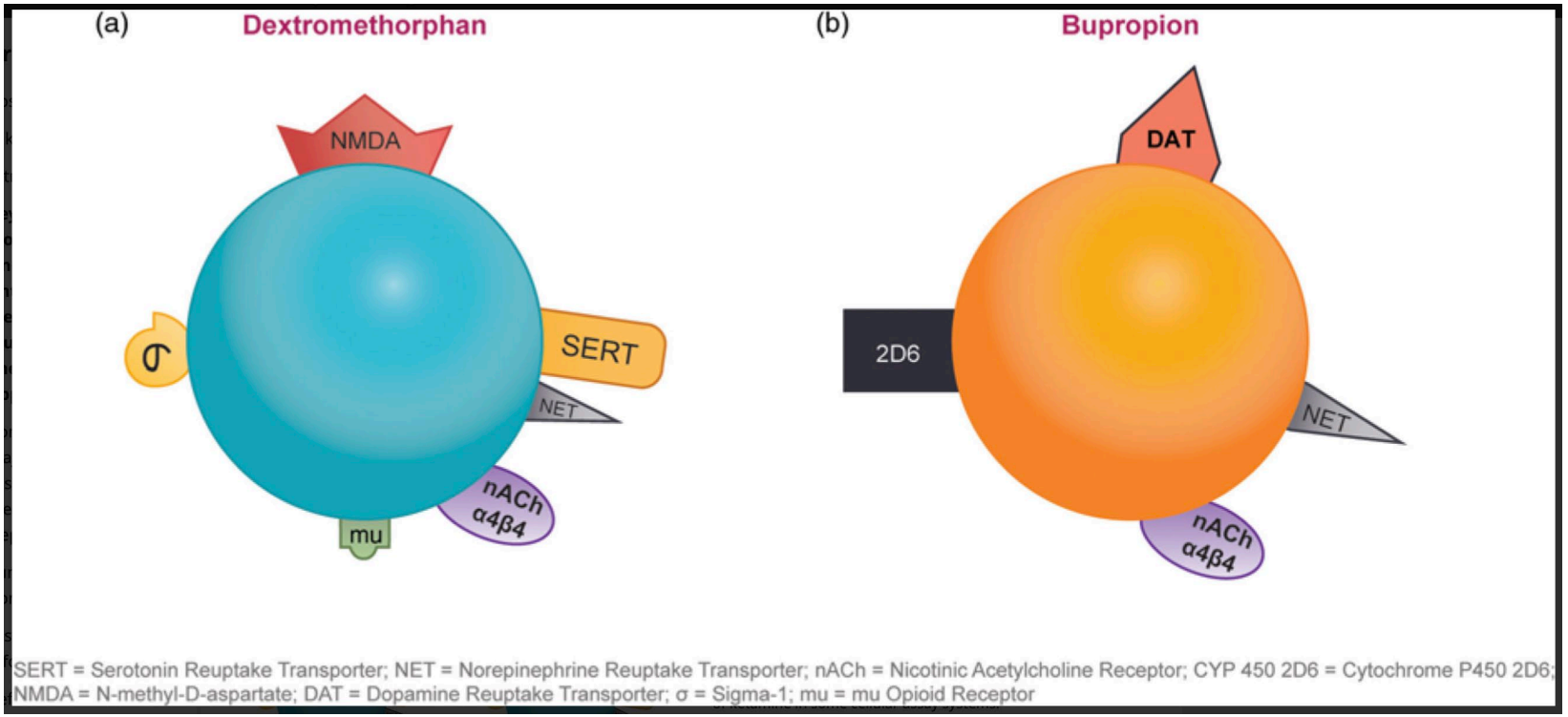
Suizidalität: Akute Effekte von i.v. Ketamin



Wilkinson et al., Am J Psychiatry. 2018, 175:150–8

August 2022 FDA breakthrough rapid acting antidepressant drug

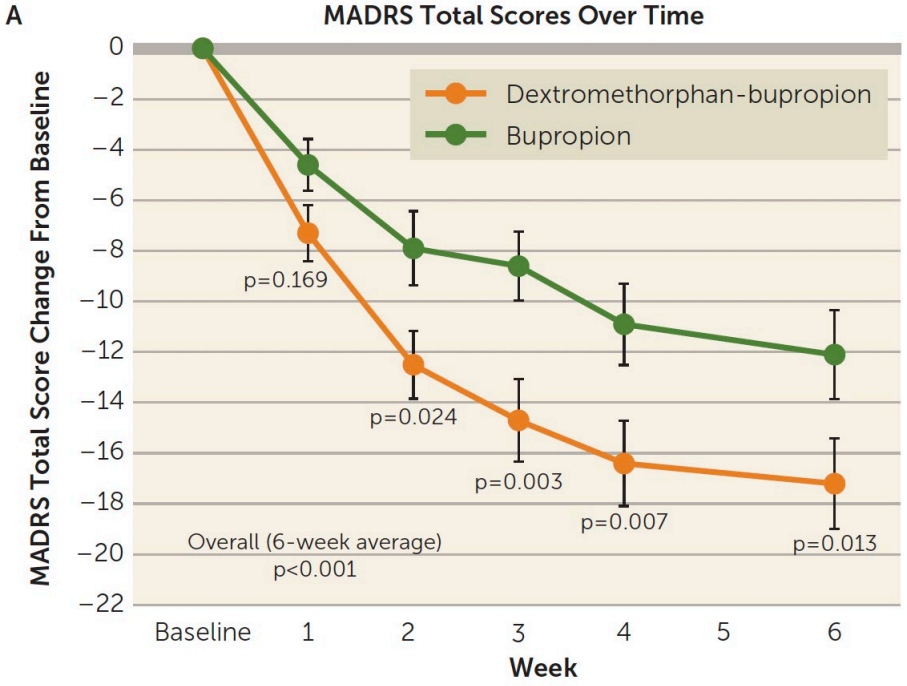
- "Auvelity": Dextometorphan + Bupropion
  - Dextrometorphan: NMDA Antagonist
  - Bupropion: CYP450-2D6 Hemmer

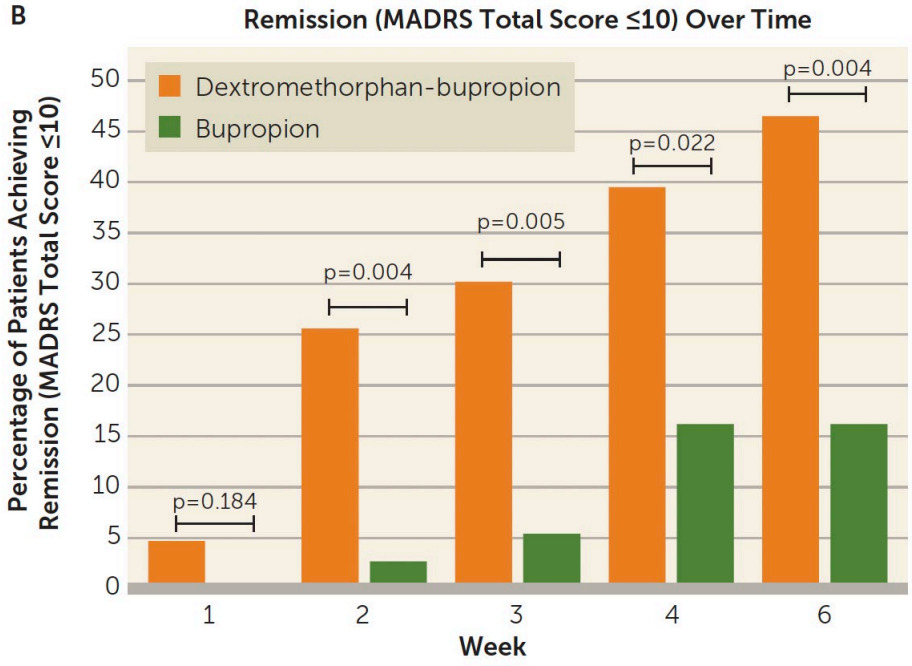


Stahl S, Dextromethorphan/bupropion: A novel oral NMDA (N-methyl-d-aspartate) receptor antagonist with multimodal activity. CNS Spectrums (2019), 24, 461–466. doi:10.1017/S1092852919001470

August 2022 FDA breakthrough rapid acting antidepressant drug

- Phase 2 RCT, 35 vs. 39 Pat., MDE, 18-65 J, mittel bis schwer depressiv
- 45 mg/105 mg (Dextrometorphan/Bupropion) p.o. vs. Bupropion 105 mg p.o.
- 1 x / Tag für 3 Tage, danach 2 x / Tag, 6 Wochen
- primärere Endpunkt: MADRS





Tabuteau et al, Effect of AXS-05 (dextromethorphan-bupropion) in major depressive disorder: A randomized double-blind controlled trial. Am J Psychiat 2022


Psilocybin
Magic Mushroom

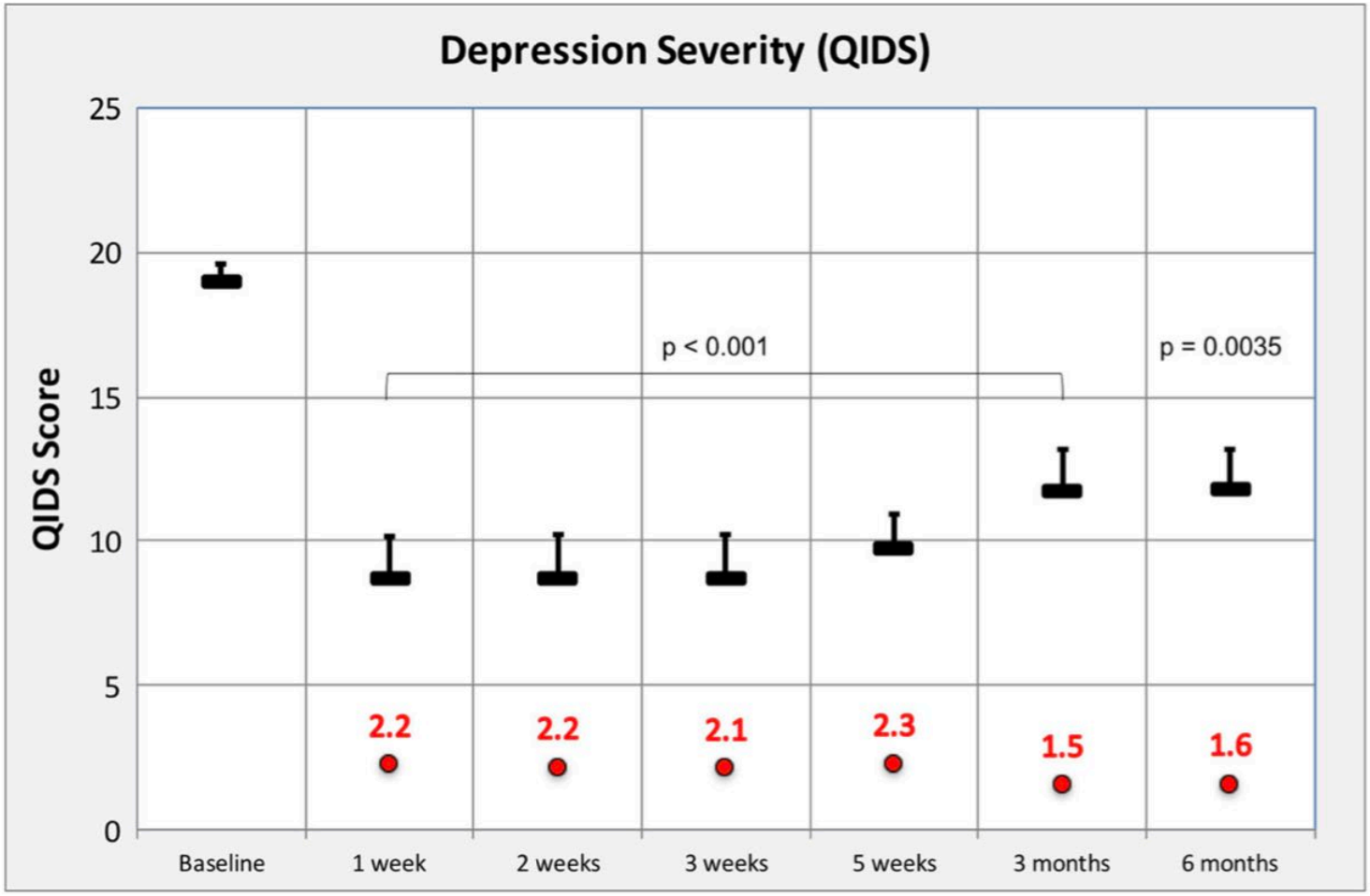
Psilocybin – psychodynamische Konzepte

clinical studies w/ **psilocybin** (1960-70ies)

- improved TRD, chronic anxiety, alcohol dependence

Hanscarl Leuner (1919-1996)
founder of Guided Affective Imagery
(also known as: KIP, Katathym-Imaginative Psychotherapy)

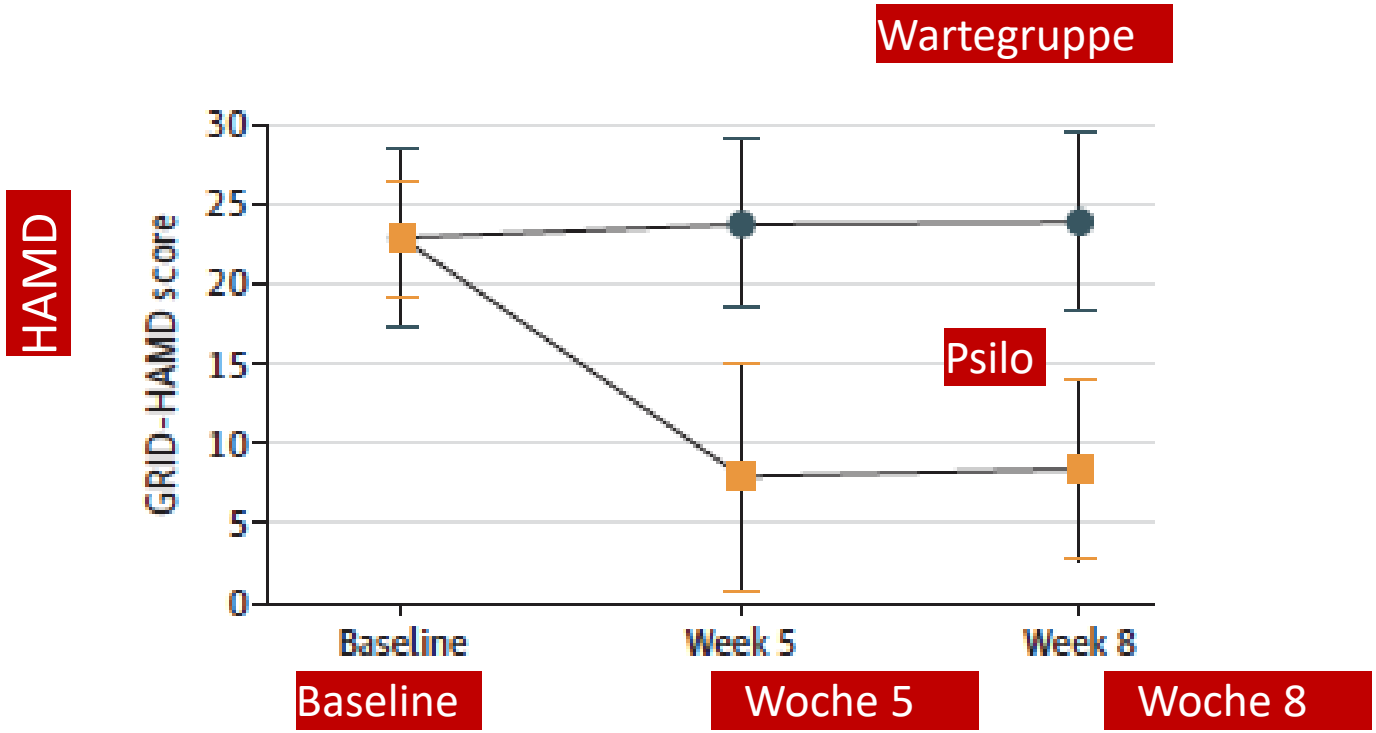
Psilocybin bei Therapie-resistenter Depression: 6 Monate später



Carhart-Harris et al, Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. Psychopharmacology (2018) 235:399–408

Psilocybin bei unmedizierten MDD Patienten

> Random. klin. Studie, N = 27 MDD Pat., unmediz., 21 - 75 J | vs Wartegruppe
  - Psilocybin Behandlungen (Session 1: 20 mg / 70 kg; Session 2: 30mg / 70 kg) + supportive Psychotherapie (ca. 11 Std)
  - 1 Session / Woche

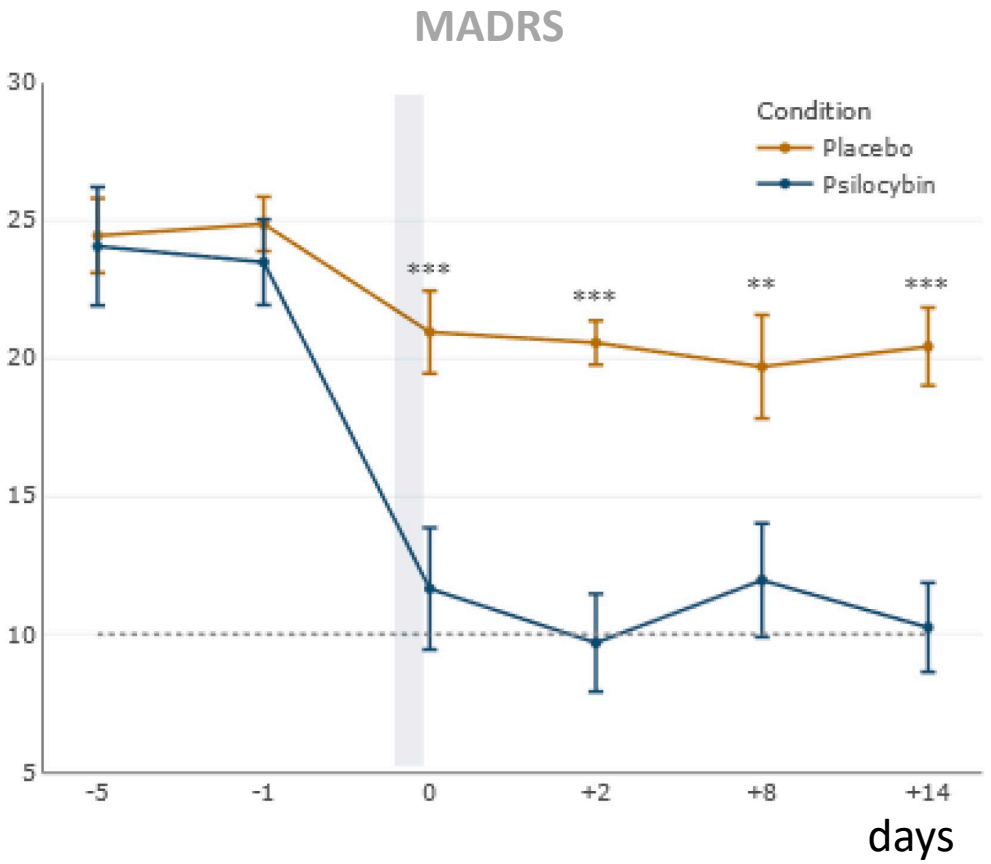


> ➔ Markanter, schneller und nachhaltiger antidepressiver Effekt bei MDD

Davis AK et al. JAMA Psychiatry 2020, doi:10.1001/jamapsychiatry.2020.3285

Single-dose, placebo-controlled, double-blind, randomised clinical trial on psilocybin-assisted therapy in MDD

- single, moderate dose (0.215 mg/kg bw) psilocybin vs placebo
- double-blind RCT
- 52 MDE patients
- primary endpoint, 14 d: MADRS / BDI

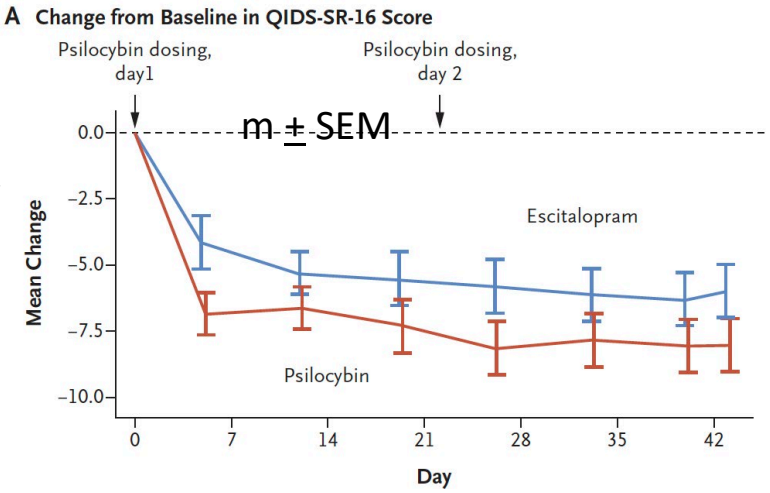


von Rotz R, Schindowski EM, Jungwirth J, Schuldt A, Rieser NM, Zahoransky K, Seifritz E, Nowak A, Nowak P, Jäncke L, Preller KH, Franz X. Vollenweider; submitted 30.08.2022

Psilocybin vs Escitalopram – RCT

QUIDS:
16-item Quick Inventory of Depressive Symptomatology – Self-Report

<u>primäre Zielvariable: ns</u>



<u>Fragen</u>:

Pat. Selektion Verzerrung? Funktionelle Enblindung? Erwartungseffekte? Placeboeffekte?
Mechanismen: pharmakolog. oder via Dissoziation? Schwer Kranke und Dissoziation? Wie geben?
Suchtpotential?

Carhart-Harris et al, NEJM 2021

Ecstasy – 3,4-Methylendioxy-N-methylamphetamin (MDMA)

MDMA bei PTSD

nature medicine

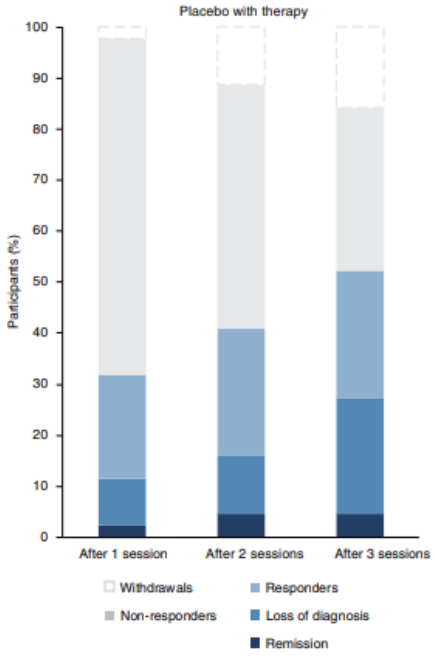
ARTICLES

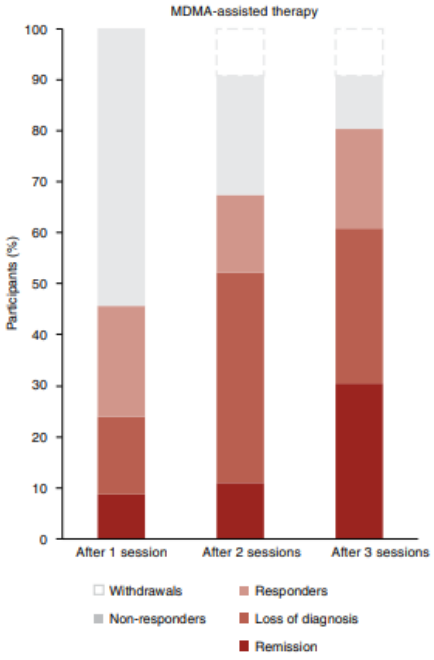
https://doi.org/10.1038/s41591-021-01336-3

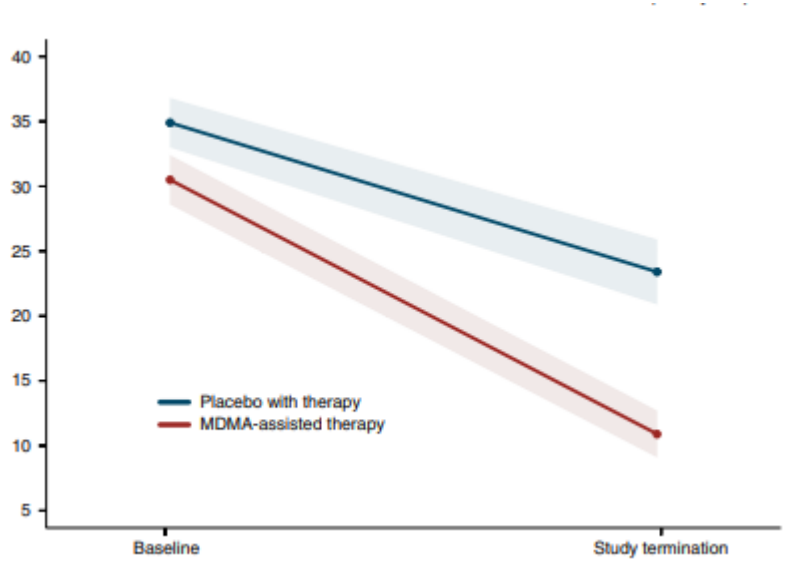
Check for updates

OPEN

MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study



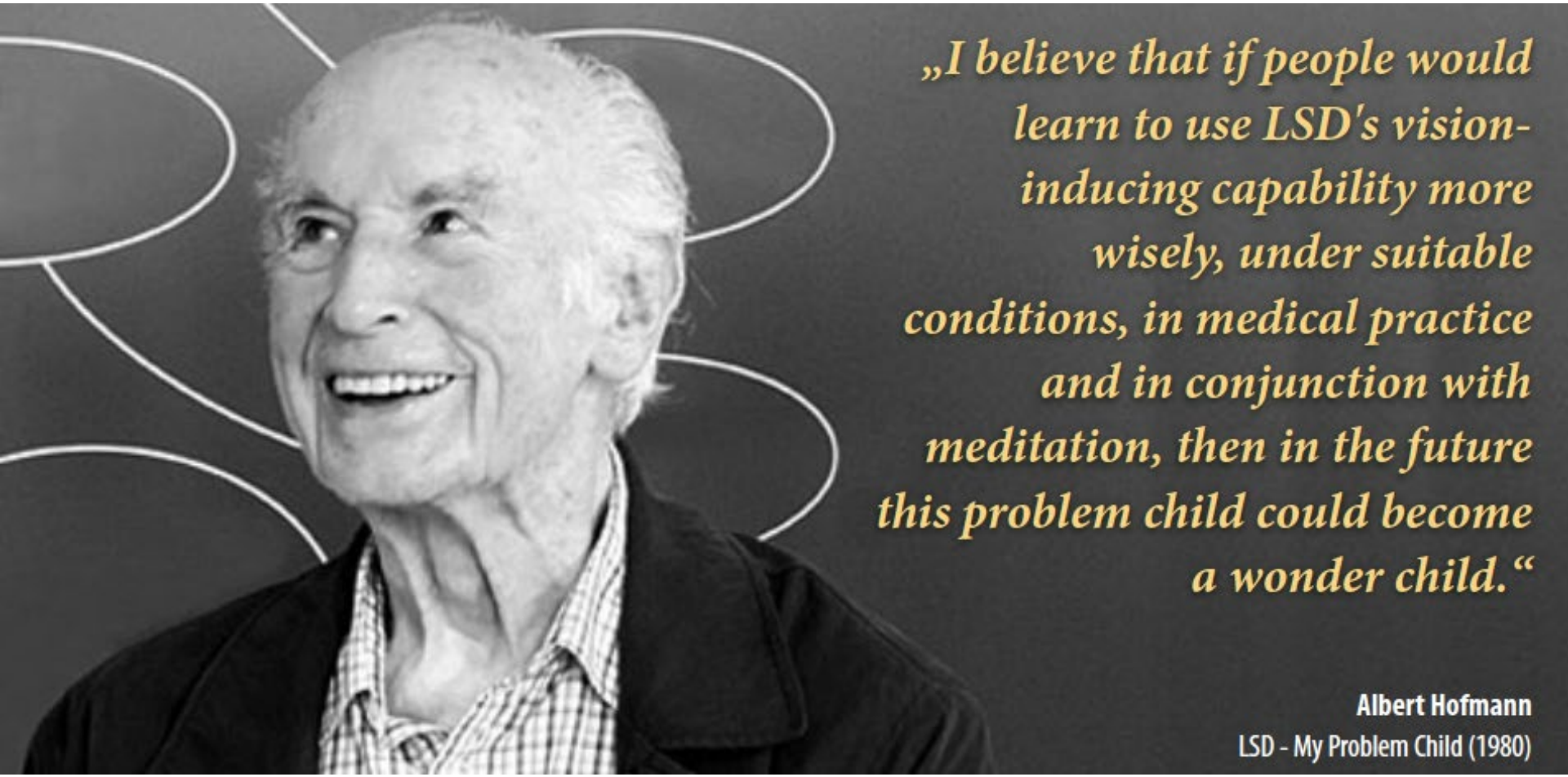




MDMA: 3,4-methyl enedioxy methamphetamine

Mitchell et al, MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study. Nat. Medicine, 27, 2021, 1025-33

LSD - lysergic acid diethylamide



Klinische Studien – LSD bei MDE unterwegs

Original Paper

Acute subjective effects in LSD- and MDMA-assisted psychotherapy

Yasmin Schmid[1,2], Peter Gasser[3], Peter Oehen[4] and Matthias E Liechti[1,2]

Psychopharm

Journal of Psychopharmacology
2021, Vol. 35(4) 362–374

DOI: 10.1177/0269881120959604
journals.sagepub.com/home/jop
SAGE

Abstract

Background: Lysergic acid diethylamide (LSD) and 3,4-methylenedioxymethamphetamine (MDMA) were used in psychotherapy in the 1960s–1980s, and are currently being re-investigated as treatments for several psychiatric disorders. In Switzerland, limited medical use of these substances is possible in patients not responding to other treatments (compassionate use).

Methods: This study aimed to describe patient characteristics, treatment indications and acute alterations of mind in patient 200 µg) and/or MDMA (100–175 mg) within the Swiss compassionate use programme from 2014–2018. Acute effects were Dimensions of Altered States of Consciousness scale and the Mystical Experience Questionnaire, and compared with those administered with LSD or MDMA and patients treated alone with LSD in clinical trials.

Results: Eighteen patients (including 12 women and six men, aged 29–77 years) were treated in group settings. Indications mostly stress disorder and major depression. Generally, a drug-assisted session was conducted every 3.5 months after 3–10 psych induced pronounced alterations of consciousness on the 5 Dimensions of Altered States of Consciousness scale, and mystical- increases in all scales on the Mystical Experience Questionnaire. Effects were largely comparable between patients in the compas and patients or healthy subjects treated alone in a research setting.

Conclusion: LSD and MDMA are currently used medically in Switzerland mainly in patients with posttraumatic stress disorder a settings, producing similar acute responses as in research subjects. The data may serve as a basis for further controlled studies psychotherapy.

subhalluzinogene Dosen

STUDY PROTOCOL Open Access

MDLSD: study protocol for a randomised, double-masked, placebo-controlled trial of repeated microdoses of LSD in healthy volunteers

Robin J. Murphy[1*], Rachael L. Sumner[1], William Evans[2], David Menkes[3], Ingo Lambrecht[4], Rhys Ponton[1], Frederick Sundram[5], Nicholas Hoeh[6], Sanya Ram[1], Lisa Reynolds[6] and Suresh Muthukumaraswamy[1]

Abstract

Background: Regular ingestion of sub-hallucinogenic doses of psychedelics, referred to as "microdosing", has gained increasing popularity and attention in the press and in online forums, with reported benefits across multiple cognitive and emotional domains. Rigorously controlled studies to date, however, have been limited in scope and have failed to produce results comparable to those reported in the grey literature.

Methods: Eighty healthy male participants will receive 14 doses of placebo or 10 µg lysergic acid diethylamide orally every 3rd day over a 6-week treatment protocol. A battery of personality, creativity, mood, cognition, and EEG plasticity measures, as well as resting-state fMRI imaging, will be administered at baseline and at the end of the protocol. Creativity, mood, and plasticity measures will additionally be assessed in the acute phase of the first dose. Daily functioning will be monitored with questionnaires and a wearable sleep and activity tracker.

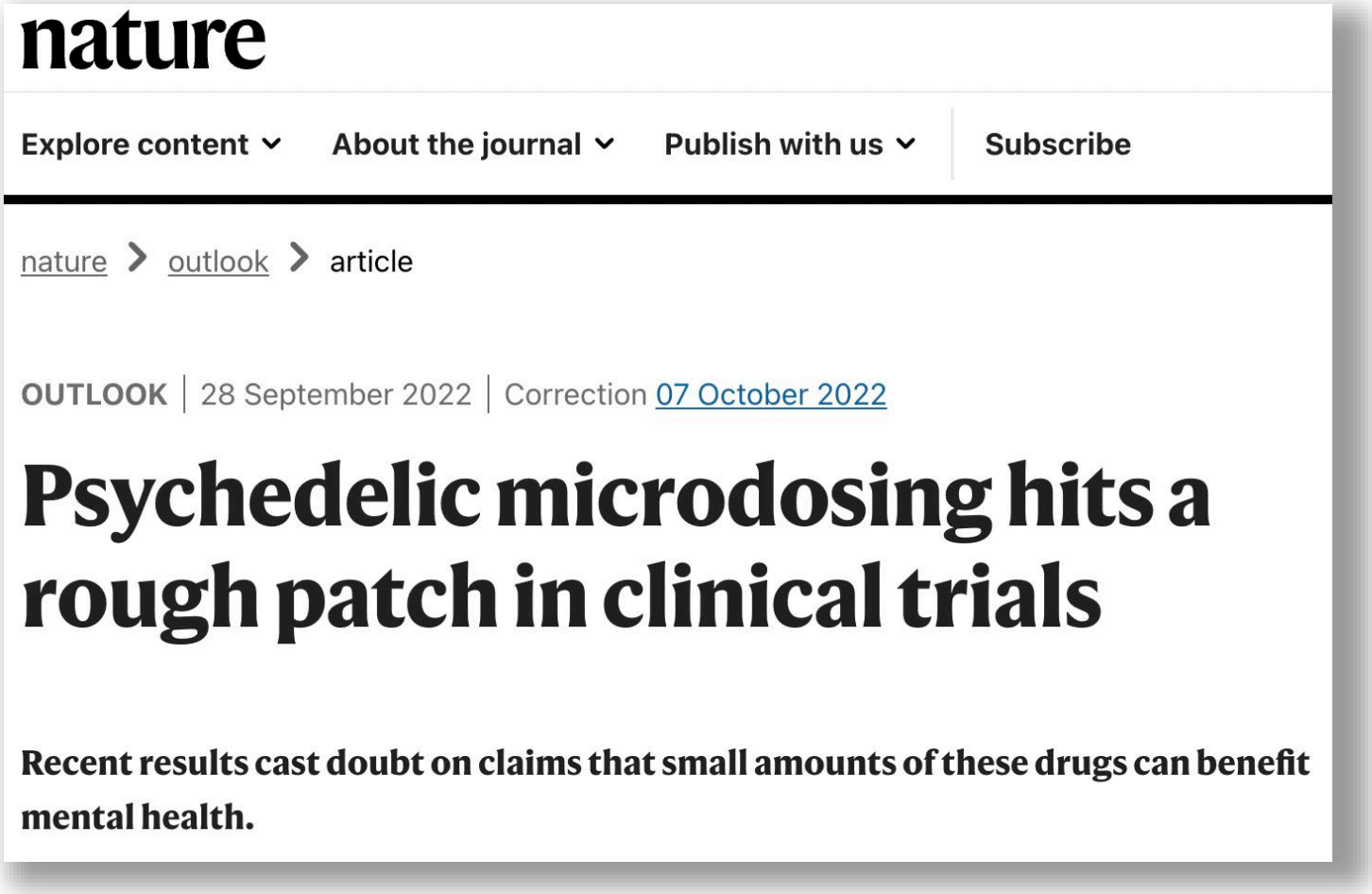
Discussion: This study will rigorously examine the claims presented in the microdosing grey literature by pairing a comparable dosing protocol with objective measures. Potential therapeutic implications include future clinical trials to investigate microdosed psychedelics as a standalone treatment or as an augmentation of psychotherapy in the treatment of depression, addiction, eating disorders, obsessive-compulsive disorders, and palliative care.

Trial registration: ACTRN12621000436875. Registered on 19 February 2021

Keywords: Microdosing, Lysergic acid diethylamide, Psychedelics, Cortical plasticity, Cortical connectivity, Personality, Creativity, Long-term potentiation, Randomised controlled trial

Schmid et al 2021, Murphy et al 2021

Microdosing LSD?



nature

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OUTLOOK | 28 September 2022 | Correction 07 October 2022

Psychedelic microdosing hits a rough patch in clinical trials

Recent results cast doubt on claims that small amounts of these drugs can benefit mental health.

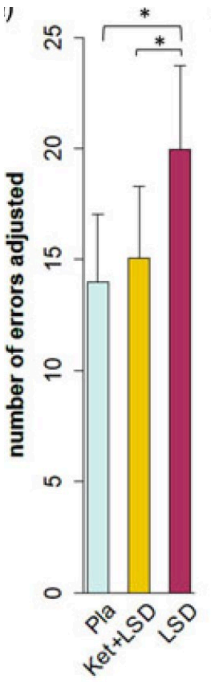
Nature Outlook September 2022

LSD Microdosingbei gesunden Probanden?

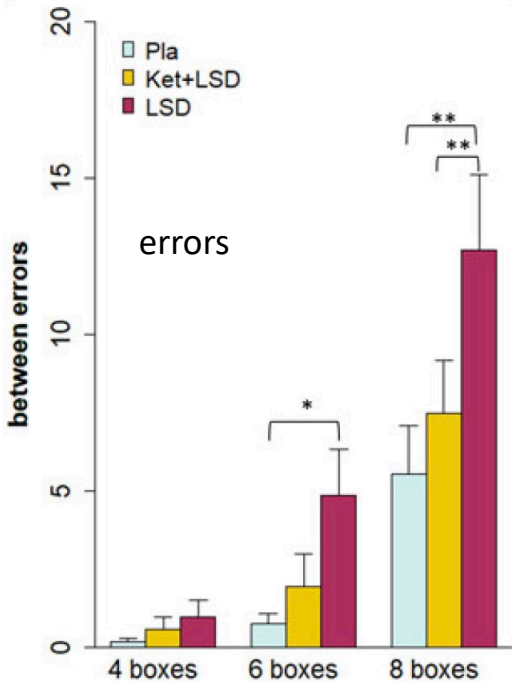
25 healthy subjects
LSD 100 ug ± Ketanserin 40 mg, placebo

executive functions, cognitive flexibility (Intra/Extra-Dimensional shift task IED)
Spatial Working Memory task (SWM)
risk-based decision-making (Cambridge Gambling Task CGT)

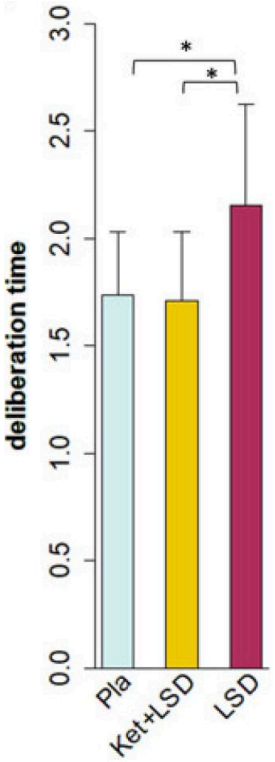
IED: errors



SWM: errors



CGT: deliberation time



Pokorny et al, Psychological Medicine 2019

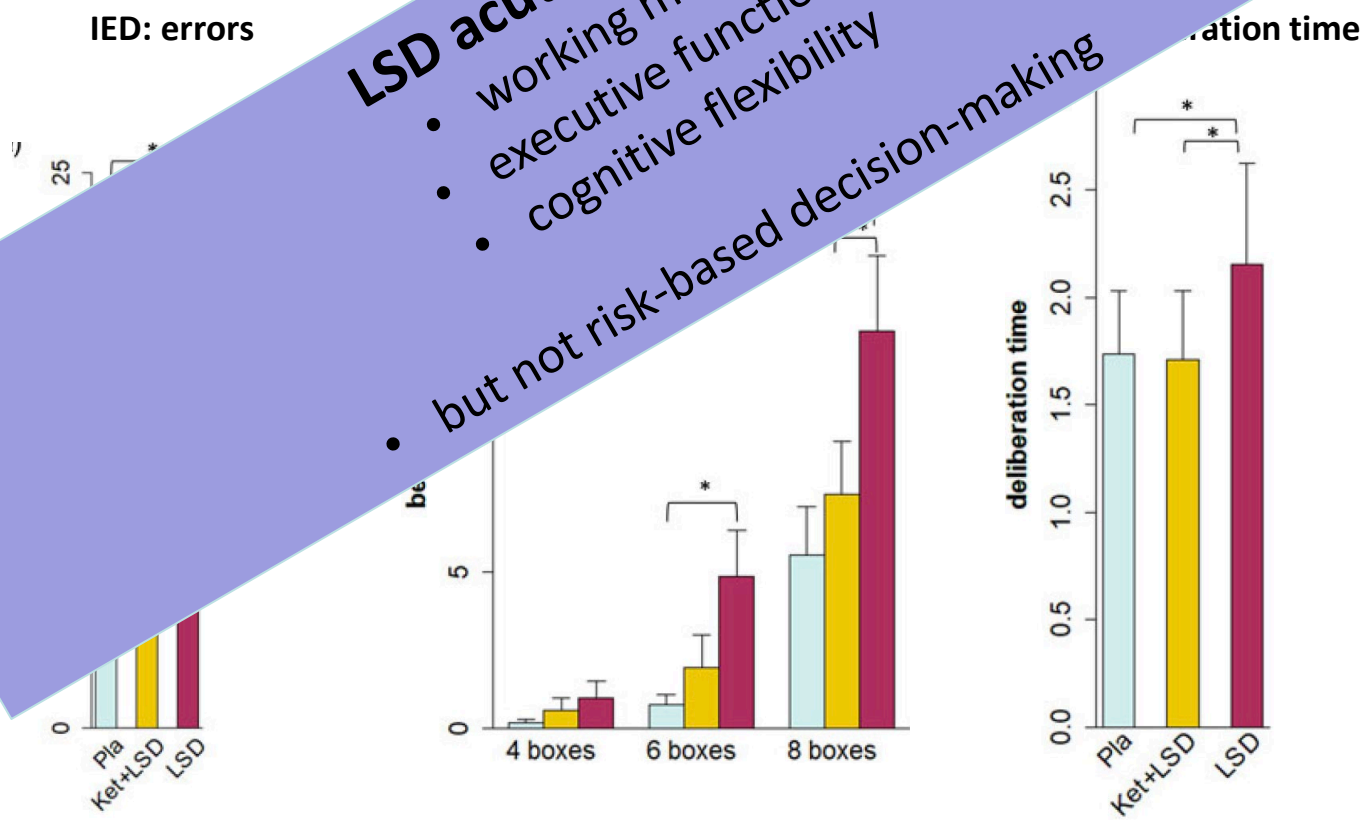
LSD Microdosingbei gesunden Probanden?

25 healthy subjects
LSD 100 ug ± Ketanserin 40 mg, placebo

executive functions, cognitive flexibility (Intra/Extra-Dimensio
Spatial Working Memory task (SWM)
risk-based decision-making (Cambridge Gambling Ta

LSD acutely impairs

- working memory
- executive functions
- cognitive flexibility
- but not risk-based decision-making

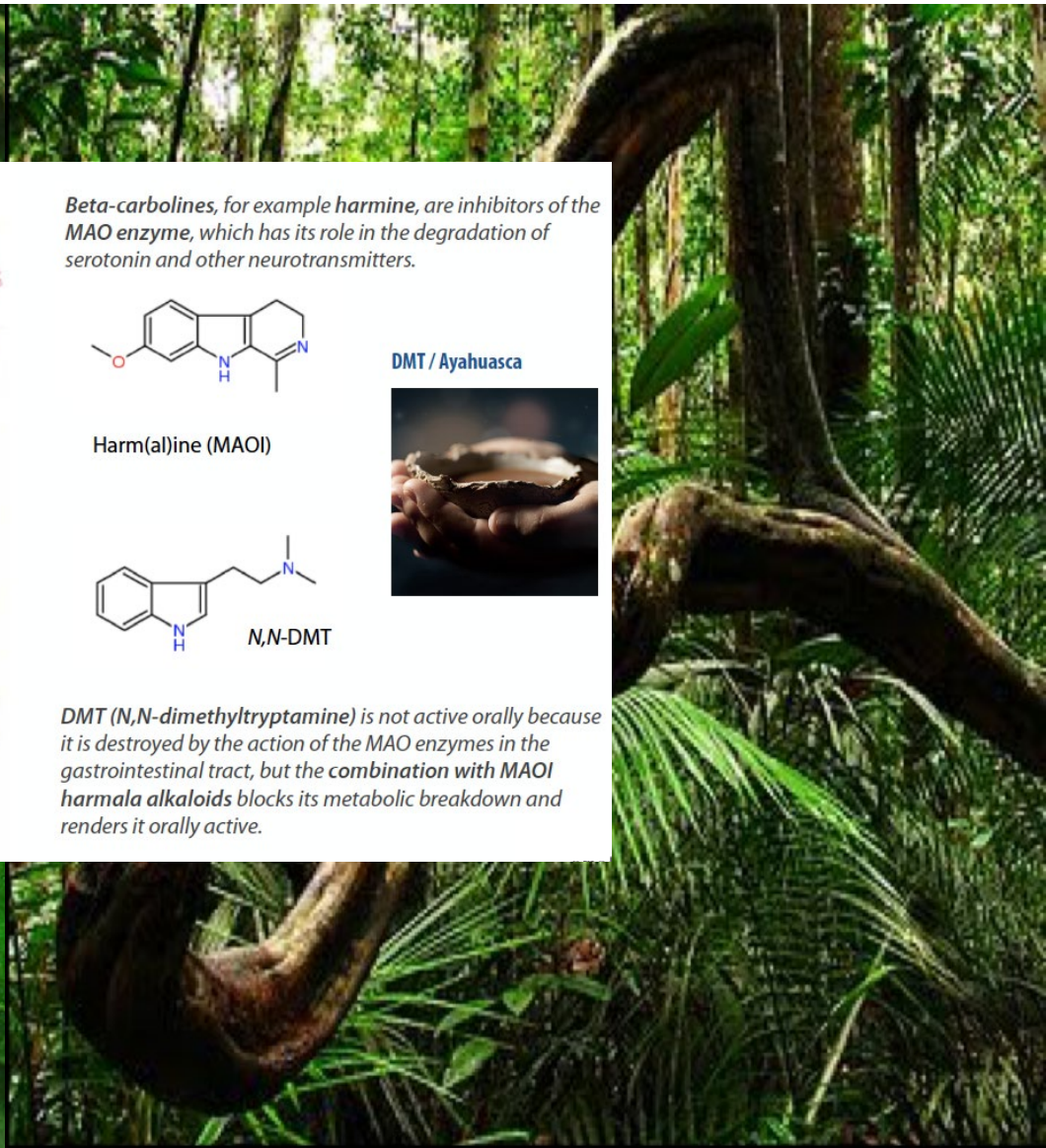


Pokorny et al, Psychological Medicine 2019

Ayahuasca

Banisteriopsis caapi –> harmaline (MAOI)

Psychotria viridis –> N,N-dimethyltryptamine (DMT)



Banisteriopsis Caapi

Psychotria Viridis

***Beta-carbolines**, for example **harmine**, are inhibitors of the **MAO enzyme**, which has its role in the degradation of serotonin and other neurotransmitters.*

Harm(al)ine (MAOI)

DMT / Ayahuasca

N,N-DMT

***DMT (N,N-dimethyltryptamine)** is not active orally because it is destroyed by the action of the MAO enzymes in the gastrointestinal tract, but the **combination with MAOI harmala alkaloids** blocks its metabolic breakdown and renders it orally active.*

nature International weekly journal of science

NATURE | NEWS

Ayahuasca psychedelic tested for depression

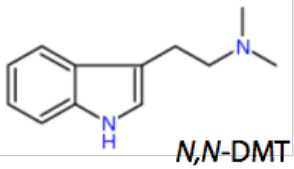
Pilot study with shamanic brew hints at therapeutic potential.

Arran Frood

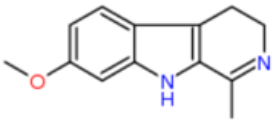
06 April 2015

Lunae Parracho/Reuters/Corbis

Ayahuasca being prepared for a healing ritual in the Brazilian village of Novo Segredo.



N,N-DMT



Harm(al)ine (MAOI)

N_2O (Distickstoffmonoxid) – Lachgas als Antidepressivum?

- 1772 vom englischen Chemiker Joseph Priestley rein dargestellt
- 1790er Jahre, englischer Apotheker Humphry Davy beschreibt psychogene und analgetische Effekte
- 1844 vom Zahnarzt H. Wells erstmals eingesetzt
- Schmerzstillende, betäubende Wirkung: Bewusstsein/Vigilanz erhalten
- Treibgas in Spraydosen und als Aufschäummittel in Sahnespenderkapseln gefüllt
- Rauschzustand: wenige Minuten. Höbere Dosis: Bewusstlosigkeit bis tödlich

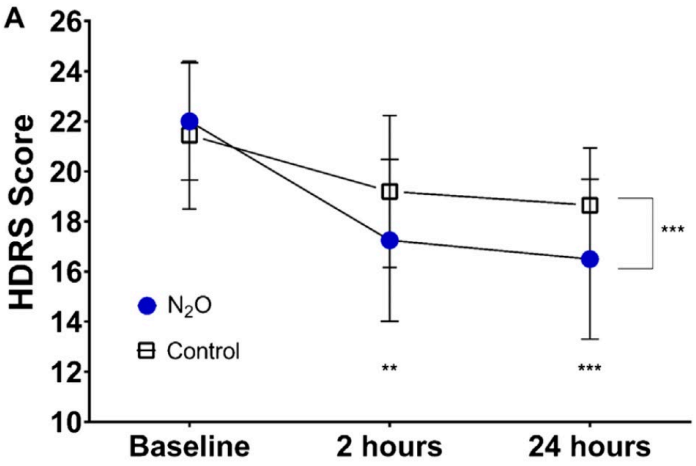
https://de.wikipedia.org/wiki/Distickstoffmonoxid

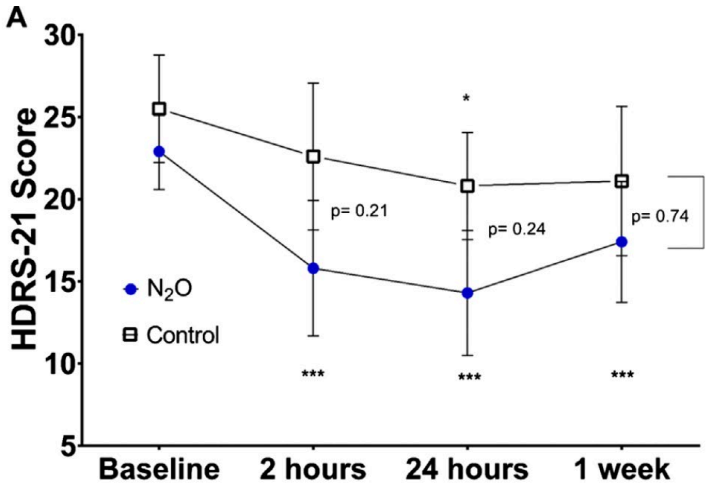
N_2O (Distickstoffmonoxid) – Antidepressivum?

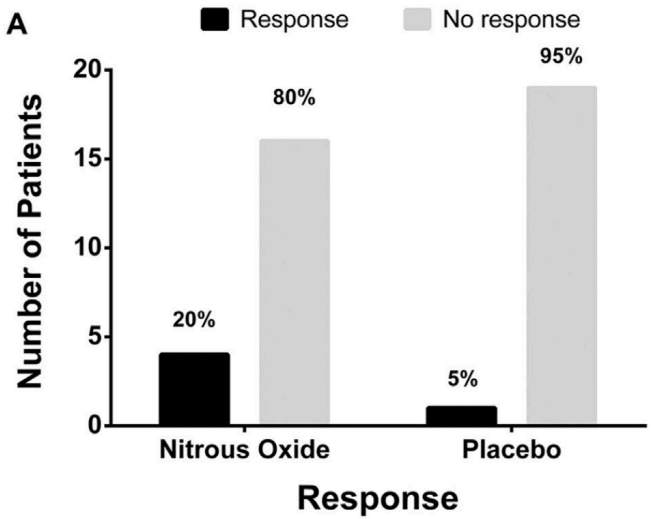
20 TRD Pat.

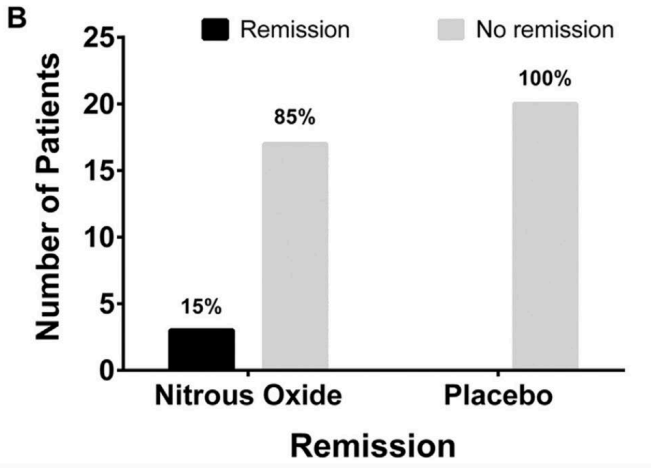
1 Std

50% N_2O vs. Nitrogen/O_2









Nagele P et al. Biol Psychiatry 2015, 78:1, 10-8, doi:10.1016/j.biopsych.2014.11.016

Afterglow von Psychedelika

- Phase nach Abklingen der Akutwirkung (bis zu 10 Tage) mit i.d.R. Wohlbefinden, erhöhter Achtsamkeit und kognitiver Flexibilität („Plastizität“).
- Diese Phase scheint besonders geeignet für psychotherapeutische Interventionen und allgemein neue Lernerfahrungen zu sein.

u.a. nach Gründer et al. 2022

Konzept der Psychedelika-unterstützten Psychotherapie

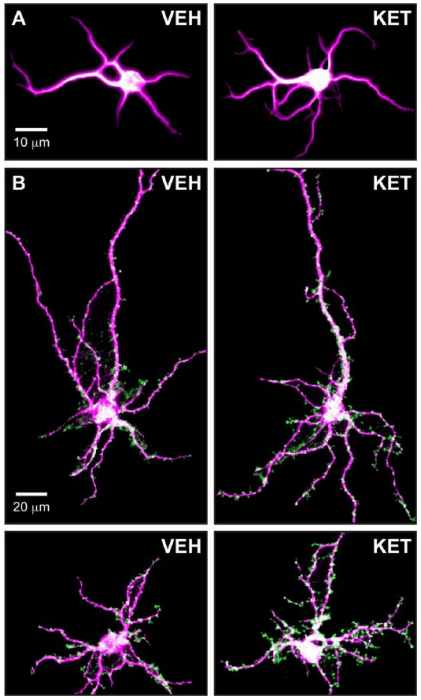
Konzept der Pharmakopsychotherapie

- neue Art der **Kombination** von Pharmakotherapie und Psychotherapie
- Pharmakon beeinflusst Art und Weise, **wie Psychotherapie wirkt**
- bestimmte **Lernvorgänge** können gezielt unterstützt werden (Empathie, Bindungserfahrung, kognitive Flexibilität, korrektive emotionale Erfahrung, Emotionsregulation)
- **integrativer Ansatz** (die Wirkung des Pharmakons hat einen direkten funktionalen Einfluss auf den Verlauf der Psychotherapie)

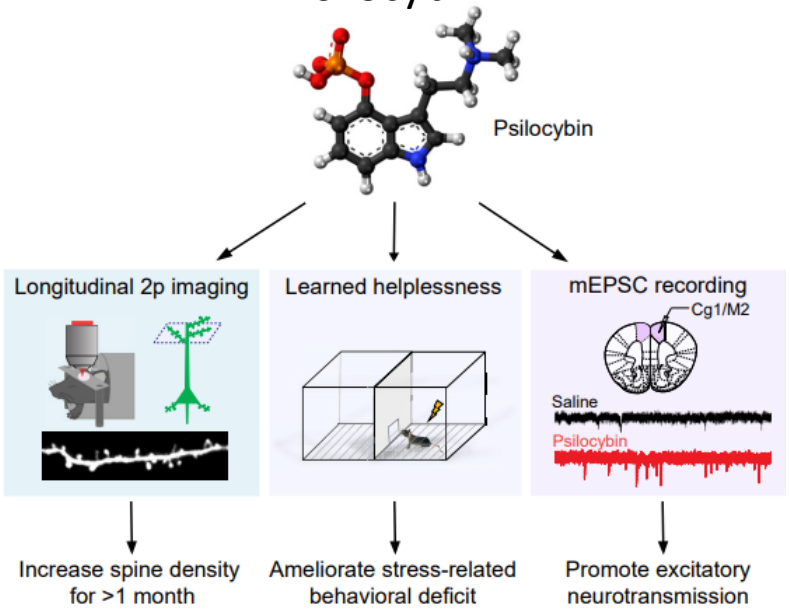
von Scheidegger M. et al, Reconnect

Neuroplastizität

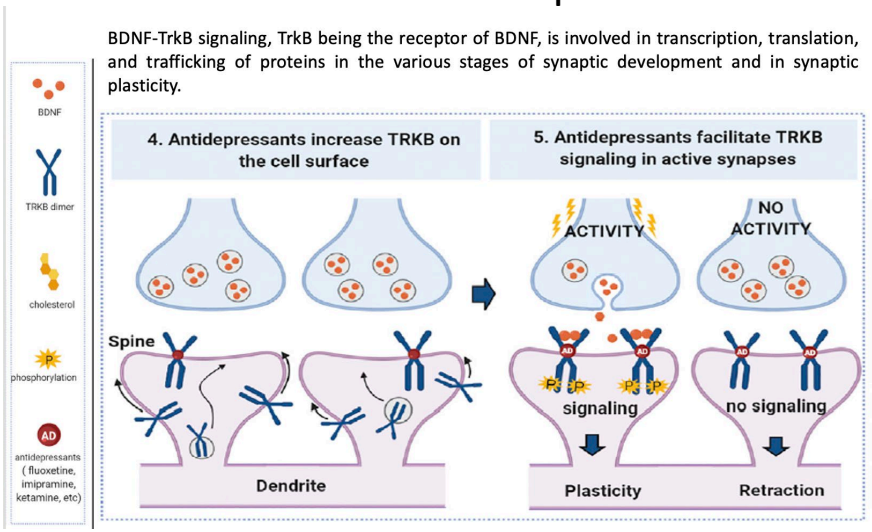
[1]Ketamin



[2]Psilocybin



[3]Klassische Antidepressiva

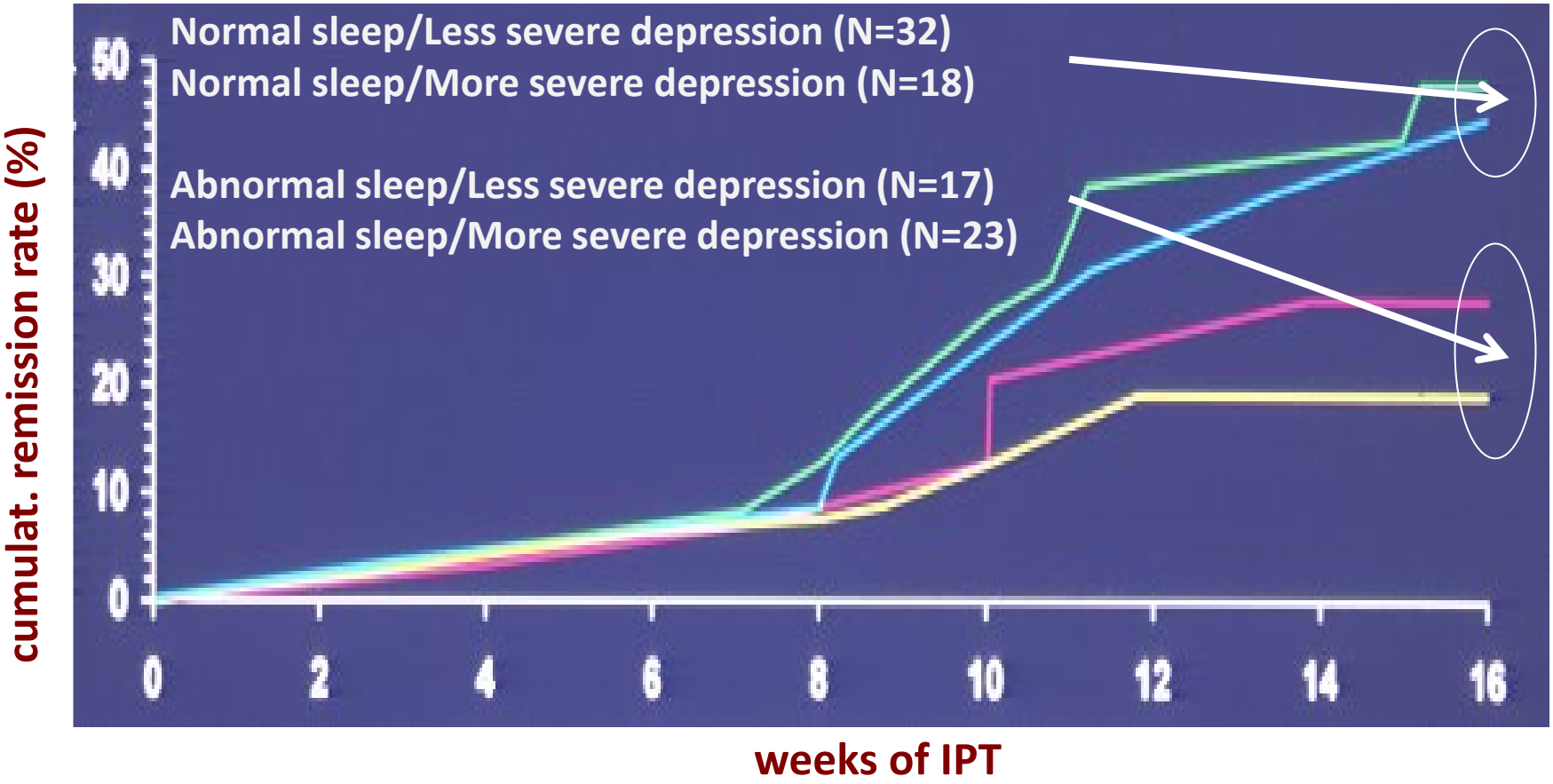


[1] Olson. Psychoplastogens: a promising class of plasticity-promoting neurotherapeutics. J Exp Neurosci, 2018

[2].Shao et al, Neuron 2021, 109, 2535 - 2544

[3].Casarotto et al., 2021, Cell 184, 1299 – 1313

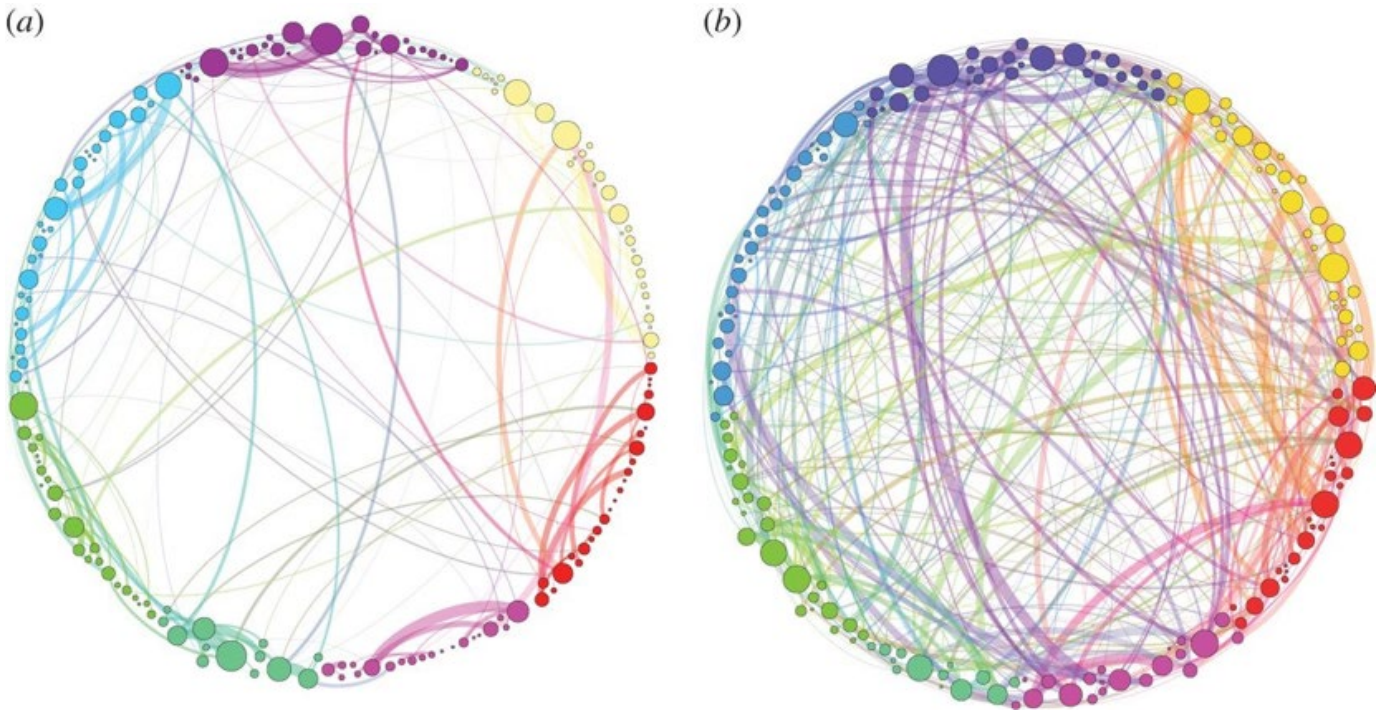
Schlaf und Wirksamkeit von Psychotherapie bei Depression



Thase et al, Am J Psychiatry 1997

Connectomix

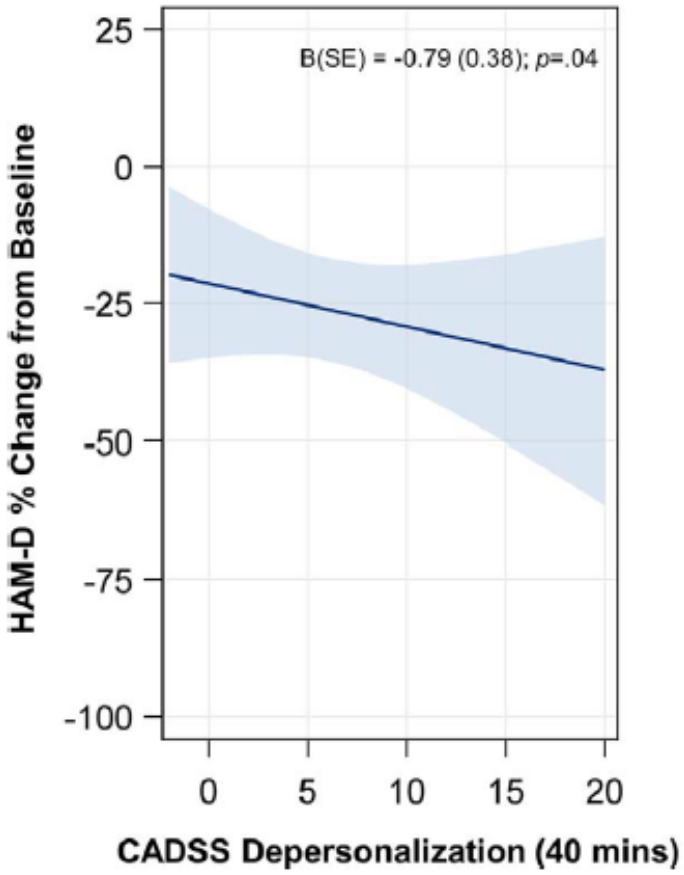
15 healthy volunteers after i.v. infusion of placebo and psilocybin



placebo psilopsybin

Petri et al, Homological scaffolds of brain functional networks. J R Soc Interface. 2014 Dec 6;11(101):20140873.

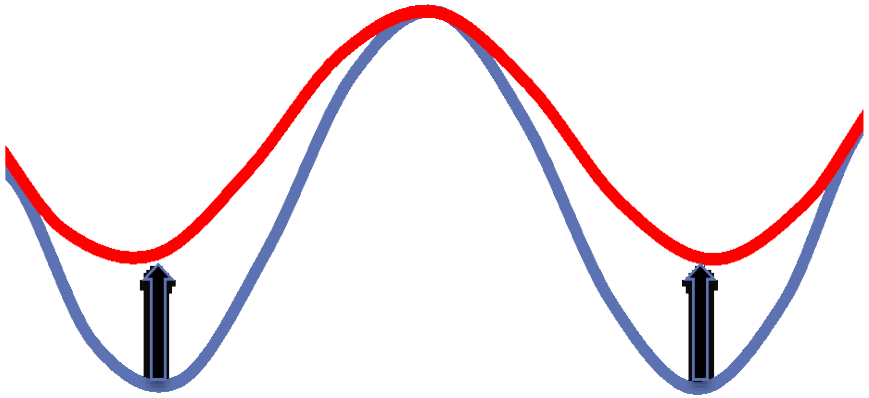
Dissoziation?



Niciu et al, Features of dissociation differentially predict antidepressant response to ketamine in treatment-resistant depression, Journal of Affective Disorders, Disorders, 232, 310–315, 2018

Katalysator für Phasenübergänge?

... we conclude that depression is better defined as the tendency to enter into, and inability to disengage from, a negative mood state rather than the mood state per se ...



Holtzheimer and Mayberg, TINS 2011

Plazebo?

“He cures most successfully in whom the people have the most confidence”

Galen, 129 – 217 AD)

bloomberg.com, 30.5.2021
psilocybin & compass

Bloomberg

Showing results for "compass psilocybin"

Wealth
Billionaire Took Psychedelics, Got Bitcoin and Is Now Into SPACs
By Devon Pendleton
German investor Christian Angermayer has made a fortune on the risky and faddish. His portfolio includes crypto, weed and space travel.
April 23, 2021

Markets
Psychedelics ETF to Launch After Sector Attracts Thiel's Money
By Michael Bellusci
The world's first exchange-traded fund for psychedelic-drug companies will debut this week in Toronto, as the investment industry tries to capitalize on rising interest in prospective mental health treatments using the drugs.
January 26, 2021

Pursuits
Psychedelic Schools Teach Mental Health Therapists MDMA, Psilocybin
By Michelle Lhooq
For hundreds or thousands of dollars, you can get certified to administer mind-altering—and some say, mind-healing—drugs.
January 18, 2021