Klinik Köln
Akademisches Lehrkrankenhaus
der Universität zu Köln

Qualität für Menschen

Ecstasy-Studien mit Spätadoleszenten in den 1990er Jahren: Welche Zukunft haben die Stimulanzien bei Jugendlichen?

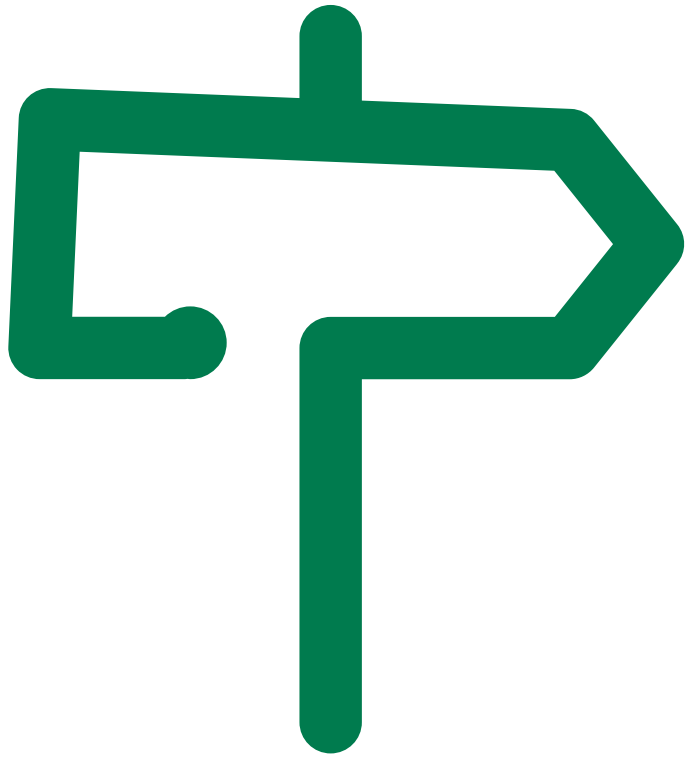
Prof. Dr. Euphrosyne Gouzoulis-Mayfrank

Symposium des DZSKJ
Suchtforschung und -therapie für Kinder und Jugendliche

Agenda

- Ecstasy – Was ist das? Erste Annäherungen
- Die Frage der Neurotoxizität
- Ecstasy – Und immer noch die Frage: Was ist das?

  ATS (Amphetamine type stimulant) oder psychedelic?
- Bedeutung heute



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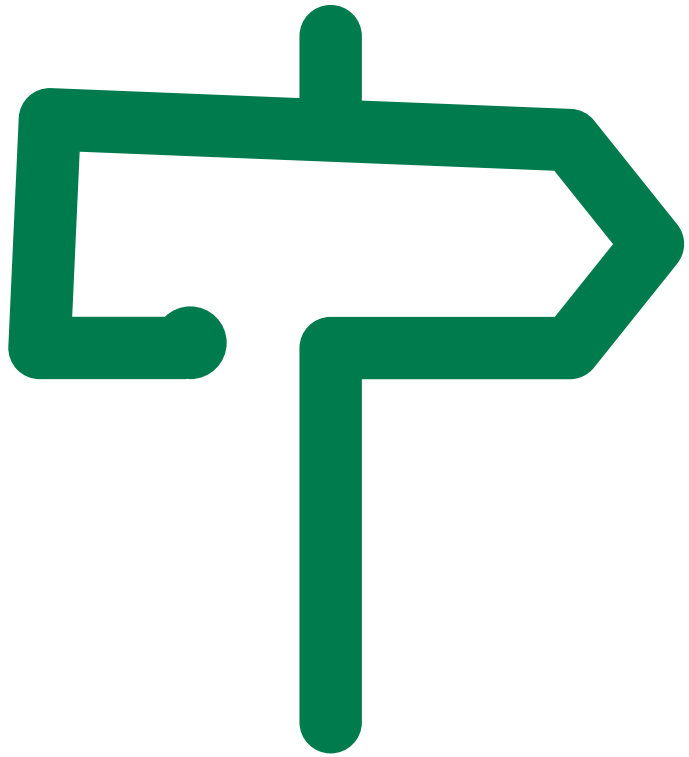
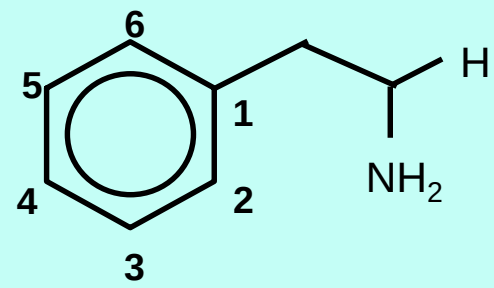
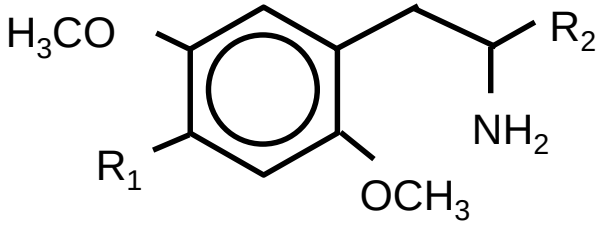


Ecstasy: (Chemische) Verwandtschaft mit Halluzinogenen und Stimulanzien



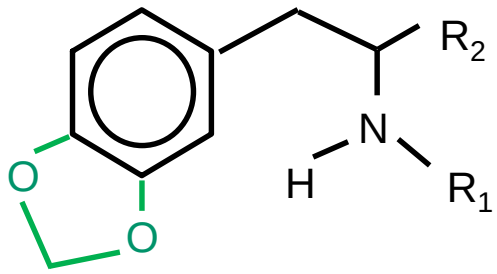
Phenethylamin

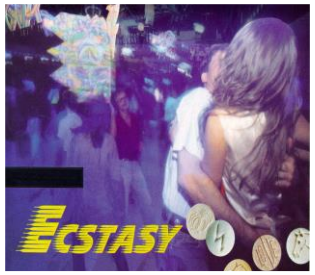
Halluzinogene



$R_1 = CH_3$; $R_2 = CH_3$: **DOM**
$R_1 = Br$; $R_2 = CH_3$: **DOB**
$R_1 = H_3CO$; $R_2 = CH_3$: **TMA**
$R_1 = H_3CO$; $R_2 = H$: **Meskalin**

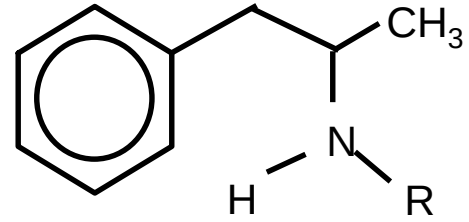
Ecstasy (Methylendioxy-amphetamine)





$R_1 = H$; $R_2 = CH_3$: **MDA**
$R_1 = CH_3$; $R_2 = CH_3$: **MDMA**
$R_1 = C_2H_5$; $R_2 = CH_3$: **MDE**
$R_1 = CH_3$; $R_2 = C_2H_5$: **MBDB**

Stimulanzien



R = H : **Amphetamin**
R = CH_3: **Methamphetamin**

Ecstasy: MDMA und Analoga

Wirklich eine neue Substanzgruppe?

Was heißt „Entaktogene“?

„en“

„tactus“

„gen“

→ to produce a touching within

Differences Between the Mechanism of Action of MDMA, MBDB, and the Classic Hallucinogens. Identification of a New Therapeutic Class: Entactogens

DAVID E. NICHOLS, PH.D.*

The widespread use of psychedelic drugs, such as lysergic acid diethylamide (LSD), during the 1960's and 1970's led to severe reactions by governmental agencies and proscriptions against their use. However, with the high degree of interest in mind-altering drugs in the United States, as evidenced by their widespread popularity, it was only a matter of time before new drugs appeared that were developed outside of the pharmaceutical companies.

Nearly 70 years after its first synthesis, 3,4-methylenedioxymethamphetamine (MDMA) was rediscovered. Although it had its more recent origin in the class of drugs that is generally defined as psychedelic or hallucinogenic, it clearly appears different from LSD. In humans, MDMA induces a state of reduced anxiety and lowered defensiveness that makes it attractive to therapists wishing to speed up the therapeutic process. However, as with all substances that produce pleasurable effects, it soon became popular as a recreational drug, and it went the same way as the psychedelics: into Schedule I.

The present author's interest in MDMA stems from longstanding efforts, spanning nearly 17 years, to understand how psychedelic substances work. In contrast to the pharmacologist, who often studies the effect of a single drug to understand how it works, the development of a potency-series is employed. That is, a series of drugs closely related in structure is prepared and the biological potency of the members of the series is measured. Then, with these numbers in hand, one attempts to develop quantitative structure-activity relationships (QSARs). Simply stated, attempts are made to find quantitative correlations (or equations) that relate biological activity to fundamental properties of the molecule. This approach is being widely developed in the pharmaceutical industry in order to understand more fully how particular types of drugs work, and to be able to predict which additional molecules should be synthesized. It should also be added that no equations have been developed that adequately correlate hallucinogenic or psychedelic activity with any particular molecular property.

In this context, it is important to define clearly the type of biological activity that is being measured. It is typical that if a molecule has several different sites of action in the brain, that each one of these actions may be related to entirely different structural features or properties of the molecule. Thus, to develop valid QSARs, one needs to measure some index of pure biological activity. It goes almost without saying that psychedelics probably do not have any one pure mechanism of action. That is, their complex array of behavioral effects is probably the net result of multiple neurochemical component processes. Martin and his colleagues (Nozaki, Vaupel & Martin 1977) at the Lexington (Kentucky) Addiction Research Center were probably the first strong proponents of this idea, but several later groups (including the present author's research team) have reiterated that these substances may all differ in the scope of their qualitative effects (Glennon & Young 1984a, 1984b, 1984c; Nichols et al. 1982). Some compounds have predominantly stimulant effects like amphetamine, while others have an action more like LSD or mescaline. In between, there is a whole

*Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana 47907.

Ecstasy: Eine neue Substanzgruppe?

Psychological Effects of MDE in Normal Subjects

Are Entactogens a New Class of Psychoactive Agents?

Leo Hermle, M.D., Manfred Spitzer, M.D., Ph.D., Dieter Borchardt, Karl-Artur Kovar, Ph.D., and Euphrosyne Gouzoulis, M.D.

The so-called entactogens 3,4-methylenedioxymethamphetamine ([MDMA] also known as "Ecstasy," or "Adam") and its analog 3,4-methylenedioxyethamphetamine ([MDE] also known as "Eve") exert similar psychotropic effects in humans. Two double-blind placebo-controlled psychometric studies with normal control subjects were conducted. Placebo or MDE (140 mg) was administered orally to eight male volunteers at 1:30 P.M. and to six subjects (3 male, 3 female) at 11 P.M. Psychologic tests and clinical ratings were performed 1 hour before the administration of the drugs, as well as 2, 5, and 24 hours after drug intake and 7 days thereafter in the first study. In the second study, measures were taken at times −1, +8.5, +24 hours, and +7 days. The majority of the psychotropic effects resembled those that have already been described in anecdotal reports. The substance produced a partially controllable state of enhanced insight, empathy, and peaceful feelings. All subjects displayed a general stimulation with increased psychomotor drive, logorrhea, and facilitation of communication. One of the fourteen volunteers developed a toxic psychosis. One volunteer displayed a dysphoric reaction, one suffered from episodes of anxiety for some days after the experiment. The findings support the hypothesis that MDMA and MDE represent a novel pharmacologic class. ***[Neuropsychopharmacology 8:171–176, 1993]***

1108 BIOL PSYCHIATRY
1992;32:1108–1117

Sleep EEG Effects of 3,4-Methylenedioxyethamphetamine (MDE; "Eve") in Healthy Volunteers

Euphrosyne Gouzoulis, Axel Steiger, Martin Ensslin, Arthur Kovar, and Leopold Hermle

Neuroendocrine and Cardiovascular Effects of MDE in Healthy Volunteers

Euphrosyne Gouzoulis, M.D., Ulrich von Bardeleben, M.D., Armin Rupp, Karl-Arthur Kovar, Ph.D., and Leopold Hermle, M.D.

The drug 3,4-methylenedioxyethamphetamine ([MDE] also known as "Eve") is a less toxic analog of 3,4-methylenedioxymethamphetamine (also known as "Ecstasy") with similar psychotropic effects in humans. In a double-blind placebo-controlled, cross-over study we administered 140 mg of MDE or placebo orally to eight healthy male volunteers at 1:30 P.M. Serum cortisol, prolactin (PRL), and growth hormone (GH) levels, as well as blood pressure, and heart rate were measured every 20 minutes until 5:00 P.M. Administration of MDE was followed by statistically significant long-lasting increases of serum cortisol, PRL, systolic blood pressure, and heart rate, and by a trend toward blunting of GH secretion. The neuroendocrine and cardiovascular effects of MDE are comparable to those of other phenethyl-amines with the exception of the effect on GH secretion. ***[Neuropsychopharmacology 8:187–193, 1993]***

Nervenarzt (1996) 67: 369–380

Die Entaktogene „Ecstasy“ (MDMA), „Eve“ (MDE) und andere ringsubstituierte Methamphetaminderivate

Eine neue Stoffklasse unter den illegalen Designerdrogen?

E. Gouzoulis-Mayfrank[1], L. Hermle[2], K.-A. Kovar[3] und H. Saß[1]
[1] *Psychiatrische Klinik, Medizinische Einrichtungen der RWTH, Aachen*
[2] *Fachkrankenhaus für Neurologie und Psychiatrie Christophsbad, Göppingen*
[3] *Pharmazeutisches Institut der Universität, Tübingen*

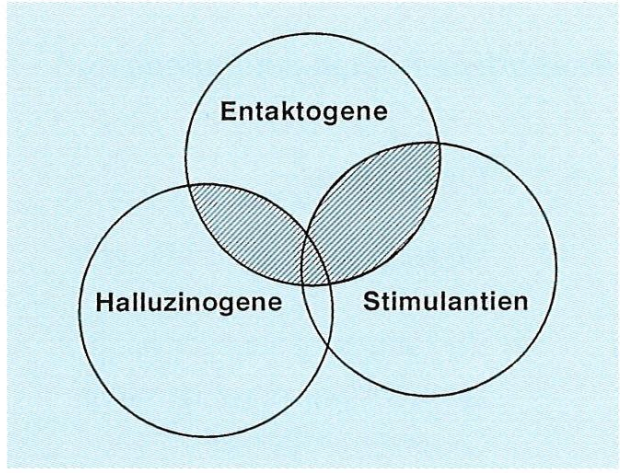


Tabelle 2
Psychische Effekte von MDE bei gesunden Probanden in eigenen experimentellen placebokontrollierten Laborstudien (*n* = 14). Ergebnisse zusammengefaßt aus: Hermle et al. (1993) [43], Gouzoulis et al. (1993) [33] sowie nach Auswertung bisher unveröffentlichter freier Versuchsprotokolle

• Beginn der Wirkung (in min nach Einnahme)	20–85	
• Dauer der Wirkung (in Stunden)	2–3	
Psychische Effekte	Serie 1[a] (*n* = 8) Anzahl der Probanden	Serie 2[b] (*n* = 6) Anzahl der Probanden
• Hypervigilanz, gesteigerter Antrieb	8	6
• Euphorie, Entspannung, friedvolle Zufriedenheit	4	3
• Dysphorie, Gereiztheit	1	0
• Glücksgefühl	2	1
• „Entaktogenes Wirkprofil“: Introspektion, Empathie, Angstfreiheit, glückliche Selbstakzeptanz, kontrollierte kommunikative Offenheit	3	0
• Verändertes Zeiterleben	2	1
• Wahrnehmungsstörungen optisch/taktil/akustisch: Farben intensiver, Konturen verzerrt, Gegenstände größer/kleiner, Geräusche lauter, Tasten „wie durch Watte“	4	3
• Depersonalisation, Derealisation	0	1
• Religiös-mystisches Erleben	1	2
• Psychotischer Rauschverlauf: akustische/optische Halluzinationen, Wahnerleben, Verlust der Ich-Kontrolle, Angst	0	1
• Erhaltene Ich-Kontrolle	8	5
• Subjektiv Konzentrationsminderung	4	2
• Grobe kognitive Einschränkung	0	?

[a] Versuche bei Tageslicht, Kontakt zum Versuchsleiter, vollständige Erfassung der psychotropen Effekte direkt während des Versuches
[b] Versuche nachts bei Dunkelheit (Schlaf-EEG-Ableitung), kein Kontakt zu Versuchsleiter, unvollständige Erfassung der psychotropen Effekte

Ecstasy: (Wirklich) eine neue Substanzgruppe?

Psychopharmacology (1999) 142 : 41–50

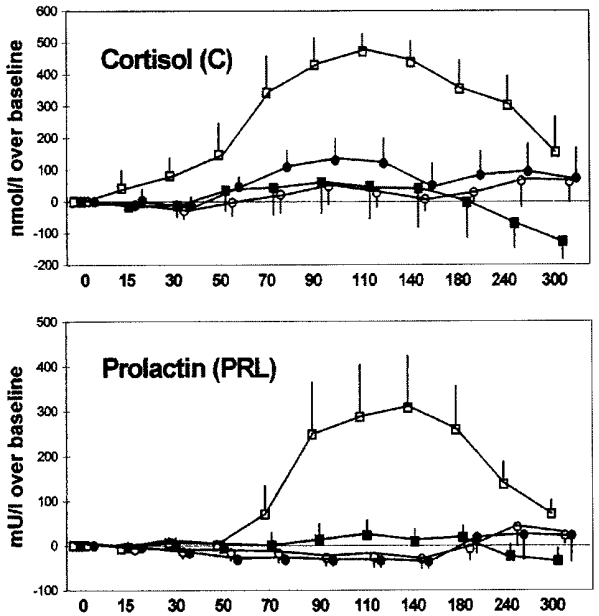
ORIGINAL INVESTIGATION

E. Gouzoulis-Mayfrank · B. Thelen · E. Habermeyer · H.J. Kunert
K.-A. Kovar · H. Lindenblatt · L. Hermle · M. Spitzer · H. Sass

Psychopathological, neuroendocrine and autonomic effects of 3,4-methylenedioxyethylamphetamine (MDE), psilocybin and *d*-methamphetamine in healthy volunteers

Results of an experimental double-blind placebo-controlled study

Received: 5 March 1998/Final version: 20 July 1998



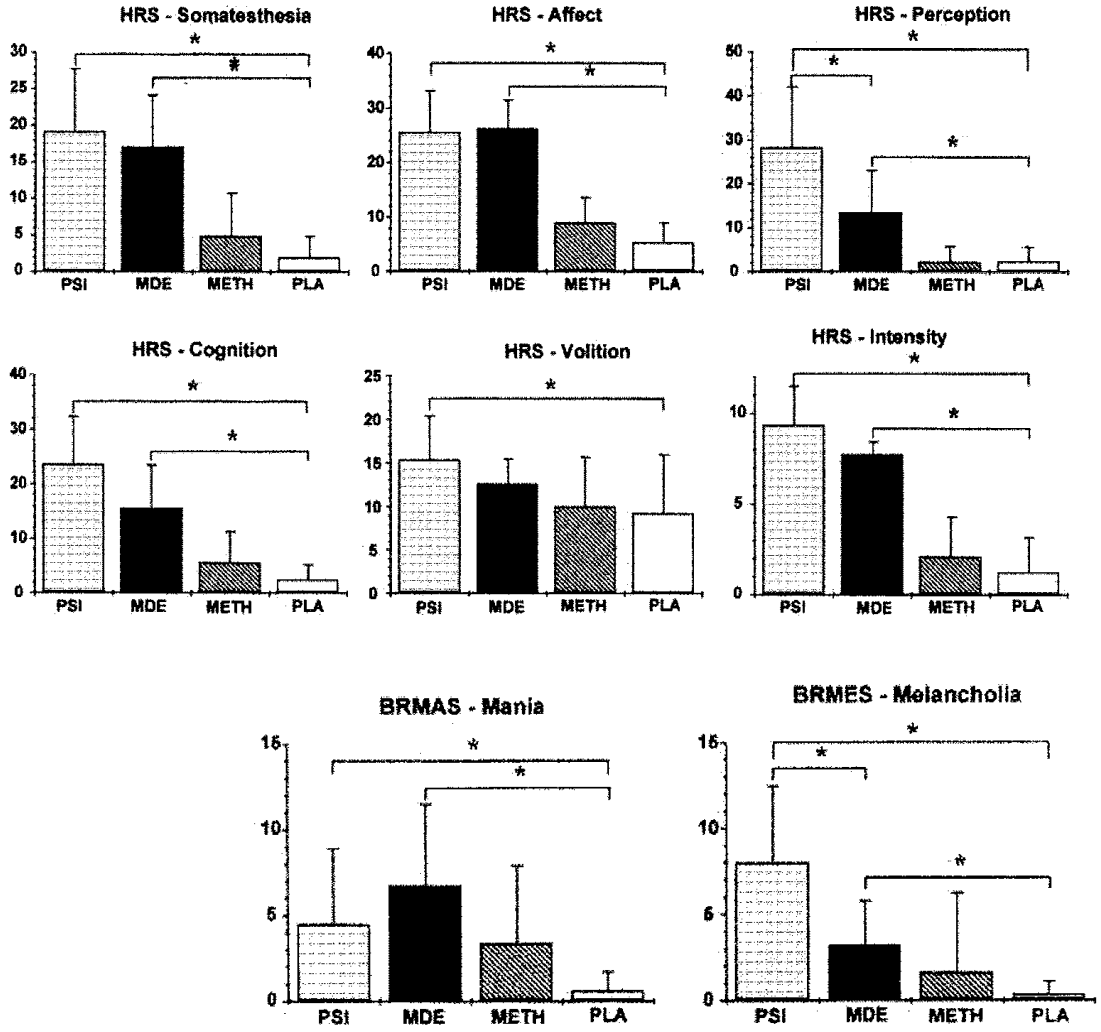


Fig. 3 Time-curves of hormonal responses (means ± SD) after intake of psilocybin (■), 3,4-methylenedioxyethylamphetamine (□, *MDE*), *d*-methamphetamine (●) and placebo (○) (each group: $n = 8$)

Ecstasy: (Wirklich) eine neue Substanzgruppe?

Neurometabolic Effects of Psilocybin, 3,4-Methylenedioxyethylamphetamine (MDE) and d-Methamphetamine in Healthy Volunteers

A Double-Blind, Placebo-Controlled PET Study with [^{18}F]FDG

Euphrosyne Gouzoulis-Mayfrank, M.D., Mathias Schreckenberger, M.D., Osama Sabri, M.D., Christoph Arning, Bernhard Thelen, M.D., Manfred Spitzer, M.D., Ph.D., Karl-Artur Kovar, Ph.D., Leopold Hermle, M.D., Udalrich Büll, M.D., and Henning Sass, M.D.

The neurometabolic effects of the hallucinogen psilocybin (PSI; 0.2 mg/kg), the entactogen 3,4-methylenedioxyethylamphetamine (MDE; 2 mg/kg) and the stimulant d-methamphetamine (METH; 0.2–0.4 mg/kg) and the drugs' interactions with a prefrontal activation task were investigated in a double-blind, placebo-controlled human [F-18]fluorodeoxyglucoseFDG-positron emission tomographicPET study (each group: n = 8). Subjects underwent two scans (control: word repetition; activation: word association) within 2–4 weeks. Psilocybin increased rMRGlu in distinct right hemispheric frontotemporal cortical regions, particularly in the anterior cingulate and decreased rMRGlu in the thalamus. Both MDE and METH induced cortical hypometabolism and cerebellar hypermetabolism. In the MDE group, cortical hypometabolism was more pronounced in frontal regions, with the exception of the right anterior cingulate, which tended to be hyperactive. Cognitive activation-related increases in left frontocortical regions were attenuated under all three psychoactive substances, but less so under MDE. Taking into account performance data and subjective reports on task difficulty, these effects may result from different mechanisms across the three groups. Our PSI data are in line with studies on acute schizophrenic patients suggesting frontal overactivity at rest, but diminished capacity to activate prefrontal regions upon cognitive demand. The MDE data support the hypothesis that entactogens constitute a distinct psychoactive substance class, which takes an intermediate position between stimulants and hallucinogens.

[Neuropsychopharmacology 20:565–581, 1999]

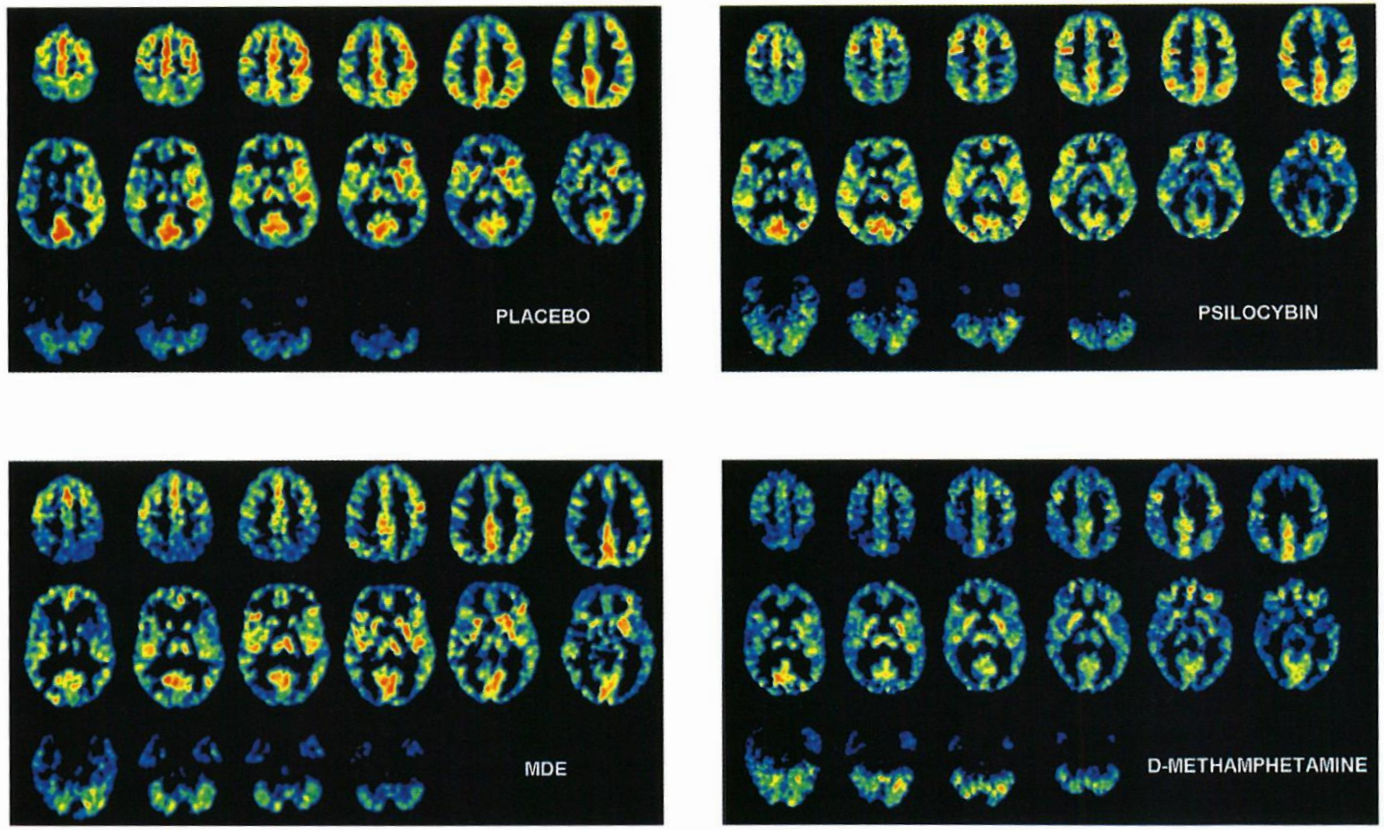


Figure 4. Representative transaxial FDG-PET images of single subjects under placebo, psilocybin, MDE, and d-methamphetamine while performing a word repetition task. Note the shifted right/left asymmetry, the increased activity of the anterior cingulate and the decreased thalamic activity in the psilocybin subject. Note the decreased cortical and increased cerebellar activity in the MDE and d-methamphetamine subjects.

Agenda

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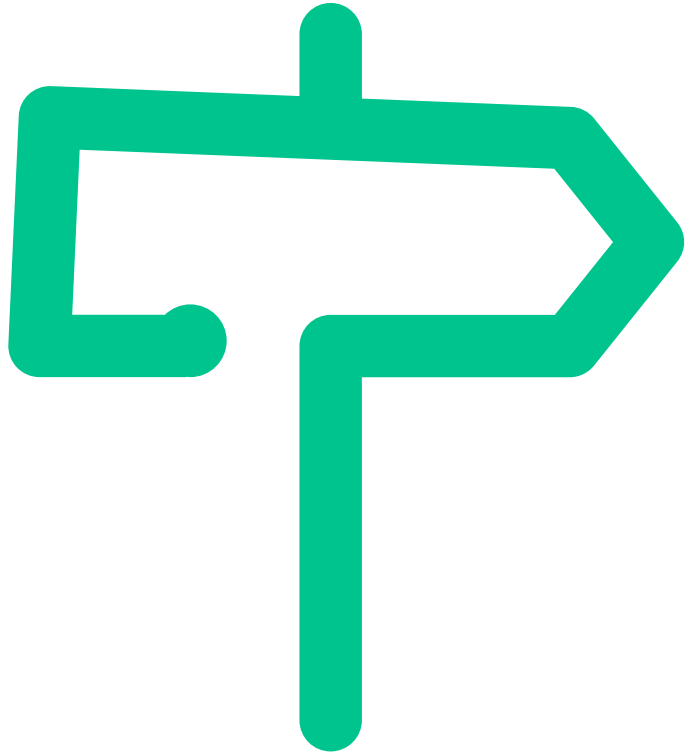
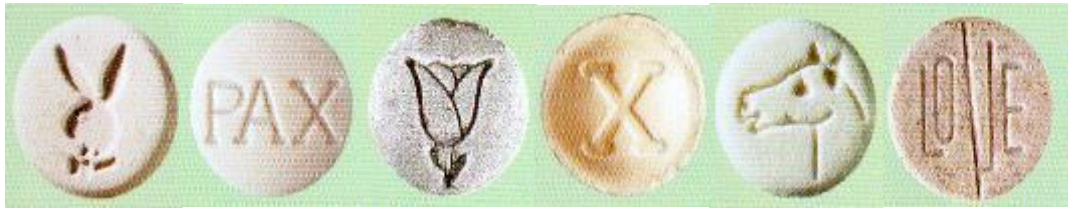
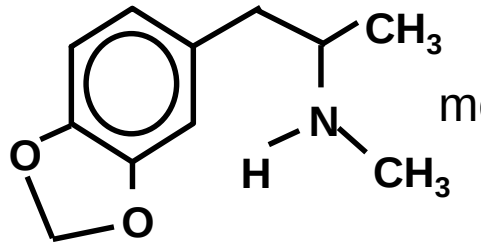


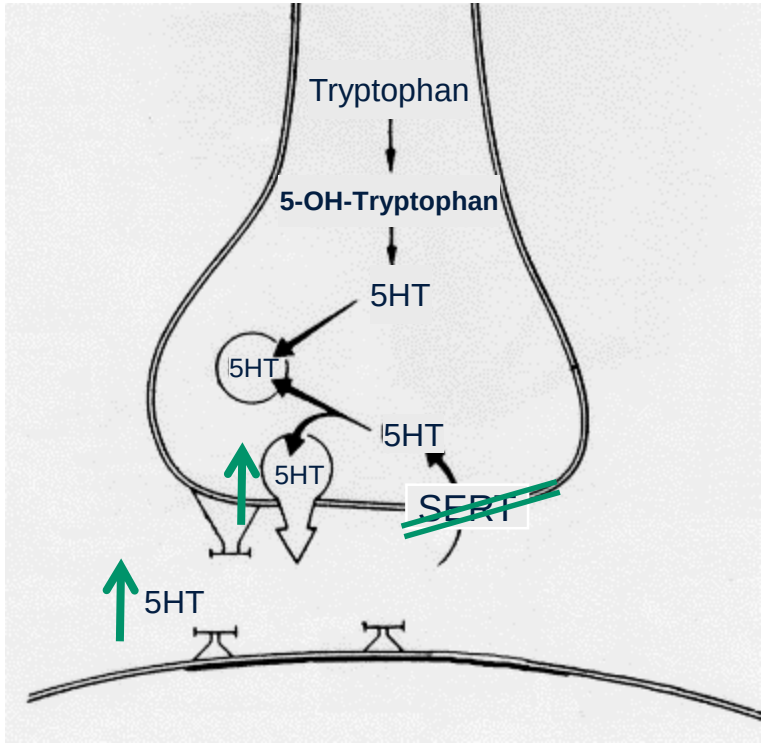
Ecstasy: Die Frage der Neurotoxizität





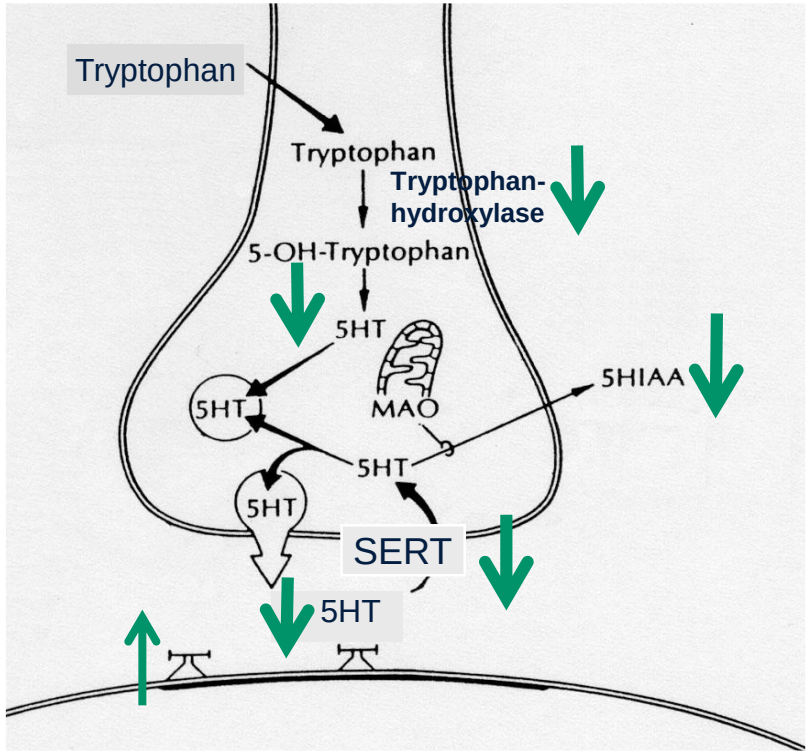
Methylendioxy-
methamphetamine

akut: indirekt serotonerg



serotonerge Synapse

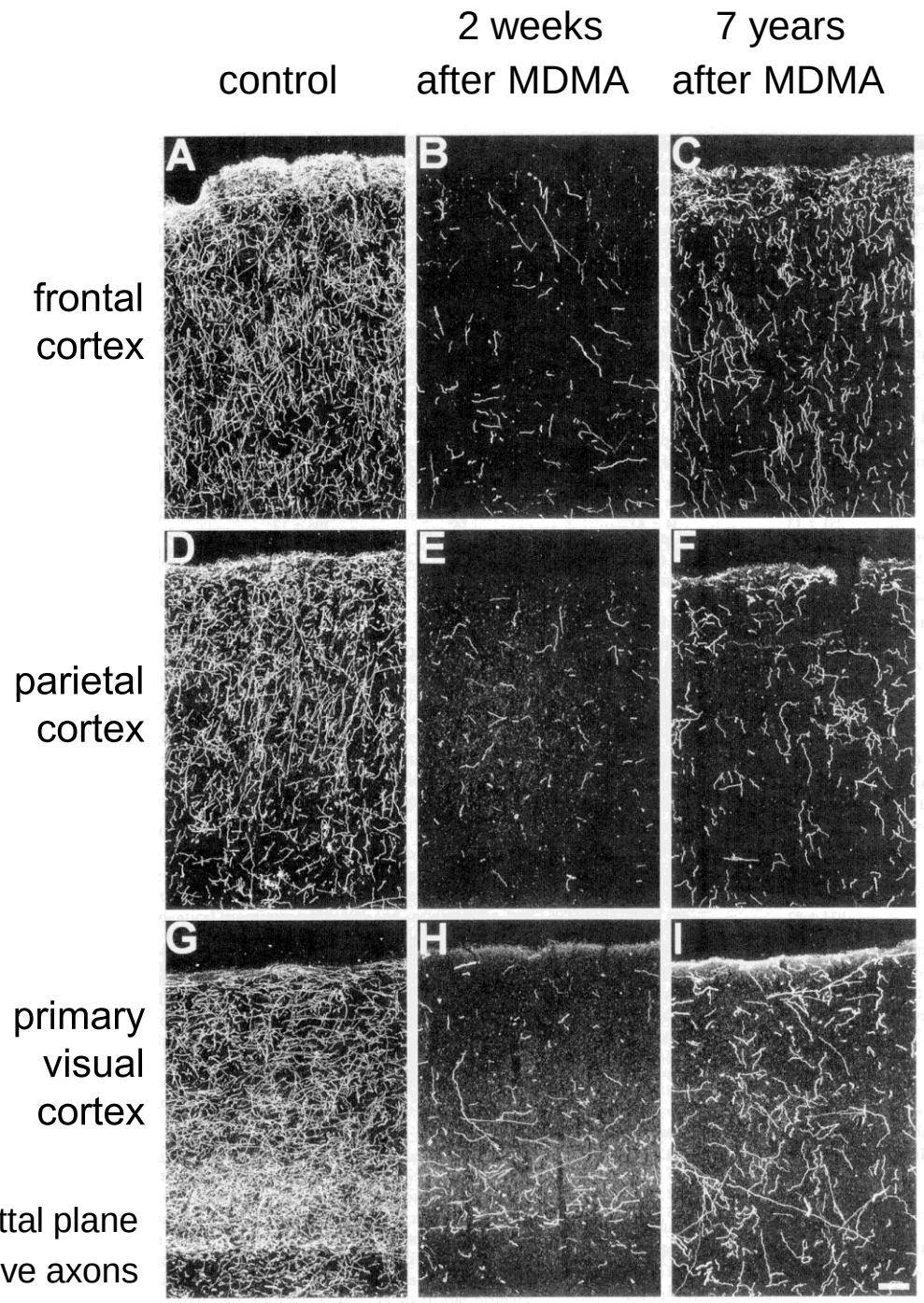
chronisch: neurotoxisch



Hatzidimitriou et al, J Neurosci 1999

Altered serotonin innervation patterns in the forebrain of ***monkeys treated with (±)3,4-Methylenedioxymethamphetamine seven years previously:***
factors influencing abnormal recovery

Relevanz für den Menschen ?



Dark-field photomicrograph, sagittal plane of 5-HT immunoreactive axons

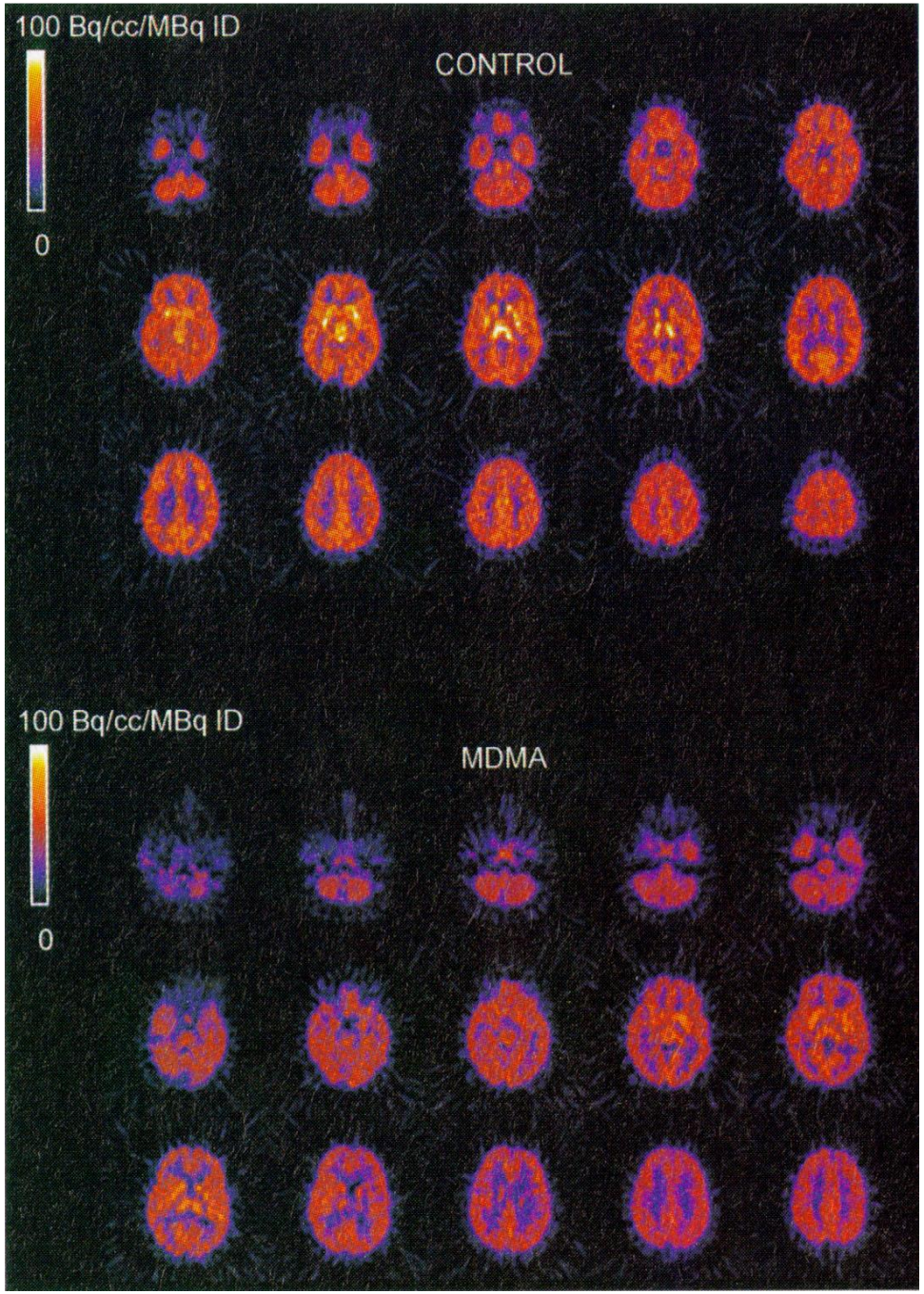
zentrale serotonerge Parameter bei Ecstasy-Konsumenten

Serotoninmetabolit 5-HIAA im Liquor

- Peroutka et al. 1987 ↔ 5-HIAA
- Ricaurte et al. 1990 ↓ 5-HIAA
- McCann et al. 1994 ↓ 5-HIAA
- Bolla et al. 1998 ↓ 5-HIAA
  assoziiert mit ↑ Ecstasy-Konsum und ↓ Gedächtnis
- McCann et al. 1999 ↓ 5-HIAA

McCann et al, THE LANCET 1998

Positron emission tomographic evidence of ***toxic effect of MDMA ("Ecstasy") on brain serotonin neurons in human beings***



PET with SERT ligand 11C-(+)-McN5652

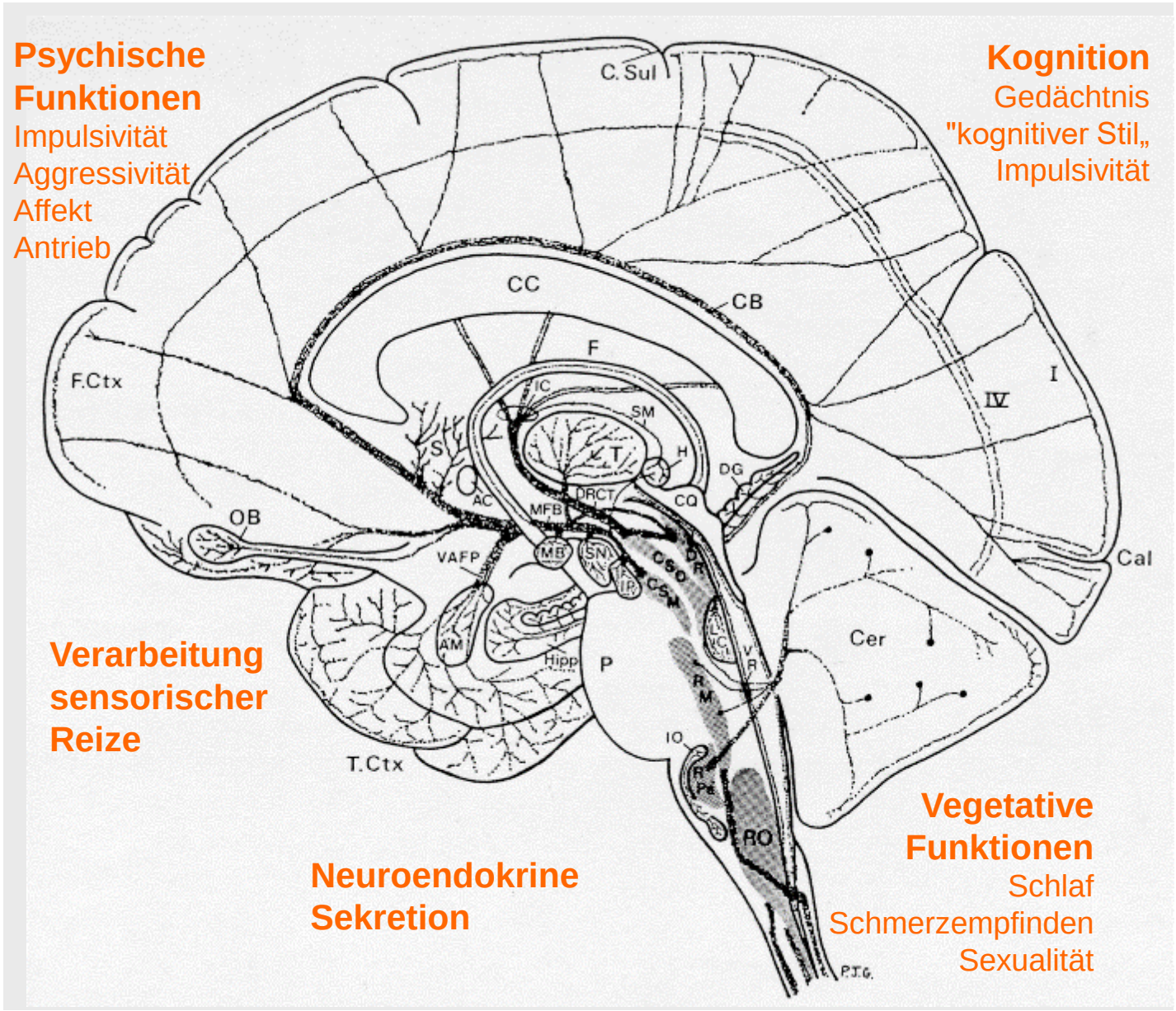
zentrale serotonerge Parameter bei Ecstasy-Konsumenten

PET und SPECT mit Serotonintransporter (SERT)-Liganden

• McCann et al. 1998	↓ Bindung, assoziiert mit ↑ Ecstasy-Konsum
• Semple et al. 1999	↓ Bindung, assoziiert mit kurzer Abstinenzdauer
• Reneman et al. 2001a	↓ Bindung nur bei aktuellen Usern
• Reneman et al. 2001b	↓ Bindung nur bei starken Usern
• Thomasius et al. 2003, 2006 Buchert et al. 2004, 2006	↓ Bindung nur bei aktuellen Usern Erholung im Längsschnittverlauf nach Abstinenz oder Reduktion des Konsums

⟹ nur transiente Veränderungen ?

Serotonerges System: Anatomie und Funktionen



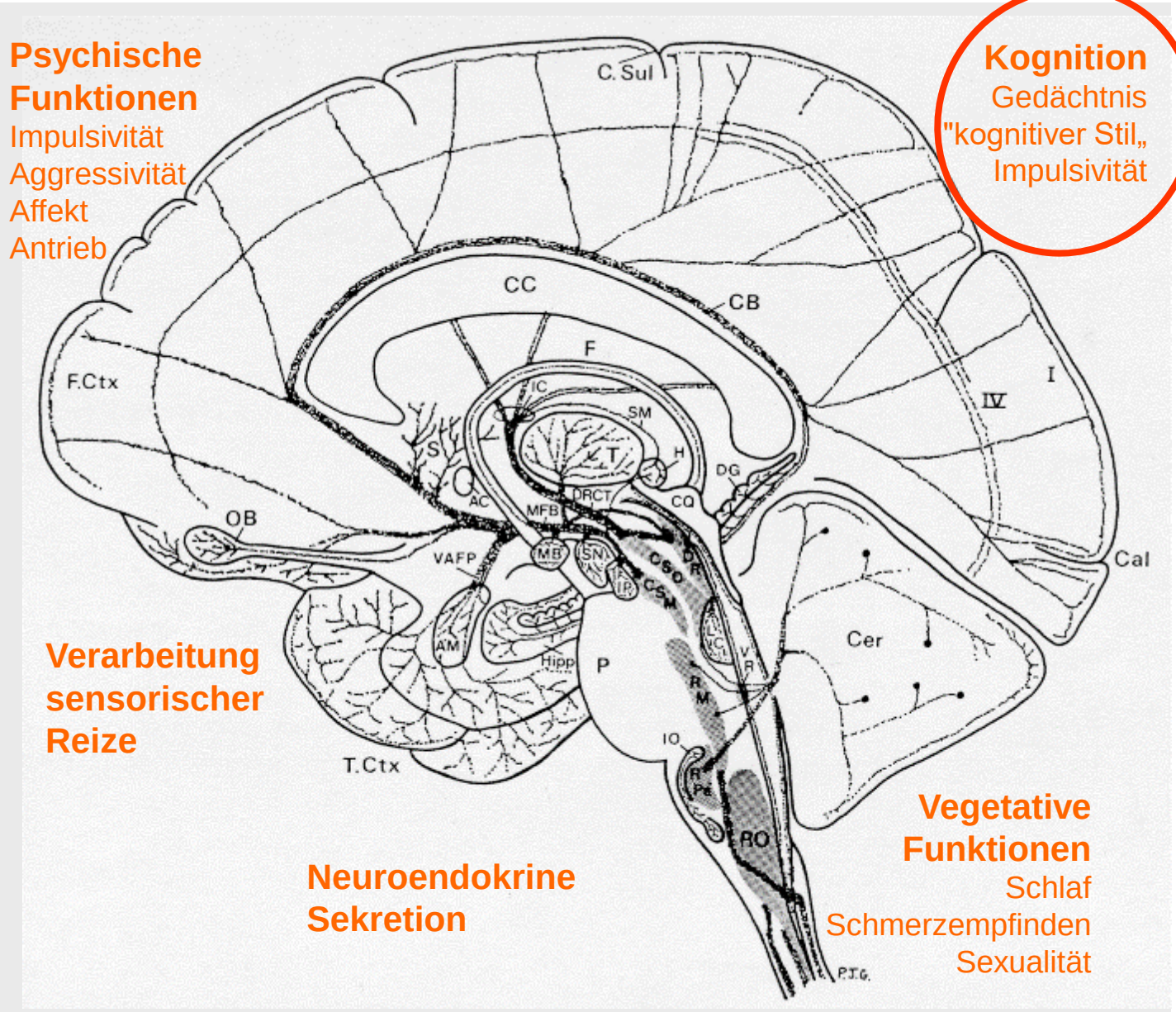
(aus: Azmitia u. Gannon 1986)

Auffälligkeiten bei Ecstasy-Konsumenten:

sind sie

Folge des Ecstasy-Konsums ?

Serotonerges System: Anatomie und Funktionen



(aus: Azmitia u. Gannon 1986)

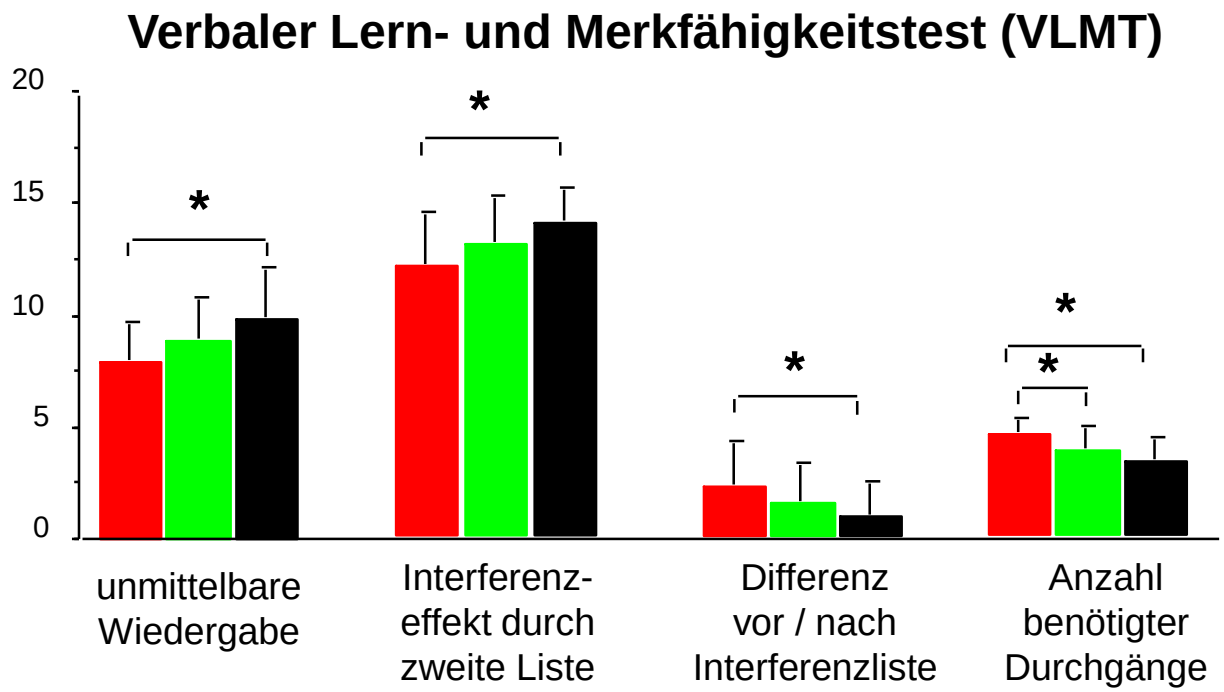
Auffälligkeiten bei Ecstasy-Konsumenten:

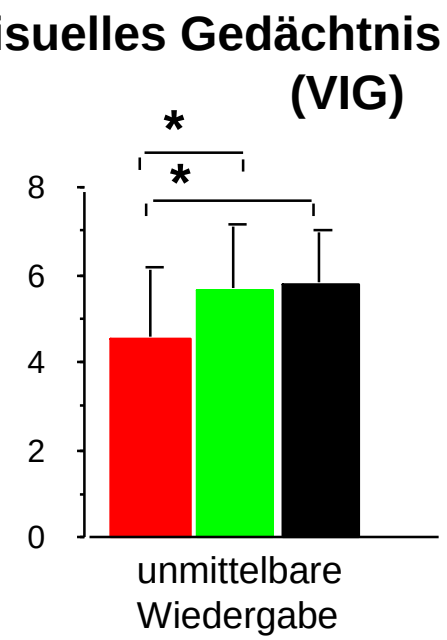
sind sie

Folge des Ecstasy-Konsums ?

- Viele Befunde wären damit vereinbar

Merkfähigkeit und Lernen





schlechtere Leistungen

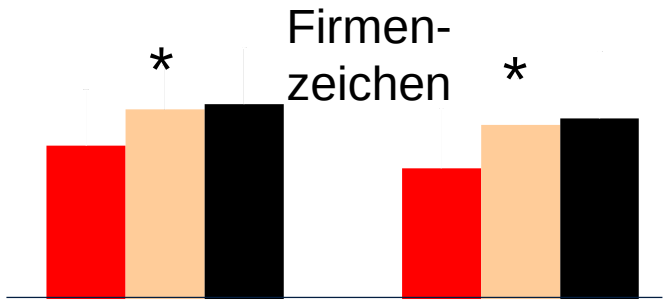
assoziiert mit

- **mehr Ecstasy**:
  höhere Lifetime-, Einmaldosis, Konsumfrequenz
- **mehr Cannabis**:
  höhere Konsumfrequenz

- Ecstasy / Cannabis user (n=28)
- Cannabis user (n=28)
- Nicht-user (n=28)

Gouzoulis-Mayfrank et al, JNNP 2000

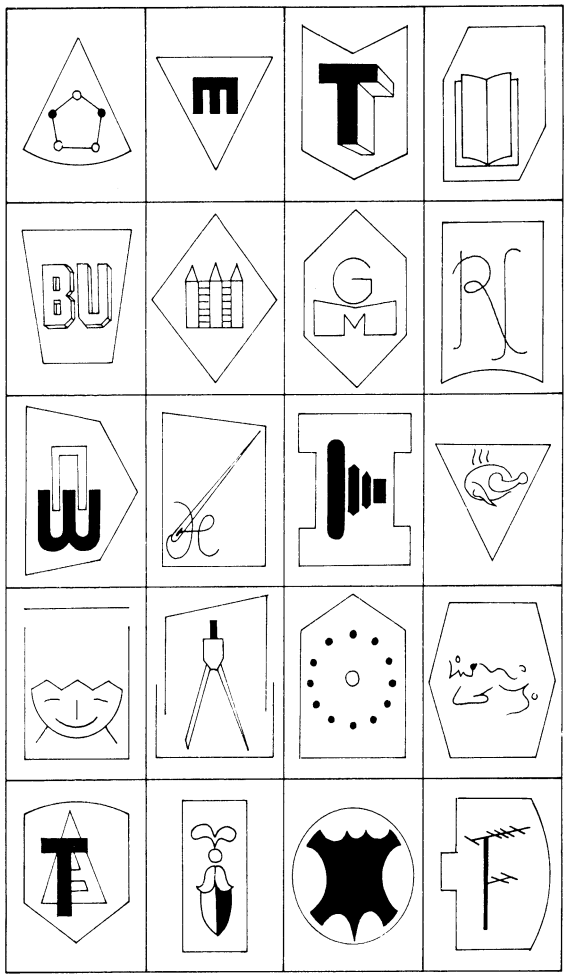
Merkfähigkeit (LGT-3)



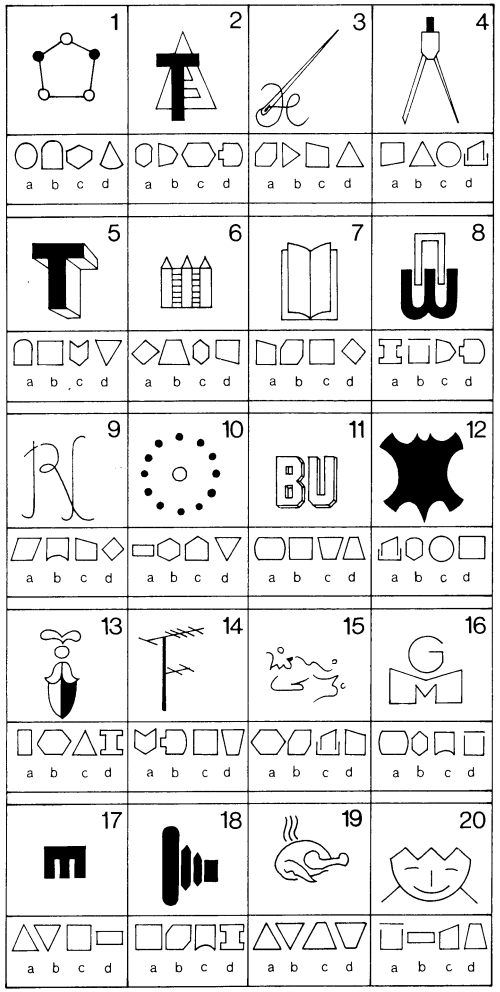
immediate recall (IR) delayed recall (DR)

- starke E-Konsumenten (+ Cannabis > Amphetamine > LSD > Kokain, n = 30)
- moderate E-Konsumenten (+ Cannabis > Amphetamine > LSD > Kokain, n = 30)
- Nicht-Konsumenten (n = 30)

Signifikanter Einfluß ausschließlich der Frequenz des Ecstasy-Konsums auf Immediate und Delayed Recall



Enkodieren

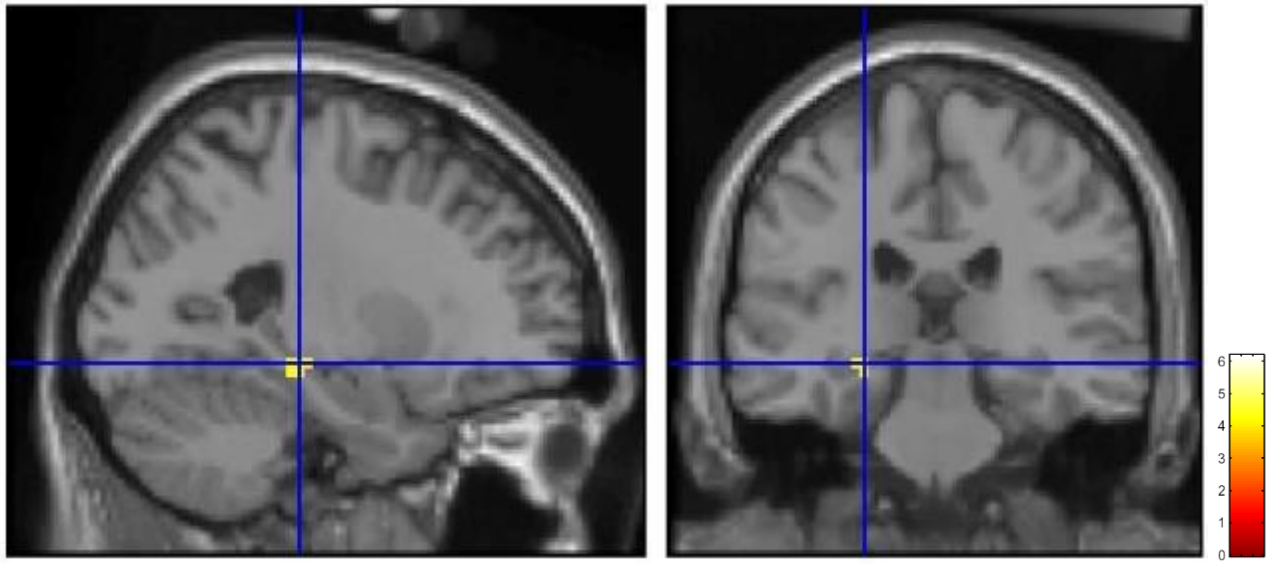


Abrufen

Gouzoulis-Mayfrank et al, Progr Neuro-Psychopharm Biol Psych 2003

Funktionelle Kernspintomographie (fMRT)

Assoziatives Lernen / Reproduktion
(Kontrollen > Konsumenten)



2-tailed t-test (p=.001 (uncorr.) /.05 (corr. sphere,10mm; n=24)

Daumann et al, Psychopharmacology 2005

Kognitive Leistungen bei Ecstasy-Konsumenten

Intraindividuell im Längsschnitt

- *Zakzanis et al 2001:*

N = 15, follow-up 12 Monate

Fortführen des Konsums ⇒ ↓ Gedächtnis

- *Zakzanis et al 2006:*

Gleiche N = 15, follow-up weitere 24 Monate

Fortführen des Konsums (n=7) ⇒ ↓ Gedächtnis

Aufhören mit Konsum (n=8) ⇒ ↑ Gedächtnis

- *Gouzoulis-Mayfrank et al 2005:*

N = 38, follow-up 18 Monate

Fortführen (n = 16) oder Aufhören mit Konsum (n = 19):

keine Veränderung bei Gedächtnis, Arbeitsgedächtnis

- *Thomasius et al 2006:*

N = 11 Akt, N = 10 Ex, N = 11 Poly, N = Kontr, Baseline + 2 Follow-up in 2 J;

keine Veränderungen bei Gedächtnis

Erste prospektive Studie

NeXT (Netherlands XTC toxicity study)

N = 25 vor und nach 2 ± 1,4 Ecstasy-Pillen

► Arbeitsgedächtnis, Selektive Aufmerksamkeit, Assoziatives Gedächtnis

► kein Unterschied behavioral und bei neuralen Korrelaten (fMRT)

Jager et al Psychopharm 2007

N = 58 vor und nach 3,2 ± 5,2 Ecstasy-Pillen (Range: 0,5 – 30; Median: 1,5)

► Verbales Gedächtnis (Immediate, Delayed Recall, Rekognition), Visuelles Gedächtnis, Aufmerksamkeit, Arbeitsgedächtnis, Mentale Rotation

► diskret ↓ verbales Gedächtnis

Schilt et al 2007

Ecstasy: Die Frage der Neurotoxizität

Baseline: n = 149 mit bis zu 5 Erfahrungen mit MDMA oder speed (+Cannabis)

Follow-Up nach 12 und 24 Monaten

*Wagner et al. A prospective study of learning, memory, and executive function in **new MDMA users**, Addiction 2013*

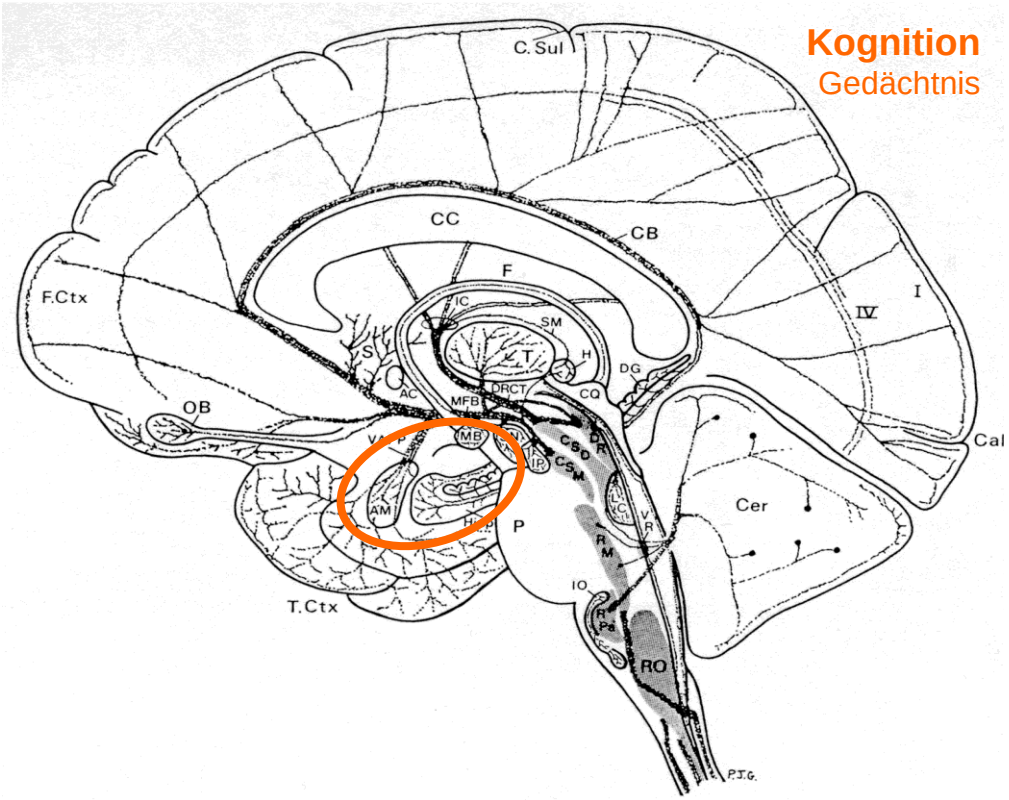
↓ Gedächtnis- u- Lernleistungen

*Kendrick et al. A prospective longitudinal study shows putamen volume is associated with moderate **amphetamine use** and resultant cognitive impairments, Psychoradiology 2021*

*Becker et al. Memory-related hippocampal functioning in **ecstasy and amphetamine users**: a prospective fMRI study, Psychopharmacology 2013*

*Koesters et al. Cortical thinning in **amphetamine-type stimulant users**, Neuroscience 2012*

Ecstasy: Die Frage der Neurotoxizität



Der Ecstasykonsum ist am deutlichsten mit kognitiven, insbes. relativen Gedächtnis- und Lernstörungen assoziiert.

► MDMA-bedingte neurotoxische Schäden am serotonergen System wahrscheinlich

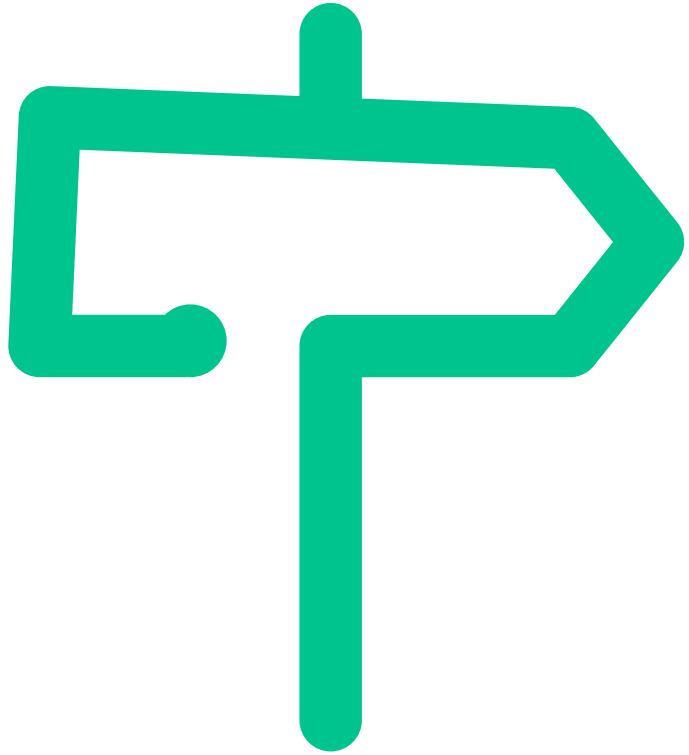
► stärkere Vulnerabilität des Hippokampus?

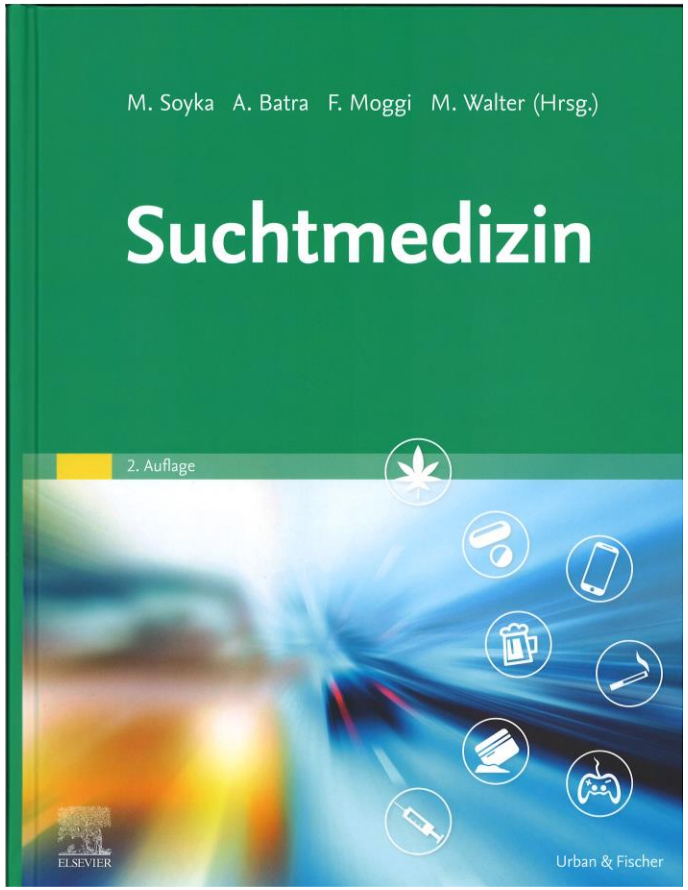
- Hippokampus weist höchste 5-HT-Depletionsraten nach MDMA auf
- Plastizität im Hippokampus am stärksten, Neurogenese noch im Erwachsenenalter
- Stimulation von 5-HT1A-Rezep-toren stimulieren Neurogenese im Hippokampus

Agenda

- Ecstasy – Was ist das? Erste Annäherungen
- Die Frage der Neurotoxizität
- **Ecstasy – Und immer noch die Frage: Was ist das?**

  ATS (Amphetamine type stimulant) oder psychedelic?
- Bedeutung heute





KAPITEL

14 Stimulanzien vom Amphetamin-Typ

Euphrosyne Gouzoulis-Mayfrank, Tomislav Majić, Michael Schaub

Reiff et al. Psychedelics and Psychedelic-Assisted Psychotherapy, Am J Psychiaty 2020

Objective: The authors provide an evidenced-based summary of the literature on the clinical application of psychedelic drugs in psychiatric disorders.

Methods: Searches of PubMed and PsycINFO via Ovid were conducted for articles in English, in peer-reviewed journals, reporting on "psilocybin," "lysergic acid diethylamide," "LSD," "ayahuasca," "*3,4*-methylenedioxymethamphetamine," and "MDMA," in human subjects. ….

Results: The most significant database exists for MDMA and psilocybin, which have been designated by the U.S. Food and Drug Administration (FDA) as "breakthrough therapies" for posttraumatic stress disorder (PTSD) and treatment-resistant depression, respectively…..

Conclusions: Randomized clinical trials support the efficacy of MDMA in the treatment of PTSD and psilocybin in the treatment of depression and cancer-related anxiety….

ICD-11

Kapitel 06 Psychische Störungen, Verhaltensstörungen oder neuromentale Entwicklungsstörungen

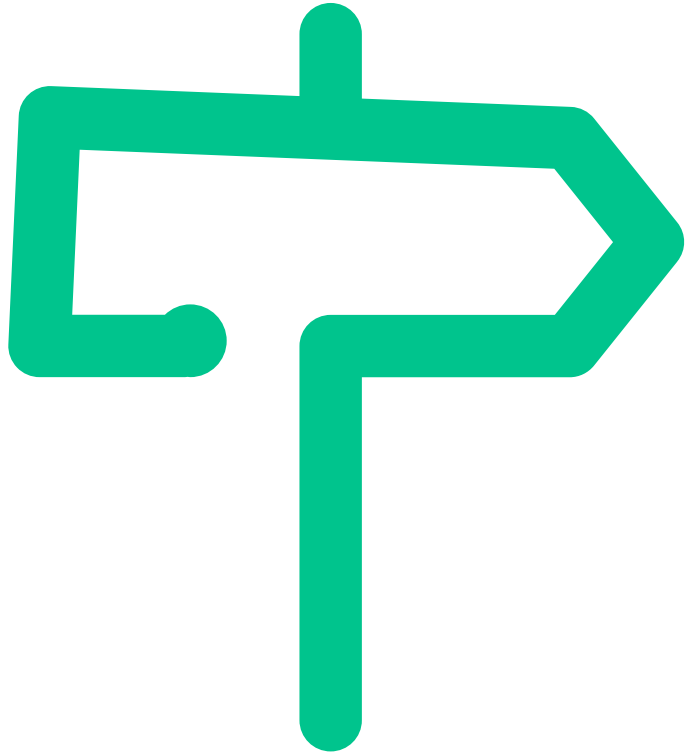
Störungen durch Substanzgebrauch

- **6C46** Störungen durch Stimulanzien, einschließlich Amphetamine, Methamphetamine oder Methcathinone
- **6C47** Störungen durch synthetische Cathinone
- **6C49** Störungen durch Halluzinogene
- **6C4C** Störungen durch MDMA oder verwandte Substanzen, einschl. MDA
- **6C4D** Störungen durch Dissoziativa, einschließlich Ketamin oder PCP [Phencyclidin]

Agenda

- Ecstasy – Was ist das? Erste Annäherungen
- Die Frage der Neurotoxizität
- Ecstasy – Und immer noch die Frage: Was ist das?

  ATS (Amphetamine type stimulant) oder psychedelic?
- **Bedeutung heute**



Prävalenz des Konsums von ATS bei Jugendlichen und Erwachsenen

Tab. 2: 12-Monats-Prävalenz des Konsums anderer illegaler Drogen als Cannabis in Deutschland

	DAS 2019 (12 bis 17 Jahre)			ESA 2021 (18 bis 64 Jahre)		
	Gesamt	Männlich	Weiblich	Gesamt	Männlich	Weiblich
Andere Drogen als Cannabis	1,1	1,1	1,0	3,6	4,4	2,9
Amphetamine	0,3	0,4	0,2	1,4	1,5	1,3
Methamphetamin	0,0	0,0	0,1	0,2	0,2	0,2
Ecstasy	0,5	0,4	0,5	1,0	1,4	0,7
LSD	0,2	0,2	0,1	0,6	0,8	0,4
Heroin/andere Opiate	0,0	0,1	0,0	0,5	0,6	0,5
Kokain/Crack	0,2	0,1	0,4	1,6	2,1	1,1
Schnüffelstoffe	0,1	0,1	0,0	0,3	0,4	0,2
Pilze	0,3	0,4	0,2	0,5	0,7	0,4
Neue psychoaktive Substanzen	0,1	0,1	0,1	1,3	1,5	1,2

ESA = Epidemiologischer Suchtsurvey. DAS = Drogenaffinitätsstudie

Quelle: Rauschert et al., 2022; Orth, Merkel, 2020

Konsum von ATS: Risikofaktor für spätere Psychose?

Article

Methamphetamine Use and Schizophrenia: A Population-Based Cohort Study in California

Russell C. Callaghan, Ph.D.
James K. Cunningham, Ph.D.
Peter Allebeck, M.D., Ph.D.
Tamara Arenovich, M.Sc.
Gautam Sajeev, M.Sc.
Gary Remington, M.D., Ph.D.
Isabelle Boileau, Ph.D.
Stephen J. Kish, Ph.D.

Objective: Clinical investigators in Japan have long suggested that exposure to methamphetamine might cause a persistent schizophrenia-like psychosis. This possibility is discounted in the Western literature. To investigate the relationship between drug use and later schizophrenia, the authors conducted a large-scale cohort study of drug users initially free of persistent psychosis.

Method: A population-based cohort study was conducted using data from California inpatient hospital discharge records from 1990 through 2000. Patients with methamphetamine-related conditions (N=42,412) and those with other drug use disorders (cannabis, cocaine, alcohol, and opioids) were propensity score-matched to individuals with primary appendicitis who served as a population proxy comparison group; the methamphetamine cohort was also matched to the other drug cohorts. Cox modeling was used to estimate differences between matched groups in the rates of subsequent admission with schizophrenia diagnoses.

Results: The methamphetamine cohort had a significantly higher risk of schizophrenia than the appendicitis group (hazard ratio=9.37) and the cocaine, opioid, and alcohol groups (hazard ratios ranging from 1.46 to 2.81), but not significantly different from that of the cannabis group. The risk of schizophrenia was higher in all drug cohorts than in the appendicitis group.

Conclusions: Study limitations include difficulty in confirming schizophrenia diagnoses independent of drug intoxication and the possibility of undetected schizophrenia predating drug exposure. The study's findings suggest that individuals with methamphetamine-related disorders have a higher risk of schizophrenia than those with other drug use disorders, with the exception of cannabis use disorders. The elevated risk in methamphetamine users may be explained by shared etiological mechanisms involved in the development of schizophrenia.

(Am J Psychiatry 2012; 169:389–396)

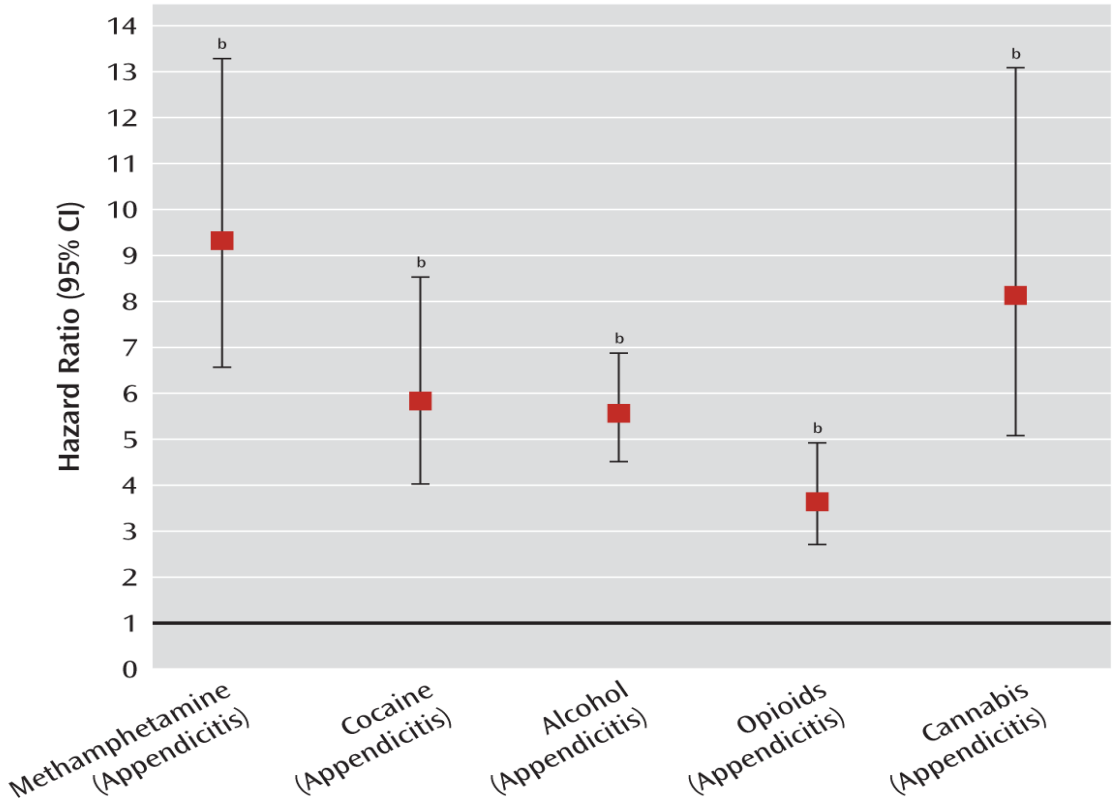


FIGURE 1. Risk of Schizophrenia in the Drug Cohorts Relative to the Population Proxy (Appendicitis) Comparison Group and in the Methamphetamine Cohort Relative to the Drug Cohort Comparison Groups[a]

[a] Reference group in parentheses.

[b] Statistically significant difference, $p<0.005$.

Konsum von ATS: Risikofaktor für spätere Psychose?

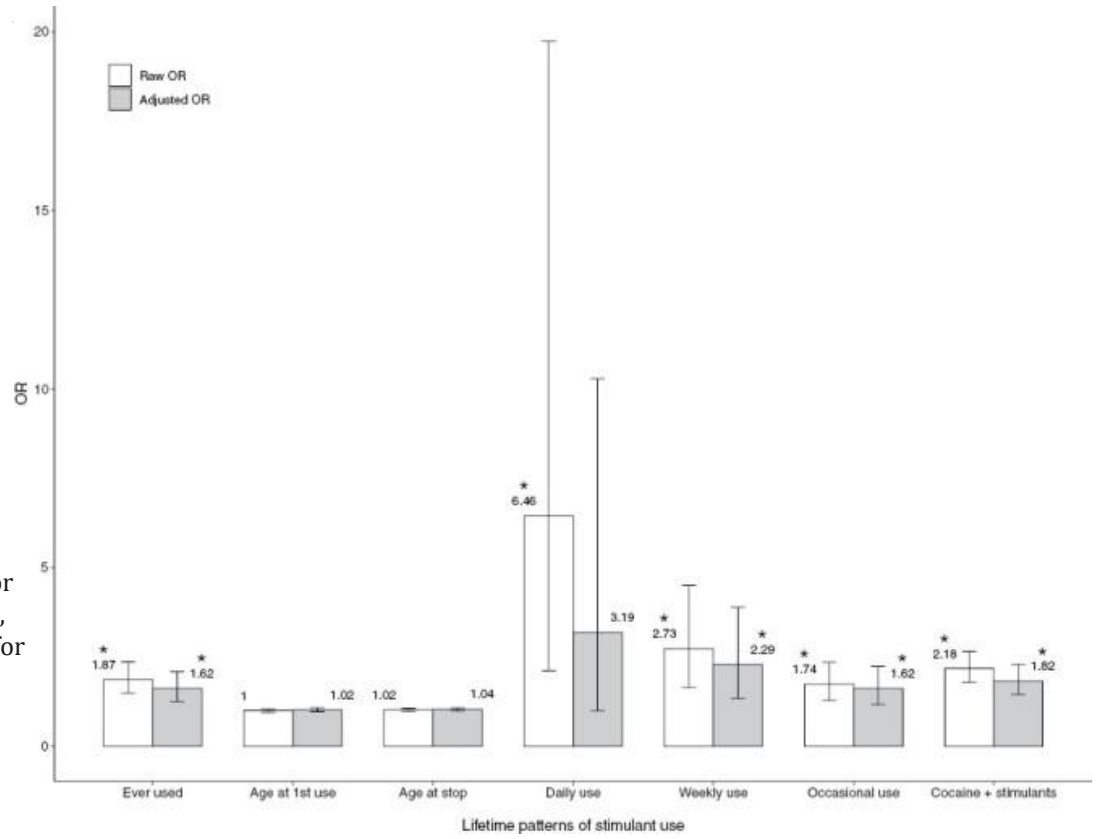
Schizophrenia Bulletin vol. 49 no. 5 pp. 1269–1280, 2023
https://doi.org/10.1093/schbul/sbad013
Advance Access publication July 19, 2023

Differences in Patterns of Stimulant Use and Their Impact on First-Episode Psychosis Incidence: An Analysis of the EUGEI Study

Elisa Rodríguez-Toscano[*,1,2,3,35,✉], Clara Alloza[3,4,35], David Fraguas[1,3,4], Manuel Durán-Cutilla[3], Laura Roldán[2], Teresa Sánchez-Gutiérrez[5,✉], Gonzalo López-Montoya[3,5], Mara Parellada[3,4], Carmen Moreno[3,4], Charlotte Gayer-Anderson[6,✉], Hannah E. Jongsma[7,8], Marta Di Forti[9], Diego Quattrone[9], Eva Velthorst[10,11,12], Lieuwe de Haan[12], Jean-Paul Selten[13,14], Andrei Szöke[15,16,17], Pierre-Michel Llorca[18], Andrea Tortelli[19], Julio Bobes[20], Miguel Bernardo[21,✉], Julio Sanjuán[22], José Luis Santos[23], Manuel Arrojo[24], Ilaria Tarricone[25], Domenico Berardi[26], Mirella Ruggeri[27], Antonio Lasalvia[27,28,✉], Laura Ferraro[29,✉], Caterina La Cascia[29], Daniele La Barbera[29], Paulo Rossi Menezes[30], Cristina Marta Del-Ben[31], EU-GEI WP2 Group, Bart P. Rutten[14], Jim van Os[14,32,33], Peter B. Jones[8,34,✉], Robin M. Murray[33], James B. Kirkbride[7,✉], Craig Morgan[6], Covadonga M. Díaz-Caneja[3,4,36,✉], and Celso Arango[3,4,36]

n = 1130 FEP,
attending psychiatric services at 17 sites
across 5 European countries and Brazil

n = 1497 controls



Raw and fully adjusted ORs of first-episode psychosis for lifetime patterns of stimulant use and the combined measure of cocaine and/or stimulant use for the whole sample. Raw ORs are adjusted for age, sex, and ethnicity, whereas fully adjusted ORs were additionally adjusted for recent and lifetime cannabis use and education level. Error bars represent 95% of CIs. The reference group for both raw and fully adjusted ORs is abstainers (recent or lifetime, accordingly). Asterisks represent significant ORs ($P < .05$). CI, confidence interval; OR, odds ratio.

Vielen Dank für Ihre Aufmerksamkeit!

Ecstasy-Studien mit Spätadoleszenten in den 1990er Jahren: Welche Zukunft haben die Stimulanzien bei Jugendlichen?

Prof. Dr. Euphrosyne Gouzoulis-Mayfrank

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Symposium des DZSKJ
Suchtforschung und -therapie für Kinder und Jugendliche
14.05.2025, UKE Hamburg