

vitos: 25 Jahre nach Millennium: Aktuelle Schlaglichter aus den (Neuro)wissenschaften

Seite 1 Vitos-Management

Universitätsklinikum Hamburg-Eppendorf

Ein Unternehmen des DLR Konzerns

Antidepressant effects of selective serotonin reuptake inhibitors (SSRIs) are attenuated by antiinflammatory drugs in mice and humans

PMID | May 26, 2011 | vol 114 | no 22 | 484

Jennifer L. Warner-Schmidt¹, Kimberly E. Vanover², Emily Y. Chen³, John J. Marshall³, and Paul Greengard¹

A Test Reactivity Test Reactivity (% control) vs VEH, CIT, FLX, IM, DM, TCP, BUP. Legend: vehicle (white), ibuprofen (black).

B Frontal Cortex Test Reactivity (% control) vs VEH, CIT, FLX, IM, DM, TCP, BUP. Legend: vehicle (white), ibuprofen (black).

Antidepressant drugs act by directly binding to TRKB neurotrophin receptors Casarotto et al., 2021, *Cell* 184, 1299-1313

BDNF-TRKB signaling, TrkB being the receptor of BDNF, is involved in transcription, translation, and trafficking of proteins in the various stages of synaptic development and in synaptic plasticity.

4. Antidepressants increase TRKB on the cell surface
5. Antidepressants facilitate TRKB signaling in active synapses

Spine: Dendrite, Plasticity, Retraction
 Signaling: NO SIGNALING, signaling, NO ACTIVITY, ACTIVITY

Neuroanatomische Veränderungen im Verlauf einer menschlichen Schwangerschaft

Pritschel T, Taylor CM, et al. Nat Neurosci. 2024 Nov;2 (in press)

Whole-brain subcortical volumes: Lateral ventricle, Caudate, Thalamus, Brain stem, Putamen, Hippocampus, Ventral DC.

Summary white matter tracts Gestation: Avg. WMV (mm³)

Das Bewusstsein erwacht

(A) Infant EEG **(B) Fetal MEG**
(C) Infant fNIRS **(D) Infant fMRI**

The case for early emergence

Late gestation Birth Early infancy Late infancy to toddlerhood

Functional connectivity networks with long-range connections (100-200) (blue)
 Attention-recruiting frontal brain networks (200-300) (green)
 Multisensory integration (McGurk effect) (300-400) (red)

fMRI: the neural network (spatial activation) needs a functional component (blue)

Science | Copyright Science, December 2013, Vol. 322, No. 12 | 1141

Das Gedächtnis erwacht

Yates et al., Science 367, 1316-1320 (2022)

THE FADING MEMORIES OF YOUTH

The mystery of "infantile amnesia" suggests memory works differently in the developing brain.

A Example segmentation (18.8-month-old) showing Whole hippocampus (x=22), Anterior hippocampus (y=23), Posterior hippocampus (y=30).

B Graph of Whole hippocampus vs Age (months) showing a positive correlation.

C Graph of Anterior hippocampus and Posterior hippocampus vs Age (months) showing different developmental trajectories.

Rückblick: 25 Jahre

Umwelt, Ernährung und Klima als Fokus-Thema

Künstliche Intelligenz in der Medizin

Genomik, Epigenetik und transgenerationale Vererbung

Immuntherapien gegen Krebs

CRISPR-Cas9: Revolution in der Gentechnik

Schlaf-Wach-Medizin und zelluläre Rhythmen

Fortschritte in der Einzelzell-Analyse z.B. mit Optogenetik

Mikroplastik und seine Auswirkungen auf die Gesundheit

mRNA-Impfstoffe und Post-COVID

Neue Medikamente durch KI

Mikrobiom



GWAS im Jahr 2025

> 5,700 GWAS for > 3,300 traits

Many complex traits highly heritable, GWAS detected many genetic variants, but only fraction of genetic variance (<5%) - effects are small, large samples needed

Current sample sizes typically 100,000's, but even > 1 million is not uncommon!



Genome-wide analysis of insomnia in 1,331,010 individuals identifies new risk loci and functional pathways

Philip B. Jones^{1,2}, Kenta Watanabe^{1,2}, Sven Dörringer^{1,2}, Nathan Stransky^{1,2}, Julia Brysler^{1,2}, Anshu K. Srivastava^{1,2}, Christian A. Lottstein^{1,2}, James E. Bumpstead^{1,2}, Anshu K. Srivastava^{1,2}, Muthu Raju^{1,2}, James E. Bumpstead^{1,2}, Haniyeh Tavakoli^{1,2}, Terry Walsh^{1,2}, The DREAM Consortium^{1,2}, Jason T. Wang^{1,2}, David A. Hinds^{1,2}, Vladimir Vukobratovic^{1,2}, David M. Altshuler^{1,2}, Sophie van der Sluis^{1,2}, Tracy L.C. Walhovd^{1,2}, Augustin B. Soria^{1,2}, David G. Lachy^{1,2}, Amy L. Van Someren^{1,2} and David M. Forster^{1,2}



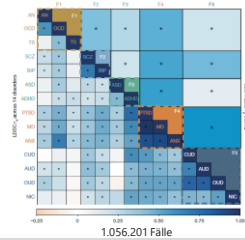
Multivariate analysis of 1.5 million people identifies genetic associations with traits related to self-regulation and addiction

Richard Karlsson-Lind¹, Tessa T. Maloney¹, Alex B. Barr¹, Sandra Sanchez-Rudez¹, James W. Mackillop¹, Morgan R. D'Esposito¹, Andy R. Green¹, Rosalind W. Young¹, Andrew D. Grotzer¹, John J. Treisman¹, James C. Svejnar¹, Margaret C. L. Saxe-Braunstein¹, Troy Skidmore¹, Hong D. Kim¹, Richard C. Anderson¹, Jeffrey A. Pankratz¹, Laura A. Harwood¹, Daping L. Liu¹, Scott Vitousek¹, ODSU Collaborators¹, Henry R. Kranzler¹, Joel Gruber¹, Kathleen Mullan-Bailey¹, Blake A. Bauer-Dronatzki¹, Paul D. Walshaw¹, Andrew A. Kuper¹, A. Pepp Harwood¹, Philipp D. Knaflitzsch¹ and Benjamin M. D'Esposito¹

Davidson Posthumus (ECNP 2025)

Kartierung der Genetik über psychiatrische Störungen

Grotzinger AD, Worme J, et al. Nature. 2025 Dec 10. doi: 10.1038/s41586-025-09820-3.



Schizophrenie und bipolare Störungen (SB-Faktor)

Exzitatorische Neuronen

Autismus-Spektrum und ADHD

Major Depression, PTBS und Angst (Internalizing Factor)

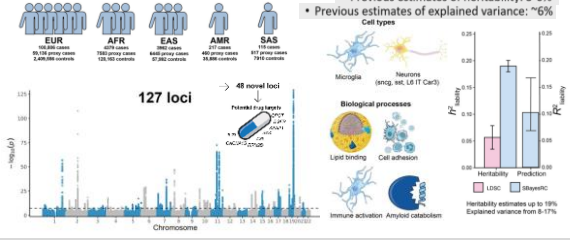
Oligodendrozyten

Hohe polygene Überschneidungen und sehr wenige störungsspezifische Loci.

Diese Beobachtungen könnten eine neurobiologisch valide psychiatrische Nosologie beeinflussen und Ziele für die therapeutische Entwicklung identifizieren.

PGC-Alzheimer im Jahr 2025

Ulfmann E, Wightman DP, et al. medRxiv [Preprint]. 2025 Oct 13:2025.10.10.25337470.



Previous estimates of heritability: 3-6%

Previous estimates of explained variance: ~6%

Cell types

Biological processes

Heritability Prediction

Heritability estimates up to 19%

Explained variance from 6-17%

Article

Rare coding variants in ten genes confer substantial risk for schizophrenia

Nature | Vol 624 | 21 April 2022 |

https://doi.org/10.1038/s41586-022-04866-w Rare coding variation has historically provided the most direct connections between

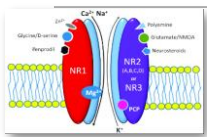
Received: 13 Aug

Accepted: 18 Feb

Published online: 21 Apr

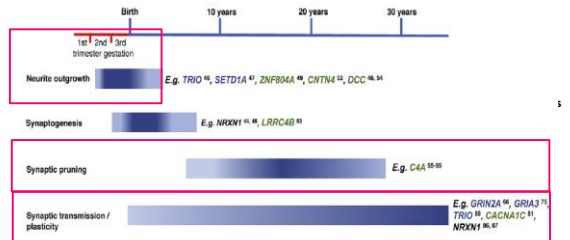
Check for updates

Mapping genomic loci implicates genes and synaptic biology in schizophrenia



Schizophrenia has a heritability of 60–80%, much of which is attributable to common risk alleles. Here, in a two-stage genome-wide association study of up to 76,725 individuals with schizophrenia and 243,649 control individuals, we report common variant associations at 287 distinct genomic loci. Associations were concentrated in genes that are expressed in excitatory and inhibitory neurons of the central nervous system, but not in other tissues or cell types. Using fine-mapping and functional genomic data, we identify 120 genes (106 protein-coding) that are likely to underpin associations at some of these loci, including ten genes with credible causal non-synonymous or untranslated region variation. We also implicate fundamental processes related to neuronal function, including synaptic organization, differentiation and transmission. Fine-mapped candidates were enriched for genes associated with synaptic transmission and synaptic plasticity, including the subunit *GRIN2A* and transcription factor *SP4*.

Schädigende Wirkung von GRIN2A- und anderen Varianten



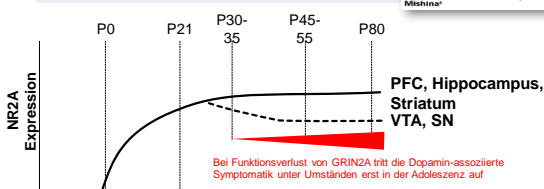
Hall J et al. Biological Psychiatry 2022;91(8):709-717

12

"Normale" Dynamik der GluN2A-Expression in Abhängigkeit vom Alter

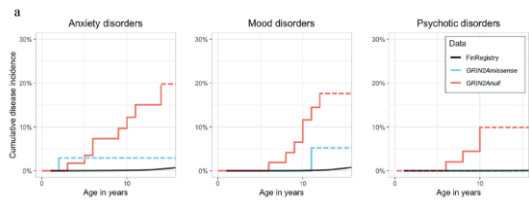
NeuronApopt 3, 1139-1146 (1994)
Developmental changes in distribution of NMDA receptor channel subunit mRNAs
 Masahiko Watanabe, Yashiro Inoue, Kenji Sakimura* and Masayoshi Mishina*

Postnataler Entwicklungsverlauf (Nagermodell)



GRIN2A null variants confer a high risk for early-onset schizophrenia and other mental disorders and potentially enable precision therapy

Molecular Psychiatry (2020) 31:374–382, <https://doi.org/10.1038/s41380-020-03279-4>



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Sichelzellerkrankheit

Thien & Howard, Blood 2018; 132 (17): 1750–1760

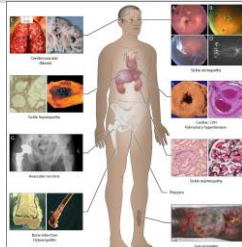
November 14, 1996, Vol. 128

SCIENCE

Sickle Cell Anemia, a Molecular Disease*

Lissa Pauling, Harry A. Boncz, J. S. Singer* and Ben C. Wick*

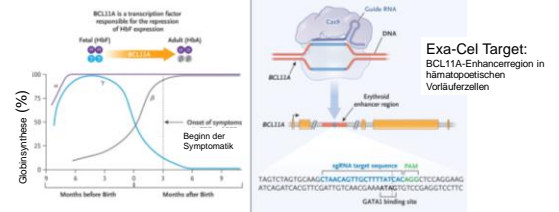
Gene and Cells (California Institute of Technology, California Institute of Technology, Pasadena, California)



Thien & Howard, Blood 2018; 132 (17): 1750–1760

Wirkmechanismus von Exa-Cel

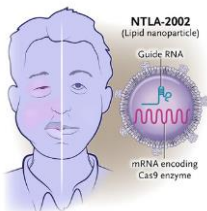
Frangoul H et al. N Engl J Med 2021;384:252-260



Exaganglogene autotzell (exa-cel) ist eine autologe Blutzustanzelltherapie mit eingeschleuster CRISPR-Cas9-Gensche

Hereditäres Angioödem

Cohn DM, et al. N Engl J Med. 2025 Jan 30;392(5):458-467.



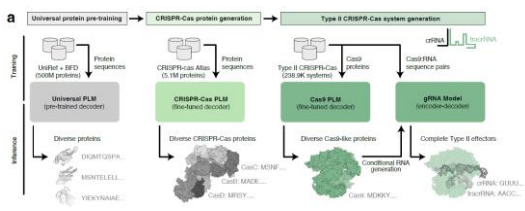
Current preventive treatments for hereditary angioedema must be used regularly. NTLA-2002 is a novel gene editing therapy based on CRISPR-Cas9 (i.e., clustered regularly interspaced short palindromic repeats [CRISPR]-CRISPR-associated protein 9). NTLA-2002 is designed to permanently disable the gene encoding kallikrein B1, a protease that is elevated in hereditary angioedema and leads to swelling.

RESULTS
 During follow-up, the estimated mean monthly angioedema attack rate was lower in both the 25-mg and the 50-mg NTLA-2002 groups than in the placebo group.
 The most common adverse events in the two active-treatment groups were headache, fatigue, and nasopharyngitis.



Weiterentwicklung von CRISPR-Geneditoren mit KI

Ruffolo, JA et al. bioRxiv preprint doi: <https://doi.org/10.1101/2024.04.22.590591> 2025



Dieser innovative Ansatz hat OpenCRISPR-1 hervorgebracht, den ersten KI-generierten Geneditor.

Optogenetik

Raster
Ort

In a roaming rat, individual grid cells fire at regularly spaced intervals (top), forming a navigational grid-place cells fire whenever an animal enters a specific spot in the environment (bottom).

NOBEL PRIZES
Brain's GPS finds top honor
"Place" and "grid" cells help explain how we navigate

RESEARCH | [sciencemag.org](https://www.sciencemag.org) | 10 OCTOBER 2014 • VOL 348 | 1331-1338

Sustained rescue of prefrontal circuit dysfunction by antidepressant-induced spine formation

Optogenetik

B Timecourse of changes: Effects on circuit function and behavior precede spine formation

C Last spine (red) / Formed spine (blue) | Optogenetic deletion of newly formed spines

Chronic COBT 10 days → Ketamine → blue light → 1d post-Rx → Deletion of newly formed spines → Disrupted maintenance of antidepressant effects on circuit function and motivated escape behavior

Mulla-Saqa et al., *Science* 2014, 344:1028-1031 | 12 April 2019

Weiterentwicklung zu LICONN

Tavakoli MR, et al. *Nature*. 2025 Jun;642(8067):398-410.

Es wurden speziell entwickelte Hydrogel-Einbettung und -Expansion mit umfassender Deep-Learning-basierter Segmentierung und Analyse der Konnektivität integriert.

EM | **LICONN**

LICONN: Lichtmikroskopie-basierte rekonstruktive Kartierung des Säugetierhirngewebes

FlyWire Brain: Konnektom der Drosophila – Brain Prize 2024

Shinomiya K, Takemura SY, et al. *Front Neural Circuits*. 2015 Jul 9;3:33.

fly - Drosophila

166,000 neurons
12,000 cell types
172 million synapses

Schoffer et al. (2020) | Denkiewicz et al. (2024) | FlyEM Project Team (2025)

FlyWire Brain

<https://www.nature.com/immersive/d42859-024-00053-4/index.html>

Serotonerge Modulation des Schluckens in einem vollständigen Vagusnerv-Konnektom der Fliegen

Schoofs A, Miroshnikow A, et al. *Curr Biol*. 2024 Oct 7;34(19):4495-4512.

Using a whole-animal serial transmission electron microscopy dataset, Schoofs et al. provide a complete reconstruction of a sensorimotor circuit underlying the *Drosophila* swallowing system. Through the vagus nerve, serotonergic neurons rate food based on mechanosensory and chemosensory information and modulate esophageal peristalsis.

Whole animal STEM | **Feeding system**

Enteric connectome: Food value signals → CNS → Convergent integration → Enteric 5-HT release → 5-HT output → Motor output (Swallowing) → Enteric sensory neurons

Enteric motor neurons | **Enteric sensory neurons**

Navigation: Wie das Insektenhirn den Raum erfasst

Webb B. *Trends Cogn Sci*. 2025 Dec;29(12):1077-1079.

Central complex (green) | Time-computed Sun compass | Transitional cells flow | Hock | Hock | Hock

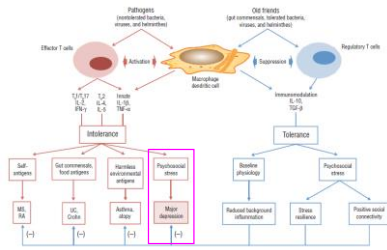
Pre-motoric bridge | Mushroom body | Hypothetical integrative memory-goal | Shift left and compare heading | Difference controls steering output

odour | heading | goal

Trends Cognitive Sciences

Gute Hinweise: Mikrobiom spielte eine kritische Rolle bei der Pathophysiologie auch von depressiven Störungen

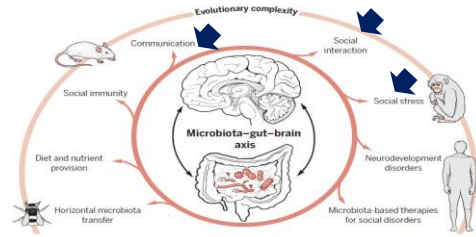
Raison CL, Lowry CA, Rook GA. Arch Gen Psychiatry. 2010; 67(12):1211-24.



Soziale Interaktion, Resilienz, Immunsystem, Darm und das Gehirn

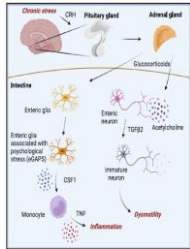
Sherwin E, Bordenstein SR, et. al Science. 2019 Nov 1;366(6465)

...sind archaisch verbunden



Das enterische Nervensystem leitet psychischen (sozialen) Stress an den Darm weiter

Schneider KM, Blank N, et. al. Cell. 2023 Jun 22;186(13):2823-2838.e20.

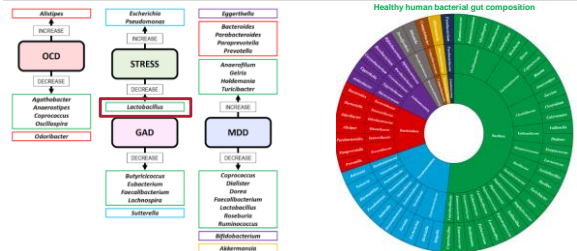


Psychological stress and chronically elevated glucocorticoid levels induce inflammatory enteric glia and transcriptional immaturity in enteric neurons, leading to dysmotility and predisposing the intestine to monocyte-mediated inflammation.

Stress provokes transcriptional immaturity in enteric neurons and dysmotility

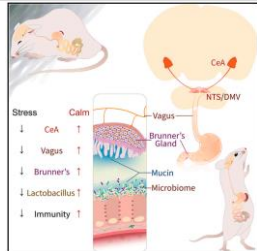
Stress, Mikrobiom und psychische Störung

Borrego-Ruiz A, Borrego JJ. Prog Neuropsychopharmacol Biol Psychiatry. 2024 Jan 10;128:110861



Stress-sensitive Gehirn-Vagus-Verbindung verändert Mikrobiome über duodenale Brunner-Drüsen

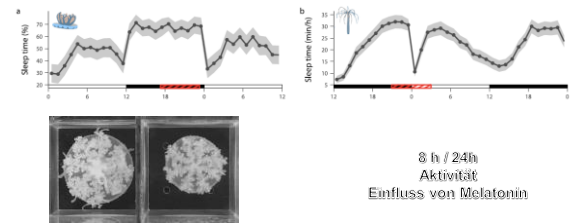
Chang H, et. al. Cell 2024 Sep 19;187(19):5393-5412.e30.



Secretions from the duodenal glands of Brunner enhance host defense by promoting gastrointestinal Lactobacilli proliferation. Chronic stress inhibited a brain-vagus nerve circuit that stimulates glandular secretion, thereby suppressing Lactobacillus populations and systemic immunity.

DNA damage modulates sleep drive in basal cnidarians with divergent chronotypes

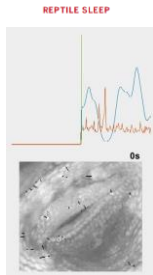
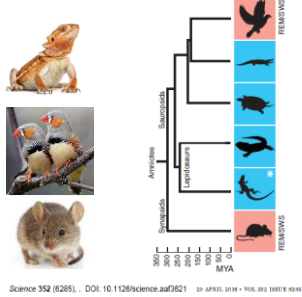
Nature Communications | 2026973



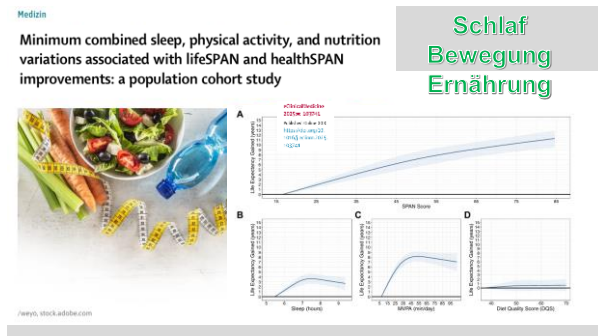
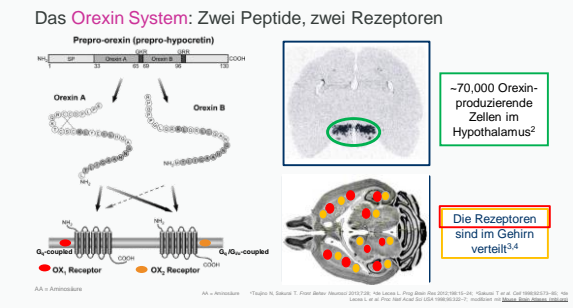
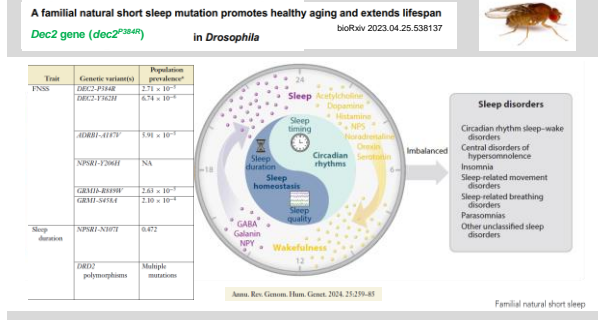
Qualle und Anemone

8 h / 24h
Aktivität
Einfluss von Melatonin

Suche nach Prinzipien des Lebens



Slow waves, sharp waves, ripples, and REM in sleeping dragons



Vor der Tür stehen in der Psychiatrie und Psychotherapie:

- KI für Diagnostik und Prognose (Expertensysteme)
- KI-gestützte Therapie-Tools
- Chatbots und virtuelle Therapeut:innen
- Voice- und Biomarker-basierte Systeme
- KI-gestützte Arzneistoffproduktion
- Service – HR – Controlling – Recalls – Onboarding...

Automatisierung mit KI im Gesundheitswesen

PSYCHOTHERAPIE MIT KI

Trügerische Seelenröster im Netz

Von Marlene Heckl
04.04.2025, 07:34 | 15:00:00 | 5 Min.

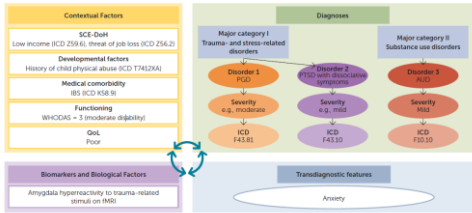
NEJM AI 2025 (4)
DOI: 10.1056/ai.2025.00002

ORIGINAL ARTICLE

Randomized Trial of a Generative AI Chatbot for Mental Health Treatment

CONCLUSIONS This is the first RCT demonstrating the effectiveness of a fully Gen-AI therapy chatbot for treating clinical-level mental health symptoms. The results were promising for MDD, GAD, and CHR-FED symptoms.

Vor der Tür stehen in der Psychiatrie und Psychotherapie:
Veränderung der Zukunft DSM



¹ AUD, alcohol use disorder; IBS, irritable bowel syndrome; PTSD, prolonged grief disorder; PTSD, posttraumatic stress disorder; QoL, quality of life; SCE-Draft, socioeconomic, cultural, and environmental determinants of health; WHODAS, World Health Organization Disability Assessment Schedule. *Am J Psychiatry* XXX:XX, XX, 2026

2026

PSYCHIATRIEUPDATE



16. Psychiatrie-Update-Seminar

27. und 28. Februar, Mainz | Livestream
06. und 07. März, Berlin | Livestream

Wissenschaftliche Leitung

Dieter F. Braus, Elvile
Katharina Domschke, Freiburg
Andreas Heinz, Berlin
Sabine Herpertz, Heidelberg



Psychiatrie LIVE



<https://streamed-up.com/>

doctopus TUTORIALS PSYCHIATRIE Therapie der Depression

Depression Zertifiziert und kostenfrei

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 2. Therapie der Depression
 3. Prävalenzen bei Depression
 4. Digitale Selbsthilfeschulungen (DSAS) als Beispiel für digitale Medizin

www.steamed.up.com