vitos:

25 Jahre nach Millennium:

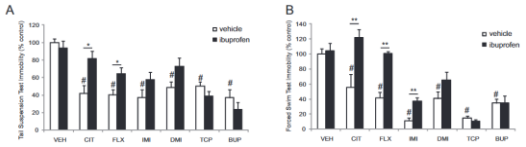
Aktuelle Shlaglichter aus den (Neuro)wissenschaften

Universitätsklinikum Hamburg-Eppendorf

Ein Unternehmen des UKE-Konzern

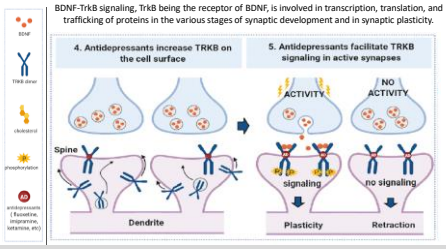
Antidepressant effects of selective serotonin reuptake inhibitors (SSRIs) are attenuated by antiinflammatory drugs in mice and humans

Jennifer L. Warner-Schmidt[a,1], Kimberly E. Vanover[b], Emily Y. Chen[a], John J. Marshall[a], and Paul Greengard[a,1]



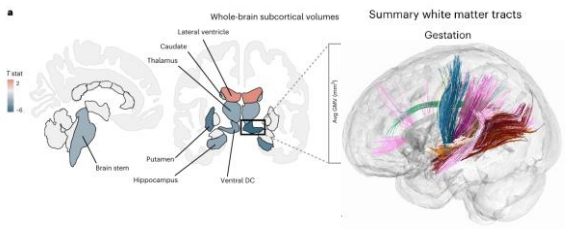
Antidepressant drugs act by directly binding to TRKB neurotrophin receptors

Casarotto et al., 2021, Cell *184*, 1299–1313

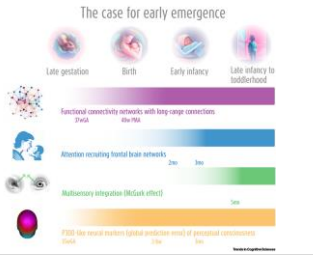


Neuroanatomische Veränderungen im Verlauf einer menschlichen Schwangerschaft

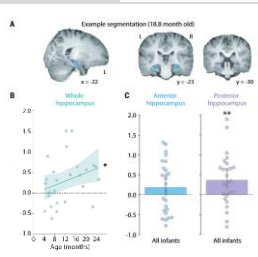
Pritschet L, Taylor CM, et. al. Nat Neurosci. 2024 Nov;2 (in press)



Das Bewusstsein erwacht



Das Gedächtnis erwacht



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

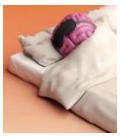
Fortschritte in der Einzelzell-Analyse z.B. mit Optogenetik

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!

ARTICLES — nature genetics

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

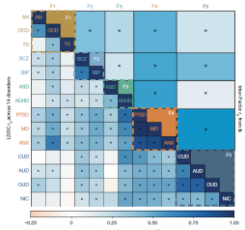
nature neuroscience — ARTICLES

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

Danielle Posthuma (ECNP 2025)

Kartierung der Genetik über psychiatrische Störungen

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



1.056.201 Fälle

Schizophrenie und bipolare Störungen (SB-Faktor)

Exzitatorische Neuronen

Autismus-Spektrum und ADHD

Major Depression, PTBS und Angst (Internalizing Factor)

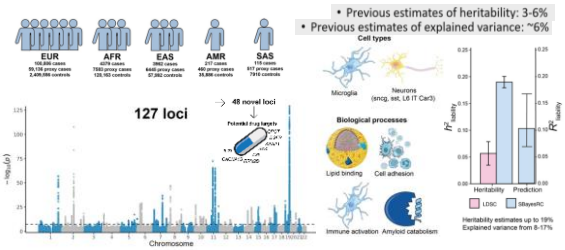
Oligodentrozyten

Hohe polygene Überschneidungen und sehr wenige störungsspezifische Loci.

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

PGC-Alzheimer im Jahr 2025

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



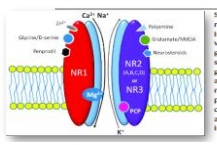
Article

Rare coding variants in ten genes confer substantial risk for schizophrenia

Nature | Vol 604 | 21 April 2022 |

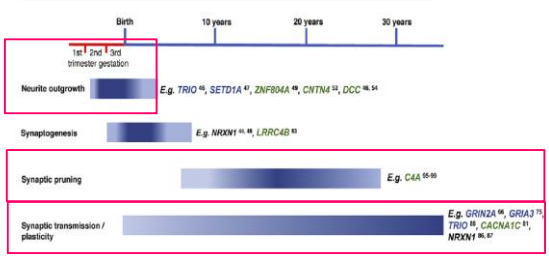
Article

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 76,755 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 16 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 [illegible] including the subunit *GRIN2A* and transcription factor *SP4*,

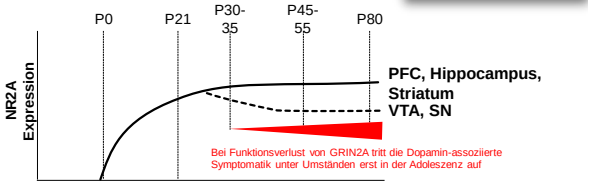
Schädigende Wirkung von GRIN2A-und anderen Varianten



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

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

Postnataler Entwicklungsverlauf (Nagermodell)

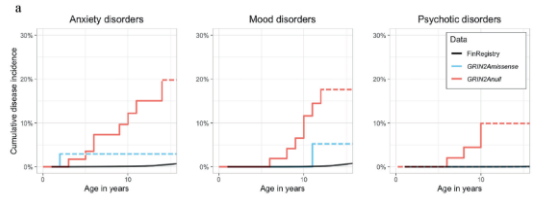


Bei Funktionsverlust von GRIN2A tritt die Dopamin-assoziierte Symptomatik unter Umständen erst in der Adoleszenz auf

13

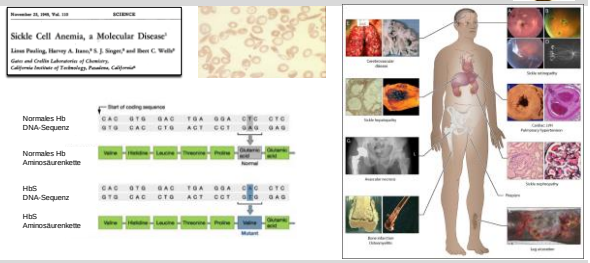
GRIN2A null variants confer a high risk for early-onset schizophrenia and other mental disorders and potentially enable precision therapy

Molecular Psychiatry (2026) 31:374–382; https://doi.org/10.1038/s41380-025-03279-4



Sichelzellkrankheit

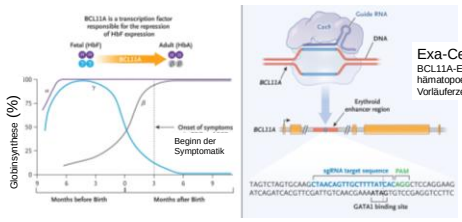
Thein & Howard, Blood 2018; 132 (17): 1750–1760



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

Wirkmechanismus von Exa-Cel

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

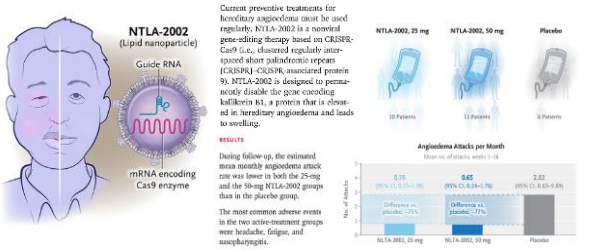


Exa-Cel Target:
BCL11A-Enhancerregion in hämatopoetischen Vorläuferzellen

Exagamglogene autotelcel (exa-cel) ist eine autologe Blutstammzelltherapie mit eingeschleuster CRISPR-Cas9-Genschere

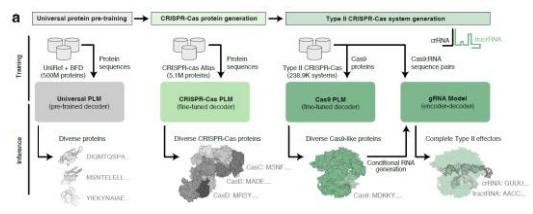
Hereditäres Angioödem

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



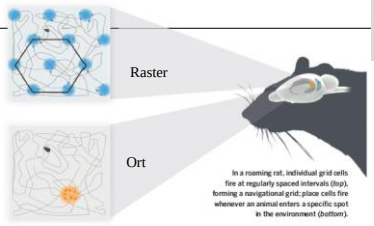
Weiterentwicklung von CRISPR-Geneditoren mit KI

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



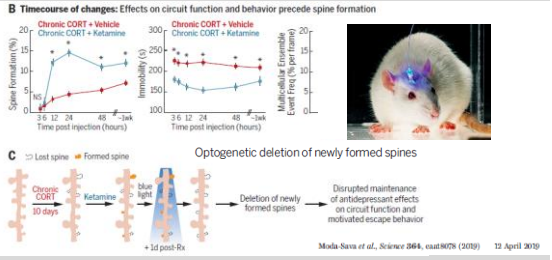
NOBEL PRIZES

Brain's GPS finds top honor

"Place" and "grid" cells help explain how we navigate

Optogenetik

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



Moda-Sava *et al., Science* **364**, eaat8078 (2019) 12 April 2019

Weiterentwicklung zu LICONN

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

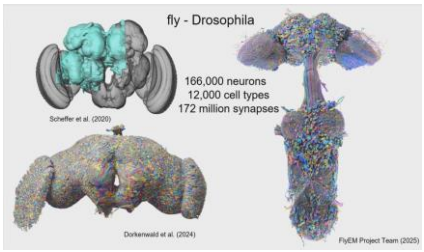
Es wurden speziell entwickelte Hydrogel-Einbettung und -Expansion mit umfassender

Deep-Learning-basierter Segmentierung und Analyse der Konnektivität integriert.

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;9:33.



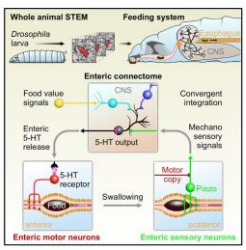
FlyWire Brain

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

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

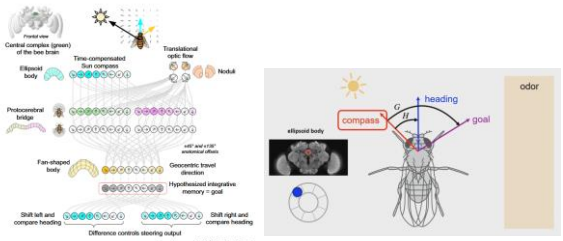
Schoofs A, Miroschnikow A, et. al.Curr Biol. 2024 Oct 7;34(19):4495-4512.

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.



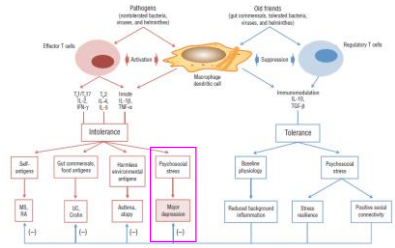
Navigation: Wie das Insektenhirn den Raum erfasst

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



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

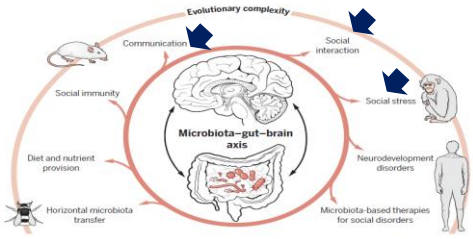
Raison CL, Lowry CA, Rook GA. Arch Gen Psychiatry. 2010; 67(12):1211-24.



Soziale Interaktion, Resilienz, Immunsystem, Darm und das Gehirn

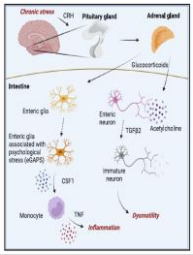
Sherwin E, Bordenstein SR, et. al Science. 2019 Nov 1;366(6465)

...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.

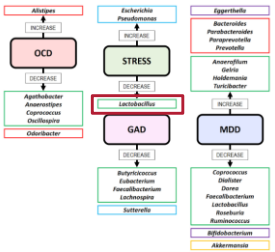


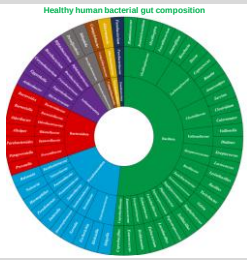
Psychological stress and chronically elevated glucocorticoid levels induce inflammatory enteric glia and transcriptional immaturity in enteric neurons, leading to dysmotility and predisposing the intestine to monocyte-mediated inflammation.

Stress provokes transcriptional immaturity in enteric neurons and dysmotility

Stress, Mikrobiom und psychische Störung

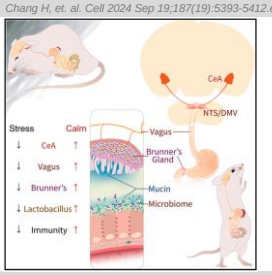
Borrego-Ruiz A, Borrego JJ. Prog Neuropsychopharmacol Biol Psychiatry. 2024 Jan 10;128:110861





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

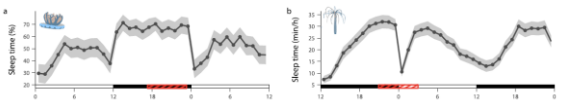
Chang H, et. al. Cell 2024 Sep 19;187(19):5393-5412.e30.

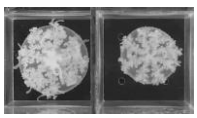


Secretions from the duodenal glands of Brunner enhance host defense by promoting gastrointestinal *Lactobacilli* proliferation. Chronic stress inhibited a brain-vagus nerve circuit that stimulates glandular secretion, thereby suppressing *Lactobacillus* populations and systemic immunity.

DNA damage modulates sleep drive in basal cnidarians with divergent chronotypes

Nature Communications | (2026)17:3

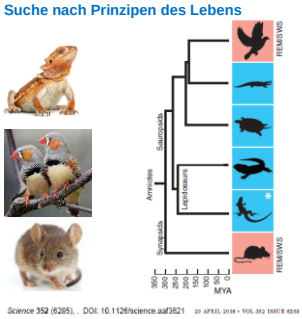


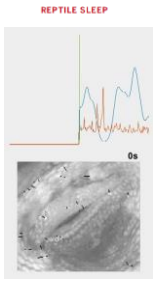


Qualle und Anemone

8 h / 24h
Aktivität
Einfluss von Melatonin

Suche nach Prinzipen des Lebens





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

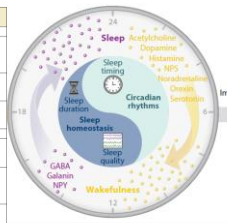
Science 352 (6285), . DOI: 10.1126/science.aaf3621 20 APRIL 2016 • VOL 352 ISSUE 6285

A familial natural short sleep mutation promotes healthy aging and extends lifespan

Dec2 gene (*dec2*^{P384R}) in *Drosophila*

bioRxiv 2023.04.25.538137

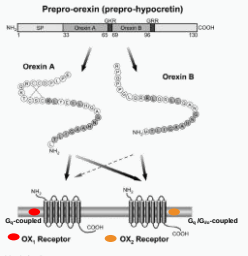
Trait	Genetic variant(s)	Population prevalence[a]
FNSS	*DEC2-P384R*	2.71×10^{-5}
	DEC2-Y362H	6.74×10^{-6}
	ADRB1-A187V	5.91×10^{-5}
	NPSR1-Y206H	NA
	GRM3A-R889W	2.63×10^{-5}
	GRM3-S458A	2.10×10^{-4}
Sleep duration	*NPSR1-N107I*	0.472
	DRD2 polymorphisms	Multiple mutations

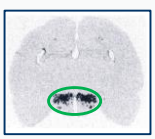


Annu. Rev. Genom. Hum. Genet. 2024. 25:259–85

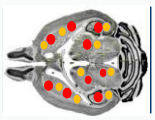
Familial natural short sleep

Das Orexin System: Zwei Peptide, zwei Rezeptoren





~70,000 Orexin-produzierende Zellen im Hypothalamus[2]

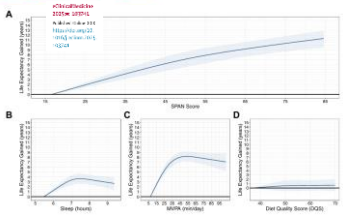


Die Rezeptoren sind im Gehirn verteilt[3,4]

Medizin

Minimum combined sleep, physical activity, and nutrition variations associated with lifeSPAN and healthSPAN improvements: a population cohort study

Schlaf
Bewegung
Ernährung



/weyo, stock.adobe.com

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…**

PSYCHOTHERAPIE MIT KI

Trügerische Seelentröster im Netz

Von Marlene Heckl

04.04.2025, 07:14 Lesezeit: 8 Min.

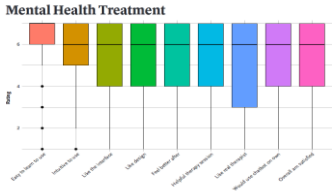
Wenn die Seele krankt und der Frust steigt, steht heute psychologische Unterstützung durch Chatbots bereit. Was die KI-Helfer können und warum der Mensch unersetzlich bleibt: Eine Recherche im therapeutischen Neuland.

NEJM AI

NEJM AI 2025;2(4)
DOI: 10.1056/AIoa2400802

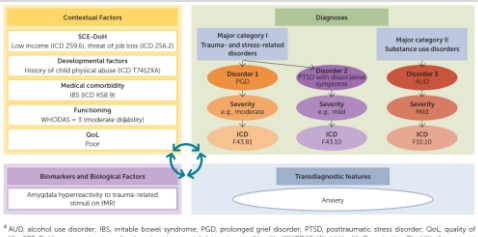
ORIGINAL ARTICLE

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



[a] AUD, alcohol use disorder; IBS, irritable bowel syndrome; PGD, prolonged grief disorder; PTSD, posttraumatic stress disorder; QoL, quality of life; SCE-DoH, socioeconomic, cultural, and environmental determinants of health; WHODAS, World Health Organization Disability Assessment Schedule.

Am J Psychiatry XX:XX, XX 20XX