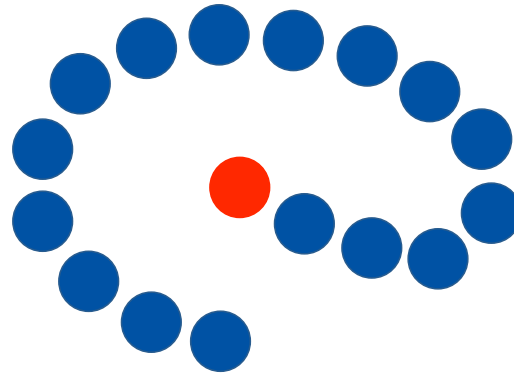


Stress, Gene und Gedächtnis: Neue Ansätze für die Therapie von Angsterkrankungen

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Faculty of Medicine & Faculty of Psychology
University of Basel
Switzerland

11. September 2001



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Gedächtnismoleküle

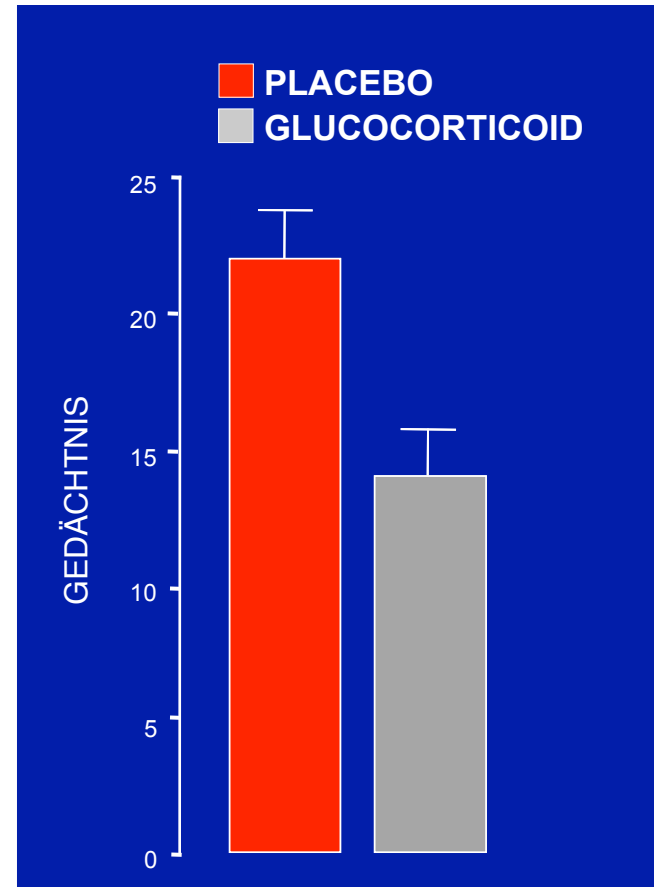
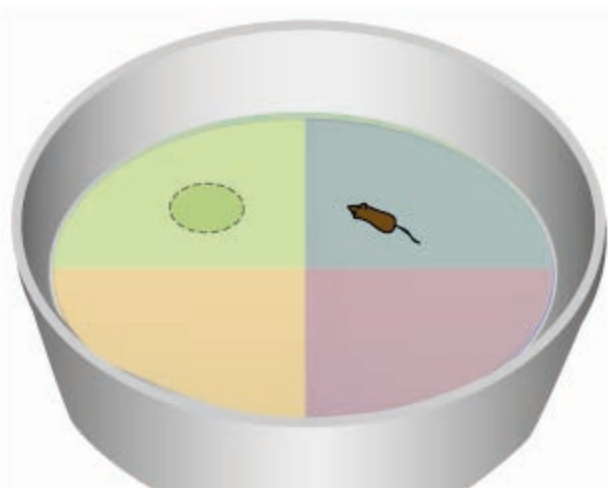


Körpereigene molekulare Mechanismen haben grossen Einfluss auf das Gedächtnis

>> Therapie für Gedächtnisstörungen



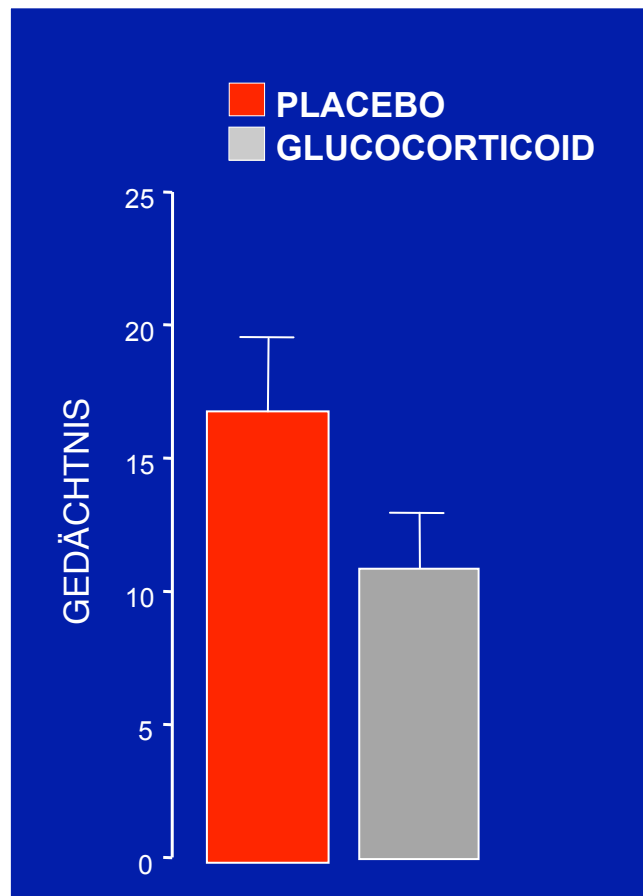
Stress vermindert Gedächtnisabruf



de Quervain, Roozendaal and McGaugh, *Nature* (1998)



Glucocorticoide vermindern Gedächtnisabruf



de Quervain et al., *Nature Neuroscience* (2000)



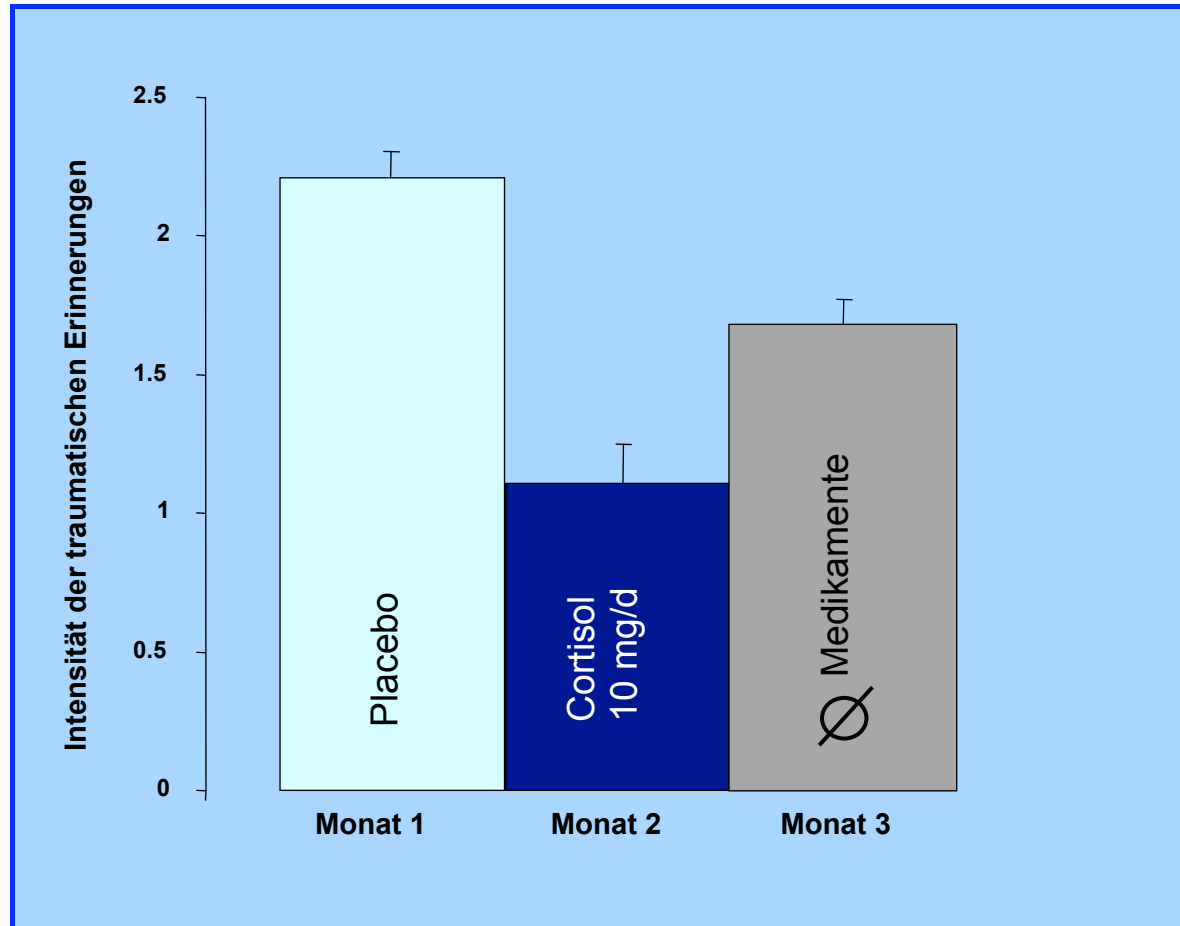
Posttraumatische Belastungsstörung



▶ Intensive schmerzhaftes Erinnerungen an das traumatische Ereignis



Posttraumatische Belastungsstörung



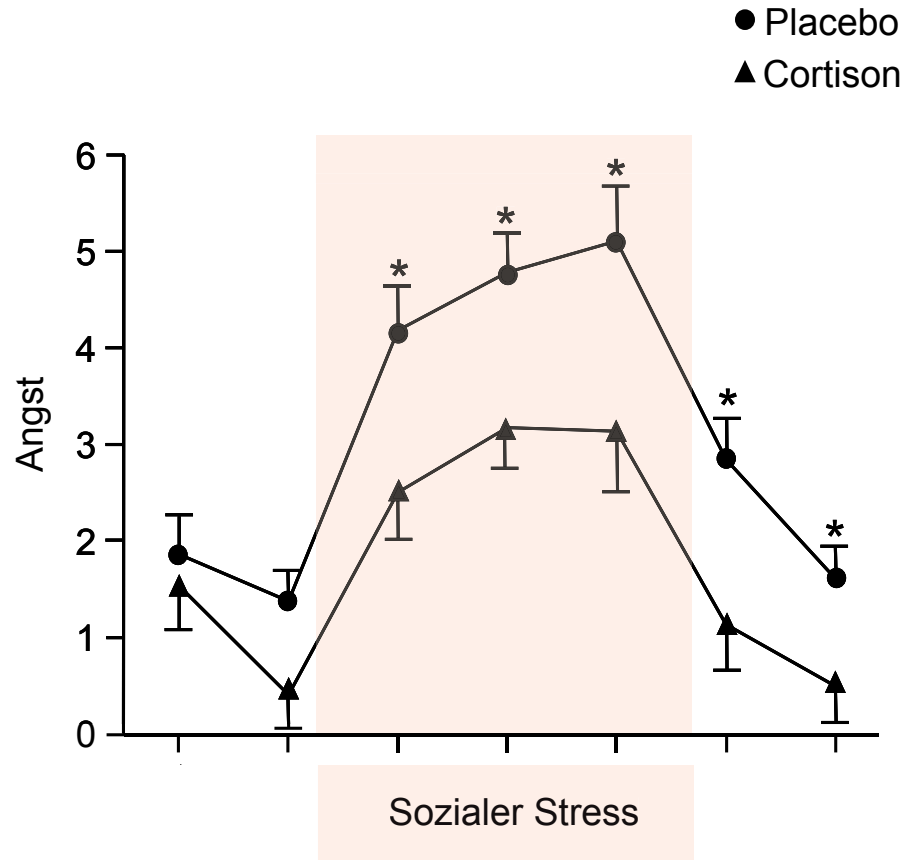
Aerni, Traber, Hock, Roozendaal, Schelling, Papassotiropoulos, Nitsch, Schnyder, & de Quervain; *American Journal of Psychiatry*, 2004



Soziale Phobie

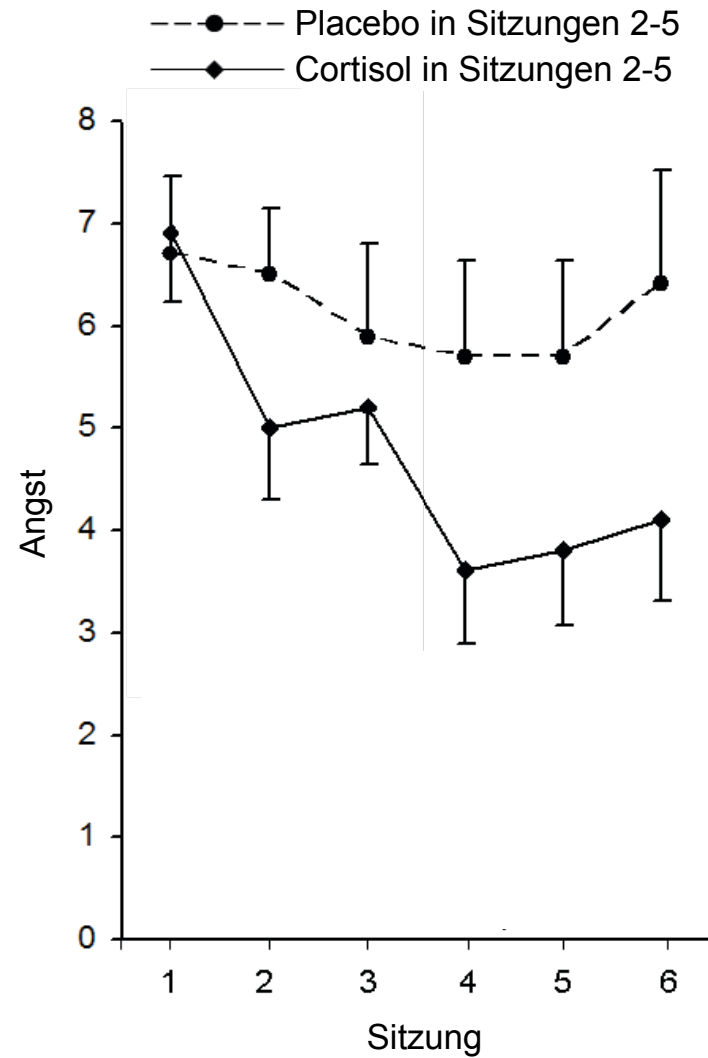


Cortison vermindert die subjektive Angst in einer sozialen Stresssituation





Spinnenphobie





Glucocorticoide in Kombination mit Verhaltenstherapie



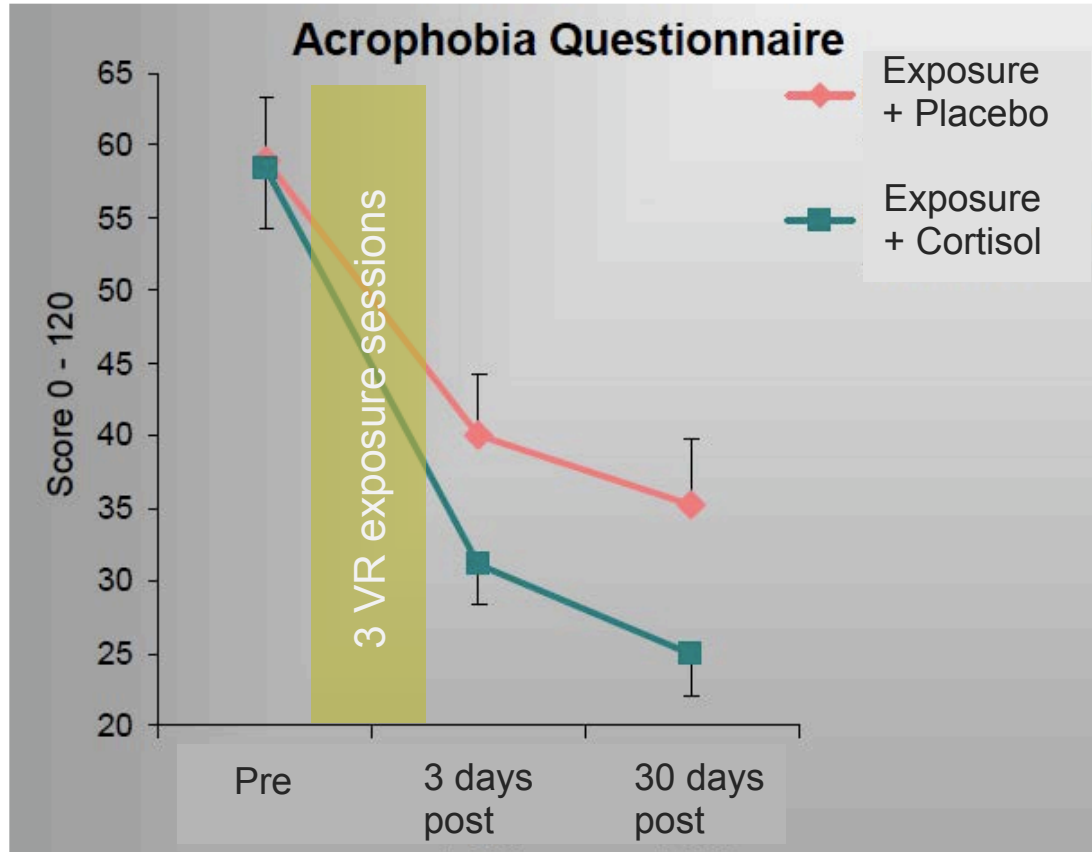


Glucocorticoide in Kombination mit Verhaltenstherapie





Glucocorticoide in Kombination mit Verhaltenstherapie



de Quervain, Bentz, Michael, Bolt, Wiederhold, Margraf, Wilhelm *PNAS* 2011

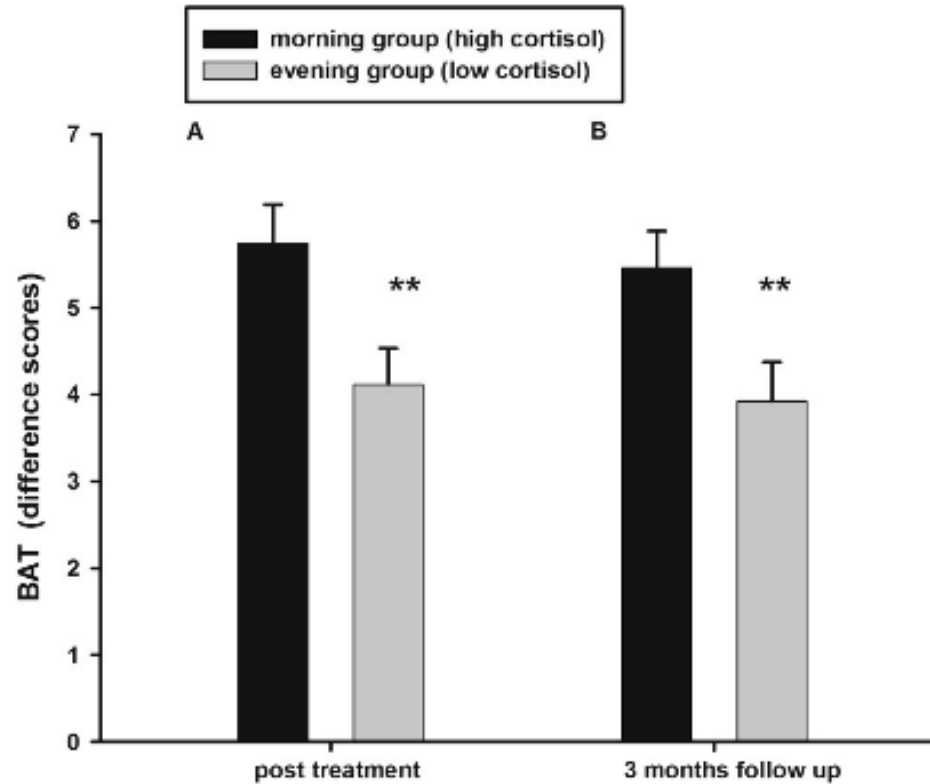
Table 1 | **Clinical trials with glucocorticoid-based interventions in fear-related disorders**

Drug	Design	Timing and duration	Memory phase exposed	Outcome	Refs
<i>Treatment of PTSD</i>					
Cort	DB, PC, CO	Daily for 30 days	Retrieval	↓ Intrusions while under treatment	130
		Daily for 7 days	Retrieval	No change in intrusions while under treatment	131
	RCT	Single dose after exposure	Extinction	↓ PTSD symptoms at 1 week	132
		20 min before exposure therapy, which was administered on 8 days	Retrieval and extinction	↓ PTSD symptoms at 6 weeks	134
<i>Prevention of PTSD</i>					
Cort	RCT	Starting <12 h after trauma, for 10 days	Consolidation and retrieval	↓ PTSD symptoms at 3 months	139
		Starting <6 h after trauma, for 6 days	Consolidation and retrieval	↓ PTSD incidence at 31 months	137
		Starting <6 h after trauma, for 4 days	Consolidation and retrieval	↓ Stress scores at 6 months	136, 138
		Single dose <6 h after trauma	Consolidation	↓ PTSD incidence at 3 months	128
Dex	RCT	Single intraoperative dose	Consolidation	No difference in PTSD incidence at 18 months	129
<i>Treatment of social phobia</i>					
Cort	RCT	Single dose 1 h before phobic stimulus	Retrieval	↓ Fear while under treatment	149
<i>Treatment of spider phobia</i>					
Cort	RCT	1 h before phobic stimulus, which was administered on 4 days	Retrieval and extinction	↓ Fear while under treatment	149
		1 h before exposure therapy, which was administered on 2 days	Retrieval and extinction	↓ Fear at 1 month	151
<i>Treatment of phobia of heights</i>					
Cort	RCT	1 h before exposure therapy, which was administered on 3 days	Retrieval and extinction	↓ Fear at 1 month	150

Only randomized controlled trials (RCT) or double-blind (DB), placebo-controlled (PC), cross-over (CO) trials are included. Cort, cortisol; Dex, dexamethasone; PTSD, post-traumatic stress disorder.



Therapie am Morgen besser?





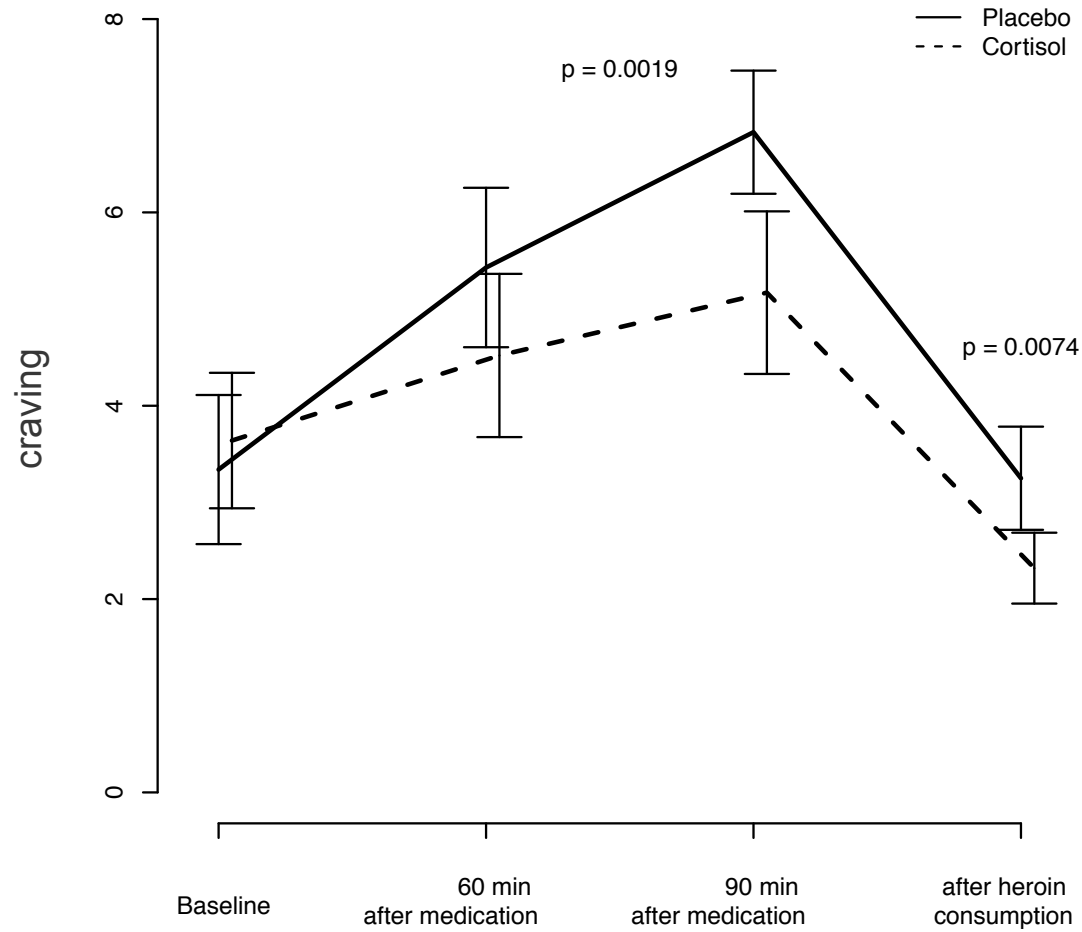
Glucocorticoide bei Sucht

Suchtgedächtnis



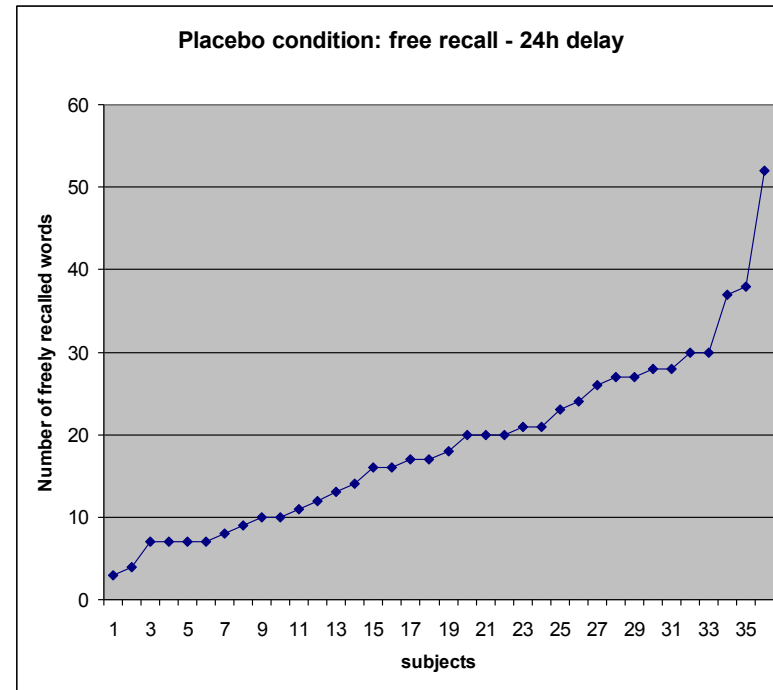
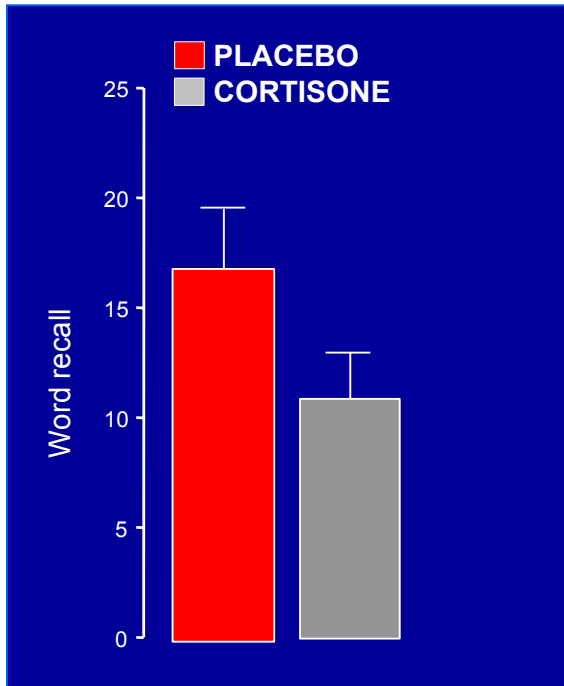


Glucocorticoide bei Sucht





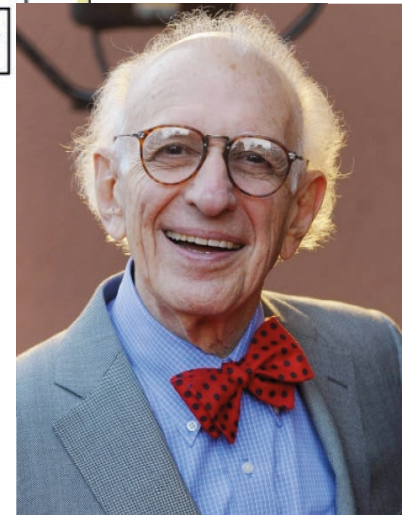
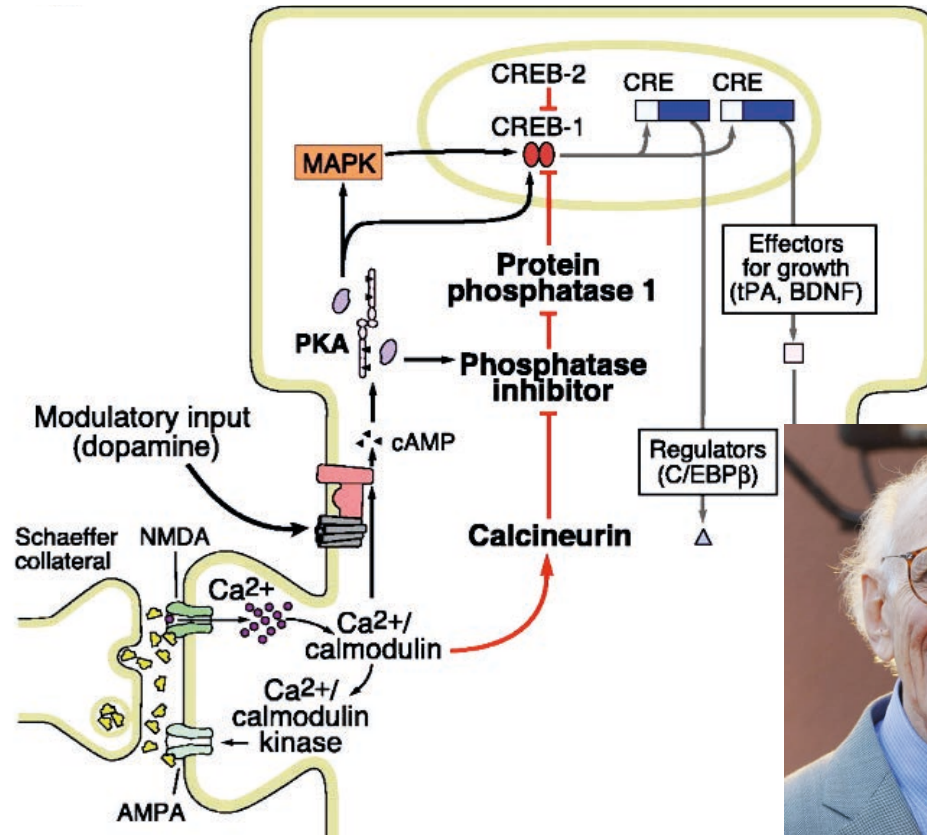
Gene und Gedächtnis



- ▶ Zwillingstudien: Variabilität wird zur Hälfte von genetischen Faktoren bestimmt
- ▶ Welche Gene?
- ▶ Projektstart 2002 mit dem Ziel, gedächtnisrelevante Gene zu identifizieren



Gedächtnisrelevante Signalkaskade beim Tier



Dr. Eric Kandel
Nobel prize 2000

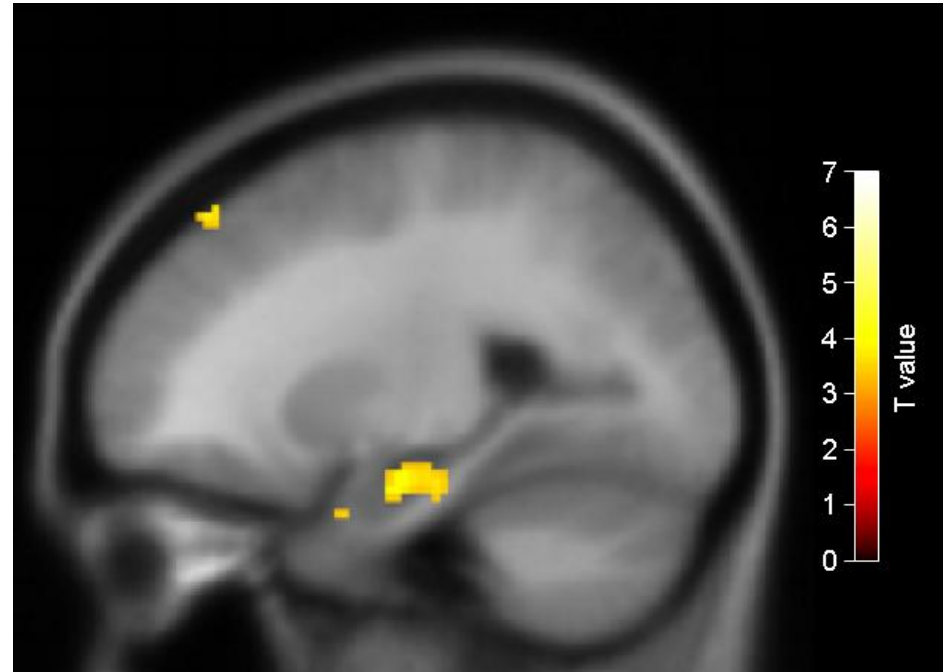
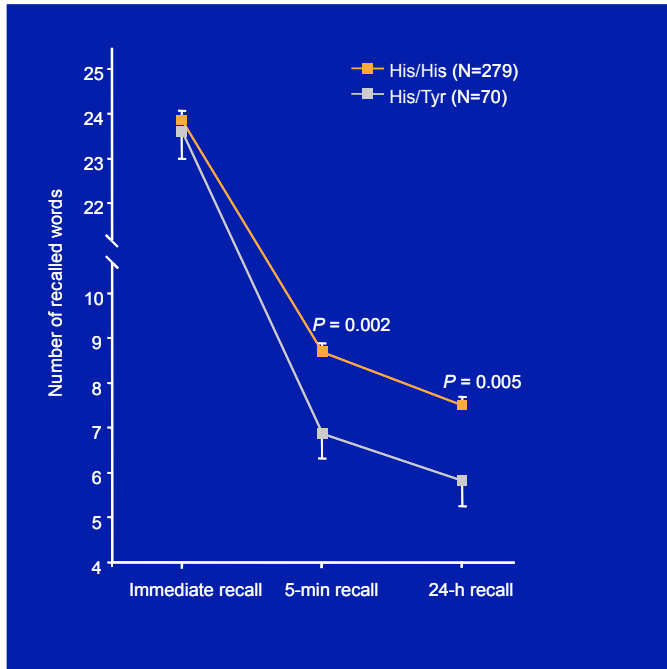


Ist diese Signalkaskade involviert beim Menschen?





Gedächtnisrelevante Gene beim Menschen



de Quervain and Papassotiropoulos, *PNAS*, 2006

de Quervain, Henke, Aerni, Coluccia, Wollmer, Hock, Nitsch, and Papassotiropoulos, *Nature Neuroscience* 2003



Gene und emotionales Gedächtnis

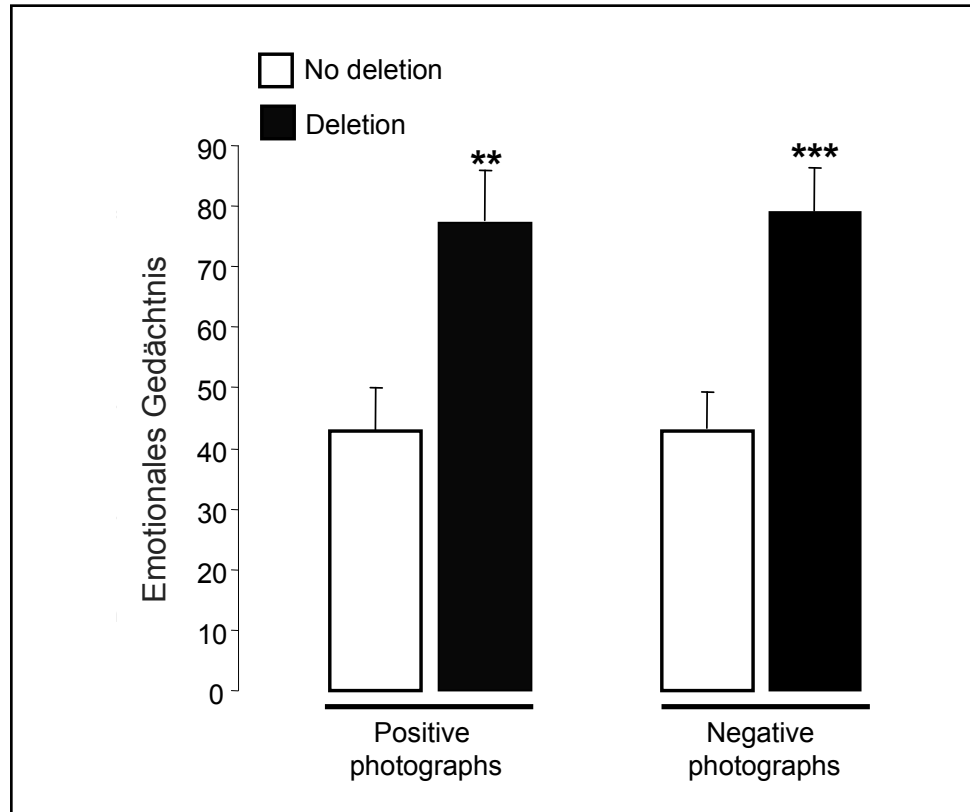


- ▶ Emotionale Information wird besser behalten als neutrale
- ▶ Dieses Phänomen hat eine adaptive Bedeutung
- ▶ Tierstudien: adrenerges Systems ist wichtig



Emotionales Gedächtnis und adrenerges System

Gesunde Probanden, $\alpha 2b$ -adrenerger Rezeptor





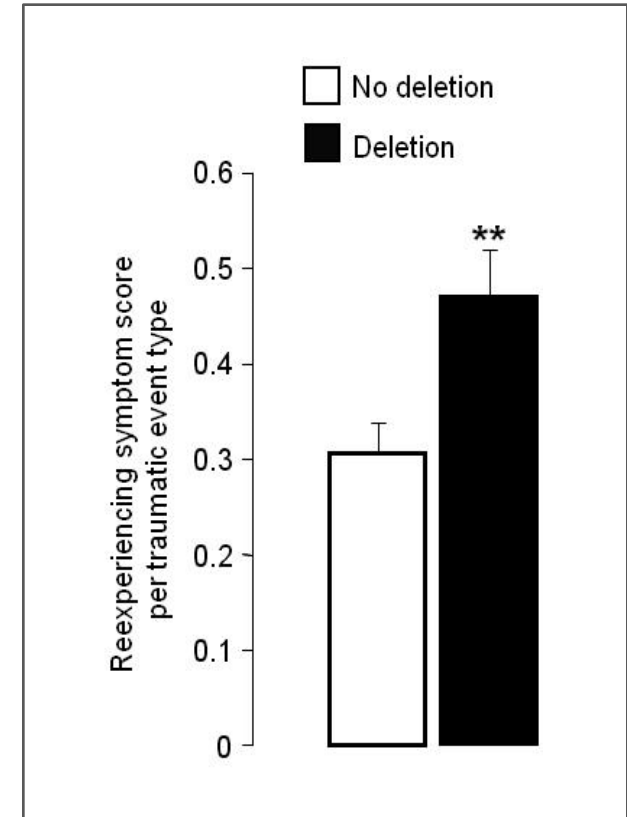
Emotionales Gedächtnis und adrenerges System

Überlebende des Bürgerkriegs in Ruanda



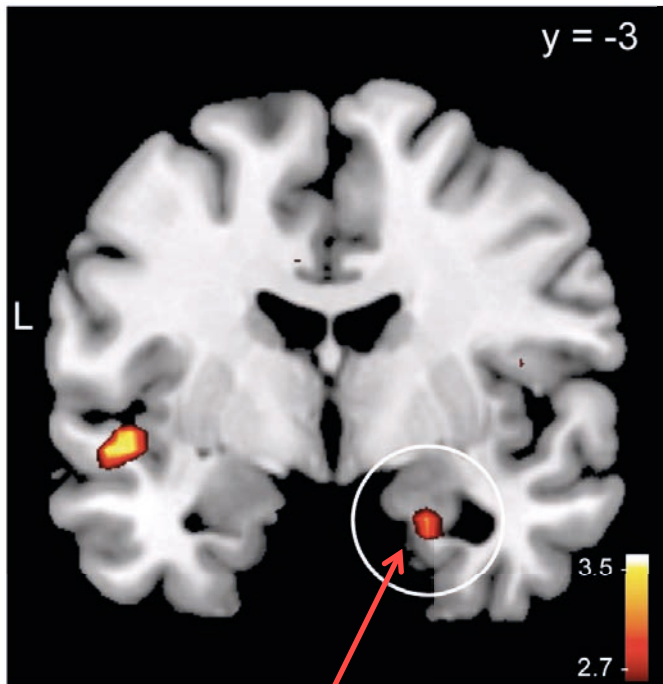


Emotionales Gedächtnis und adrenerges System

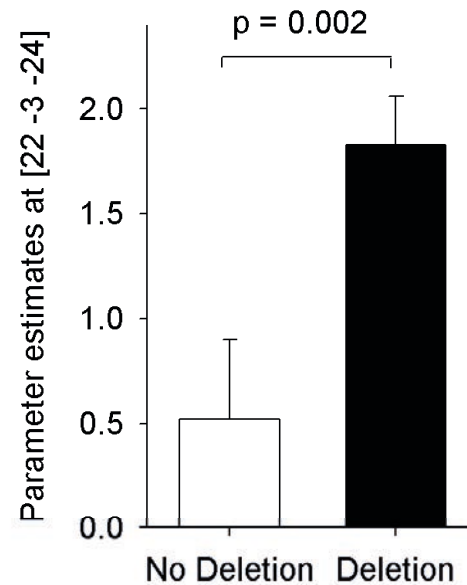




Emotionales Gedächtnis und adrenerges System



Amygdala

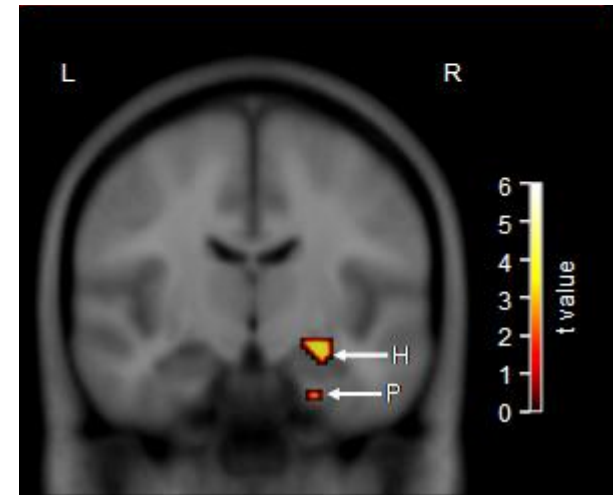
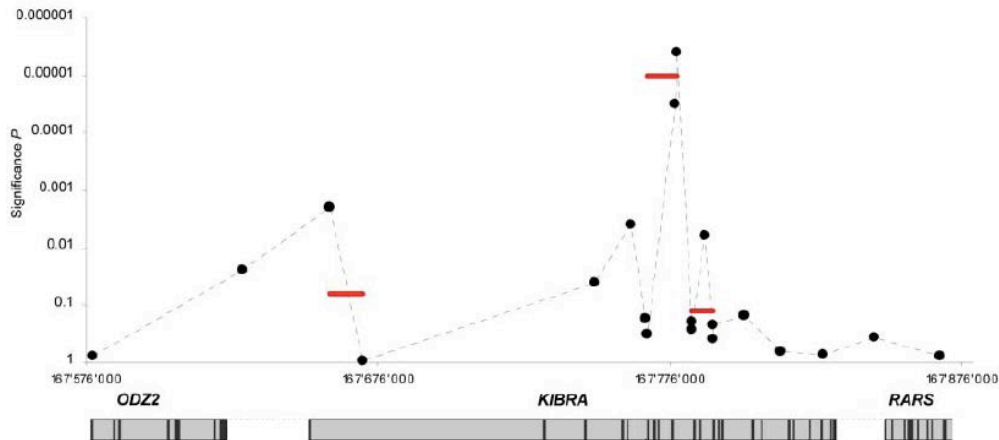




Genomweite Studien



KIBRA wichtig für episodisches Gedächtnis

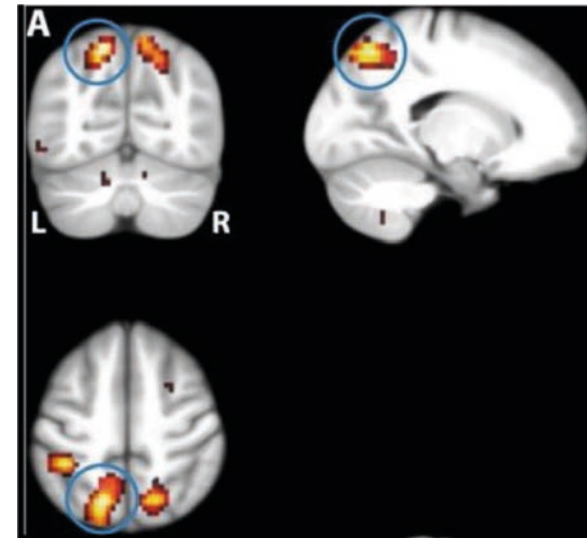
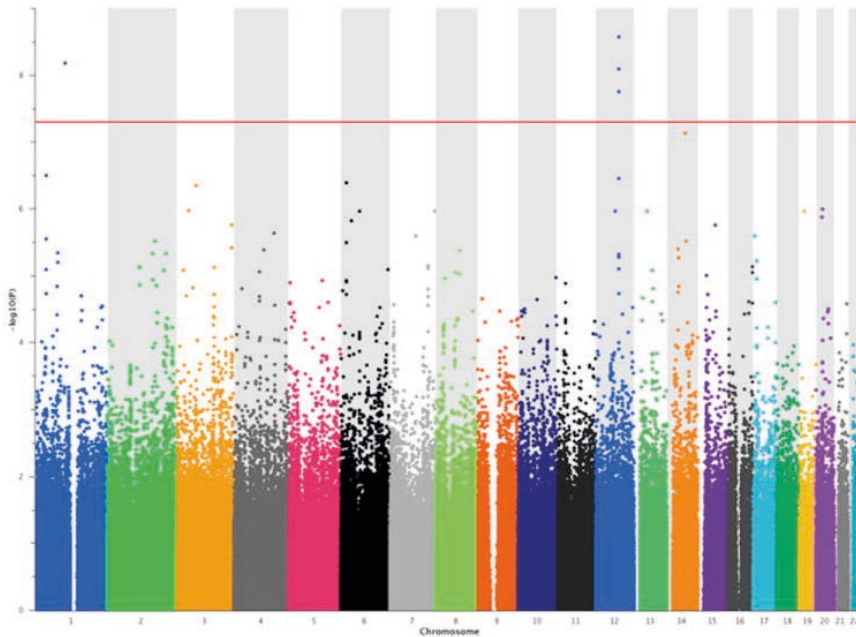




Genomweite Studien



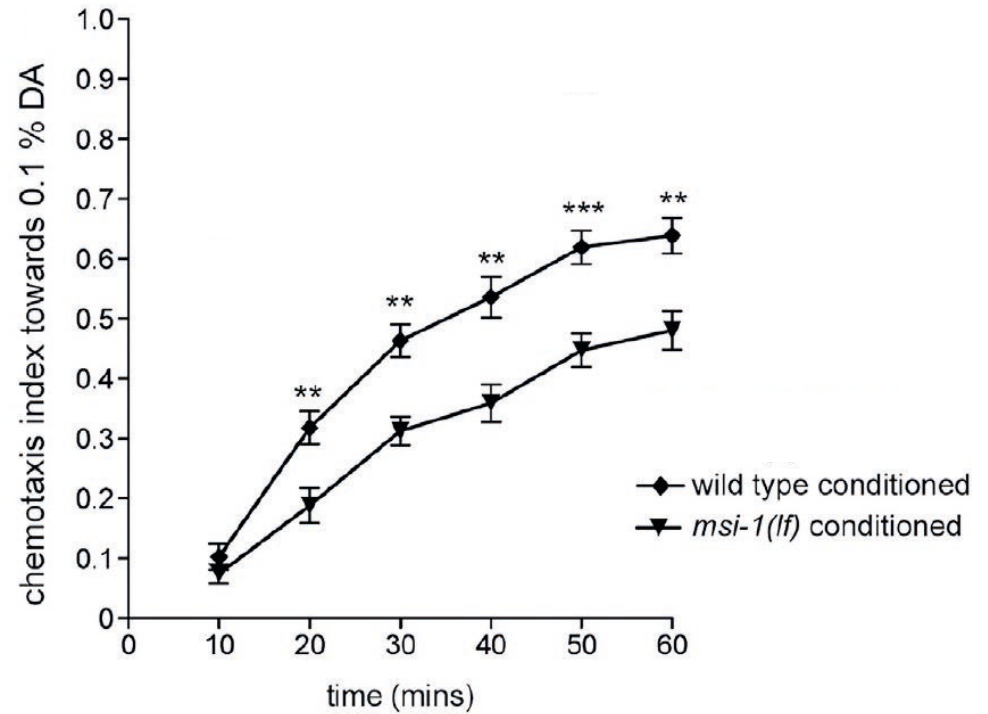
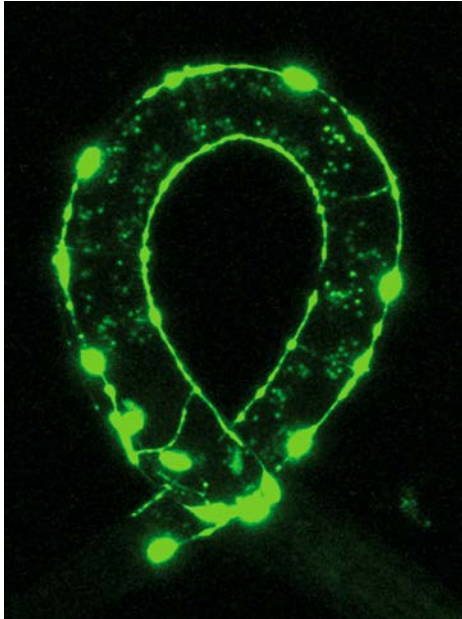
Voltage-gated cation channel activity gene set
für Arbeitsgedächtnis

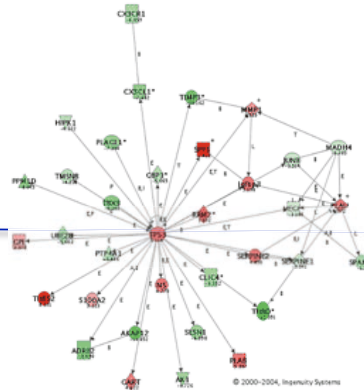
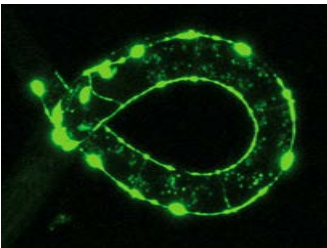
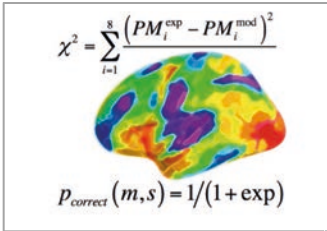
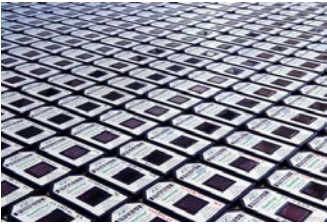




C. elegans

Musashi, ein Gen zum Vergessen





Ziel: Durch die Kombination von Verhaltens- und Bildgebungsdaten mit Human- und Molekulargenetik, neue Therapien zu entwickeln



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