Stress

Montag 12:15 – 13:45 Uhr

HZO 80

Prof. Oliver T. Wolf

FAKULTÄT FÜR PSYCHOLOGIE
Arbeitseinheit Kognitionspsychologie
www.cog.psy.ruhr-uni-bochum.de

Terminübersicht

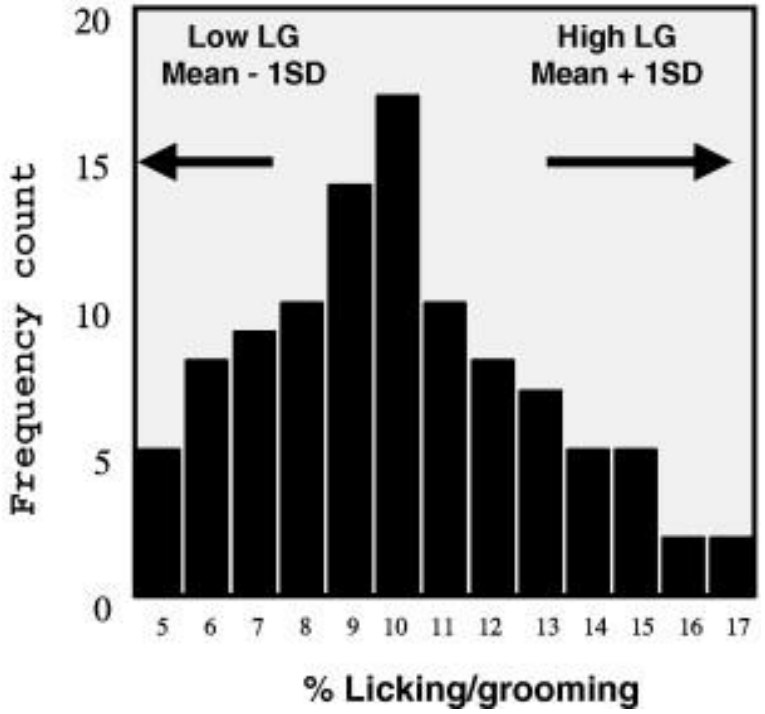
20.10.25	Übersicht und Einführung
27.10.25	Stress und das SNS: Walter Cannon (Dr. Katja Langer)
03.11.25	Stress und die HHNA: Hans Selye
10.11.25	Stress und die HHNA: Munck und Sapolsky Die kognitive Wende: Lazarus
17.11.25	Stress und Gesundheit: McEwen und die allostatische Belastung Stress im Arbeitsleben: Siegrist und die Effort Reward Imbalance
24.11.25	Burnout (Dipl. Psych. Natalie Freund)
01.12.25	Soziale Evaluation als bedeutsamer Stressor: Dickerson & Kemeny (Dr. Katja Langer)
08.12.25	Soziale Unterstützung als Stresspuffer/Oxytozin
15.12.25	Stress und Gehirn: akute und chronische Effekte
12.01.26	Pränataler Stress und seine Folgen
(Aufzeichnung)	Frühkindlicher Stress und seine Folgen (Prof. Robert Kumsta)
19.01.26	Posttraumatische Belastungsstörung

Wiederholung

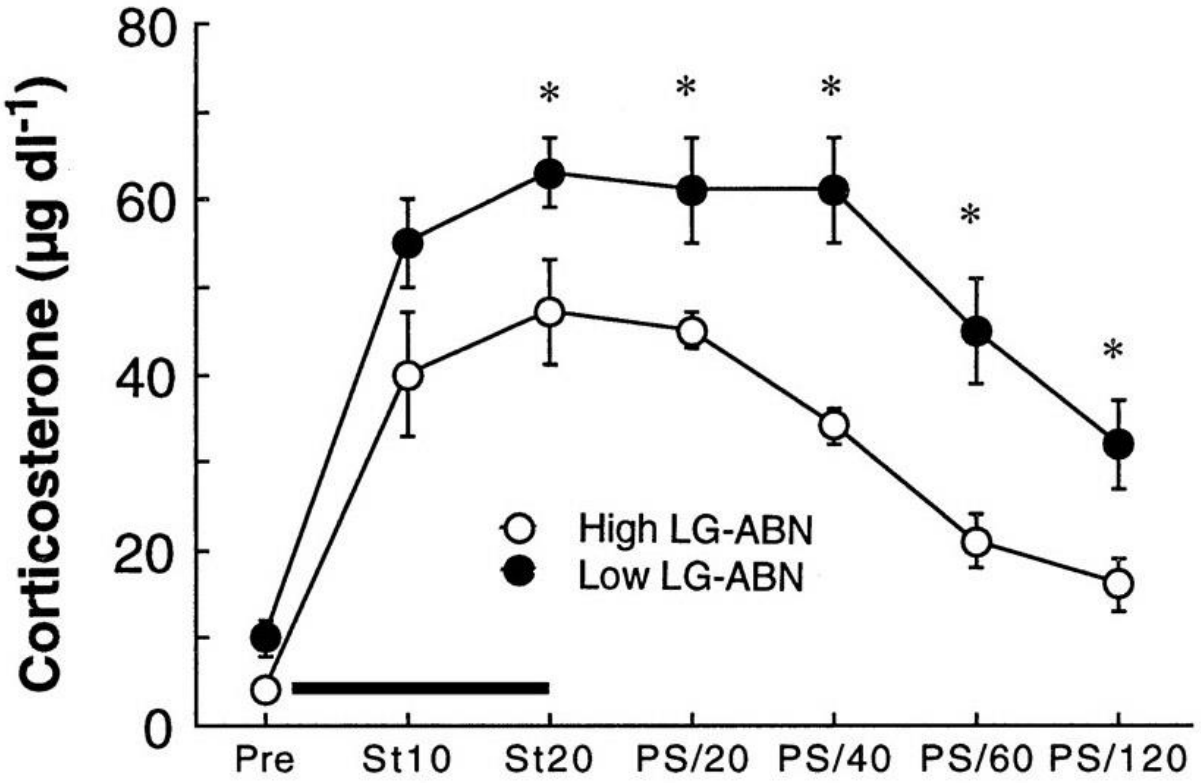
Intensives mütterliches Pflegeverhalten führt bei Rattenkindern zu…

a) erhöhter Reaktivität auf Stress	**c) erniedrigter Reaktivität auf Stress**
b) reduzierter Anzahl an GRs im Hippocampus	**d) erhöhter Anzahl an GRs in der Amygdala**

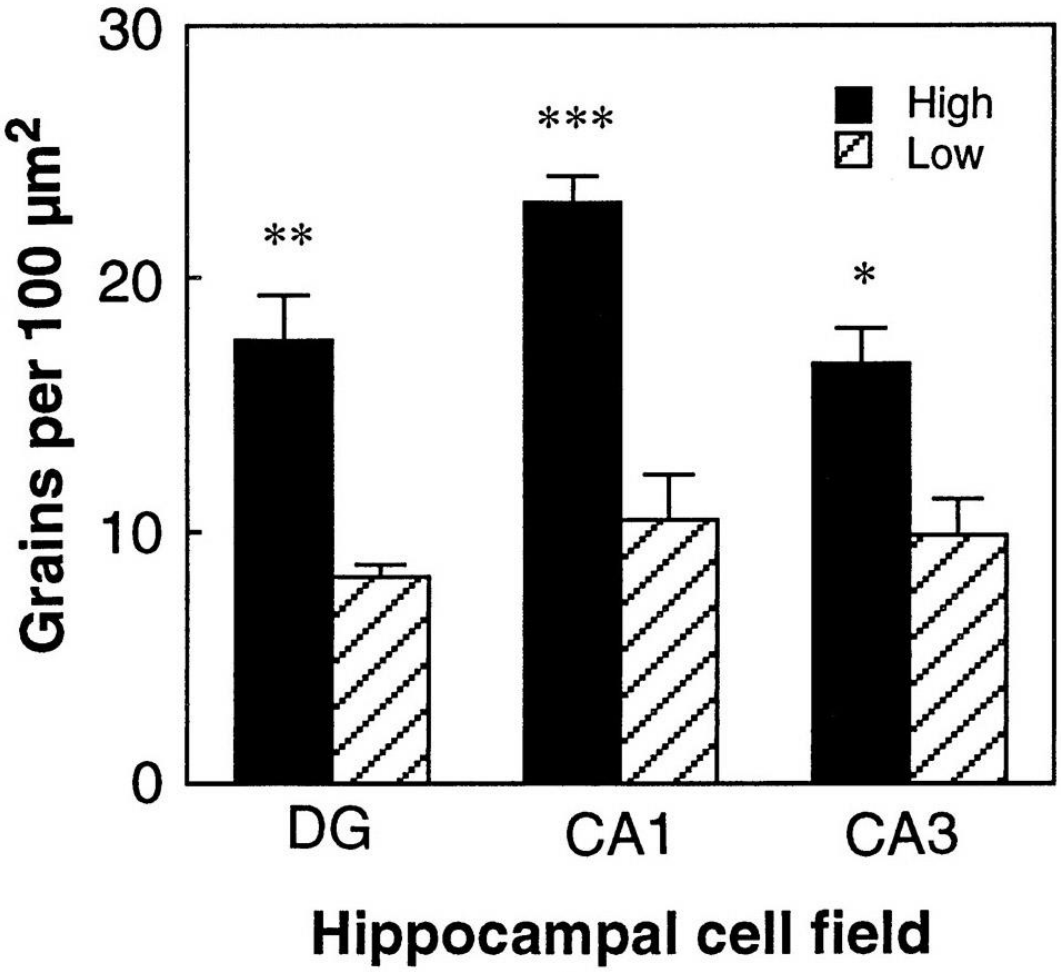
Tiermodelle: Unterschiede im mütterlichen Pflegeverhalten



Tiermodelle: mütterliche Pflege & Stressreaktivität (Liu et al., 1997)



Tiermodelle: mütterliche Pflege & GRs im Hippocampus (Liu et al., 1997)



Epigenetik: mütterliches Pflegeverhalten von Ratten

Maternal care as a model for experience-dependent chromatin plasticity?

Michael J. Meaney[1] and Moshe Szyf[2]

[1]Douglas Hospital Research Center, 6875 LaSalle Boulevard, Montréal, Québec H4H 1R3, Canada
[2]Department of Pharmacology and Therapeutics, McGill University, 3655 Sir William Oslar Promenade, Montréal, Québec H3G 1Y6, Canada

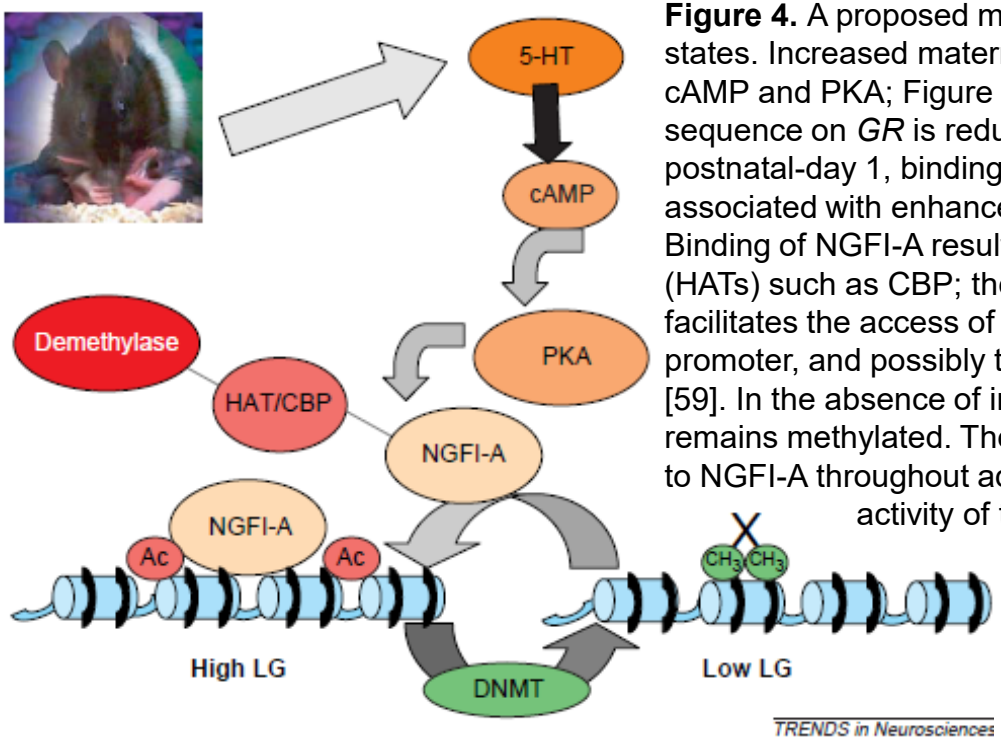


Figure 4. A proposed model for maternal programming of *GR* epigenetic states. Increased maternal LG activates NGFI-A expression (via 5-HT, cAMP and PKA; Figure 2). Although the affinity of NGFI-A to its recognition sequence on *GR* is reduced by the methylation of this element on postnatal-day 1, binding occurs through the increased levels of NGFI-A associated with enhanced tactile stimulation derived from maternal LG. Binding of NGFI-A results in recruitment of histone acetyltransferases (HATs) such as CBP; these increase histone acetylation (Ac), which in turn facilitates the access of demethylase and demethylation of the *GR* promoter, and possibly the recruitment of methylated DNA-binding proteins [59]. In the absence of increased LG and NGFI-A expression, the promoter remains methylated. The unmethylated promoter will maintain high affinity to NGFI-A throughout adulthood, resulting in greater NGFI-A-induced activity of the *GR* promoter in adult offspring of high-LG mothers, whereas the methylated *GR* promoter exhibits reduced affinity for NGFI-A, resulting in low activity of the *GR* in adult offspring of low-LG mothers. Abbreviation: DNMT, DNA methyltransferase.

Epigenetik: Relevanz für den Menschen?

RUB

ARTICLES

nature neuroscience

Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse

Patrick O McGowan[1,2], Aya Sasaki[1,2], Ana C D'Alessio[3], Sergiy Dymov[3], Benoit Labonté[1,4], Moshe Szyf[2,3], Gustavo Turecki[1,4] & Michael J Meaney[1,2,5]

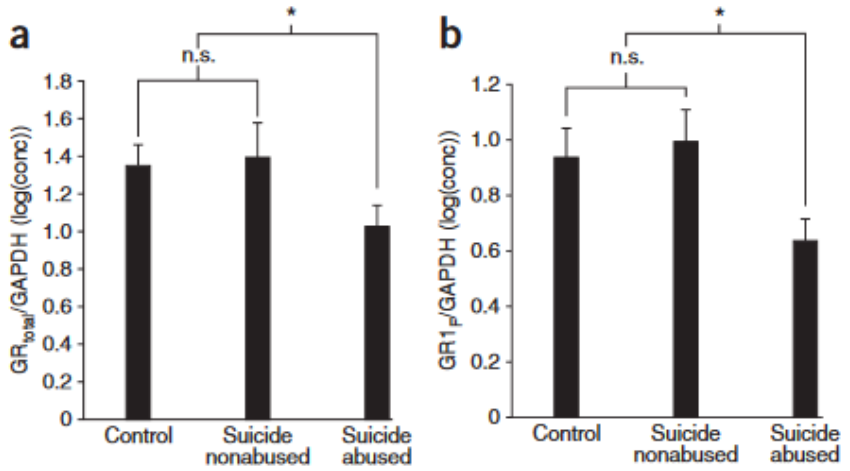


Figure 1 Hippocampal glucocorticoid receptor expression. (**a**,**b**) Mean ± s.e.m. expression levels of total glucocorticoid receptor (GR) mRNA (**a**) and glucocorticoid receptor 1_F (GR1_F) in 12 suicide victims with a history of childhood abuse, 12 nonabused suicide victims and 12 control subjects (**b**). Outliers excluded from analysis included $n = 2$ control subjects, $n = 1$ suicide victims with a history of childhood abuse for glucocorticoid receptor 1_F and an additional $n = 1$ suicide victim with a history of childhood abuse, and $n = 3$ nonabused suicide victims for overall levels of glucocorticoid receptor. * indicates $P < 0.05$; n.s. indicates not statistically significant.

Epigenetik: Relevanz für den Menschen?

ARTICLES

nature neuroscience

Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse

Patrick O McGowan[1,2], Aya Sasaki[1,2], Ana C D'Alessio[3], Sergiy Dymov[3], Benoit Labonté[1,4], Moshe Szyf[2,3], Gustavo Turecki[1,4] & Michael J Meaney[1,2,5]

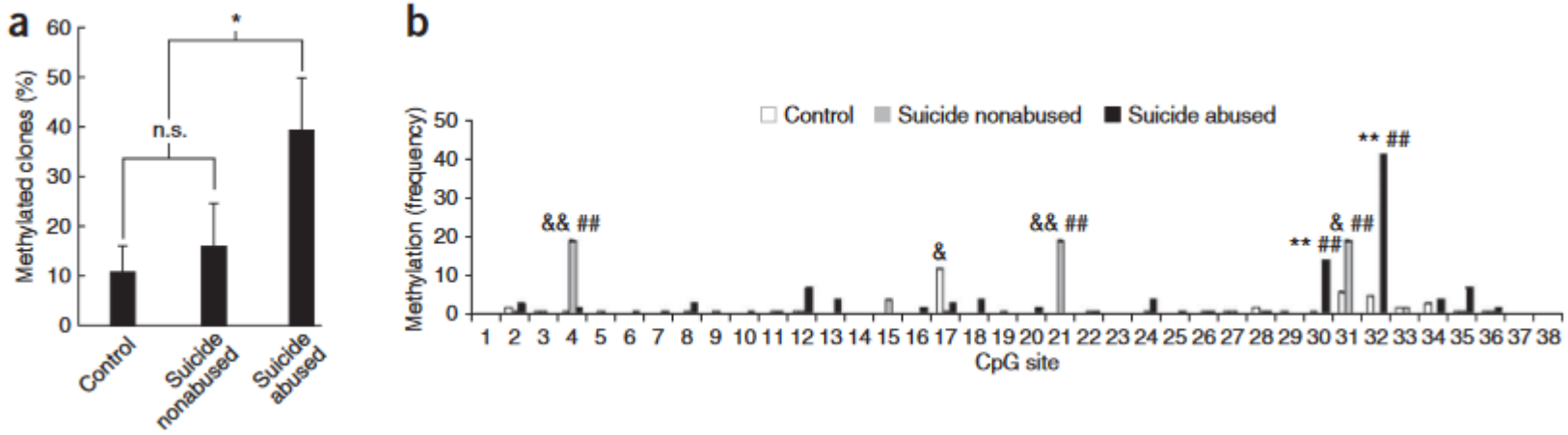


Figure 2 Methylation of the *NR3C1* promoter in the hippocampus. Twenty clones were sequenced for each subject for methylation mapping. (**a**) Mean ± s.e.m. percentage of methylated clones for suicide victims with a history of childhood abuse ($n = 12$), suicide victims without a history of childhood abuse ($n = 12$) and controls ($n = 12$). The methylation percentage was calculated as the number of clones with at least one methylated CpG site divided by the total number of clones (* indicates $P \leq 0.05$; n.s. indicates not statistically significant). (**b**) Methylation of the *NR3C1* promoter region, showing the frequency of methylation observed at each CpG site for suicide victims with a history of childhood abuse, suicide victims with no history of childhood abuse and control subjects ($^{*}P < 0.05$, $^{**}P < 0.001$, abused suicides versus controls; $^{\&}P < 0.05$, $^{\&\&}P < 0.001$, non-abused suicides versus controls; $^{\#}P < 0.05$, $^{\#\#}P < 0.001$, abused suicides versus non-abused suicides; Bonferroni *post hoc* comparisons).

Wiederholung

Welche Veränderungen werden bei Major Depression typischerweise beobachtet?

a) erhöhte Cortisolspiegel	**c) verkleinertes Hippocampusvolumen**
b) erhöhte CRF-Spiegel	**d) verkleinertes PFC-Volumen**

PTBS: HNNA-Veränderungen (Yehuda, 2002)

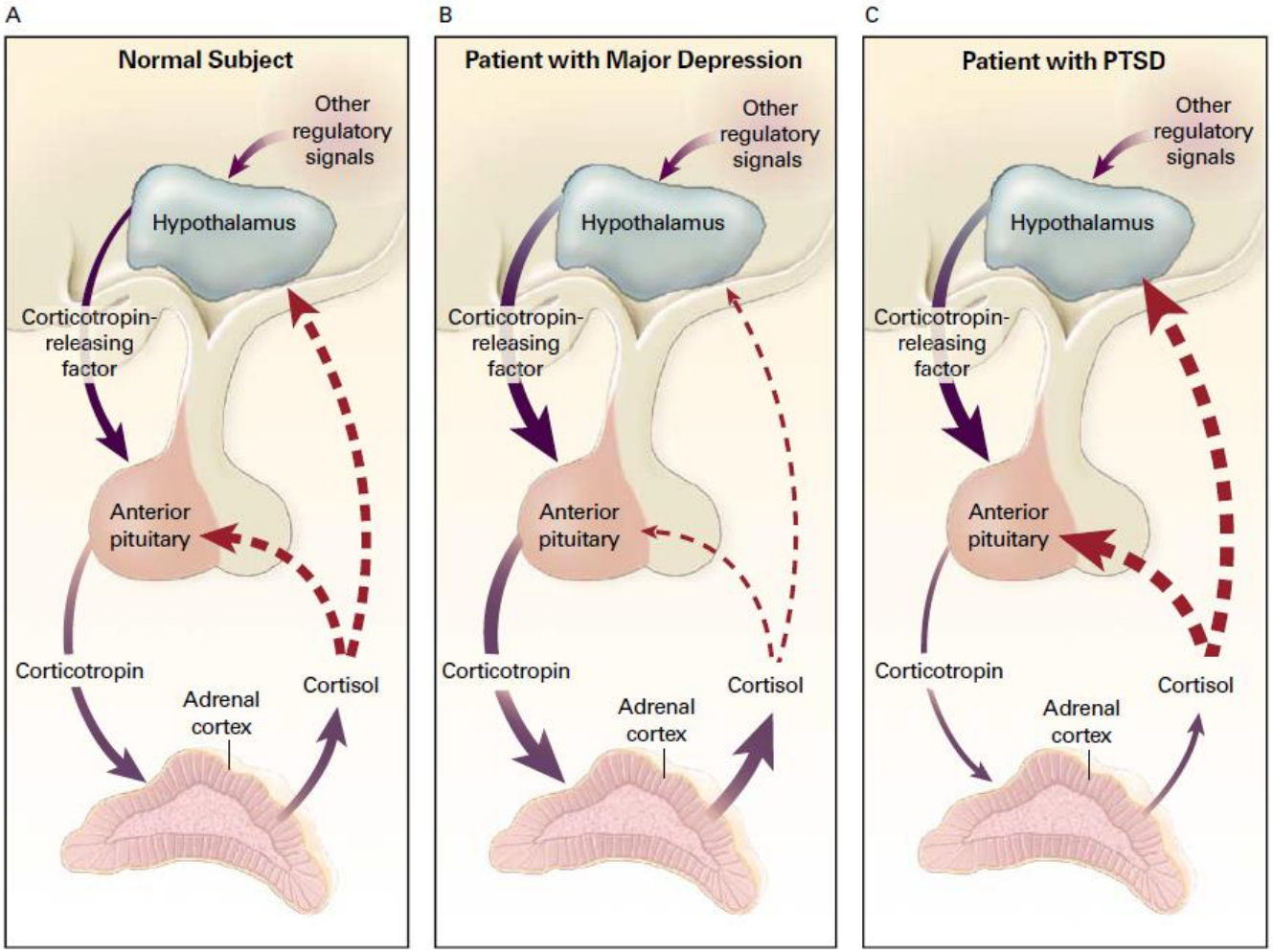
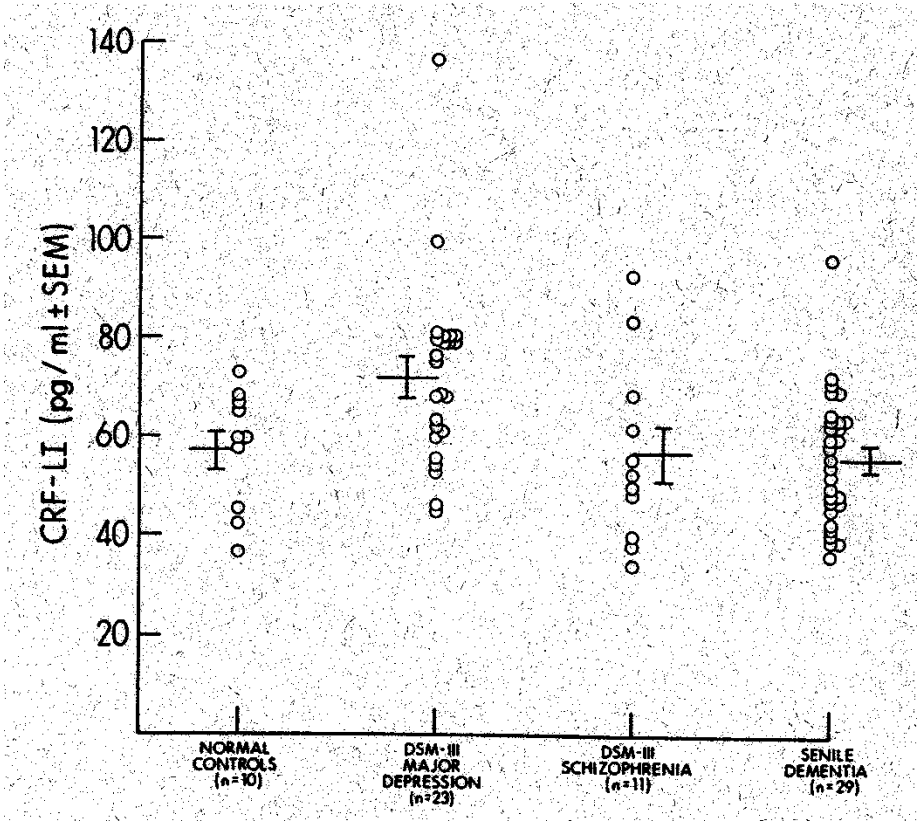


Figure 1. Response to Stress in a Normal Subject (Panel A), a Patient with Major Depressive Disorder (Panel B), and a Patient with PTSD (Panel C).

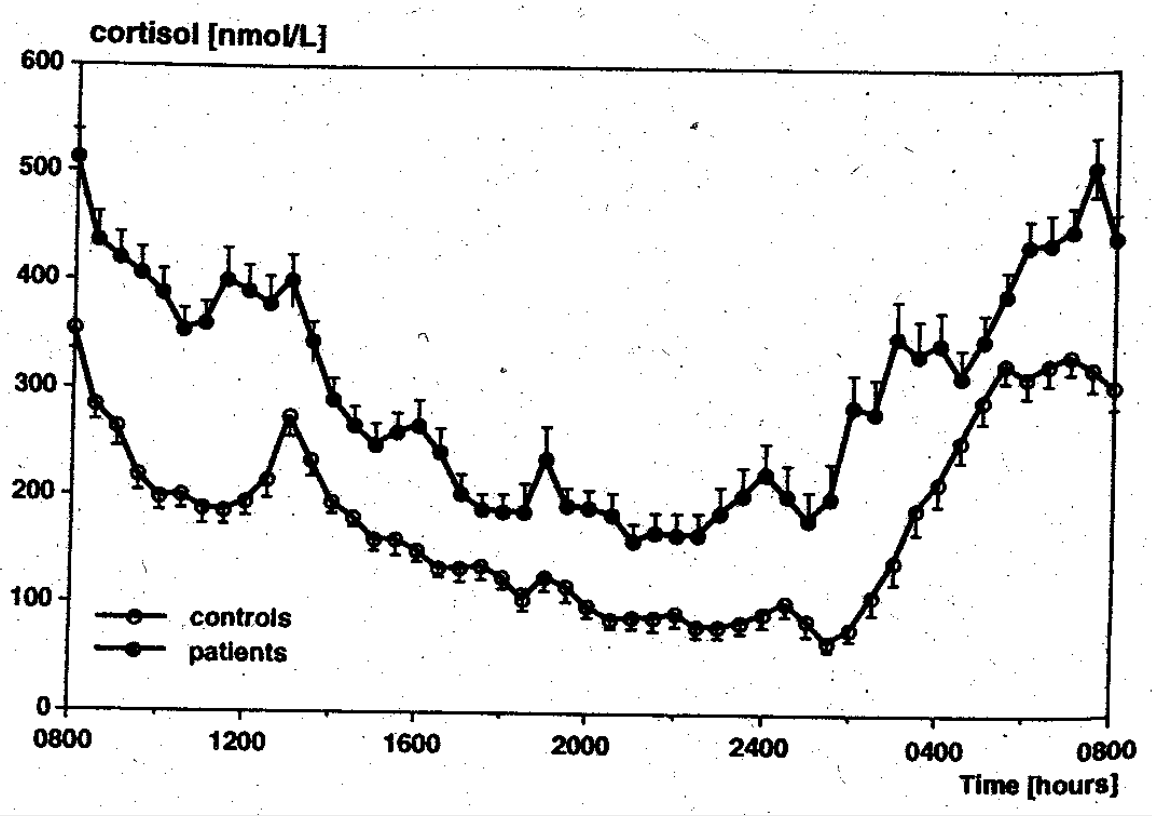
Depression & HHNA: CRF-Konzentration (Nemeroff et al., 1994)

erhöhte CRF-Konzentrationen im Liquor von Patienten mit Major Depression:

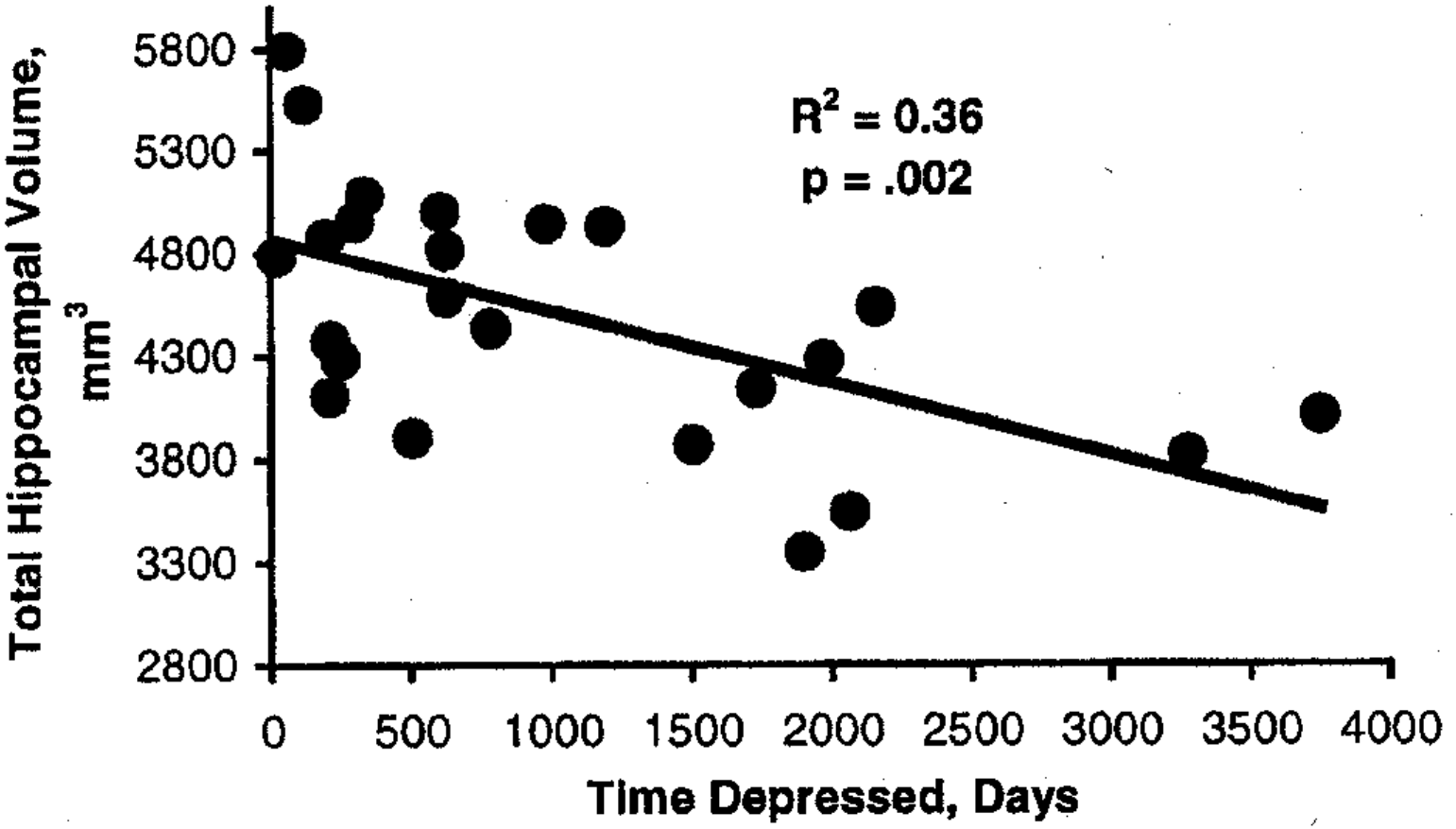


Depression & HHNA: Cortisol-Konzentration (Heuser et al., 1998)

erhöhte 24h-Cortisol-Konzentrationen bei Patienten mit Major Depression:



Depression & HHNA: Depressionsdauer & Hippocampus-Volumen (Sheline et al., 1999)



Depression & HHNA: Depressionsdauer & Hippocampus-Volumen (MacQueen et al., 2003)

RUB

Table 2. Hippocampus-dependent recollection memory function, perceived memory impairment (CFQ), and hippocampus volumes

Variable	FE depression ($n = 20$)	Controls ($n = 20$)	ME depression ($n = 17$)	Controls ($n = 17$)
CVLT-total recalled*	49.3 ± 14.5	55.3 ± 13.9	39.2 ± 16.3	53.7 ± 13.6
Process dissociation				
Recollection	0.35 ± 0.20	0.53 ± 0.14	0.40 ± 0.20	0.51 ± 0.10
Habit	0.60 ± 0.12	0.60 ± 0.08	0.61 ± 0.10	0.62 ± 0.07
Guessing	0.65 ± 0.12	0.66 ± 0.10	0.63 ± 0.11	0.65 ± 0.11
CFQ	54.8 ± 16.0	26.9 ± 9.6	66.0 ± 18.0	26.8 ± 10.1
Right HC volume, mm^3	2,793 ± 303.8	2,784 ± 342.2	2,392 ± 256.7	2,692 ± 190.1
Left HC volume, mm^3	2,738 ± 301.1	2,761 ± 368.4	2,381 ± 273.5	2,703 ± 249.0

*CVLT, California verbal learning test.

Literatur für die heutige Vorlesung

- Yehuda, R. (2002). Post-Traumatic Stress Disorder. *The New England Journal of Medicine, 346,* 108-114.

- Gilbertson, M.W., Shenton, M.E., Ciszewski, A., Kasai, K., Lasko, N.B., Orr, S.P., & Pitmann, R.K. (2002). Smaller Hippocampal Volume Predicts Pathologic Vulnerability to Psychological Trauma. *Nature Neuroscience, 15,* 1242-1247.

Posttraumatische Belastungsstörung

Gliederung

- Überblick
- HNNA-Veränderungen
- Hippocampusvolumen
- Klausurinfos

Current Concepts

POST-TRAUMATIC STRESS DISORDER

RACHEL YEHUDA, PH.D.

PTBS: Merkmale

- Flashbacks
- Albträume
- Hypervigilanz

PTBS: Prävalenz nach Art des Traumas (Yehuda, 2002)

Traumatic Event	Prevalence of Event		Rate of PTSD in Response to Event	
	Men	Women	Men	Women
	percent			
Rape*	0.7	9.2	65.0	45.9
Molestation*	2.8	12.3	12.2	26.5
Physical assault*	11.1	6.9	1.8	21.3
Accident*	25.0	13.8	6.3	8.8
Natural disaster*	18.9	15.2	3.7	5.4
Combat*	6.4	0.0	38.8	—
Witnessed death or injury†	40.1	18.6	9.1	2.8
Learned about a traumatic event†	63.1	61.8	1.4	3.2
Sudden death of loved one†	61.1	59.0	12.6	16.2
Any traumatic event*	60.7	51.2	8.1	20.4
Any traumatic event†	92.2	87.1	6.2	13.0

*Data are from Kessler et al.[4]

†Data are from Breslau et al.[16,17]

PTBS: HNNA-Veränderungen (Yehuda, 2002)

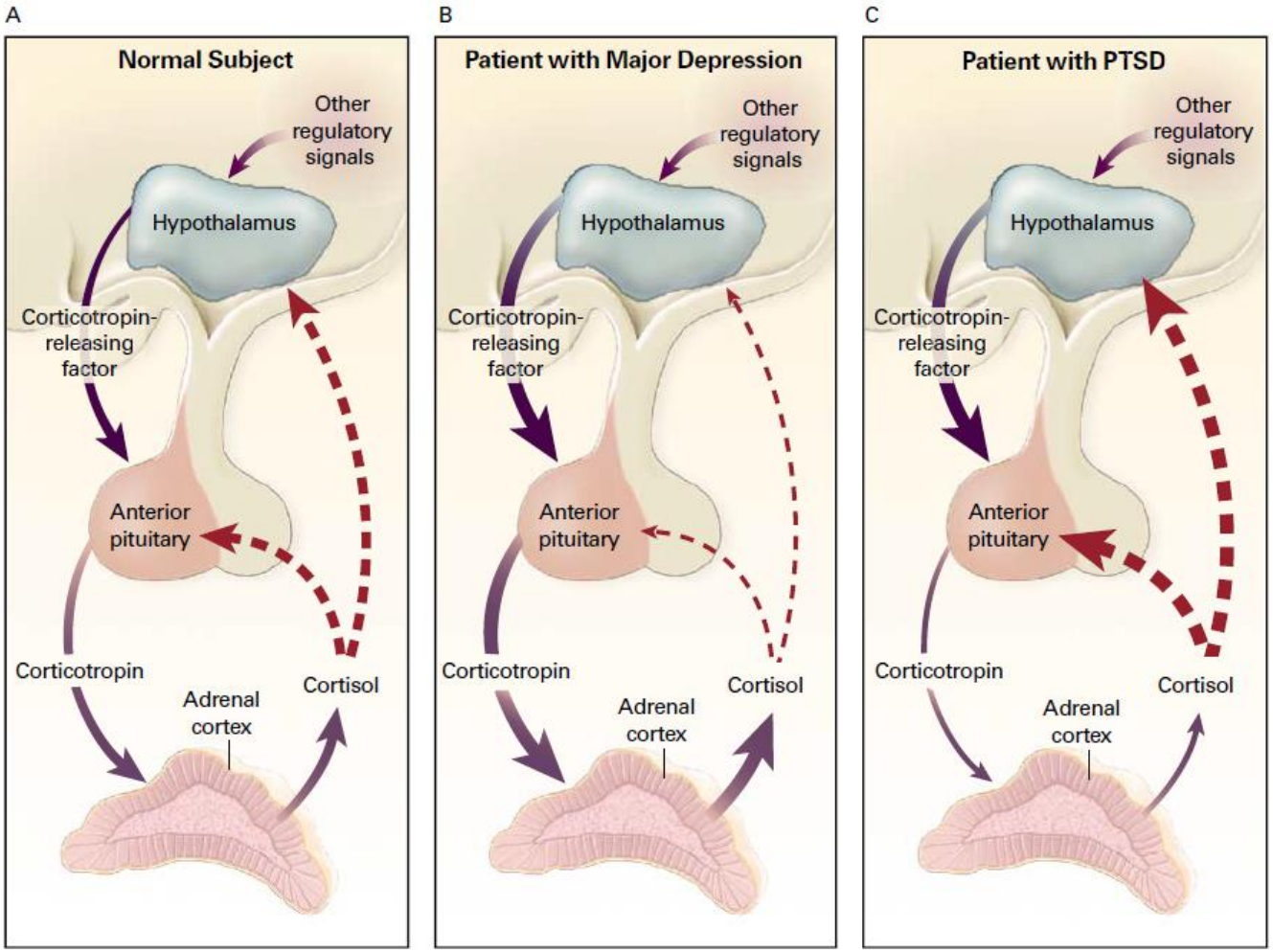
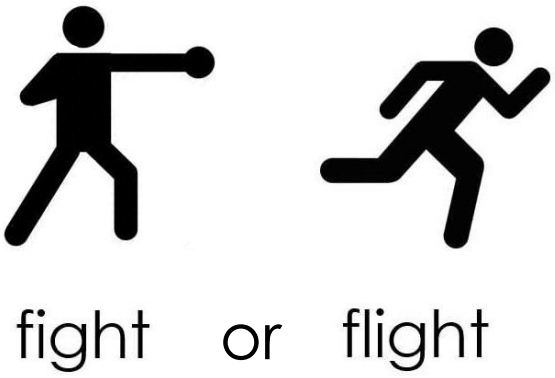
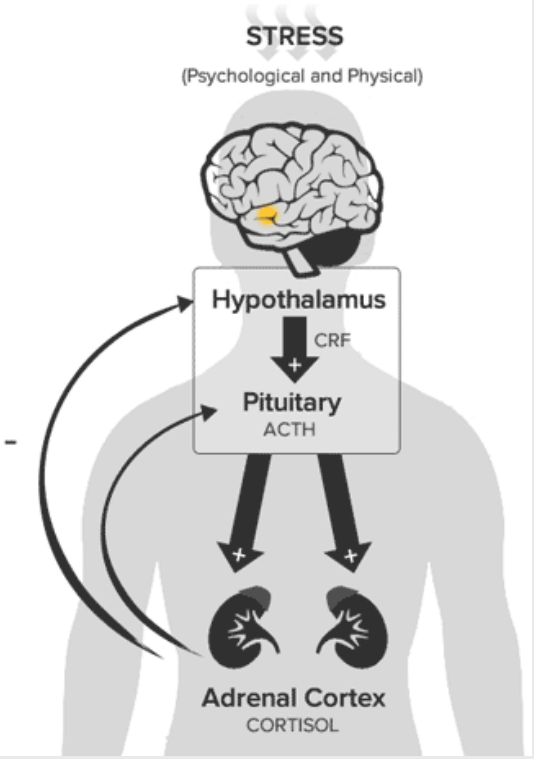


Figure 1. Response to Stress in a Normal Subject (Panel A), a Patient with Major Depressive Disorder (Panel B), and a Patient with PTSD (Panel C).

PTBS: HNNA-Veränderungen

- niedrigere basale Cortisolspiegel
- verstärkte Suppression der HHNA nach Dexamethasone-Gabe
- erhöhte Cortisolreaktion auf psychosozialen Stress (?)
- erhöhte Aktivität des SNS





PTBS & HHNA: niedrigere basale Cortisolspiegel

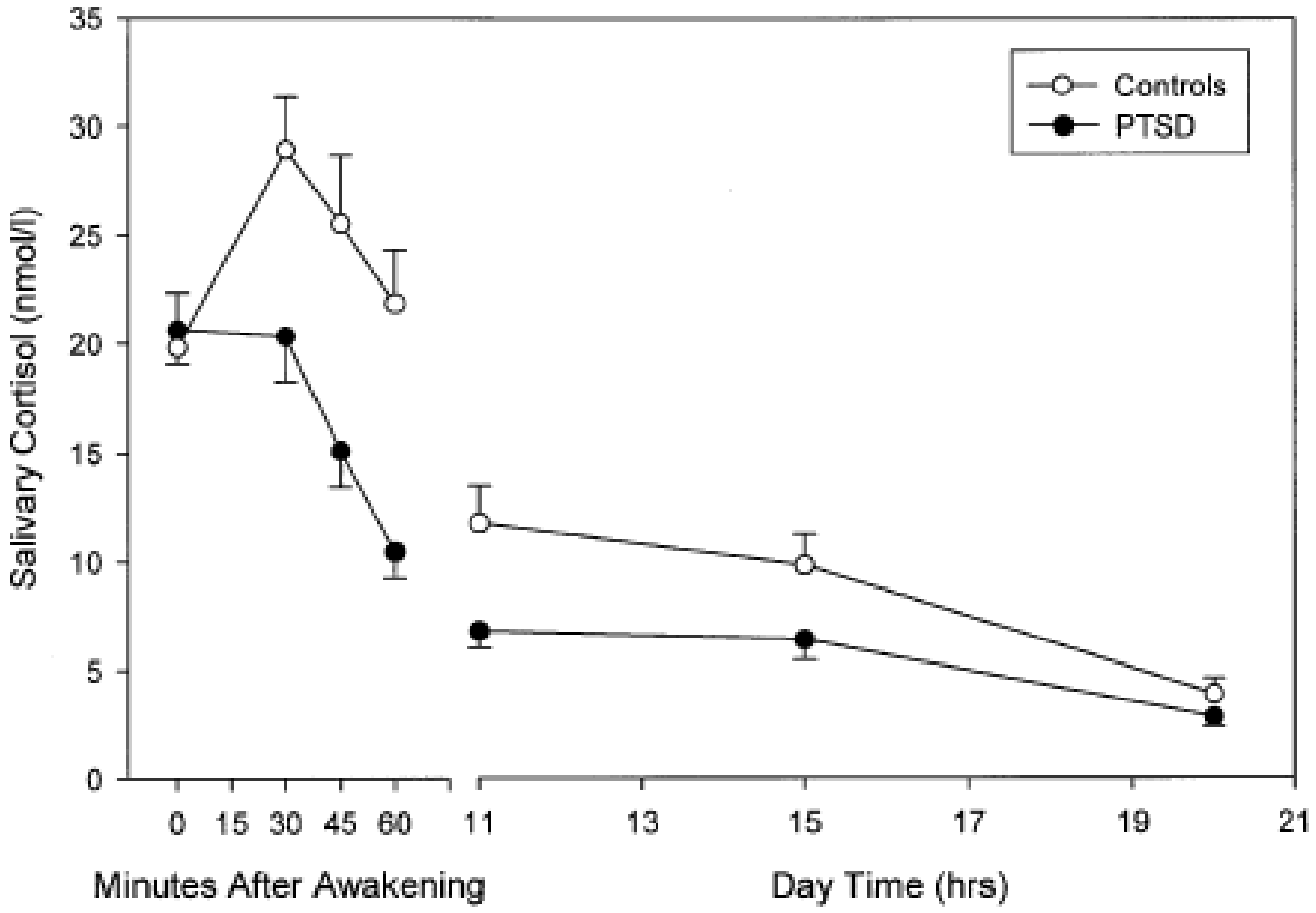
Table 1. Summary of data from studies of 24-h urinary cortisol excretion in adults with PTSD

Author(s), year	Cortisol µg/day (*n*)			
	Trauma survivors with PTSD (*n*)	Trauma with/without PTSD	Normal comparison	Psychiatric comparison
Mason et al., 1986*	33.3 (9)			48.5 (35)
Kosten et al., 1990*	50.0 (11)		55.0 (28)	70.0 (18)
Pitman and Orr, 1990**	107.3 (20)	80.5 (15)		
Yehuda et al., 1990*	40.9 (16)		62.8 (16)	
Yehuda et al., 1993*	38.6 (8)			69.4 (32)
Yehuda et al., 1995*	32.6 (22)	62.7 (25)	51.9 (15)	
Lemieux and Coe, 1995**	111.8 (11)	83.1 (8)	87.8 (9)	
Maes et al., 1998**	840.0 (10)		118 (17)	591.0 (10)
Thaller et al., 1999*	130.9 (34)		213.9 (17)	
Baker et al., 1999	84.4 (11)		76.2 (12)	
DeBellis et al., 1999**	57.3 (18)		43.6 (24)	56.0 (10)
Yehuda et al., 2000*	48.3 (22)		65.1 (15)	
Rasmusson et al., 2001	42.8 (12)		34.6 (8)	
Glover and Poland, 2002*[a]	9.8 (14)	16.5 (7)	12.8 (8)	

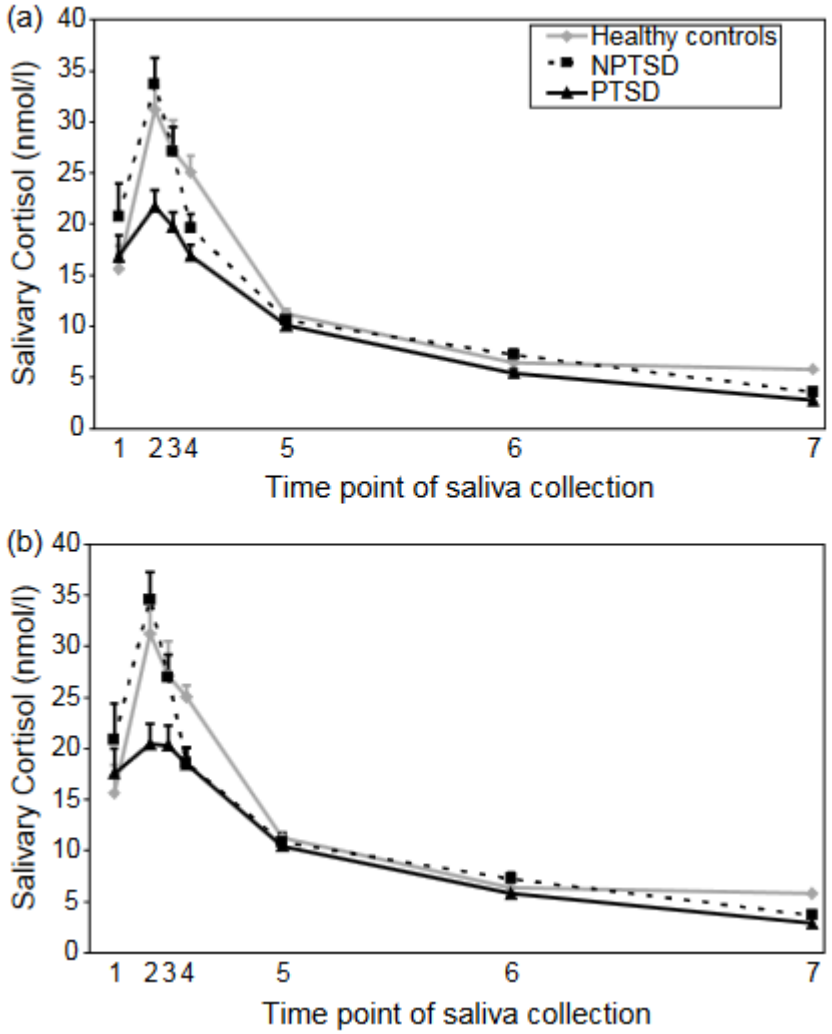
*Denotes findings in which cortisol levels were significantly lower than comparison subjects, or, in the case of Kosten et al., from depression only.
**Denotes findings in which cortisol levels were significantly higher than comparison subjects.
[a]Results are from a 12 h rather than 24 h urine collection and are expressed as ug/12 h.

Steckler, Kalin & Reul (2005). *Handbook of Stress and the Brain Part 2.*

PTBS & HHNA: Cortisolspiegel bei Patienten (Rohleder et al., 2004)



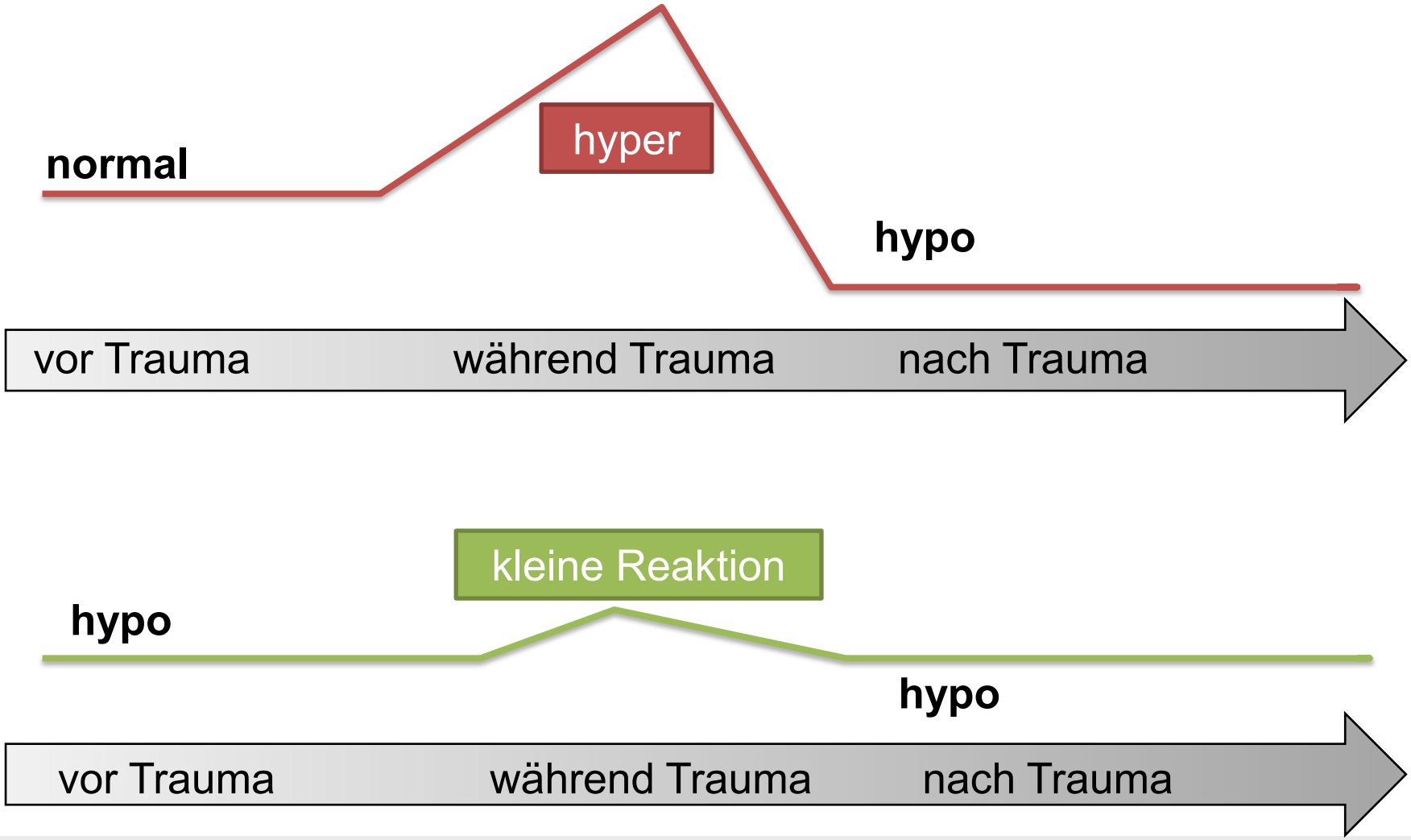
PTBS & HHNA: Cortisolspiegel bei Patienten (Wessa et al., 2005)



Unglück in Ramstein 1988

Figure 1 Salivary cortisol response to awakening (1 = awakening, 2 = 30 min after awakening, 3 = 45 min after awakening, 4 = 60 min after awakening) and daytime profile (5 = 1100 h, 6 = 1500 h and 7 = 2000 h) in (a) patients with posttraumatic stress disorder (PTSD; *N* = 29), trauma-exposed persons without PTSD (NPTSD; *N* = 19) and healthy controls (HC; *N* = 15) and (b) trauma-exposed subjects with and without PTSD, comorbid depression excluded (PTSD: *N* = 19; NPTSD: *N* = 19) and healthy controls (*N* = 15).

PTBS & HHNA: Cortisol – mögliche Verlaufsformen



PTBS & HHNA: niedrige Cortisolspiegel als Risikofaktor?

(Delahanty et al., 2000)

Table 2. Means (SDs) of Urinary Hormones and IES Scores for the PTSD and Non-PTSD Groups

	PTSD (n = 9)	Non-PTSD (n = 46)
Cortisol (μg/dL; square root transformations)	2.93 (1.42)[b]	5.10 (2.60)
Cortisol (μg/15 hours; square root transformations)	11.45 (5.24)[c]	21.04 (9.83)
Epinephrine (μg/15 hours)	14.78 (8.78)	27.63 (24.11)
Norepinephrine (μg/15 hours; square root transformations)	5.43 (1.10)[a]	7.17 (2.57)
Dopamine (μg/dL)	0.12 (.06)	0.16 (.11)
Total IES score	48.67 (11.60)[d]	17.31 (14.22)
IES intrusion subscale score	25.44 (5.7)[d]	9.18 (7.24)
IES avoidance subscale score	23.22 (7.56)[d]	8.13 (7.67)

PTBS & HHNA: Haarcortisol als Biomarker (Luo et al., 2012)

RUB

Hair Cortisol Level as a Biomarker for Altered Hypothalamic-Pituitary-Adrenal Activity in Female Adolescents with Posttraumatic Stress Disorder After the 2008 Wenchuan Earthquake

Hongrong Luo, Xun Hu, Xiang Liu, Xiaohong Ma, Wanjun Guo, Changjian Qiu, Yingcheng Wang, Qiang Wang, Xiaowei Zhang, Wei Zhang, Gregory Hannum, Kang Zhang, Xiehe Liu, and Tao Li

Background: The present study evaluated the accumulated changes in hair cortisol levels of patients with posttraumatic stress disorder (PTSD) attributed to the 2008 Wenchuan earthquake in China.

Methods: Sixty-four female adolescents from two townships who experienced the earthquake were recruited 7 months after the disaster, including 32 subjects with PTSD (PTSD group) and 32 subjects without PTSD (non-PTSD group). Twenty matched adolescents were recruited from an area that was not affected significantly by the earthquake as the control group. Hair cortisol concentrations were measured by the electrochemiluminescence immunoassay in each 3-cm segment of hair sample from the scalp.

Results: There was no significant difference at the baseline hair cortisol level in the three groups before the traumatic event ($p > .6$). Hair cortisol levels changed over time and differed among groups ($p = .0042$). The hair cortisol levels among the PTSD and non-PTSD subjects were elevated, suggesting increasing levels in response to stress. However, these two groups differed in their response. The non-PTSD subjects showed a significantly higher cortisol level than the PTSD group between month 2 and month 4 ($p = .0137$) and also between month 5 and month 7 ($p = .0438$) after the traumatic event.

Conclusions: This study revealed a blunted response curve to the disaster among PTSD subjects compared with subjects without PTSD. These findings suggest that hair cortisol level could be used to assess the integrated hypothalamic-pituitary-adrenal activity over a period of months after traumatic events and be used to serve as a biomarker in patients with PTSD.

PTBS & HHNA: Haarcortisol als Biomarker (Luo et al., 2012)

Table 1. Demographic and Clinical Features of the Study Cohort

	PTSD ($n = 32$)	Traumatized–non-PTSD ($n = 32$)	Nontraumatized Control ($n = 20$)	Statistic	p
Demographic Data (Mean ± SD)					
Age (years)	13.81 ± .93	13.84 ± .95	14.40 ± 1.67	$F = 1.877$	.160
Number of Subjects Who Experienced Certain Traumatic Events Due to the Earthquake, *n* (%)					
Being buried/injured	1 (3.13%)	0 (.0%)		–	1.000
Family member(s) died/severely injured	2 (6.25%)	0 (.0%)		–	.492
Classmate(s)/friend(s) died	15 (46.88%)	17 (53.13%)		$X^2 = .250$	.617
Estate destroyed	25 (78.13%)	21 (65.63%)		$X^2 = 1.237$	.266
Witnessed someone dying	10 (31.25%)	17 (53.13%)		$X^2 = 3.319$	.076
Witnessed buried/terribly wounded	25 (78.13%)	26 (81.25%)		–	1.000
CRIES Score (13-Items) (Mean)					
Total	42.94 ± 5.63	8.66 ± 5.91		$t = 23.752$	<.0001
Intrusion factor	3.31 ± .95	.68 ± .52		$t = 13.752$	<.0001
Avoidance factor	3.36 ± .89	.73 ± .97		$t = 11.294$	<.0001
Arousal factor	3.25 ± .71	.60 ± .49		$t = 17.299$	<.0001

CRIES Score and traumatic events due to the earthquake among PTSD and traumatized–non-PTSD were measured.
CRIES, Children's Revised Impact of Event Scale; PTSD, posttraumatic stress disorder.

PTBS & HHNA: Haarcortisol als Biomarker (Luo et al., 2012)

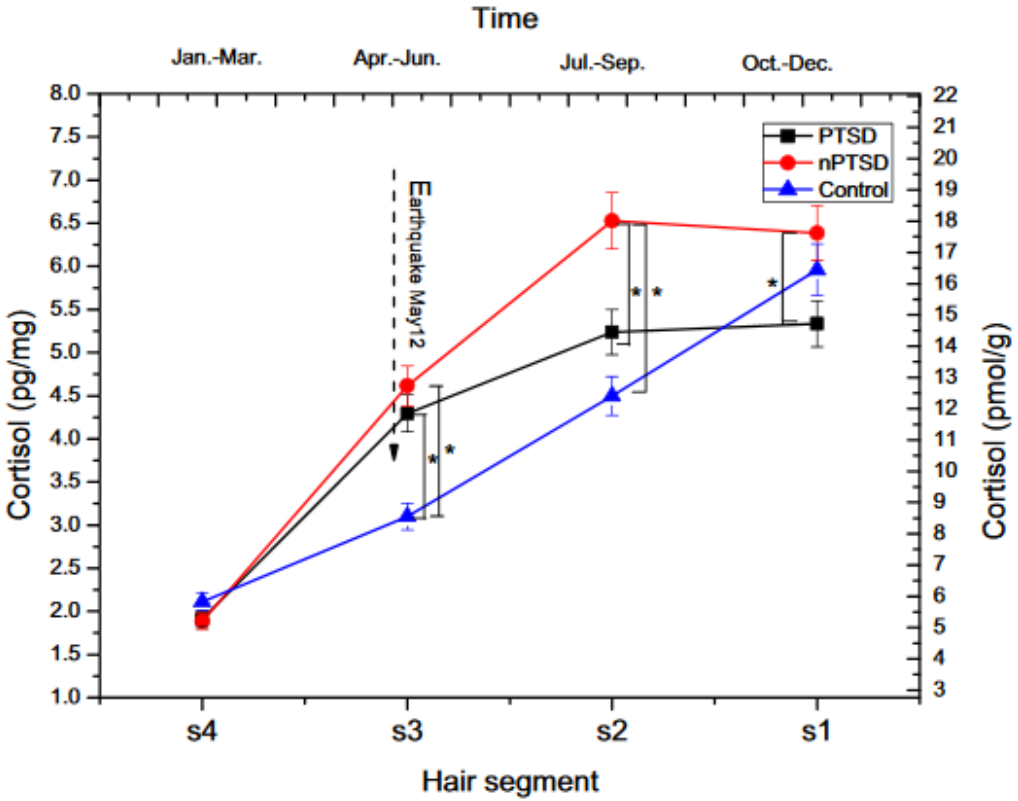


Figure 1. Analysis of cortisol levels in 3-cm hair segments (S1, S2, S3, or S4) from posttraumatic stress disorder (PTSD) ($n = 32$), non-PTSD (nPTSD; $n = 32$), and nontraumatized control ($n = 20$) groups (*$p < .05$ significance, error bar: 95% confidence interval). S1, period of 5 to 7 months after the earthquake; S2, period of 2 to 4 months after the earthquake; S3, period between 2 months before and 1 month after the earthquake; S4, period of 3 months before the earthquake.

PTBS & HHNA: Epigenetische Übertragungen – Video

PTBS & HHNA: Epigenetik

0021-972X/05/$15.00/0
Printed in U.S.A.

The Journal of Clinical Endocrinology & Metabolism 90(7):4115–4118

doi: 10.1210/jc.2005-0550

BRIEF REPORT

Transgenerational Effects of Posttraumatic Stress Disorder in Babies of Mothers Exposed to the World Trade Center Attacks during Pregnancy

Rachel Yehuda, Stephanie Mulherin Engel, Sarah R. Brand, Jonathan Seckl, Sue M. Marcus, and Gertrud S. Berkowitz

Traumatic Stress Studies Program, Department of Psychiatry (R.Y., S.R.B.), Department of Community and Preventive Medicine (S.M.E., G.S.B.), and Division of Biostatistics, Department of Psychiatry (S.M.M.), Mount Sinai School of Medicine, Bronx Veterans Affairs Medical Center, Bronx, New York 10471; and Molecular Medicine Centre, Western General Hospital (J.S.), University of Edinburgh, Edinburgh EH4 2XU, United Kingdom

Context: Reduced cortisol levels have been linked with vulnerability to posttraumatic stress disorder (PTSD) and the risk factor of parental PTSD in adult offspring of Holocaust survivors.

Objective: The purpose of this study was to report on the relationship between maternal PTSD symptoms and salivary cortisol levels in infants of mothers directly exposed to the World Trade Center collapse on September 11, 2001 during pregnancy.

Design: Mothers (n = 38) collected salivary cortisol samples from themselves and their 1-yr-old babies at awakening and at bedtime.

Results: Lower cortisol levels were observed in both mothers ($F = 5.15$, $df = 1, 34$; $P = 0.030$) and babies of mothers ($F = 8.0$, $df = 1, 29$; $P = 0.008$) who developed PTSD in response to September 11 compared with mothers who did not develop PTSD and their babies. Lower cortisol levels were most apparent in babies born to mothers with PTSD exposed in their third trimesters.

Conclusions: The data suggest that effects of maternal PTSD related to cortisol can be observed very early in the life of the offspring and underscore the relevance of *in utero* contributors to putative biological risk for PTSD. (***J Clin Endocrinol Metab* 90: 4115–4118, 2005**)

PTBS & HHNA: Epigenetik (Yehuda et al., 2005)

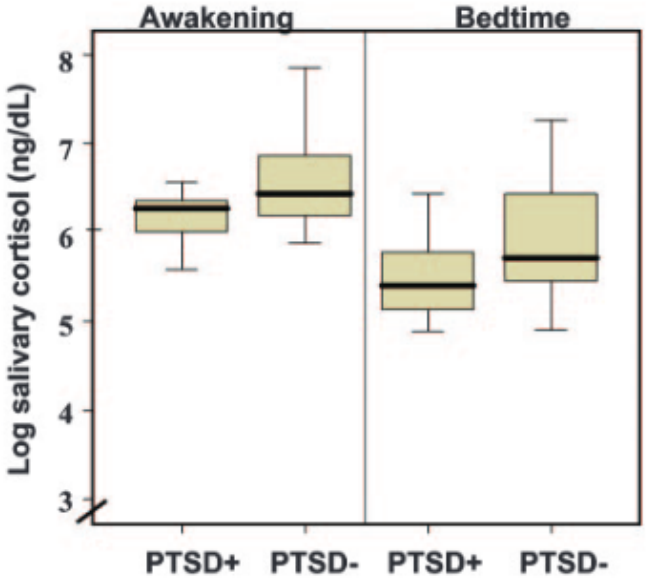
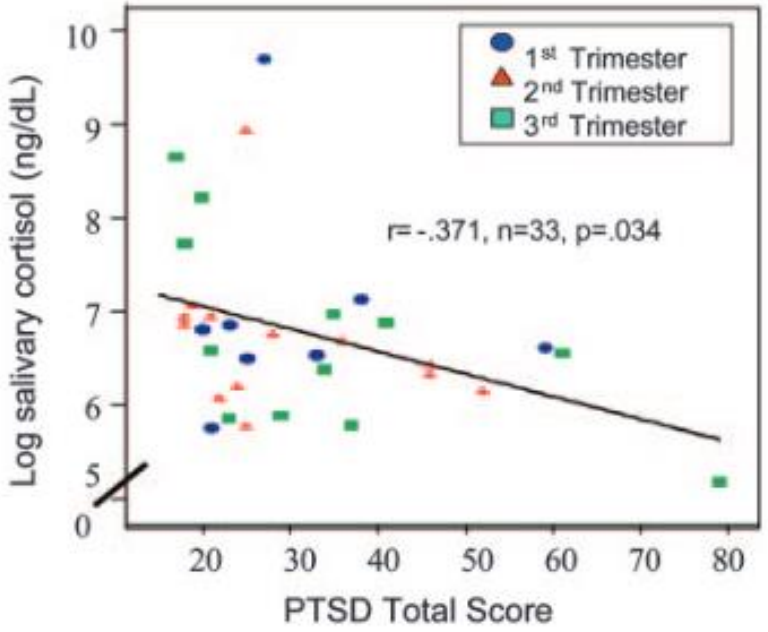


FIG. 1. Infant cortisol levels at awakening and bedtime, divided on the basis of presence or absence of maternal PTSD. The *darkened vertical lines* in each *box* represent the median values for the data, with the *boxes* representing data points within the upper and lower hinges (75th and 25th percentiles). No data points were more than 1.5 times the interquartile range from the median (*i.e.* outliers). The log-transformed mean awakening cortisol levels in infants with and without maternal PTSD, respectively, were 6.39 ± 0.51 (176.30) and 7.14 ± 1.14 (196.99) pmol/liter, and bedtime levels were 4.90 ± 0.79 (135.19) and 7.14 ± 1.14 (196.99) pmol/liter.

FIG. 2. Correlation between maternal PTSD symptom severity and infant log-transformed salivary cortisol levels at awakening. *Circles*, Data from mothers exposed in their first trimester ($r = -0.029$, $n = 8$; $P = 0.945$); *triangles*, data from mothers exposed in their second trimester ($r = -0.293$, $n = 13$; $P = 0.331$); *squares*, mothers exposed in their third trimester ($r = -0.605$, $n = 12$; $P = 0.037$). Mean salivary cortisol levels of infants of mothers with and without PTSD exposed at first trimester were 6.70 ± 0.29 (184.85) and 7.29 ± 1.69 (201.13) pmol/liter, respectively; second trimester, 6.46 ± 0.25 (178.23) and 6.84 ± 0.97 (188.72) pmol/liter, respectively; and third trimester, 6.16 ± 0.66 (169.95) and 7.51 ± 1.00 (207.20) pmol/liter, respectively.



PTBS & HHNA: integratives Modell

Neuroscience and Biobehavioral Reviews 69 (2016) 124–135

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review article

An integrative model linking traumatization, cortisol dysregulation and posttraumatic stress disorder: Insight from recent hair cortisol findings

Susann Steudte-Schmiedgen*, Clemens Kirschbaum, Nina Alexander, Tobias Stalder

Department of Psychology, Technische Universität Dresden, 01062 Dresden, Germany

PTBS & HHNA: integratives Modell

(Steudte-Schmiedgen et al., 2016)

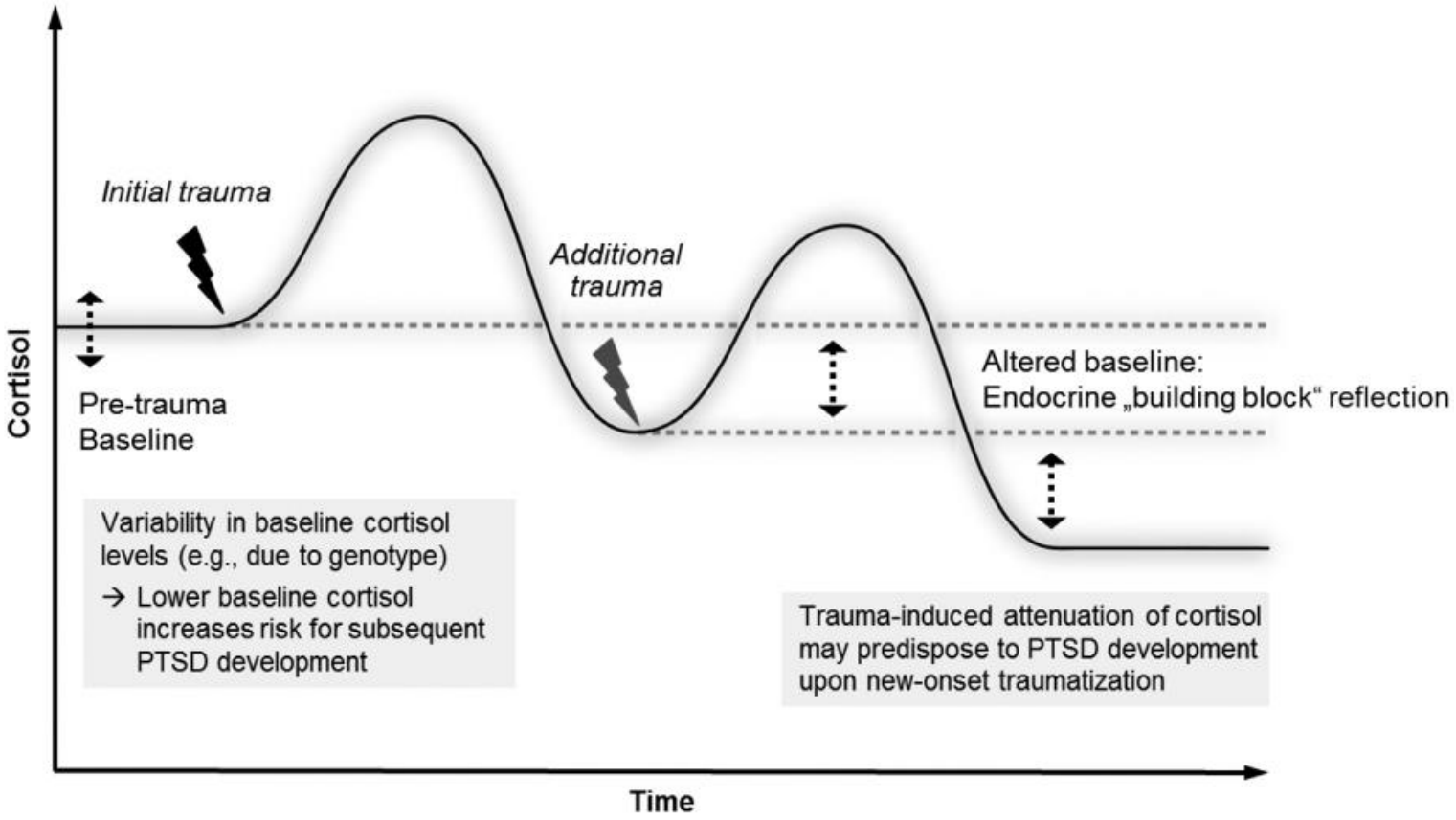
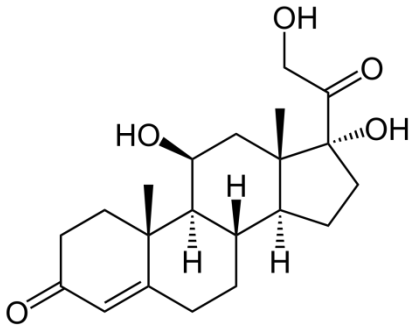


Fig. 1. Integrative model linking long-term cortisol secretion, traumatization and subsequent PTSD development. It is proposed that trauma exposure induces an initial upregulation of cortisol secretion which, over time, turns into a dose-dependent attenuation that may occur with or without the presence of PTSD. The variability in cortisol levels before traumatization (both initial and follow-on trauma) may be an important factor contributing to differential PTSD vulnerability. This may be explained by central glucocorticoid-mediated effects on the processing of trauma-related memories (e.g., Holz et al., 2014). Combined, these postulated processes may provide a psychoendocrine mechanism underlying previous findings of a dose-response relationship between the number of different lifetime traumatic events and the severity of PTSD symptoms (i.e., "building block effect"; Neuner et al., 2004).

PTBS & HHNA: positive Effekte von Cortisol?

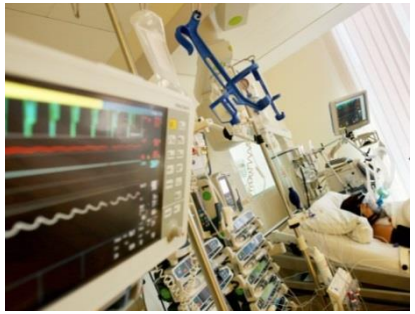
- möglicherweise „korrektere“ Speicherung des Traumas (d.h. Verknüpfung mit Raum- & Zeit-Informationen)
- möglicherweise kein spontaner Abruf der Trauma-Erinnerung (‚impaired retrieval of emotional material‘)
- eventuell Verringerung der erhöhten CRF-Freisetzung im ZNS mittels negativem Feedback



PTBS & HHNA: PTBS-Prävention durch Cortisolbehandlung? (Schelling et al., 2001)

The Effect of Stress Doses of Hydrocortisone During Septic Shock on Posttraumatic Stress Disorder in Survivors

Gustav Schelling, Josef Briegel, Benno Roozendaal, Christian Stoll, Hans-Bernd Rothenhäusler, and Hans-Peter Kapfhammer



Studiendesign:

- Patienten auf Intensivstation („intensive care unit“)
- Cortisol vs. Placebo während & nach OP
- AV: Anzahl der Patienten mit PTBS danach

PTBS & HHNA: PTBS-Prävention durch Cortisolbehandlung? (Schelling et al., 2001)

Ergebnisse:

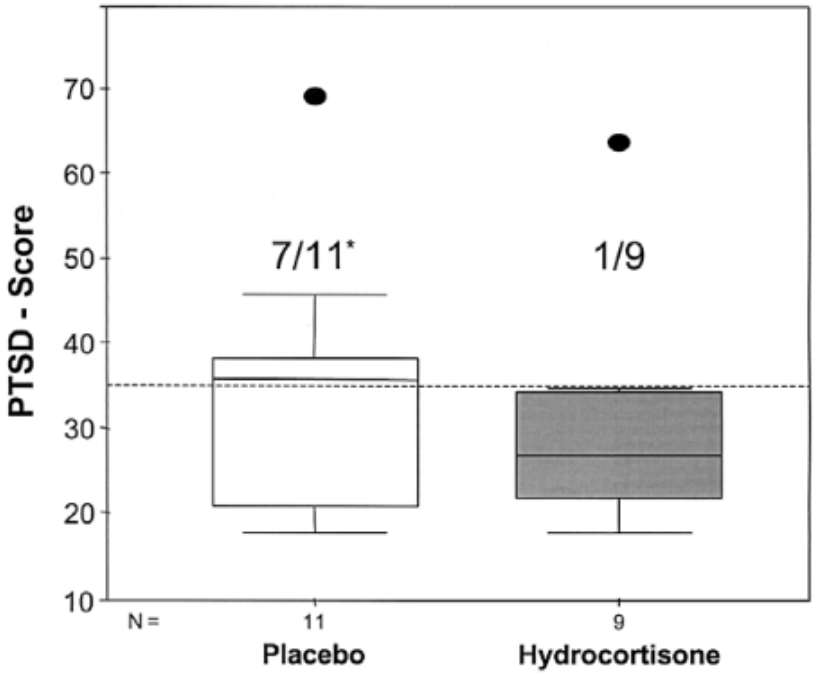


Figure 1. Boxplots comparison of PTSD scores between patients from the hydrocortisone and the placebo group. The broken line shows the 35 point cut off value of the PTSD questionnaire for diagnosis of PTSD (Stoll et al 1999). The numbers above the individual plots indicate the number of patients in both groups with PTSD scores above the threshold value of the questionnaire for diagnosis of PTSD (*p = .02). PTSD was confirmed by psychiatric interview in all patients. The "whiskers" at the top and bottom of each box indicate the minimal and maximal values of the distribution, respectively; the top and bottom of each box the 75th and 25th percentiles; the line through the box the median (the 50th percentile) and "●" indicates outliers (defined as a data value between 1.5 and 3 box lengths from the upper or lower edge of the box, the box length is the interquartile range).

PTBS & HHNA: PTBS-Therapie durch Cortisolbehandlung? (Aerni et al., 2004)

Low-Dose Cortisol for Symptoms of Posttraumatic Stress Disorder

Amanda Aerni, B.S.
Rafael Traber, M.S.
Christoph Hock, M.D.
Benno Roozendaal, Ph.D.
Gustav Schelling, M.D.
Andreas Papassotiropoulos, M.D.
Roger M. Nitsch, M.D.
Ulrich Schnyder, M.D.
Dominique J.-F. de Quervain, M.D.

Objective: Because elevated cortisol levels inhibit memory retrieval in healthy human subjects, the present study investigated whether cortisol administration might also reduce excessive retrieval of traumatic memories and related symptoms in patients with chronic posttraumatic stress disorder (PTSD).

Method: During a 3-month observation period, low-dose cortisol (10 mg/day) was administered orally for 1 month to three patients with chronic PTSD in a double-blind, placebo-controlled, crossover design.

Results: In each patient investigated, there was a significant treatment effect, with cortisol-related reductions of at least 38% in one of the daily rated symptoms of traumatic memories, as assessed by self-administered rating scales. In accordance, Clinician-Administered PTSD Scale ratings assessed after each month showed cortisol-related improvements for reexperiencing symptoms and, additionally, in one patient for avoidance symptoms.

Conclusions: The results of this pilot study indicate that low-dose cortisol treatment reduces the cardinal symptoms of PTSD.

(Am J Psychiatry 2004; 161:1488–1490)

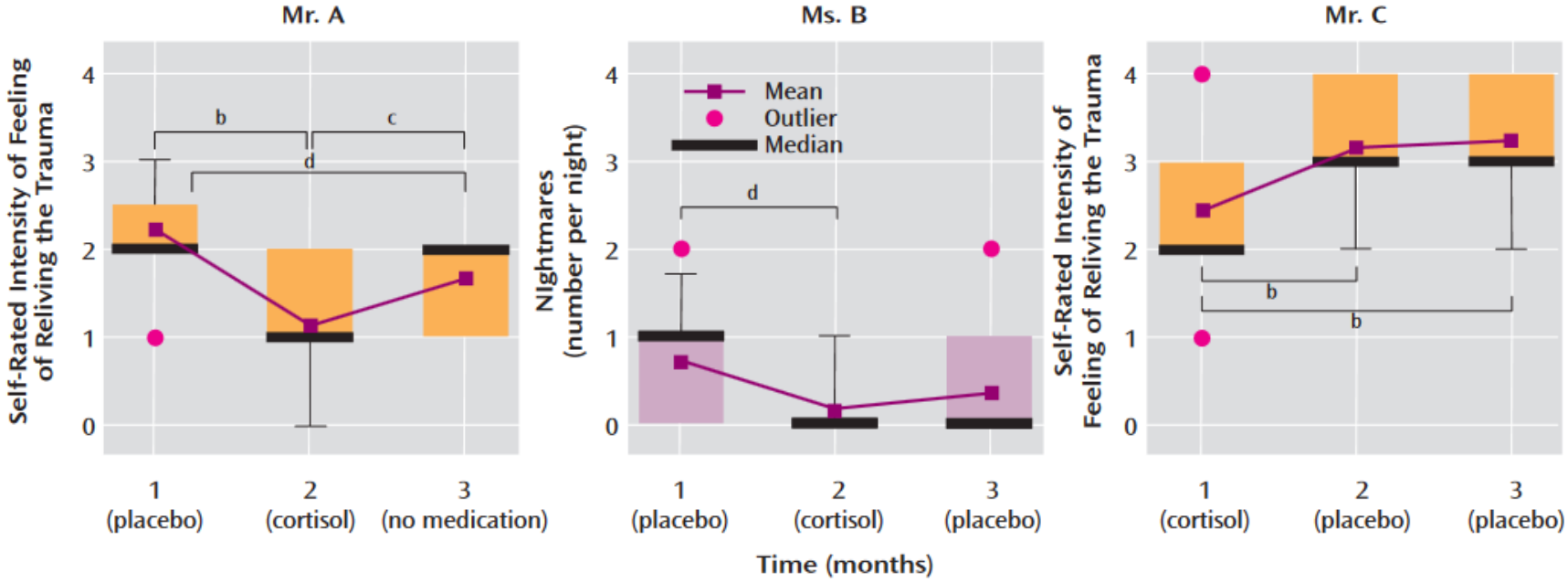
Studiendesign:

- 3 Patienten mit chronischer PTBS
- Cortisol (10 mg) vs. Placebo
- doppelblinde Crossover-Studie
- AV: berichtete Symptome

PTBS & HHNA: PTBS-Therapie durch Cortisolbehandlung? (Aerni et al., 2004)

Ergebnisse:

FIGURE 1. Effects of Cortisol Administration on Symptoms of Three Patients With Chronic PTSD[a]



PTBS & HHNA: PTBS-Therapie durch Cortisolbehandlung? (Yehuda et al., 2015)

Psychoneuroendocrinology (2015) 51, 589–597

Cortisol augmentation of a psychological treatment for warfighters with posttraumatic stress disorder: Randomized trial showing improved treatment retention and outcome

Rachel Yehuda[a,b,*], Linda M. Bierer[a,b], Laura C. Pratchett[a,b], Amy Lehrner[a,b], Erin C. Koch[a], Jaklyn A. Van Manen[a], Janine D. Flory[a,b], Iouri Makotkine[a,b], Tom Hildebrandt[b]

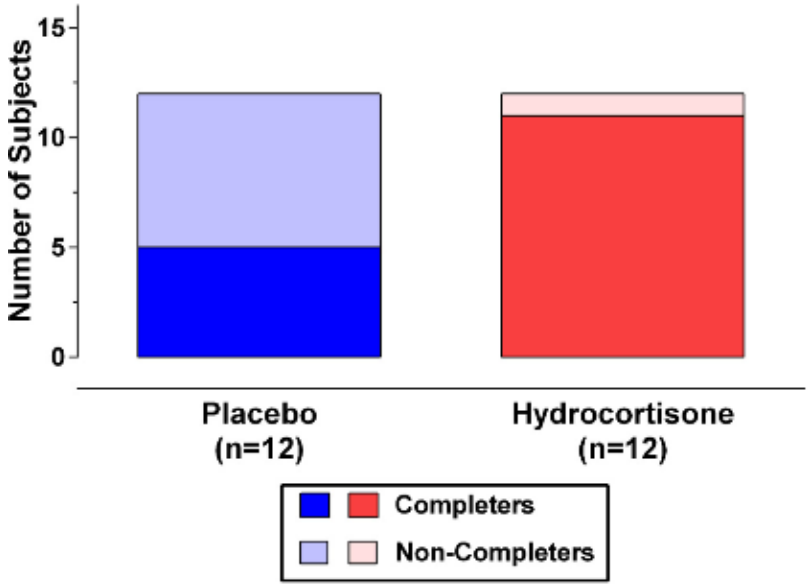


Figure 1 Comparison of treatment retention of randomized participants receiving placebo and hydrocortisone augmentation. As indicated in the text, hydrocortisone administration appeared to prevent the high rate of treatment associated drop-out.

PTBS & HHNA: PTBS-Therapie durch Cortisolbehandlung? (Yehuda et al., 2015)

Beziehung zur Glukocorticoidsensitivität?

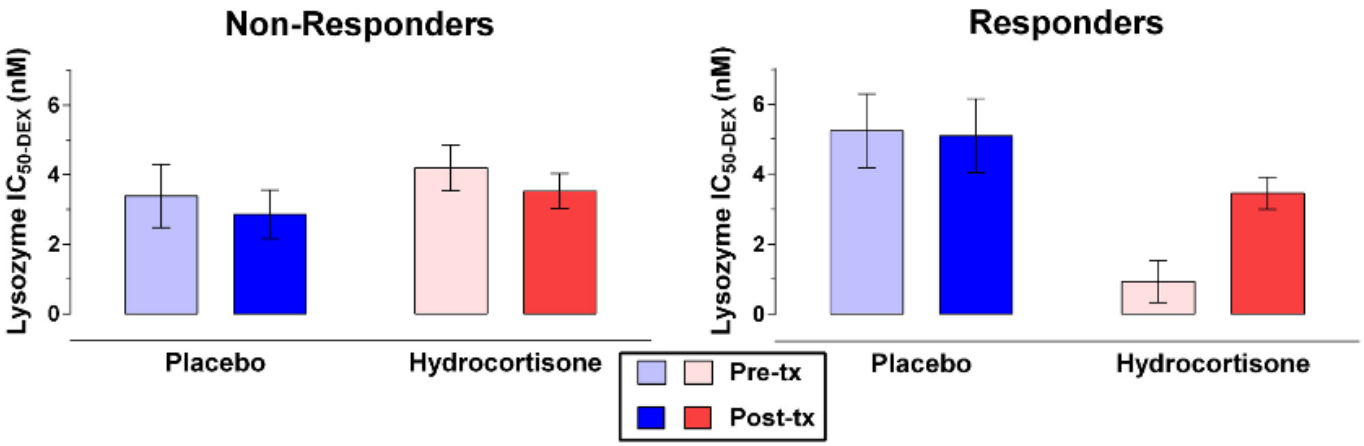


Figure 2 Comparison of glucocorticoid receptor sensitivity as reflected by the lysozyme inhibition test in responders vs. non-responders to treatment, showing a significant interaction of treatment condition and responder status. Figure depicts marginal means after accounting for age and current major depressive disorder, as described in the text.

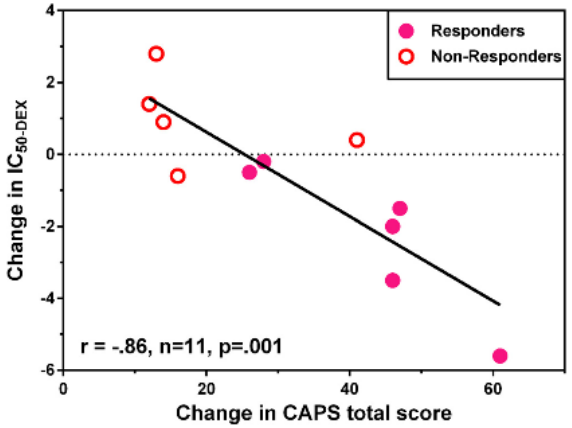


Figure 3 Relationship of PE associated clinical improvement (change in CAPS total score) with change in glucocorticoid sensitivity as assessed by the lysozyme $IC_{50\text{-}DEX}$ from pre- to post-treatment.

PTBS-Therapie durch Cortisolbehandlung?

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

Drug	Design	Timing and duration	Memory phase exposed	Outcome	Refs
Treatment of PTSD					
Cort	DB, PC, CO	Daily for 30 days	Retrieval	↓ Intrusions while under treatment	Aerni et al. 2004
Cort	DB, PC, CO	Daily for 7 days	Retrieval	No change in intrusions while under treatment	Ludascher et al. 2015
Cort	RCT	Single dose after exposure	Extinction	↓ PTSD symptoms at 1 week	Suris et al. 2010
Cort	RCT	20 min before exposure therapy, on 8 days	Retrieval and extinction	↓ PTSD symptoms at 6 weeks	Yehuda et al. 2015
Prevention of PTSD					
Cort	RCT	Starting < 12 h after trauma, for 10 days	Consolidation and retrieval	↓ PTSD symptoms at 3 months	Delahanty et al. 2013
Cort	RCT	Starting < 6 h after trauma, for 6 days	Consolidation and retrieval	↓ PTSD incidence at 31 months	Schelling et al. 2001
Cort	RCT	Starting < 6 h after trauma, for 4 days	Consolidation and retrieval	↓ Stress scores at 6 months	Schelling et al. 2004
Cort	RCT	Starting < 6 h after trauma, for 4 days	Consolidation and retrieval	↓ Stress scores at 6 months	Weis et al. 2006
Cort	RCT	Single dose < 6 h after trauma	Consolidation	↓ PTSD incidence at 3 months	Zohar et al. 2011
Dex	RCT	Single intraoperative dose	Consolidation	No difference in PTSD incidence at 18 months	Kok et al. 2016
Treatment of social phobia					
Cort	RCT	Single dose 1 h before phobic stimulus	Retrieval	↓ Fear while under treatment	Soravia et al. 2006
Treatment of spider phobia					
Cort	RCT	1 h before phobic stimulus, on 4 days	Retrieval and extinction	↓ Fear while under treatment	Soravia et al. 2006
Cort	RCT	1 h before exposure therapy, on 2 days	Retrieval and extinction	↓ Fear at 1 month	Soravia et al. 2014
Treatment of phobia of heights					
Cort	RCT	1 h before exposure therapy, on 3 days	Retrieval and extinction	↓ Fear at 1 month	de Quervain et al. 2011

Only randomized controlled trials (RCT) or double-blind (DB), placebo-controlled (PC), cross-over (CO) trials are included. Cort: Cortisol; Dex: Dexamethasone. Adapted from (de Quervain et al. 2017)

de Quervain, Wolf & Roozendaal, 2019

Pharmacological prevention and early treatment of post-traumatic stress disorder and acute stress disorder: a systematic review and meta-analysis

Laurence Astill Wright[1], Marit Sijbrandij[2], Rob Sinnerton[1], Catrin Lewis[1], Neil P. Roberts[1,3] and Jonathan I. Bisson[1]

Abstract

Post-traumatic stress disorder (PTSD) is a common mental disorder associated with significant distress and reduced functioning. Its occurrence after a severe traumatic event and association with characteristic neurobiological changes make PTSD a good candidate for pharmacological prevention and early treatment. The primary aim for this systematic review and meta-analysis was to assess whether pharmacological interventions when compared to placebo, or other pharmacological/psychosocial interventions resulted in a clinically significant reduction or prevention of symptoms, improved functioning or quality of life, presence of disorder, or adverse effects. A systematic search was undertaken to identify RCTs, which used early pharmacotherapy (within three months of a traumatic event) to prevent and treat PTSD and acute stress disorder (ASD) in children and adults. Using Cochrane Collaboration methodology, RCTs were identified and rated for risk of bias. Available data was pooled to calculate risk ratios (RR) for PTSD prevalence and standardised mean differences (SMD) for PTSD severity. 19 RCTs met the inclusion criteria; 16 studies with adult participants and three with children. The methodological quality of most trials was low. Only hydrocortisone in adults was found to be superior to placebo (3 studies, *n* = 88, RR: 0.21 (CI 0.05 to 0.89)) although this was in populations with severe physical illness, raising concerns about generalisability. No significant effects were found for the other pharmacotherapies investigated (propranolol, oxytocin, gabapentin, fish oil (1470 mg DHA/147 mg EPA), fish oil (224 mg DHA/22.4 mg EPA), dexamethasone, escitalopram, imipramine and chloral hydrate). Hydrocortisone shows the most promise, of pharmacotherapies subjected to RCTs, as an emerging intervention in the prevention of PTSD within three months after trauma and should be a target for further investigation. The limited evidence for hydrocortisone and its adverse effects mean it cannot be recommended for routine use, but, it could be considered as a preventative intervention for people with severe physical illness or injury, shortly after a traumatic event, as long as there are no contraindications. More research is needed using larger, high quality RCTs to establish the most efficacious use of hydrocortisone in different populations and optimal dosing, dosing window and route. There is currently a lack of evidence to suggest that other pharmacological agents are likely to be effective.

PTBS: Hippocampusvolumen

- Überblick
- HNNA-Veränderungen
- **Hippocampusvolumen**

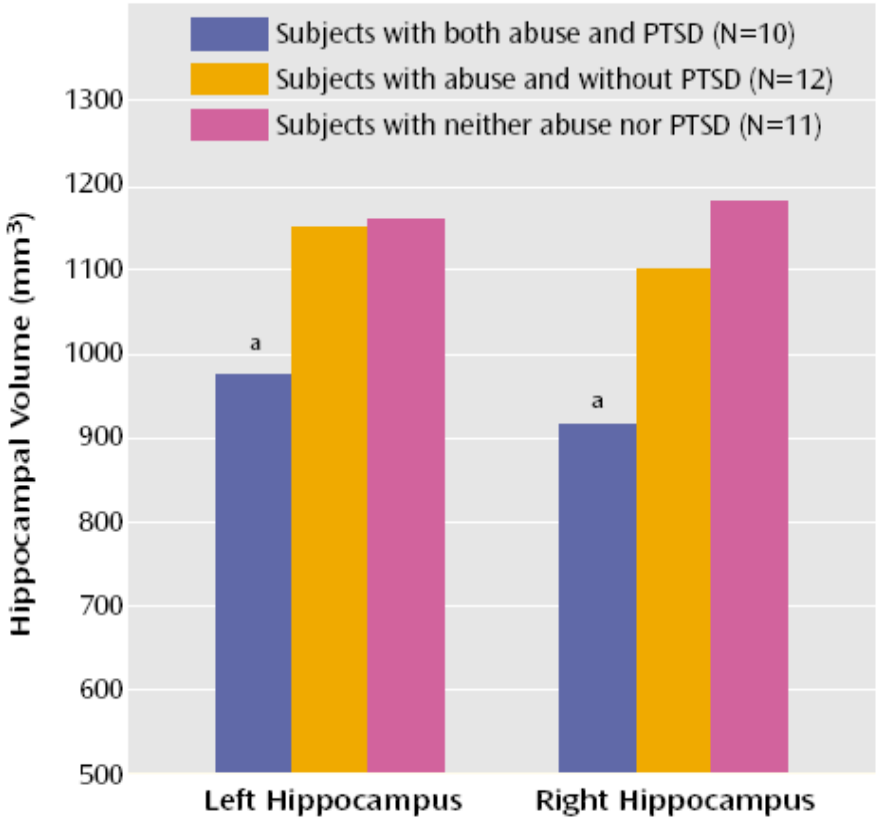
Current Concepts

POST-TRAUMATIC STRESS DISORDER

RACHEL YEHUDA, PH.D.

PTBS & Hippocampusvolumen: Missbrauch (Bremner et al., 2003)

FIGURE 1. Left and Right Hippocampal Volumes as Measured With MRI in Women With and Without Childhood Sexual Abuse and PTSD



[a] Women with abuse and PTSD differed significantly from women

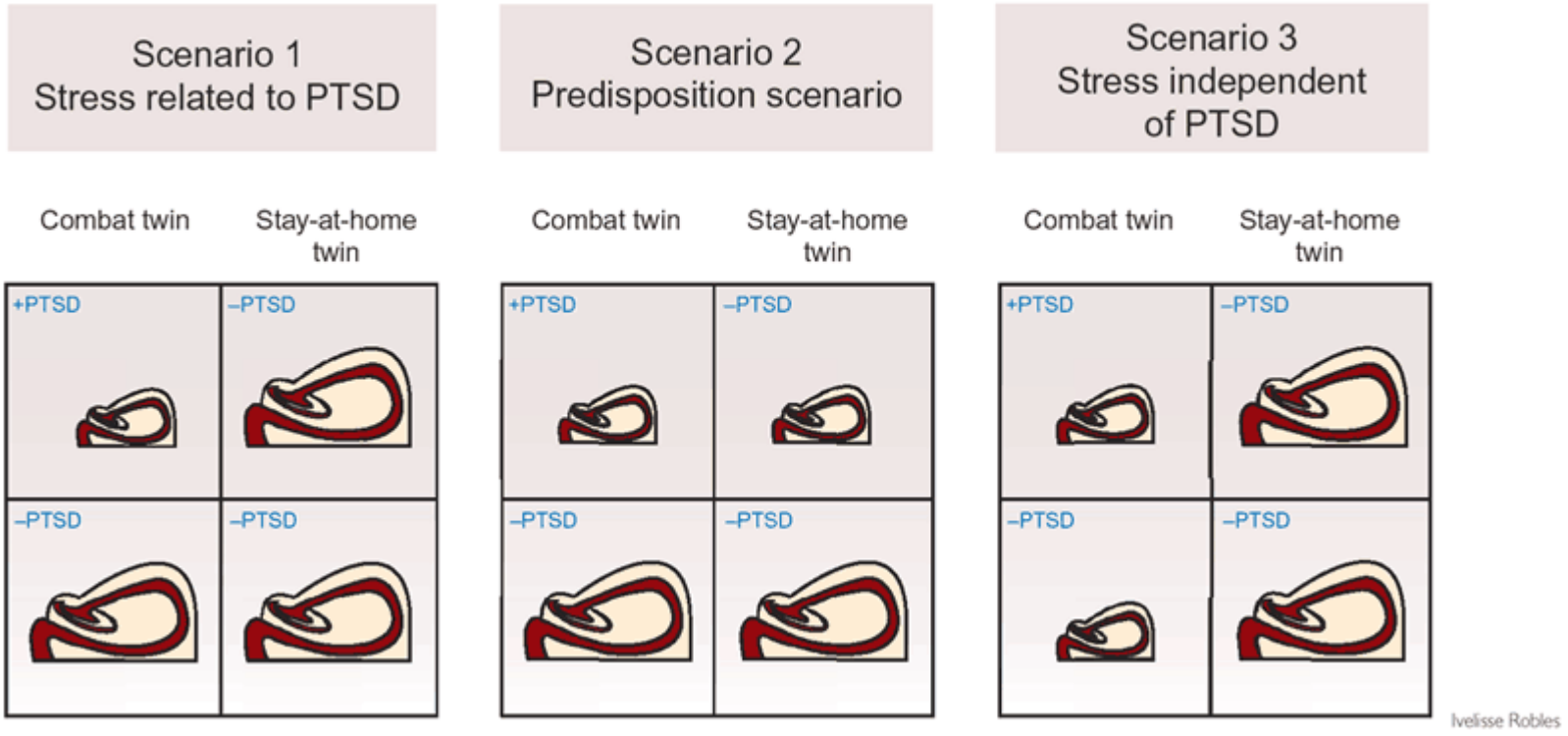
PTBS & Hippocampusvolumen: offene Fragen

RUB

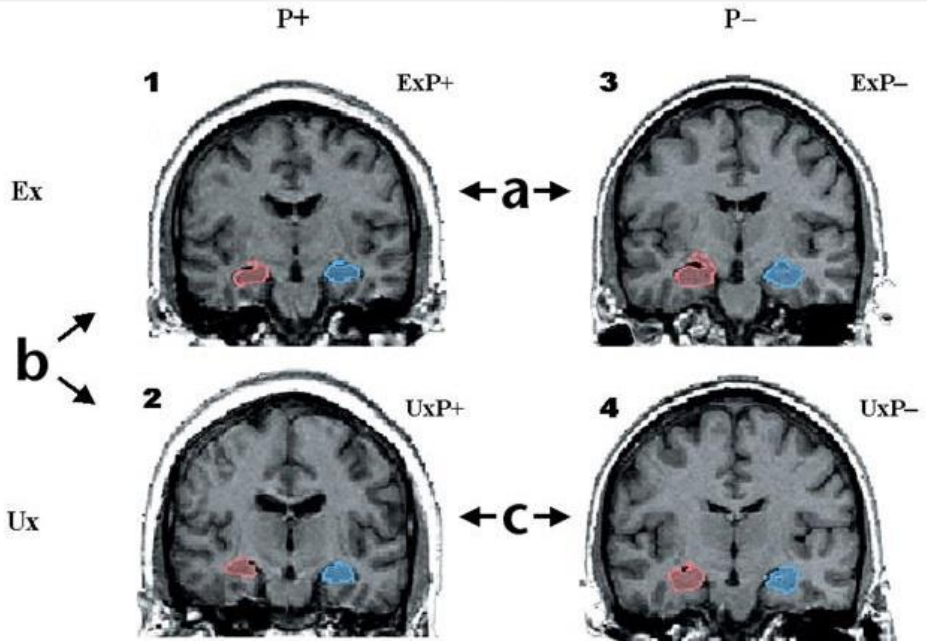
Ursache-Wirkungs-Beziehung?

- Wie könnte man das empirisch testen?
- Studienvorschläge?

PTBS & Hippocampusvolumen: Zwillingsstudie (Sapolsky, 2002)

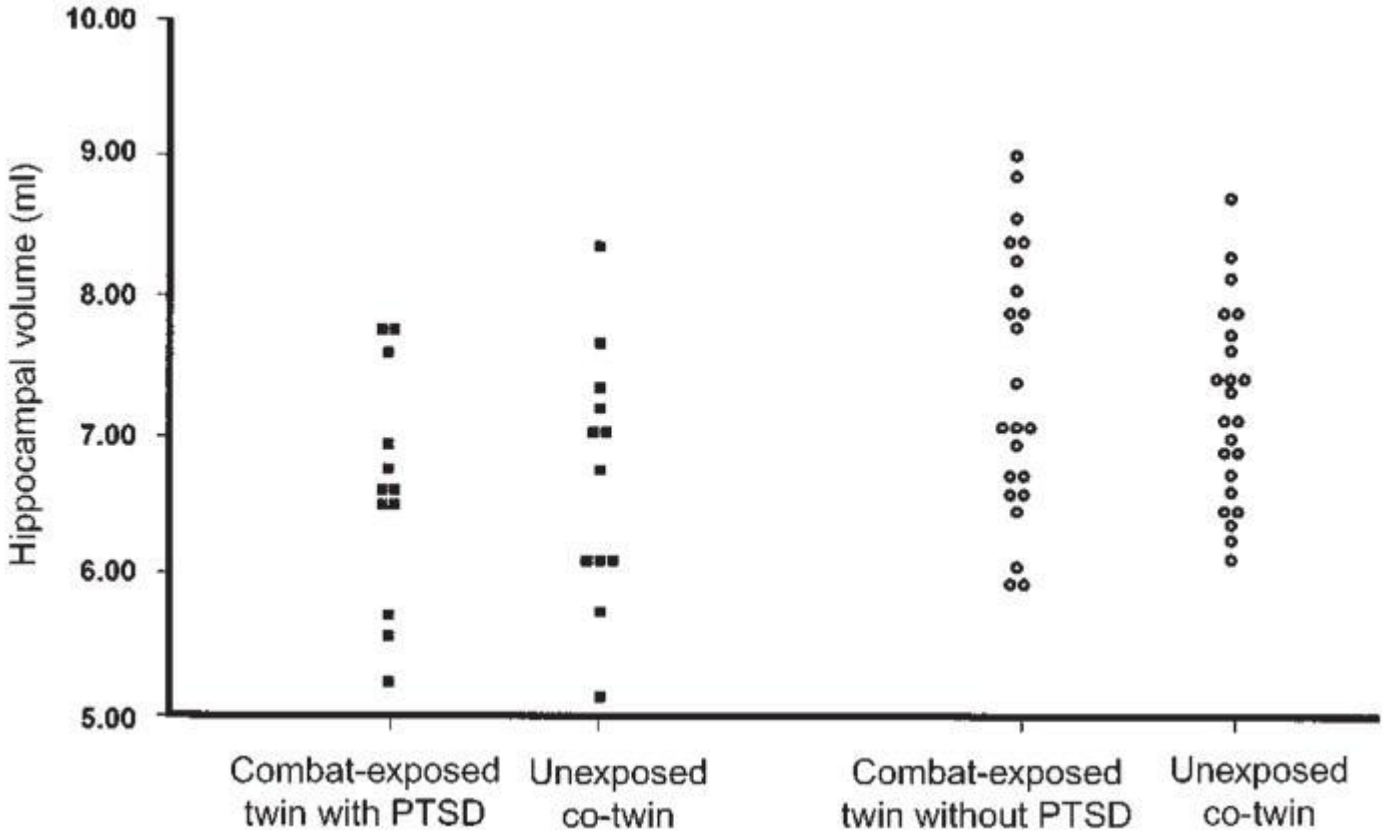


PTBS & Hippocampusvolumen: Zwillingsstudie (Gilbertson et al., 2002)



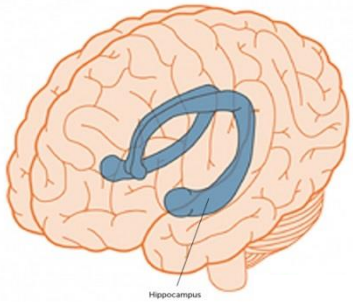
Discordant monozygotic twin paradigm for assessing MRI differences in PTSD. Sample coronal MRI images of right (red) and left (blue) hippocampi in a PTSD and a non-PTSD twin pair. Images represent four subject groups: (1) combat-exposed (Ex) subjects who developed chronic PTSD (ExP+); (2) their combat-unexposed (Ux) co-twins with no PTSD themselves (UxP+); (3) Ex subjects who never developed PTSD (ExP−) and (4) Ux co-twins also with no PTSD (UxP−). Contrast (**a**) provides a replication of previous work demonstrating smaller hippocampal volumes in combat veterans with versus without PTSD. Contrast (**b**) identifies the neurotoxicity effect—hippocampal reduction—as environmentally acquired, by contrasting hippocampal volumes in combat-exposed PTSD veterans with their unexposed co-twins. Contrast (**c**) examines pre-existing vulnerability by contrasting hippocampal volumes in the two groups of combat-unexposed co-twins whose combat-exposed brothers did versus did not develop PTSD. Model is tested by a diagnosis (P+ versus P−) × exposure (Ex versus Ux) ANOVA. Diagnosis refers to combat-exposed twin only. If hippocampal volume represents a vulnerability factor, the model predicts a significant main effect of diagnosis in the absence of a diagnosis × exposure interaction (that is, PTSD combat-exposed veterans and their unexposed co-twins show the same pattern). If hippocampal reduction results from neurotoxicity, the model predicts a significant main effect of exposure and/or a significant diagnosis × exposure interaction.

PTBS & Hippocampusvolumen: Zwillingsstudie (Gilbertson et al., 2002)

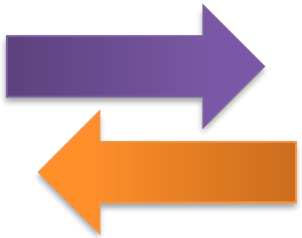


PTBS: viele offene Fragen!

- basal niedrigere Cortisolspiegel?
- kleinere Hippocampi



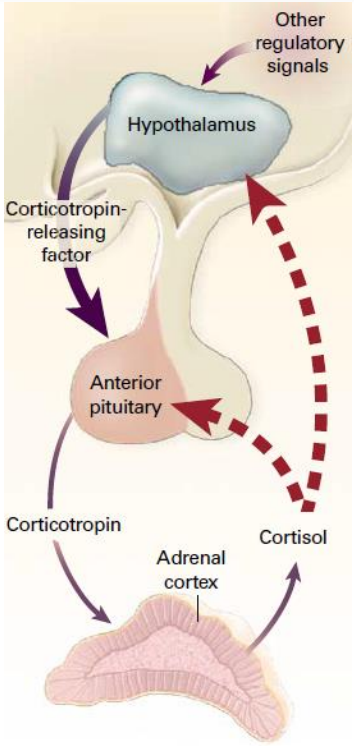
- Risikofaktoren oder Folge von frühkindlichem Stress?



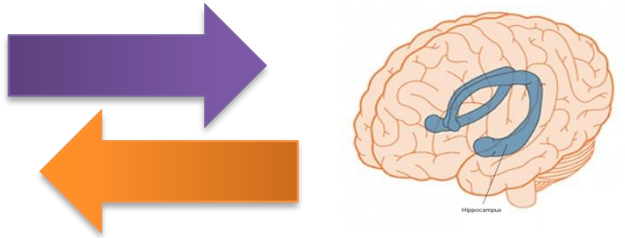
- Wirkung von Cortisol-Therapie? Falls ja, wie?

Zusammenfassung

- **HHNA-Veränderungen**:
  - Hypocorticolismus (basal)
  - reduzierte Cortisol-Aufwachreaktion
  - positive Effekte von Cortisol?
    → Prävention & Therapie?



- **Hippocampusvolumen**:
  - verkleinert
    → Folge vs. Risikofaktor?



Hinweise zur Klausur

- Multiple Choice Klausur im K-prim Format
  - Jede Frage hat vier Antwortmöglichkeiten die jeweils (!) nach wahr oder falsch beurteilt müssen.
  - Stoffplan sind die Schnittmenge aus den Vorlesungen und der Prüfungsliteratur

Beurteilen Sie die folgenden Aussagen über den Schlaf

Antwort	wahr	falsch
In der ersten Nachthälfte dominiert der REM Schlaf		
In der zweiten Nachthälfte dominiert der SWS Schlaf		
In der ersten Nachthälfte sind die körpereigenen Cortisol-spiegel erhöht		
In der ersten Nachthälfte sind die körpereigenen Acetylcholin Spiegel erniedrigt		

Hinweise zur Klausur

- Am 19.2.26 von 15:00 bis 16:00
- 60 Minuten Schreibzeit
- GAFO E-Exam

Feedback

- Was fanden Sie interessant?
- Was kam zu kurz?
- Was war zu viel?

Zum Schluss…

- viel Erfolg bei der Klausur!

- viel Spaß weiterhin im Studium!
- schöne Semesterferien!
- bei Interesse an einer Masterarbeit zum Thema Stress gerne jederzeit bei uns melden!