

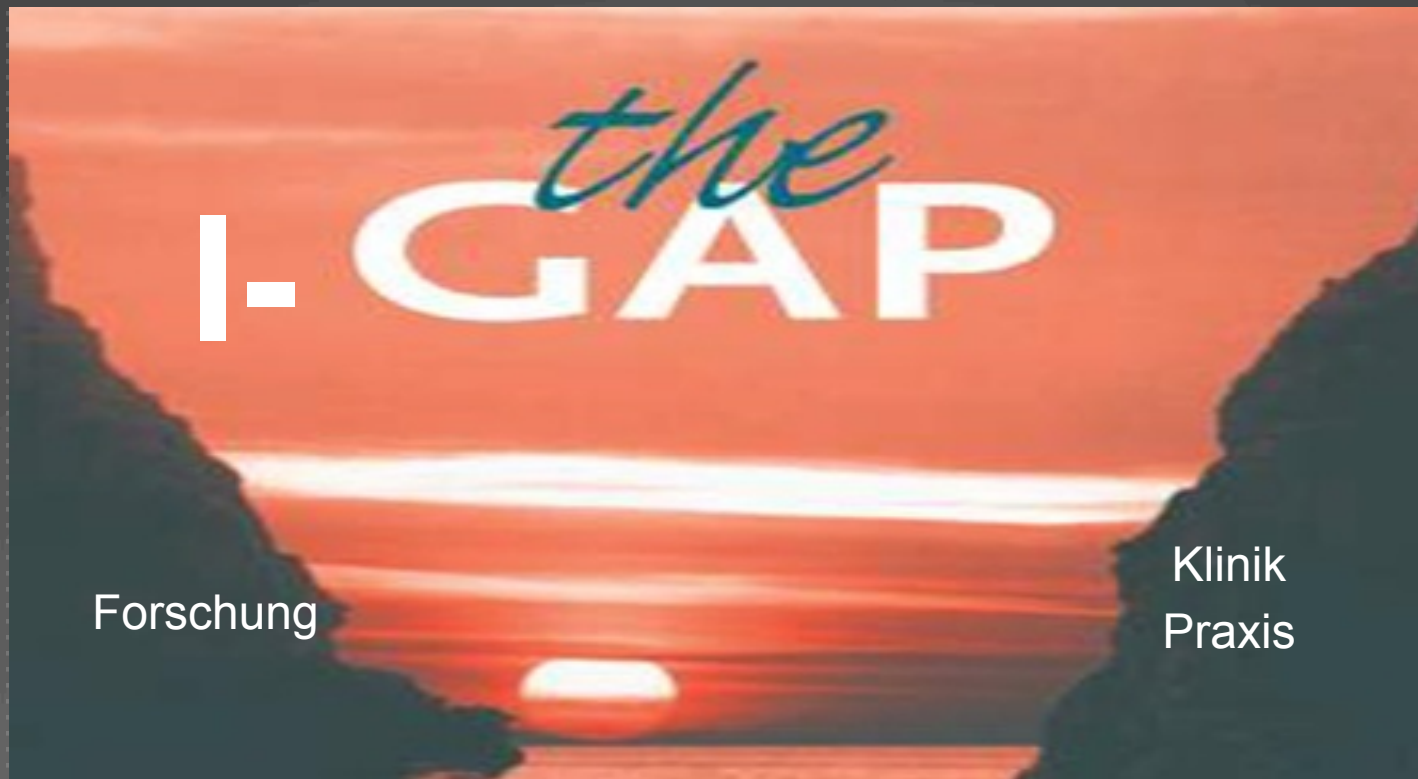
Stress-Burnout- Chronic Fatigue Syndrome Differentialdiagnose und Mikronährstofftherapie

**Assoc.
Prof.Drmed.Dr.habil.Dr.phil(PhD)
Claus Muss**

St.Elisabeth Univeriät für Forschung und
Soziales Bratislava (EU)Lehrstuhl für Public
Health –Öffentliches Gesundheitswesen

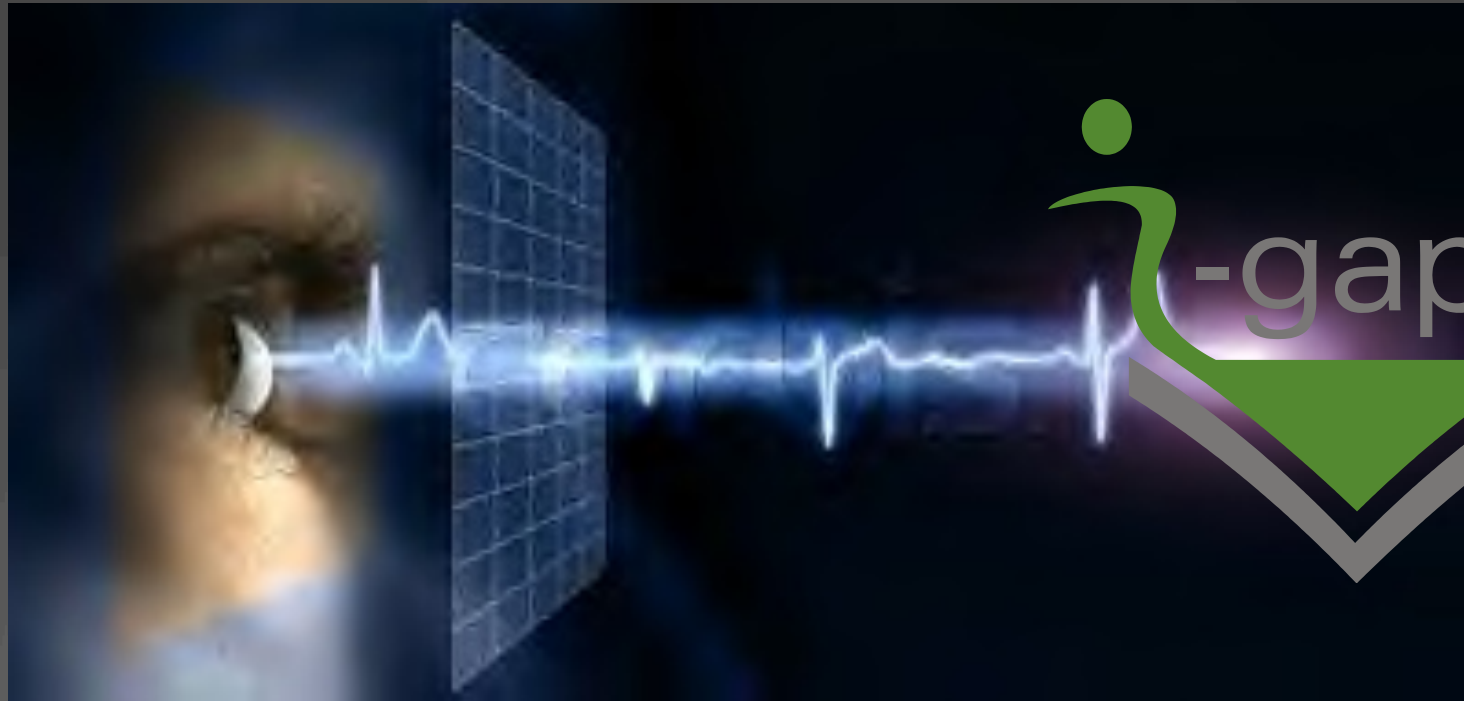
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- ▶ Unterstützung bei Therapiefragen
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- ▶ Hotline Befundinterpretation(Biovis)

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- ▶ Wissenschaftliche Studien (Labor/Biomarker, medizinische Zusammenhänge, Produktstudien)
- ▶ Vermittlung von Fachjuristen bei Rechtsfragen

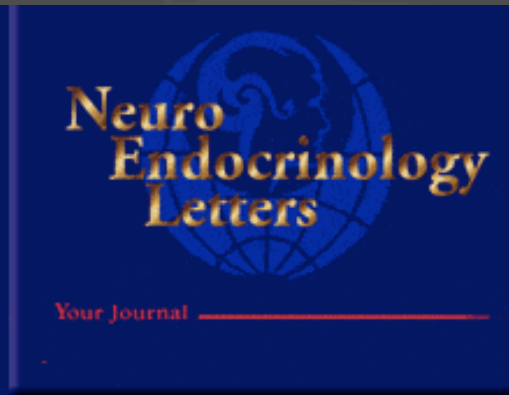
Ausbildung

- ▶ Seminare online
- ▶ Nebenberufliche Studiengänge Präventionsmedizin, Doktoranden Betreuung

**ST. ELISABETH UNIVERSITY
BRATISLAVA
*NEUROENDOCRINOIMMUNOLOGY***



PEER VIEWED PUBMED LISTED



NEUROENDOCRINOLOGY LETTERS

**Included Psychoneuroimmunology, Neuropsychopharmacology, Reproductive Medicine,
Chronobiology and Human Ethology - ISSN 0172-780X Copyright © 2013
Neuroendocrinology Letters**

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WAS IST STANDARD IN DER PRÄVENTIONSMEDIZIN?



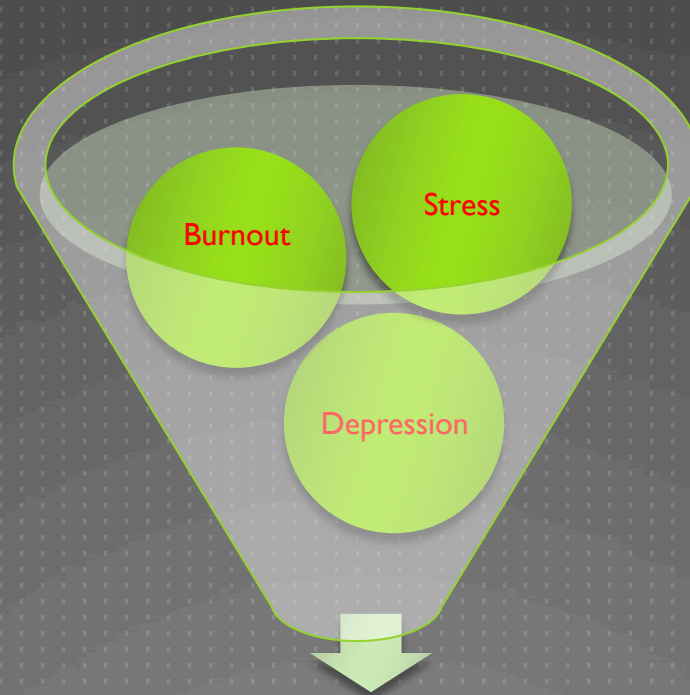
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„Wo kämen wir hin, wenn jeder sagte, wo kämen wir hin und keiner ginge, um zu sehen, wohin wir kämen, wenn wir gingen.“

Kurt Marti

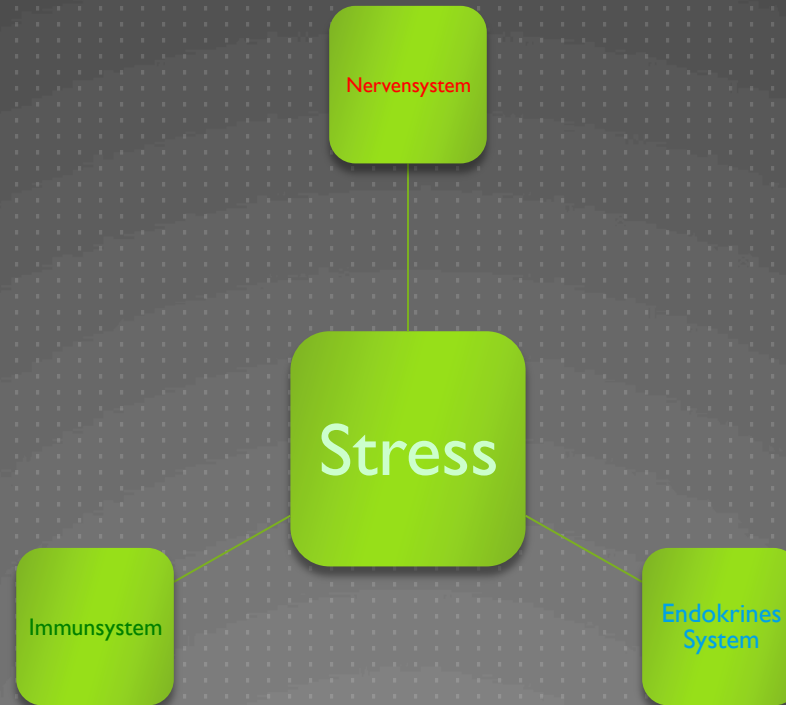


Molekularbiologische Überlegungen zum THEMA STRESS



Neuroendokrinoimmunologie

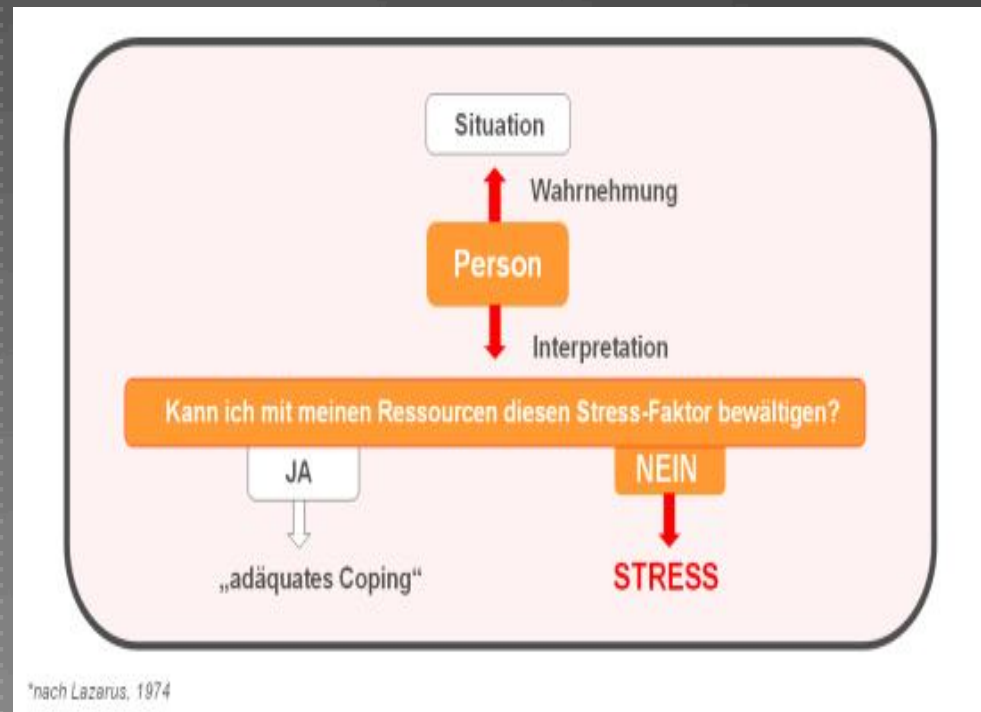
Stress wirkt auf Die grundregulation großer Organsysteme



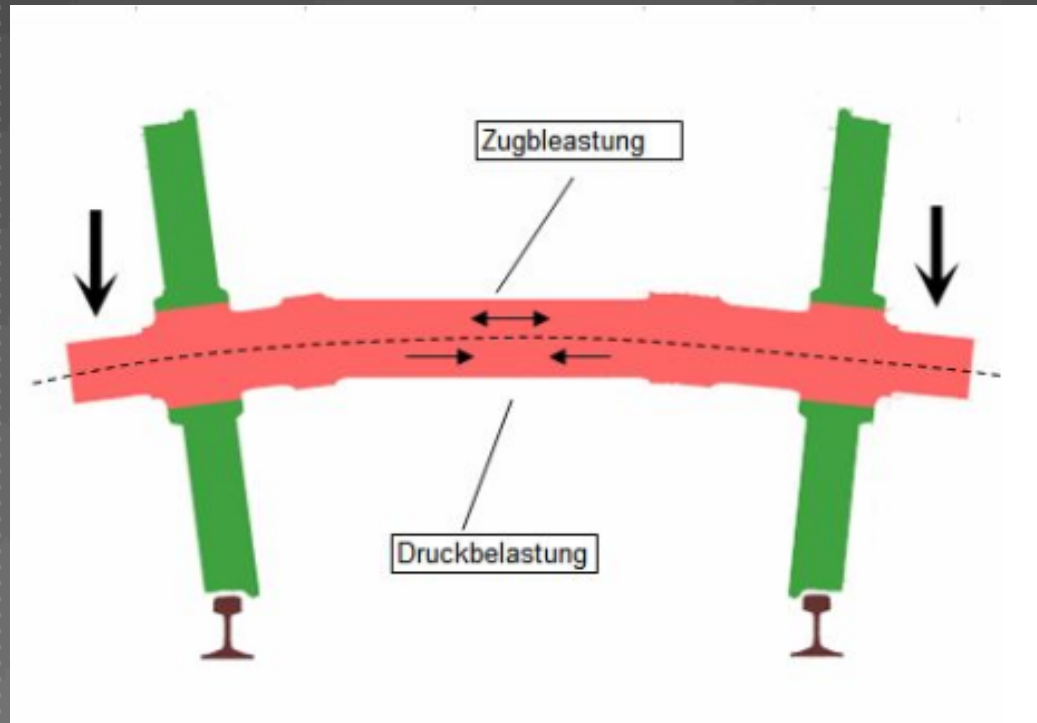
DEFINITION STRESS ?

- Stress ist ein Missverhältnis zwischen den Anforderungen und individuellen Ausgleichsmöglichkeiten, wie positives Erleben, Selbstbestätigung, Entspannung und Ähnliches.

„Lazarus Modell“

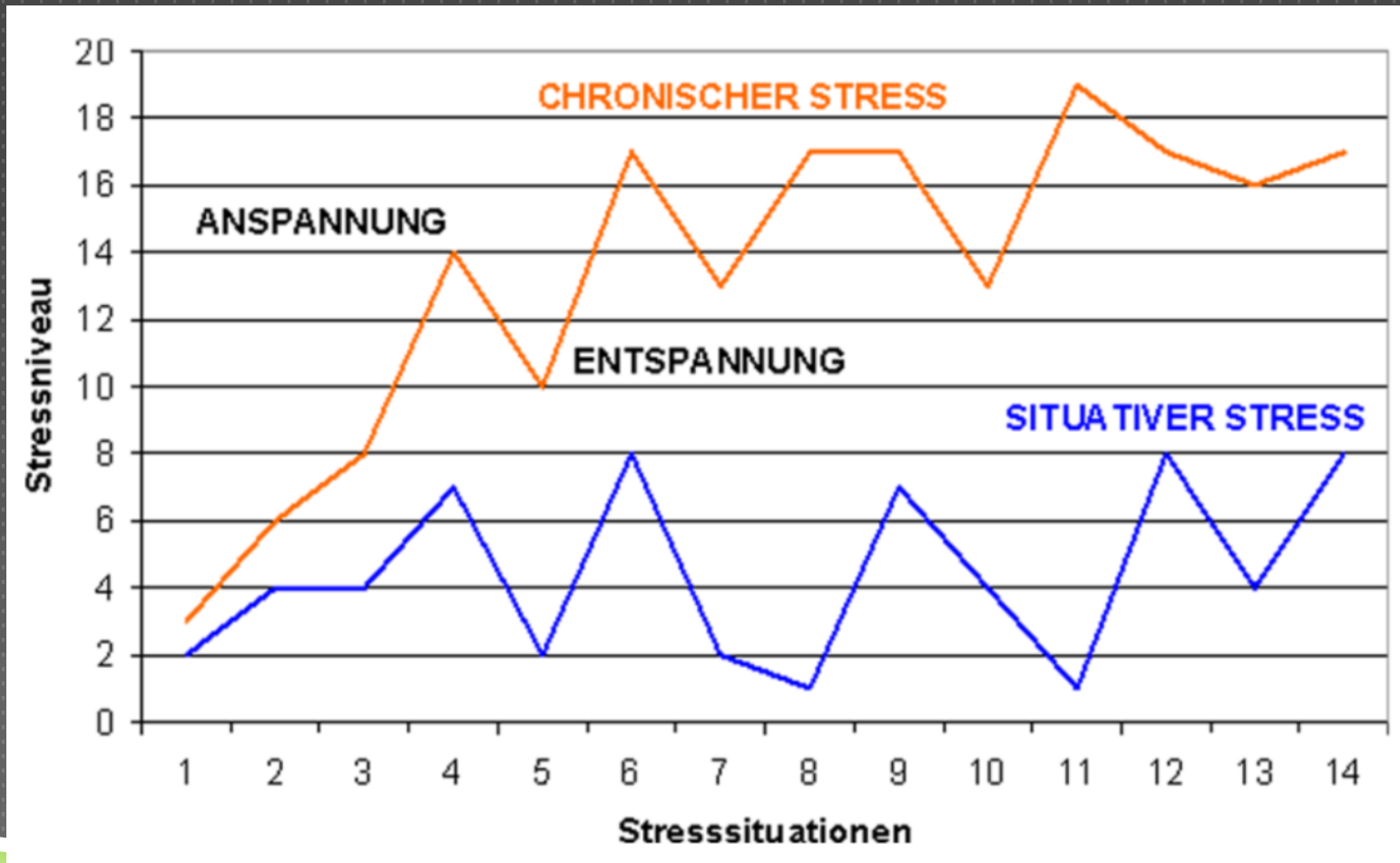


STRESS LÖST ZUG UND DRUCK (IM KÖRPER) AUS



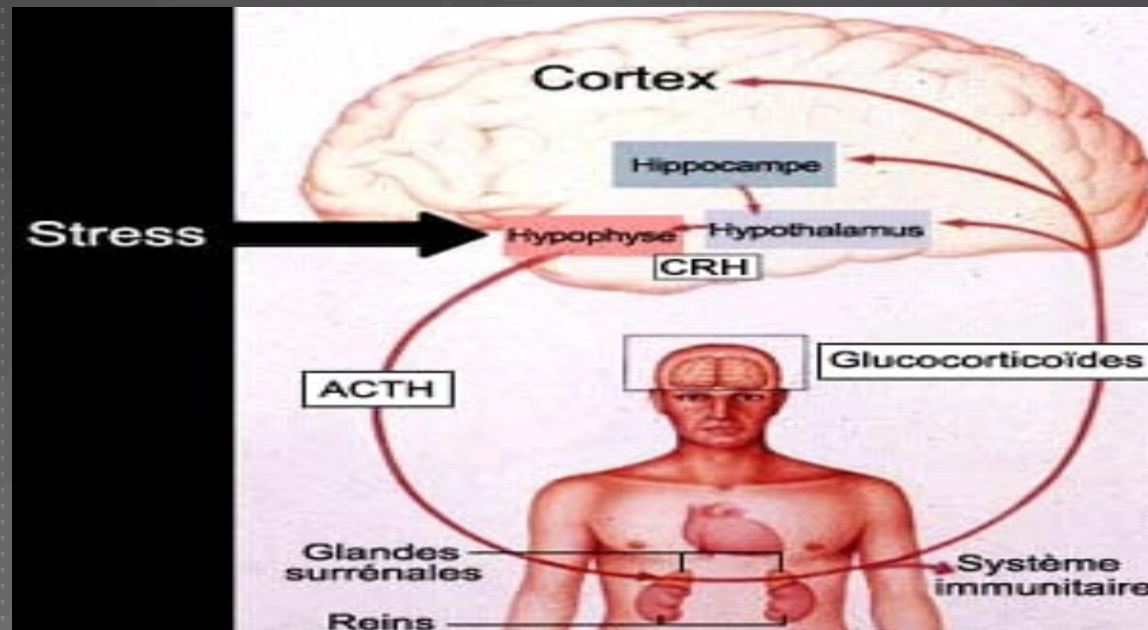
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STRESSADAPTION



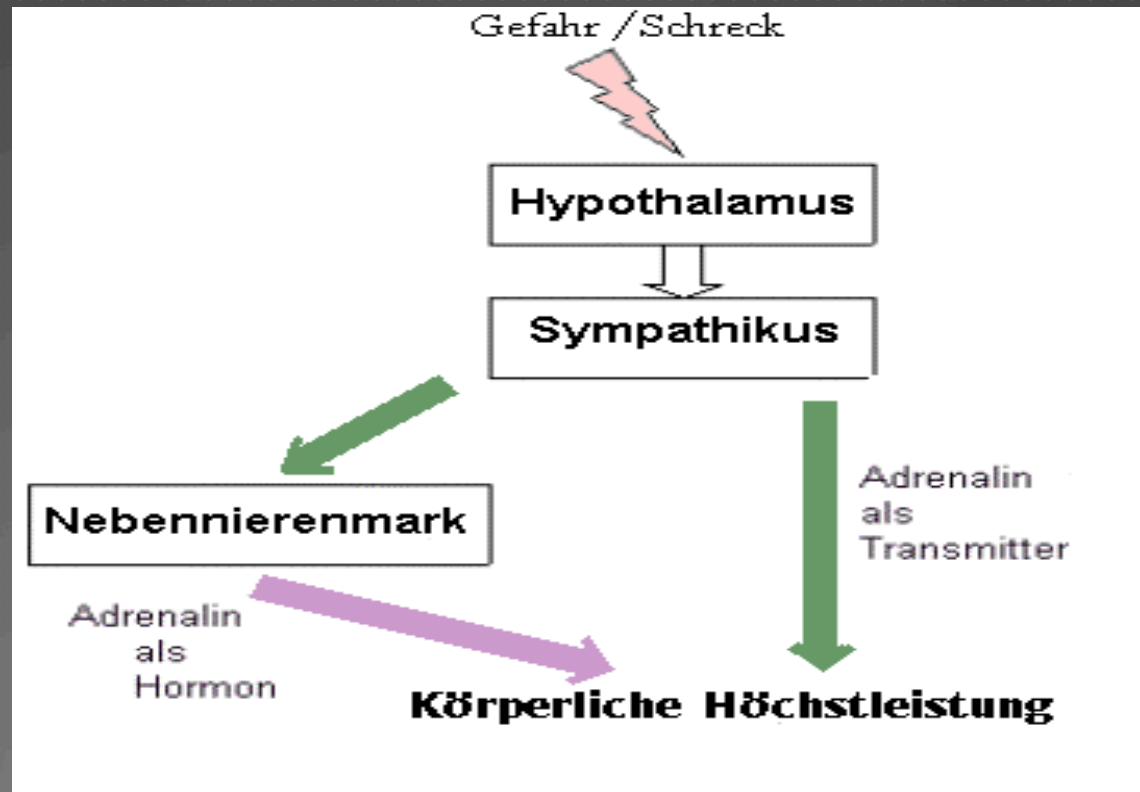
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für angewandte Präventionsmedizin
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STRESS KREISLAUF DER NEUROTRANSMITTER

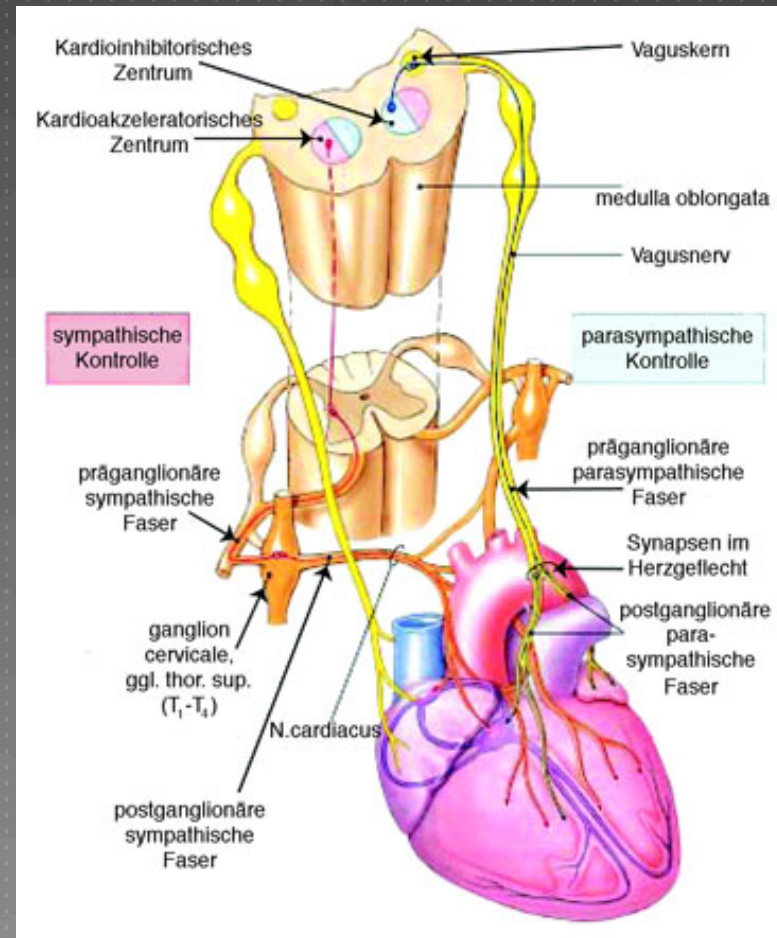


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UNMITTELBARE AKUTE STRESS ANTWORT



Das Vegetativum – Unser unbekanntes Wesen-

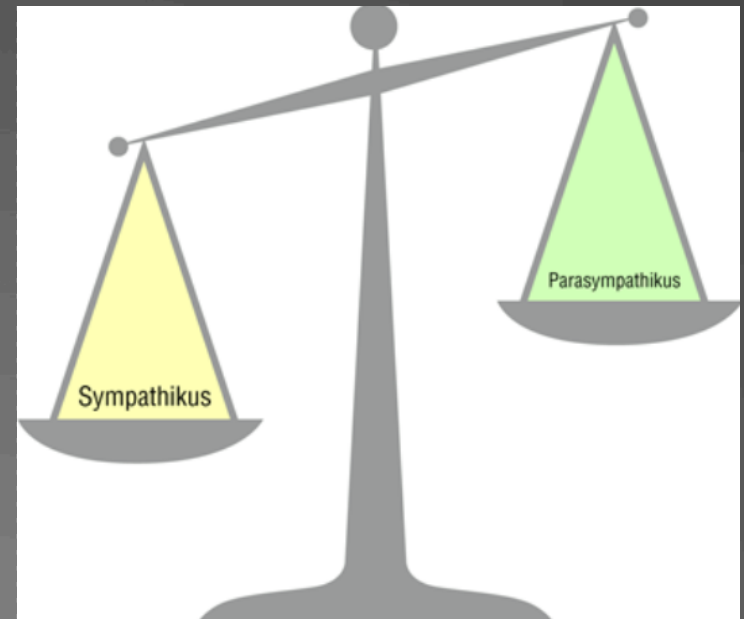


FUNKTIONSUNTERSCHIEDE SYMPATIKUS/PARASYMPATIKUS

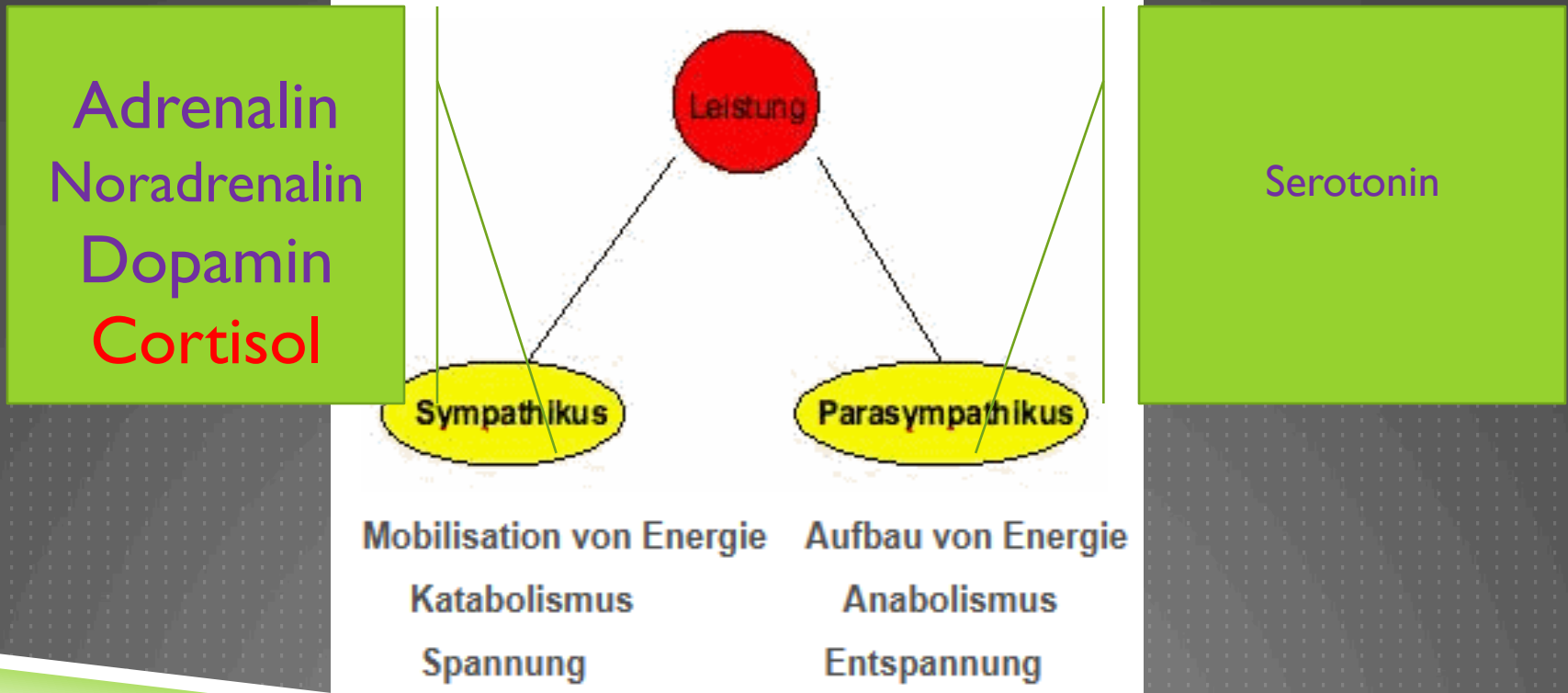
| Organ | Sympathikus | Parasympathikus |
|-----------------------------|---|---|
| Koronargefäße | Dilatation | Konstriktion |
| Pupillen | Erweiterung | Verengung |
| Bronchien | Dilatation | Konstriktion |
| Speiseröhre | Erschlaffung | Kontraktion |
| Magen | Hemmung | Anregung |
| Dünn- und Dickdarm | Hemmung | Anregung |
| Leber | Glykogenolyse, Gluconeogenese | – |
| Blase | Harnretention, Hemmung des Detrusors, Erregung des Sphinkters | Harnentleerung, Anregung des Detrusors, Erschlaffung des Sphinkters |
| Genitalien | Vasokonstriktion | Vasodilatation und Erektion |
| Nebennieren | Anregung der Adrenalinsekretion | Hemmung der Adrenalinsekretion |
| Stoffwechsel | Steigerung der Dissimilation | Steigerung der Assimilation |
| Pankreas (Insulinsekretion) | Hemmung | Anregung |
| Schilddrüse (Sekretion) | Anregung | Hemmung |

SYMPATHIKUS/ PARASYMPATHIKUS

| Elementarsituationen des Lebens | Zwei Teile des Vegetativums |
|--|--------------------------------|
| z.B. Agression, Angst, Sport, Straßenverkehr, Stress, Beruf | Sympathikus |
| z.B. Nahrungs- aufnahme, Verdauung, Ruhe, Erholung, Sexualität | Para- Sympathikus |

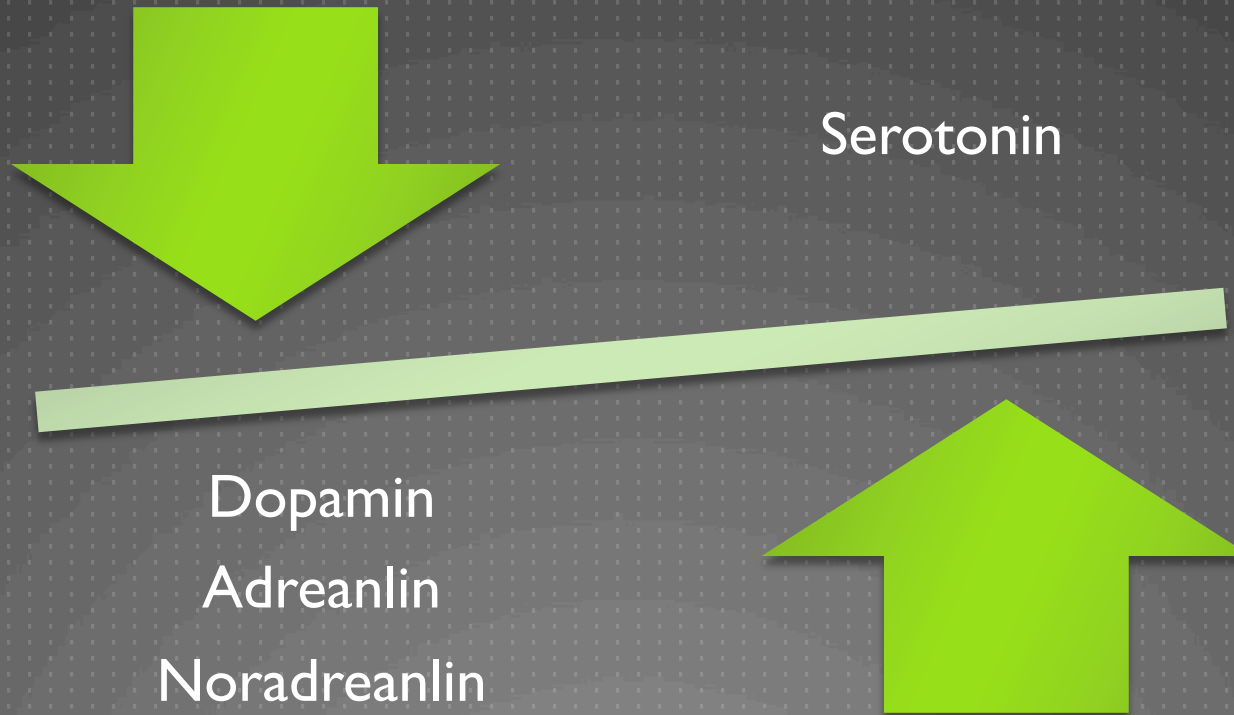


GRUNDREGULATION UND NEUROTRANSMITTER

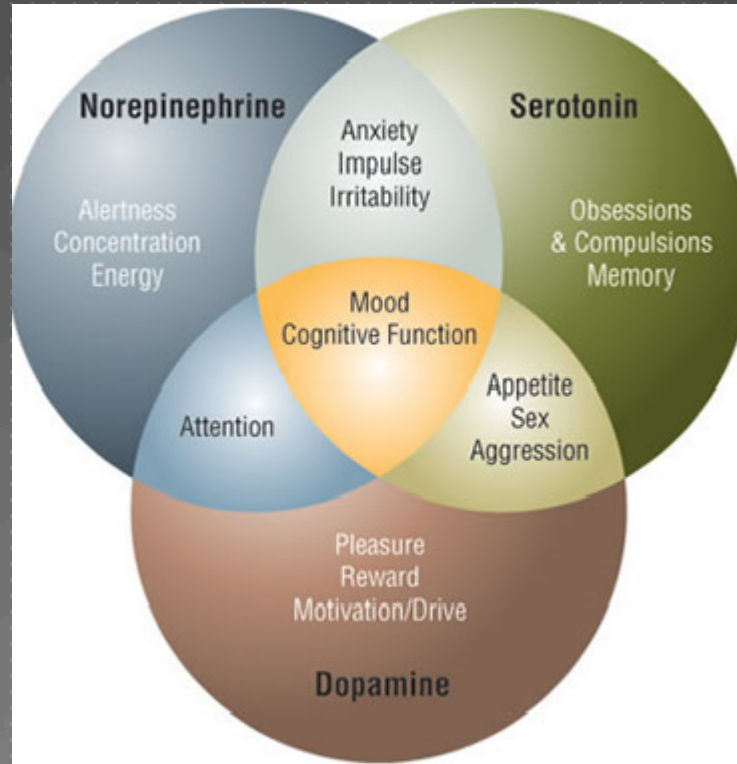


NEUROTRANSMITTER IM STRESS

-VEREINFACHTES MODELL BIOLOGISCHER
STRESSREGULATION-



EFFEKTE DER NEUROTRANSMITTER



Wie hängt das Nervensystem mit dem Stoffwechsel und Immunsystem zusammen?



ENDOKRINER SYMPATIKOTONUS

-VEREINFACHTES MODEL DES LANGFRISTIGEN STRESSES-



Cortisol

Insulin



Serotonin

DHEA

LANGZEIT STRESS AUF NT UND ENDOKRINUM

KLINISCHE UNTERSUCHUNG N=103 PATIENTEN

Interaction of Serotonin and Insulin production

Distribution of Serotonin and Insulin activity (Adiponectin)

| | N | Minimum | Maximum | Mean Average | Standard Deviation |
|---------------|-----|---------|---------|--------------|--------------------|
| SEROTONIN | 103 | 21,80 | 1233,80 | 151,0180 | 161,7139 |
| ADIPONECTIN | 100 | 1,40 | 26,00 | 8,0277 | 4,7075 |
| Valid results | 96 | | | | |

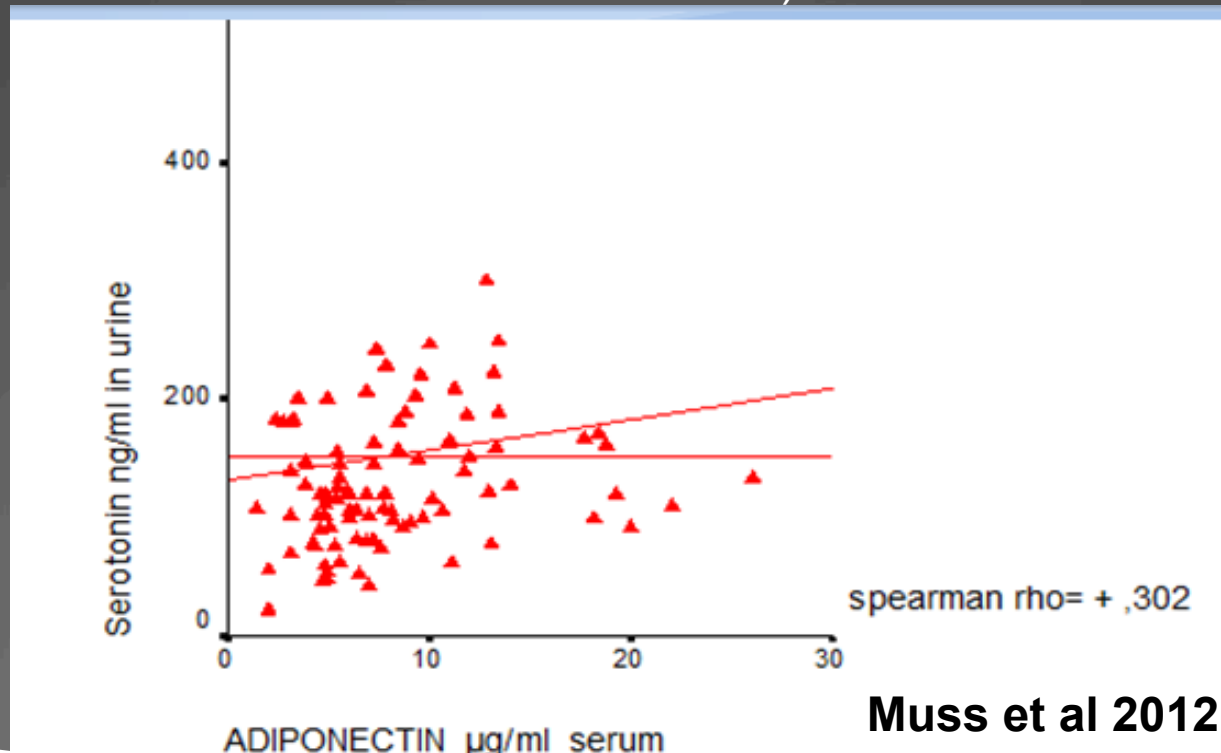
Correlation between Serotonin and Adiponectin in female and male

| | | Serotonin | Adiponectin |
|--------------|----------------|-----------|-------------|
| Spearman-Rho | Serotonin | 1,000 | ,302** |
| | Correlation | | ,003 |
| | Sig. (2-sided) | | ,003 |
| | | N | 96 |
| Adiponectin | Adiponectin | ,302** | 1,000 |
| | Correlation | | ,003 |
| | Sig. (2-sided) | | ,003 |
| | | N | 96 |

** . Significant correlation on the basis of $p < 0,01$ (two-sided).

NEGATIVE CORELATION OF SEROTONIN AND ADIPONECTIN IN SERUM

(CLINICAL SURVEY WITH N=103 PATIENTS)



WECHSELWIRKUNG DER NT IM CHRONISCHEM STRESS



Insulin



Serotonin

Kurzfristige Insulinausschüttung erhöht Serotonin Metabolismus
Langfristige Insulinausschüttung reduziert Serotonin Metabolismus

SEROTONIN CONTROLS INSULIN SECRETION



Serotonin and insulin release in vitro

| | |
|-------------------|--------------------------------------|
| Zeitschrift | Diabetologia |
| Verlag | Springer Berlin / Heidelberg |
| ISSN | 0012-186X (Print) 1432-0428 (Online) |
| Heft | Volume 4, Number 5 / November 1968 |
| Kategorie | Originals |
| DOI | 10.1007/BF01309896 |
| Seiten | 253-256 |
| Fachgebiete | Medizin |
| SpringerLink Date | Donnerstag, 31. März 2005 |

 PDF (473,5 KB)

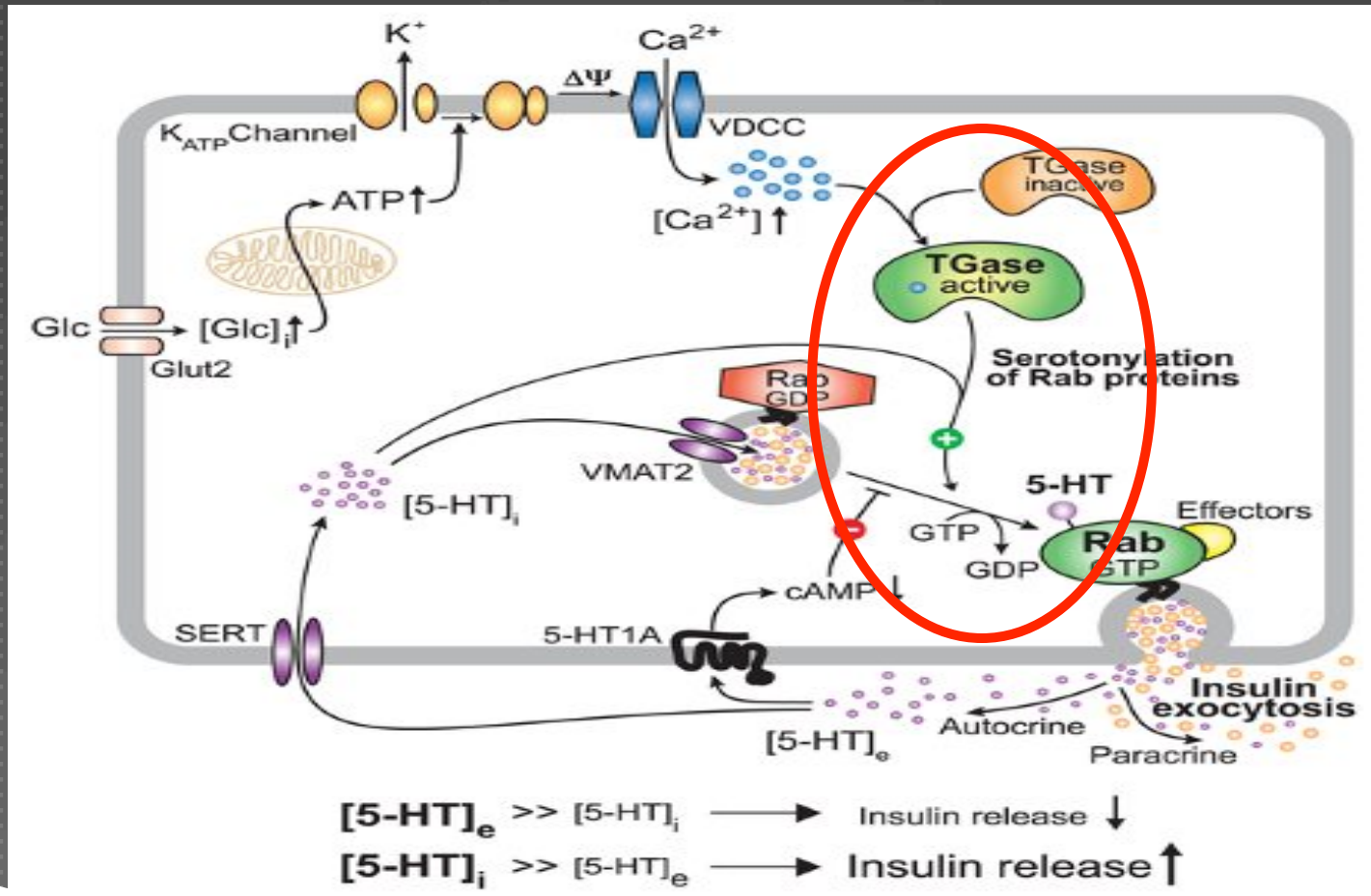
M. Telib¹, S. Raptis¹, K. E. Schröder¹ and E. F. Pfeiffer¹

(1) Department of Clinical Endocrinology and Metabolism, Centre of Medicine, University of Ulm, Donau, Sweden

„Serotonylsation“

- ▶ Insulin production in β cells depend on the ratio of intracellular and extracellular tryptophan levels. When internal serotonin levels are high, insulin and serotonin are cosecreted. The secreted serotonin **then inhibits further insulin release.**
- ▶ Gradually the secreted serotonin is taken up again by the beta cells, until there's more inside the cell than outside the cell. Then the cell can secrete more insulin.

SEROTONYLATION



[Changes in cerebra serotonin synthesis induced by insulin-dependent diabetes mellitus]

[Article in Spanish]

Manjarrez-Gutiérrez G, Herrera-Márquez JR, Molina-Hernández A, Bueno-Santoyo S, González-Ramírez M, Hernández J.

Laboratorio de Neuroquímica del Desarrollo, Hospital de Especialidades, Centro Médico Nacional Siglo XXI (CMN), Instituto Mexicano del Seguro Social (IMSS), México, D.F. México.

Abstract

OBJECTIVE: Evaluate if the rats with diabetes mellitus insulin-dependent have a minor activity of the serotonergic biosynthetic pathway through the decrease of the free fraction of L-tryptophan in plasma.

METHODS: Diabetes mellitus was induced in rats, and the brain serotonergic biosynthetic activity was evaluated at 7, 14, and 21 days after streptozotocin administration.

RESULTS: The diabetic animals showed a general decrease in body weight. In plasma they had a decrease in the free fraction of L-tryptophan. Also, in the brain they show low levels of the amino acid, as well as decrease of the activity of the limiting enzyme tryptophan-5-hydroxylase and its product serotonin. Interestingly, the activity of the enzyme was higher in the brainstem from day 14, accompanied with an elevation of the neurotransmitter.

CONCLUSIONS: The results confirm that diabetes mellitus insulin-depend induce chronic undernourishment. The low levels of L-tryptophan in blood of the diabetic animals suggest a minor transport of the amino acid to the brain and a decrease in serotonin synthesis, in cerebral cortex and hypothalamus. Besides, during the evolution of the disease, the activity of tryptophan hydroxylase was elevated, independently of L-tryptophan concentration in the brainstem of diabetic animals, suggesting a different response according to the brain region and possibly a different functional change, accompanied by an increase in the

Rev Invest Clin. 1999 Sep-Oct;51(5):293-302

CENTRAL SEROTONIC ACTIVITY AND INSULIN

The relationship between central serotonergic activity and insulin sensitivity in healthy volunteers.

Horáček J, Kuzmiaková M, Höschl C, Anděl M, Bahbonh R.

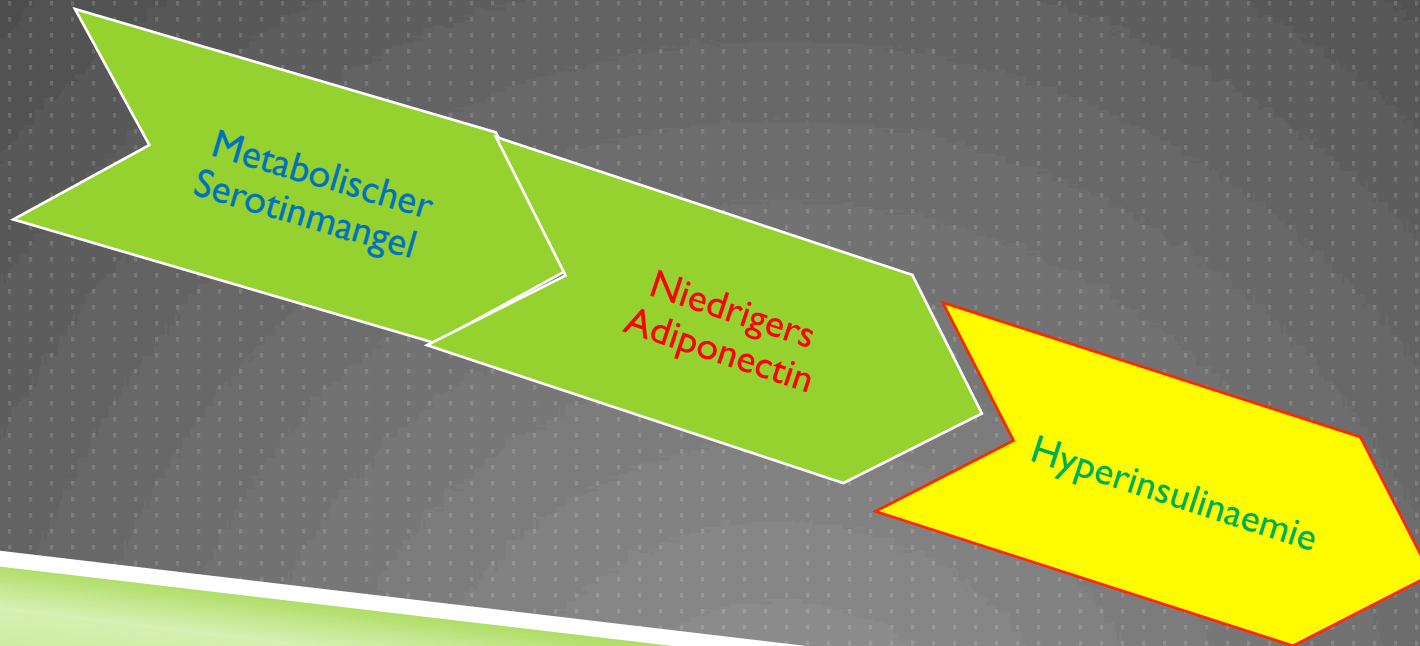
3rd Faculty of Medicine, Charles University, Prague, Czech Republic. horacek@pcp.lf3.cuni.cz

Abstract

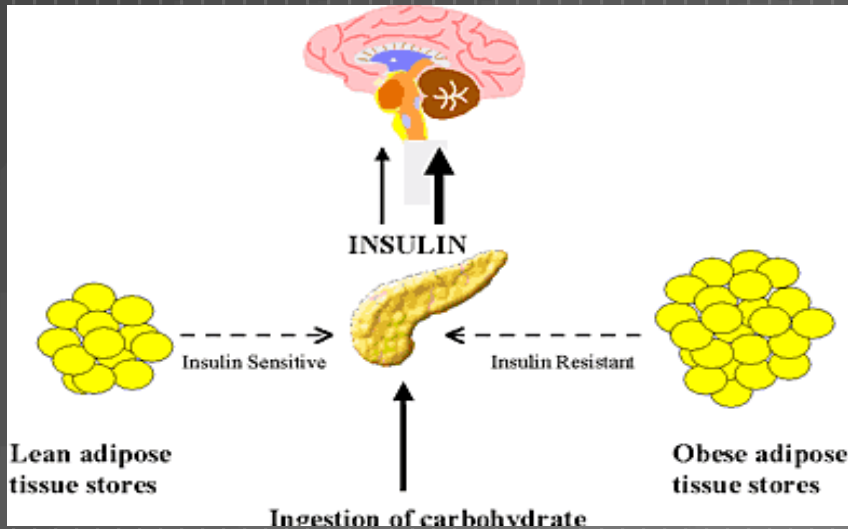
In order to determine whether central serotonin (5-HT) activity is related to sensitivity of insulin receptors, 19 healthy volunteers with normal basal glycemia and HbA1c were studied. The relationship between prolactin response to D-fenfluramine (delta PRL) in a challenge test and metabolic clearance rates (MCR) of glucose during the hyperinsulinemic-euglycemic clamp technique was evaluated. delta PRL had been chosen as a correlate of central 5-HT activity. Two levels of insulin concentration of approximately 70 mU/l (MCRsubmax) and 2000 mU/l (MCRmax) were used in a clamp, each for a duration of 120 min. A negative correlation was found between delta PRL and MCRsubmax ($r = -0.55$, $P < 0.02$) and between delta PRL and MCRmax ($r = -0.51$, $P < 0.03$). We did not find any correlation between the prolactin response to D-fenfluramine and body weight, body mass index (BMI) or waist and hip circumference (WHR). The data support the hypothesis of a close connection between 5-HT activity in the brain and peripheral sensitivity to insulin. The possible physiological mechanisms of this connection are discussed.

Horáček J, Kuzmiaková M, Höschl C, Anděl M, Bahbonh R. *Psychoneuroendocrinology*. 1999 ;24(8):785-97:.

IMPACT OF LOW SEROTONIN ON ENERGY METABOLISM (INSULIN)



HYPERINSULINAEMIE



Kohlehydratstoffwechsel und Serotonin Mangel->

Relativer Hypoglykämie, BZ-Dumpings

Symptomatik:

✓ Kohlehydrathunger

✓ Gewichtszunahme

✓ Energiespeicherung

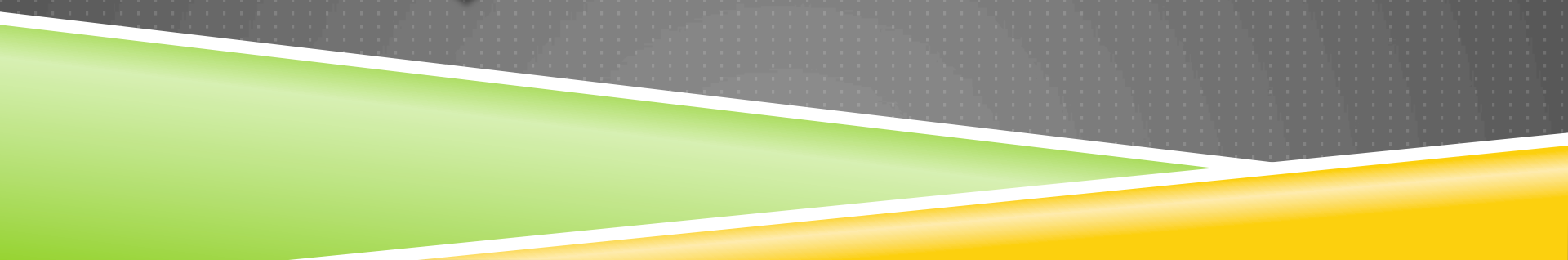
ZUSAMMENFASSUNG SEROTONIN/ INSULIN



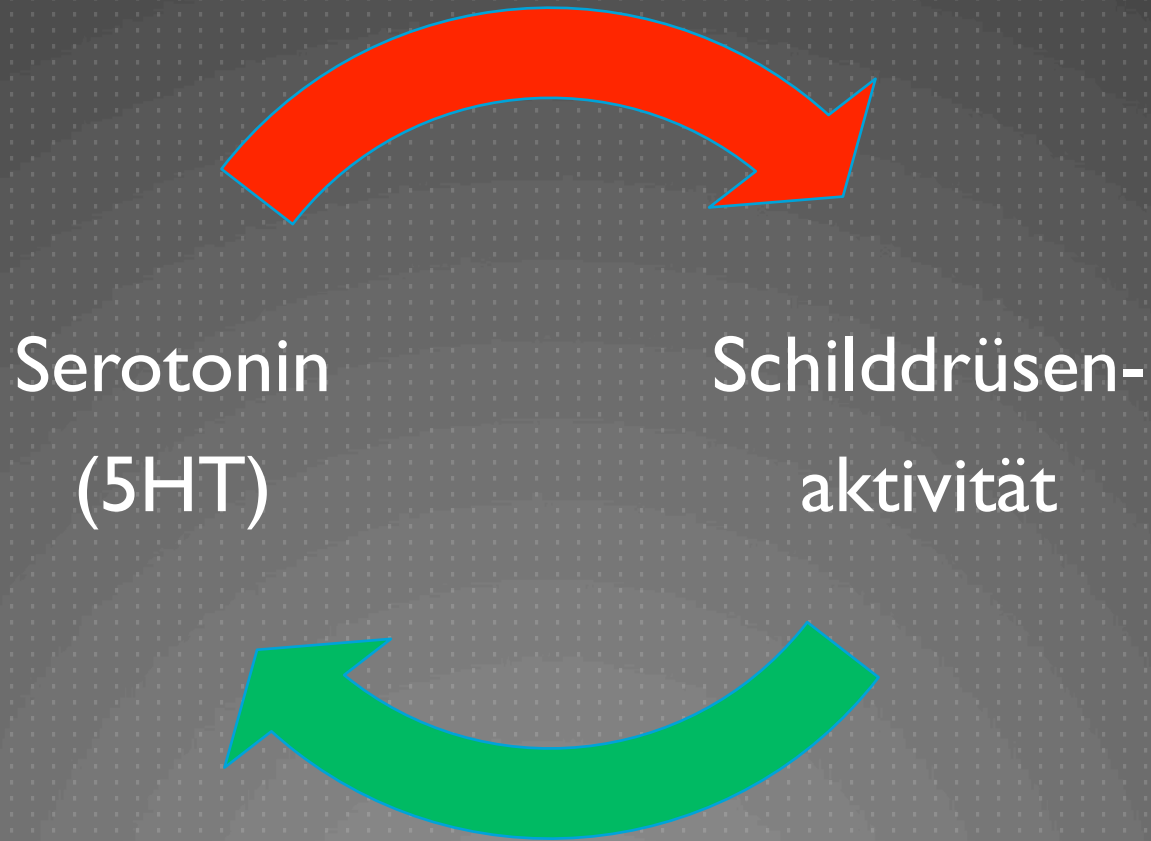
Insulin/
Cortisol



Serotonin



5hT kontrolliert Schilddrüsenaktivität



5-HT AKTIVATVIERT 5- DEJODINASE

Can J Physiol Pharmacol. 2003 Jul;81(7):747-51.

Serotonin effect on deiodinating activity in the rat.

Sullo A, Brizzi G, Maffulli N.

Second University of Naples, Faculty of Medicine and Surgery, Department of Experimental Medicine, Human Physiology Section, Napoli, Italy.

Abstract

Serotonin (5-HT) and thyroid hormones are part of a complex system modulating eating behaviour and energy expenditure. 5-Deiodinase (5-D) converts the relatively inactive thyroxine (T4) to triiodothyronine (T3), and its activity is an indirect measure of T3 production in peripheral tissues, particularly in the brain, intrascapular brown adipose tissue (IBAT), heart, liver, and kidney. We evaluated the effect of 5-HT on 5'-D activity during basal conditions and after short (30 min) cold exposure (thyroid stimulating hormone stimulation test, TST). 5'-D activity was assessed in the liver, heart, brain, kidney, and IBAT. TST increases 5'-D activity in the brain, heart, and IBAT and decreases it in kidney, leaving it unchanged in the liver. 5-HT alone did not modify 5'-D activity in the organs under study but decreased it in the IBAT, heart, and brain when injected before the TST was administered. Our results confirm the important role of 5-HT in thermoregulation, given its peripheral site of action, in modulating heat production controlling intracellular T3 production. These effects are more evident when heat production is upregulated during cold exposure in organs containing type II 5'-D, such as the brain, heart, and IBAT, which are able to modify their function during conditions that alter energy balance. In conclusion, 5-HT may also act peripherally directly on the thyroid and organs containing type II 5'-D, thus controlling energy expenditure through heat production.

Short communication

Decreased central serotonin function in hypothyroidism

Andrea Vaccari^a

^aInstitute of Pharmacology, School of Pharmacy, University of Genova, Via Capo S. Chiara 5, 16146 Genova, Italy

Received 14 June 1982; accepted 16 June 1982. Available online 1 November 2002.

Abstract

Male rats born of mothers kept on an iodide-free diet from day 15 of pregnancy up to day 4 post-delivery, were rendered hypothyroid by a daily s.c. injection of methimazole, 20–25 mg/kg from day 1 up to day 30 of age. Two days after the last injection, euthyroid and hypothyroid rats were given 220 mg/kg i.p. of L-5-hydroxytryptophan (5-HTP). The resulting behavioral syndrome was much less intense in hypothyroids, compared to euthyroids, thus suggesting a state of serotonergic hypoactivity.

Keywords: Hypothyroidism; 5-HT syndrome; 5-Hydroxytryptophan; 5-HTP decarboxylase

HYPOTHYREOIDISMUS UND 5-HTP

Thyroid hormones, serotonin and mood: of synergy and significance in the adult brain.

Bauer M, Heinz A, Whybrow PC

University of California Los Angeles (UCLA), Neuropsychiatric Institute & Hospital, Department of Psychiatry and Biobehavioral Sciences, 760 Westwood Plaza, Los Angeles, CA 90024, USA. mjbauer@mednet.ucla.edu

Abstract

The use of thyroid hormones as an effective and long-term treatment for affective disorders has been studied over the past three decades and has been confirmed repeatedly. Interaction of the thyroid and monoamine neurotransmitter systems has been suggested as a potential underlying mechanism of action. While catecholamine and thyroid interrelationships have been reviewed in detail, the serotonin system has been largely neglected. Thus, the goal of this article is to review the literature on the relationships between thyroid hormones and the brain serotonin (5-HT) system, limited to studies in adult humans and adult animals. In humans, neuroendocrine challenge studies in hypothyroid patients have shown a reduced 5-HT responsiveness that is reversible with thyroid replacement therapy. In adult animals with experimentally-induced hypothyroid states, increased 5-HT turnover in the brainstem is consistently reported while decreased cortical 5-HT concentrations and 5-HT_{2A} receptor density are less frequently observed. In the majority of studies, the effects of thyroid hormone administration in animals with experimentally-induced hypothyroid states include an increase in cortical 5-HT concentrations and a desensitization of autoinhibitory 5-HT_{1A} receptors in the raphe area, resulting in disinhibition of cortical and hippocampal 5-HT release. Furthermore, there is some indication that thyroid hormones may increase cortical 5-HT₂ receptor

Syngierismus

zwischen L-Thyroxin
and 5-HTP

T3 erhöht 5HT-Aktivität

Curr Drug Targets. 2006 Feb;7(2):203-10.

Basic mechanisms of augmentation of antidepressant effects with thyroid hormone.

Lifschytz T, Segman R, Shalom G, Lerer B, Gur E, Golzer T, Newman ME.

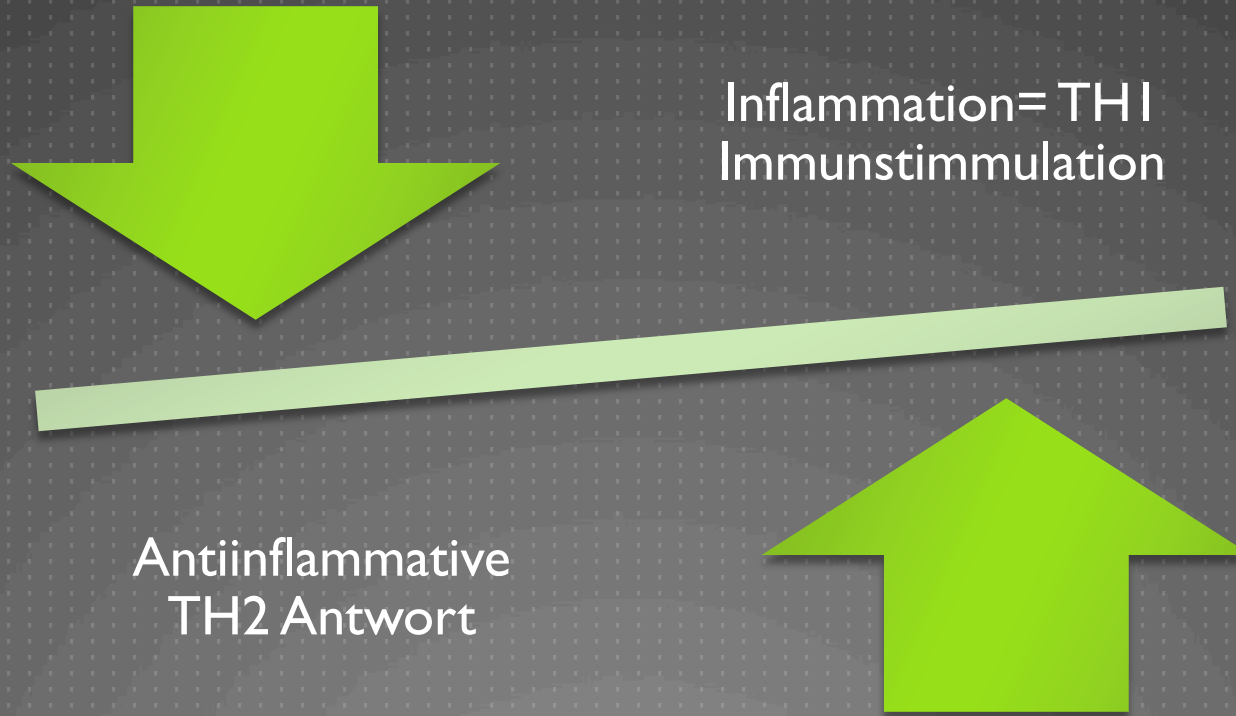
Biological Psychiatry Laboratory, Department of Psychiatry, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

Abstract

The thyroid hormone triiodothyronine (T3) has been used both to augment and accelerate the clinical effects of antidepressants, particularly the tricyclics. More recent work indicates that it may have similar actions with regard to the SSRIs. Two main mechanisms have been put forward to explain its antidepressant actions. (a) an action at the nuclear level involving stimulation of gene transcription; (b) an action at the cell membrane level involving potentiation of neurotransmission. In particular, there is considerable evidence for potentiation by T3 of the actions of the neurotransmitter 5-HT or serotonin. This evidence, which is mainly based on in vivo microdialysis studies, is reviewed, and evidence based on human and animal neuroendocrine studies considered. The effects of T3, alone and together with the SSRI fluoxetine, on mRNA levels for the 5-HT_{1A} and 5-HT_{1B} autoreceptors, which mediate serotonergic neurotransmission by feedback actions at the levels of cell firing (somatodendritic 5-HT_{1A} autoreceptors) and neurotransmitter release (nerve terminal 5-HT_{1B} autoreceptors) were also determined. Administration of a combination of fluoxetine and T3 induced reductions in the transcription of these autoreceptors, which may explain the clinical potentiating effects of this combination, and thus link the nuclear and neurotransmitter hypotheses of T3 action.

SYMPATIKOTONE IMMUNOLOGIE

-VEREINFACHTES MODELL-

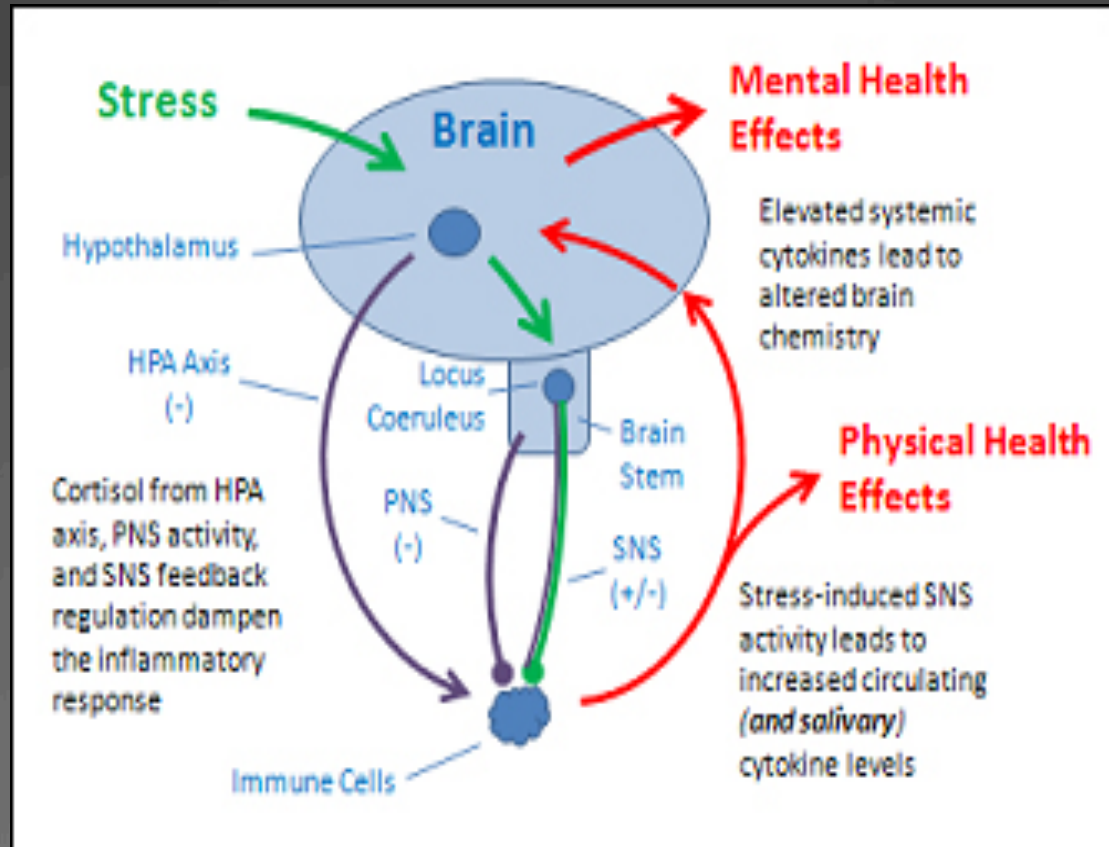


Inflammation= TH1
Immunstimulation

Antiinflammative
TH2 Antwort

Muss et al 2014

Stress und Entzündung



VNS PROTECTS FROM PERIPHERAL VASCULAR INSULT

[Basic Res Cardiol](#). 2013;108(3):345. doi: 10.1007/s00395-013-0345-1. Epub 2013 Mar 22.

Vagal stimulation triggers peripheral vascular protection through the cholinergic anti-inflammatory pathway in a rat model of myocardial ischemia/reperfusion.

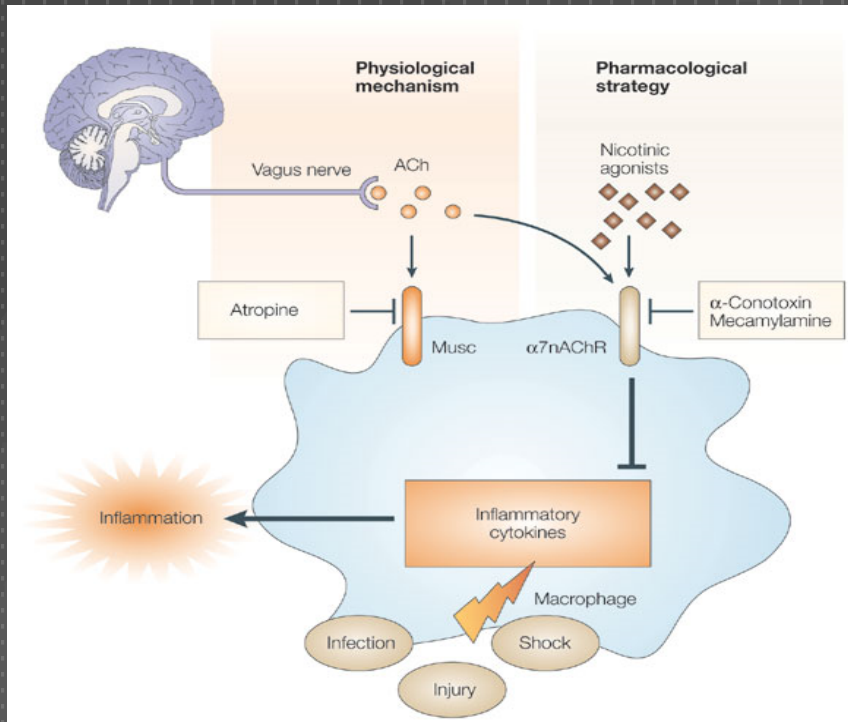
[Zhao M¹](#), [He X](#), [Bi XY](#), [Yu XJ](#), [Gil Wier W](#), [Zang WJ](#).

Author information

Abstract

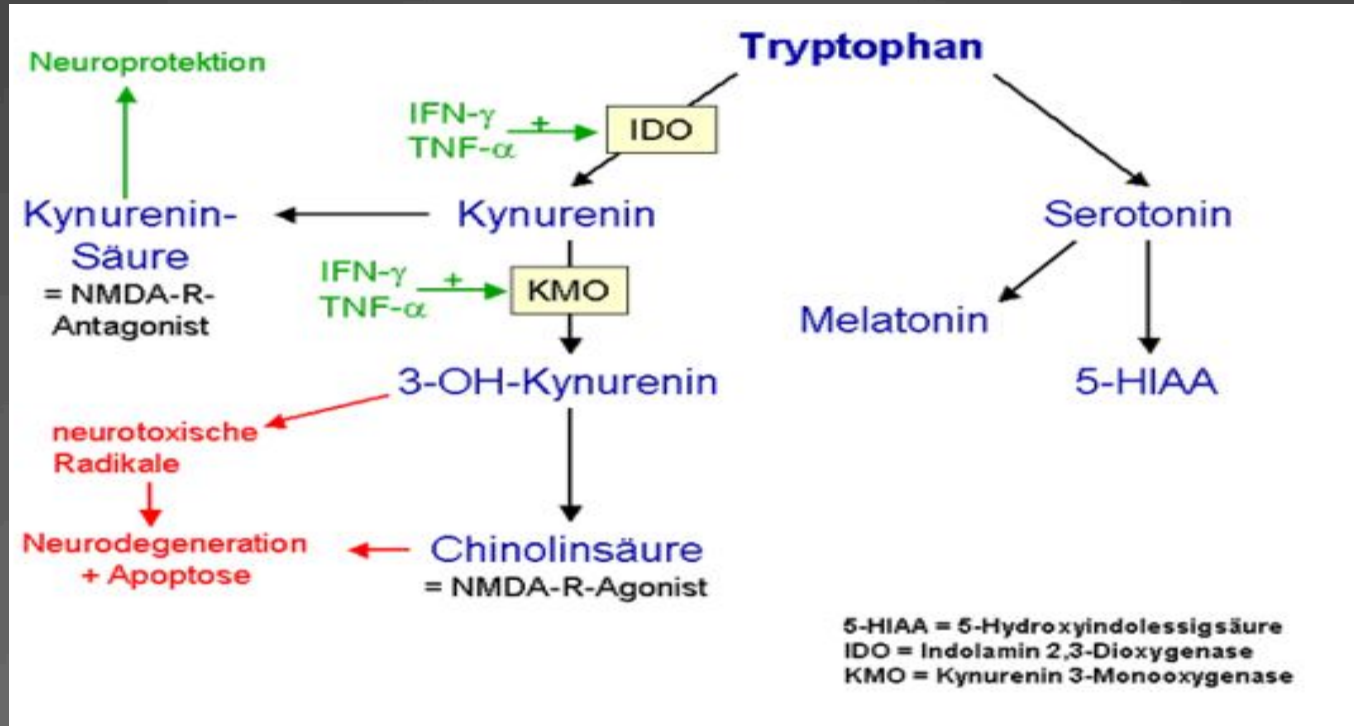
Myocardial ischemia/reperfusion (I/R) induces inflammatory response that may lead to remote vascular injury. Vagal nerve elicits the cholinergic anti-inflammatory pathway by activating $\alpha 7$ nicotinic acetylcholine receptors ($\alpha 7$ nAChR). Nevertheless, the role of vagal nerve-mediated anti-inflammatory pathway in the vasculature has not been studied previously. Therefore, we aimed to clarify the potential role of vagal stimulation (VNS) in regulating remote vascular injury after myocardial I/R. Adult male Sprague-Dawley rats were subjected to VNS starting 15 min prior to ischemia until the end of reperfusion. VNS not only reduced infarct size and improved cardiac function, but also ameliorated myocardial I/R-induced dysfunctional vasoconstriction and vasodilatation and degradation of endothelial structure in mesenteric arteries. VNS decreased serum and vascular levels of tumor necrosis factor- α and IL-1 β . Interestingly, *in vivo* microdialysis studies demonstrated that VNS increased ACh concentration in the mesenteric circulation. Furthermore, VNS up-regulated expressions of muscarinic ACh receptors-3 (M3AChR) and $\alpha 7$ nAChR in mesenteric arteries. Preserved endothelial relaxations by VNS were inhibited by atropine or methyllycaconitine, indicating that functional protection was associated with M3 and $\alpha 7$ nAChR activation. Finally, VNS increased STAT3 phosphorylation and inhibited NF- κ B activation in mesenteric arteries, and these effects were abolished by $\alpha 7$ nAChR shRNA treatment, indicating VNS-mediated anti-inflammatory effect mainly involved $\alpha 7$ nAChR. **These results demonstrated for the first time that VNS protected against remote vascular dysfunction, through the cholinergic anti-inflammatory pathway which is dependent on $\alpha 7$ nAChR. Our findings represent a significant addition to the understanding of vagal nerve-mediated pathways and the potential roles they play in regulating the vasculature.**

VAGALE (CHOLINERGE) STIMULATION WIRKT ANTI-INFLAMMATIV



Choline attenuates immune inflammation and suppresses oxidative stress in patients with asthma. Mehta AK, Singh BP, Arora N, Gaur SN. Immunobiology. 2010 Jul;215(7):527-34.

ENTZÜNDUNGEN UND STRESS HEMMEN SEROTONIN-METABOLISMUS



KYNUREINSYNTHESE UND ZELLULÄRE IMMUNITÄT

- ▶ 90% des enteralen Tryptophans wird für die Kynureinsynthese verwendet.
- ▶ Moduliert die **zelluläre (TH1) Immunität**
- ▶ Bei chronischem Virusload, z.B. chronische Herdentzündung, NMU, Autoimmunerkrankungen-> Aktivierung der zellulären Immunität-> Steigerung des Kynureinbedarfs->
- ▶ **relativer Tryptophanmangel !!!**

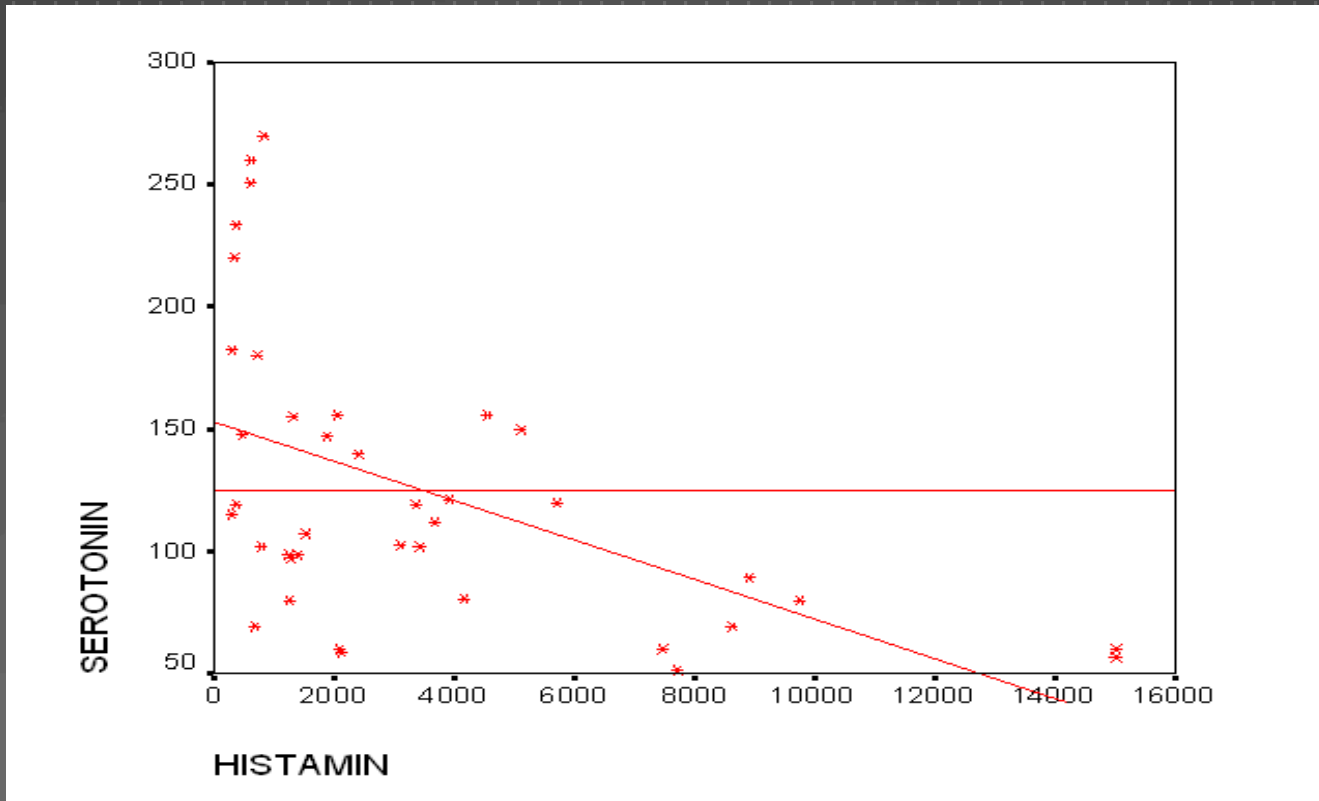
PARASYMPATHIKTNER ANTI-STRESS FAKTOR SEROTONIN

▶ Die Vulnerabilität gegenüber Stress nimmt unter Tryptophan-Mangel deutlich zu(Firk et Markus 2008).

▶ **Erklärung:**


▶ **Tryptophan → 5TP-→ Serotonin
(„Glückshormon“)**

NEGATIVE CORRELATION OF HISTAMIN AND SEROTONIN



INTERACTION INFLAMMATION & SEROTONIN

Serotonin

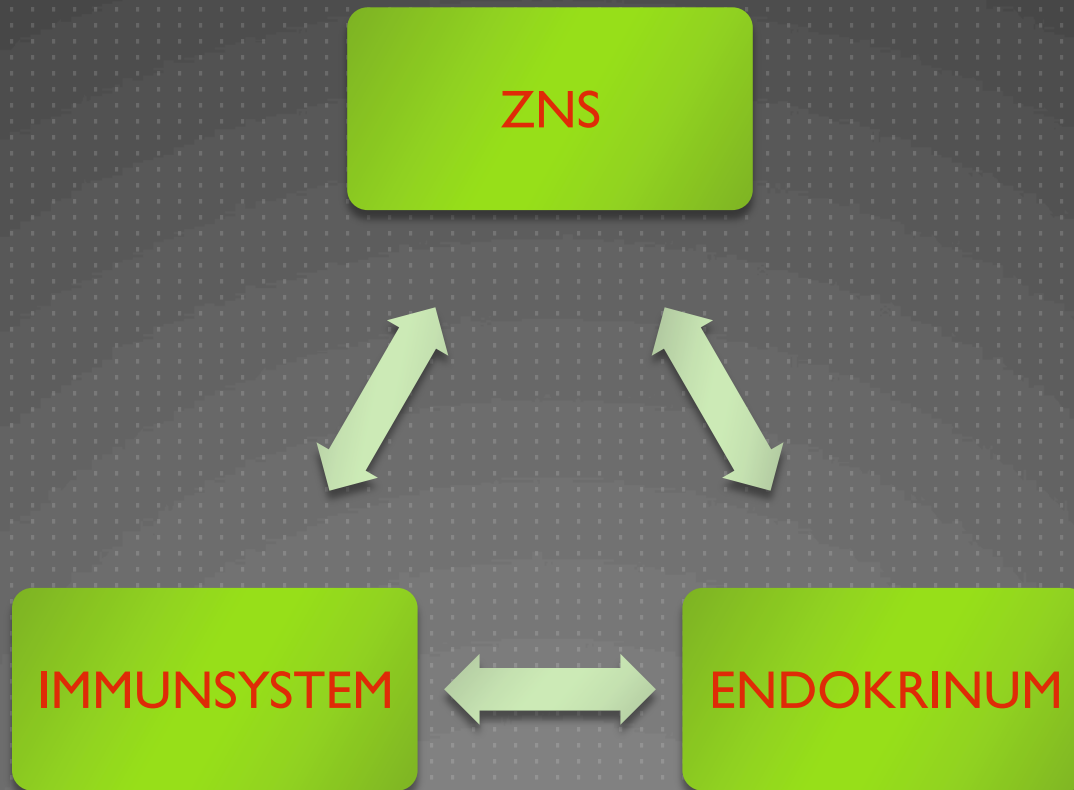


| | N | Minimum | Maximum | Mean Average | Standard Deviation |
|---------------|-----|---------|----------|--------------|--------------------|
| HISTAMIN | 104 | 21,40 | 15000,00 | 2802,2692 | 3607,6853 |
| SEROTONIN | 103 | 21,80 | 1233,80 | 151,0180 | 161,7139 |
| Valid Results | 100 | | | | |

Inflammation
(Histamin)



WECHSELWIRKUNG NEUROENDOKRINOIMMUNOLOGIE

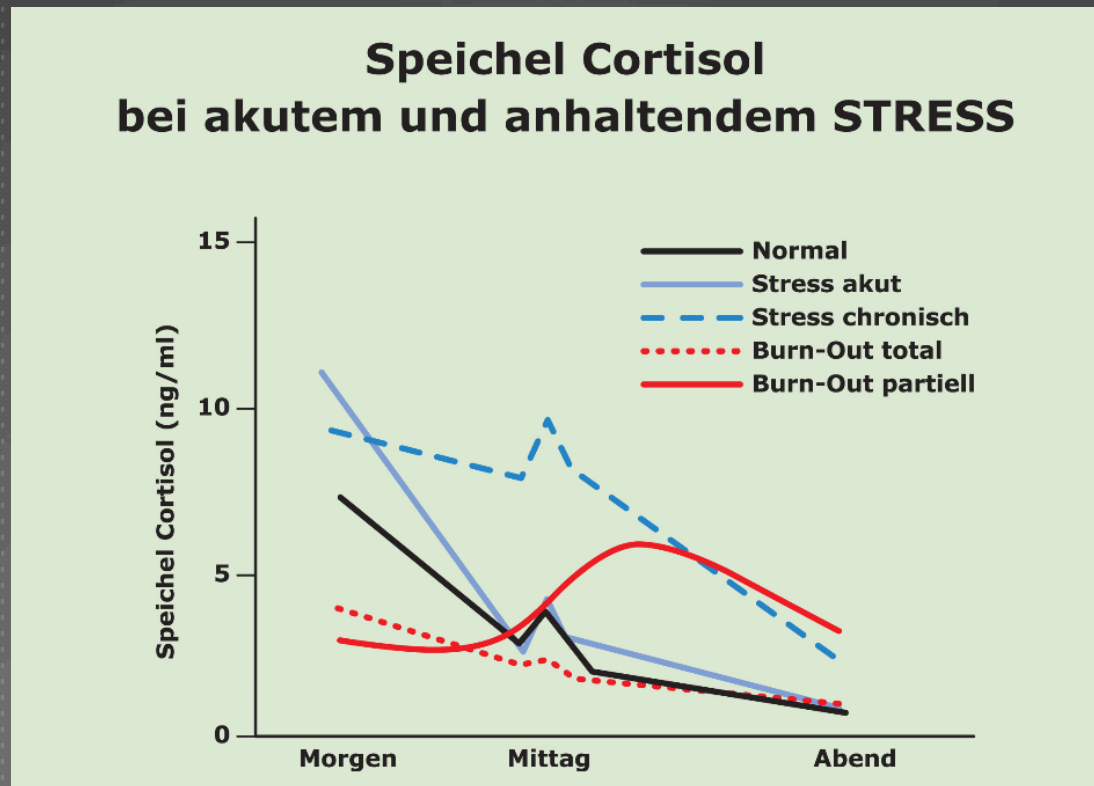


MODERNE LABORDIAGNOSTIK HILFT ZUR DIFFERENZIERUNG IM KLINISCHEN ALLTAG

- ▶ Quantitative Bestimmung akuter Stress-Botenstoffe Adrenalin und Noradrenalin + Dopamin
- ▶ Cortisol-Tagesprofil
- ▶ Serotonin-Stoffwechsel



CORTISOLPROFIL IN VERSCHIEDENEN STRESSPHASEN



MALABSORPTION TRYPTOPHAN

BIOVIS
DIAGNOSTIK

Zweiglaborierung Limburg
Dr. med. Burkhard Schütz
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Justus-Staudt Straße 2
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Tel: 06431 212 46 0 Email: info@biovis.de
 Fax: 06431 212 48 66 Web: <http://www.biovis.de>

Externe Nr.

| | | |
|------------------------------------|-----------------------------------|-----------------------------------|
| Name | Geburtsdatum | Auftrag Nr. |
| Vorname | Geschlecht weiblich | Eingang am 23.09.2011 |
| Probenentnahme am 23.09.2011 10:47 | Validiert von Dr. Herbert Schmidt | Befundstatus Endbericht |
| Probenmaterial | Validiert am 30.09.2011 | Befundstatus am 30.09.2011 |

Allergien, Nahrungsmittelenverträglichkeiten

| | | | | | |
|---------------|--------------|----------------|------|--|------|
| Diaminoxidase | 37,60 | HDU/ml | >80 | | SEC* |
| | | Optimalbereich | > 90 | | |

Bitte beachten Sie den geänderten Referenzbereich !

Sonstiges

Serotonin/Tryptophan/Kynurenin (Bloodspot)

| | | | | | |
|--|---------------|-------|----------------------------------|--|-------|
| Kynurenin (Bloodspot-Test) | 273,00 | ng/ml | 300 - 400 | | KAPB* |
| Serotonin (DBS) | 131,00 | ng/ml | > 140 | | KAPB* |
| | | | Achtung geänderter Normbereich ! | | |
| Tryptophan (Bloodspot-Test) | 7,10 | mg/dl | 8 - 12 | | KAPB* |
| Kynurenin/Tryptophan-Ratio (Bloodspot) | 38,45 | | 25 - 35 | | KBN* |

FORSCHUNGSANSATZ

Ziel:

- ▶ Klinische Differenzierung von Stress , Burnout und psychiatrischer Krankheitsbilder künftig unter Einschluss quantitativ messbarer neurovegetativer Funktionsparameter.
- ▶ Korrelation mit bislang etablierten Kriterien?

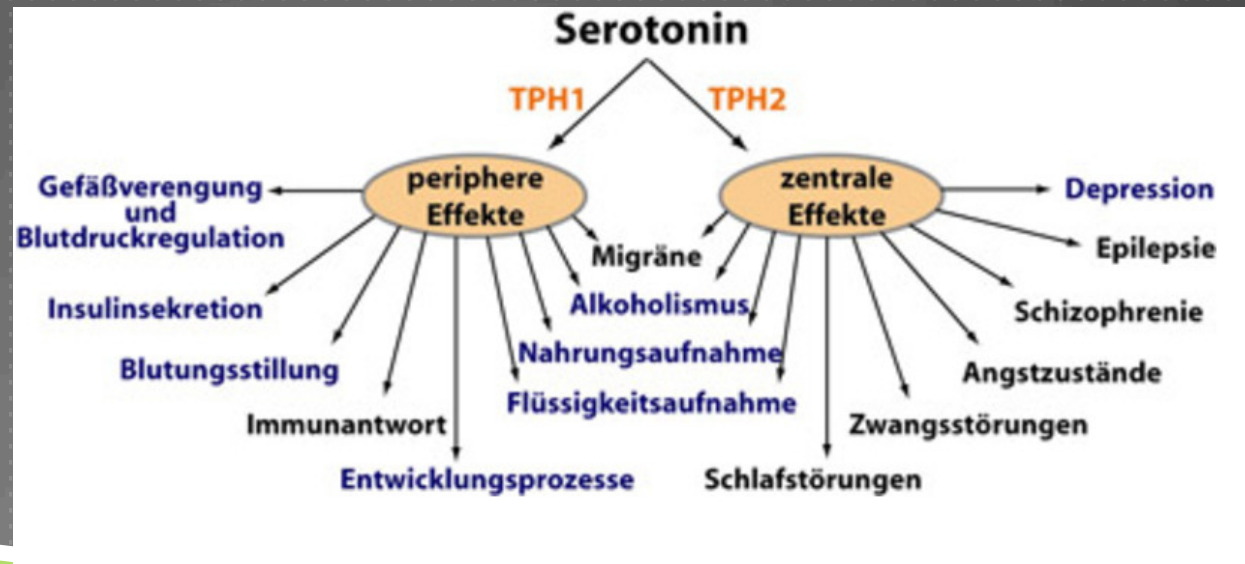
RESUMEE

NEUROENDOKRINOIMMUNOLOGISCHE ASPEKTE DES STRESS/BURNOUT

- ▶ Chronischer Stress und konsekutiver Burnout stellen eine psychovegetative Adaption des Organismus unter Einschluss verschiedener Organsysteme dar.
- ▶ Die Prävention/Therapie sollte daher integrative Konzepte berücksichtigen, die eben auf diesen verschiedenen Ebenen (neuronal, endokrin und Immunsystem) interagieren.
- ▶ Psychopharmaka erfüllen diese Forderung nicht!

Neue Präventionsstrategien ?

- ▶ Medikamente haben keine periphere neurotrope Effekte
- ▶ Unterschiedliche 5HT Rezeptoren zwischen ZNS und Körperperipherie



UAW's

Serotoninwiederaufnahmehemmer (SSRI)



Gastrointestinal

Appetitlosigkeit, Übelkeit,
Erbrechen und Durchfall

Gastrointestinale Blutungen
Risiko 2x

ASS 4x

In Kombi mit NSAR 9x

Kellner: *Antidepressiva können
den Magen zusätzlich
angreifen.* MMW-Fortschr.
Med Nr. 51–52/2009 (151.
Jg.)



Sexualleben

Erektionsfähigkeit,
Ejakulationsstörungen,
Orgasmusschwierigkeiten,
passagere Abnahme der
Spermienqualität]

A. Opbroek et. al.: Emotional
blunting associated with
SSRI-induced sexual
dysfunction. Do SSRIs inhibit
emotional responses?
International Journal of
Neuropsychopharmacology
(2002), 5, S. 147–151.



Zahnprobleme

Karies
Mundtrockenheit

E. Bassuk, S. Schoonover:
*Rampant dental caries in the
treatment of depression.* In: *J
Clin Psychiatry.* 39, Nr. 2, 1978,

Citalopram erhöht das Suicidrisiko 15 x ???

Fergusson, S. Doucette, K. C. Glasset et al.: *Association between suicide attempts and selective serotonin reuptake inhibitors: systematic review of randomised controlled trials.* In: *BMJ (Clinical Research Ed.)*. 330, Nr. 7488, Februar 2005, S. 396.

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AMITRYPTILIN BLOCKIERT STOFFWECHSEL UND MACHEN UNFIT

Helmar Tal
NetDoktor.de - Donnerstag, 4. September 2014

Rauben Antidepressiva geistige Fitness?

Antidepressiva helfen Menschen mit dunklen Wolken ums Gemüt. Aber sie können auch für Lücken im Gedächtnis sorgen.

Depressionen sind eine weit verbreitete Krankheit. Menschen mit Depressionen sind antriebslos, wirken nach außen müde und schlapp. Doch innerlich sind sie angespannt und das Gehirn arbeitet auf Hochtouren. Eine der wirksamsten Therapien ist nach wissenschaftlichen Erkenntnissen die Unterdrückung des REM-Schlafs mit bestimmten Antidepressiva. Aber: In diesen Schlafphasen finden nicht nur die meisten Träume statt, sondern es werden auch Erinnerungen im Gedächtnis verfestigt. Die Unterdrückung des REM-Schlafes könne gleichzeitig das Lernen beeinträchtigen und Gedächtnisstörungen hervorrufen, stellten Wissenschaftler der Charité – Universitätsmedizin Berlin jetzt fest.

Muster merken vor dem Schlafen

Bisherige Studien zeigten, dass depressive Menschen in ihrem prozeduralen Lernen beeinträchtigt sind – das sind automatisierte Lernvorgänge wie beispielsweise Klavierspielen oder Fahrradfahren. Außerdem haben sie ein erhöhtes Risiko an kognitiven Störungen oder

Demenz zu erkranken. Sind diese Symptome Ausdruck der Erkrankung oder werden sie erst durch die Antidepressiva hervorgerufen? Dieser Frage ging die Arbeitsgruppe um Privatdozent Dr. Dieter Kunz vom Institut für Physiologie der Charité in einer experimentellen Studie nach.

Vor dem Zubettgehen sollten sich 25 gesunde Teilnehmer visuelle Muster merken. Anschließend bekamen sie entweder ein Placebo oder das Antidepressivum Amitriptylin verabreicht. Am nächsten Abend wurde der Lernerfolg getestet: Die Probanden mit dem Placebo-Präparat konnten die Muster deutlich schneller erkennen als diejenigen, die Amitriptylin erhalten hatten.

Antidepressiva verursachen Störungen im Kopf
„Unsere Ergebnisse lassen vermuten, dass kognitive Störungen bei depressiven Patienten



Johan Larson/Fotolia.com

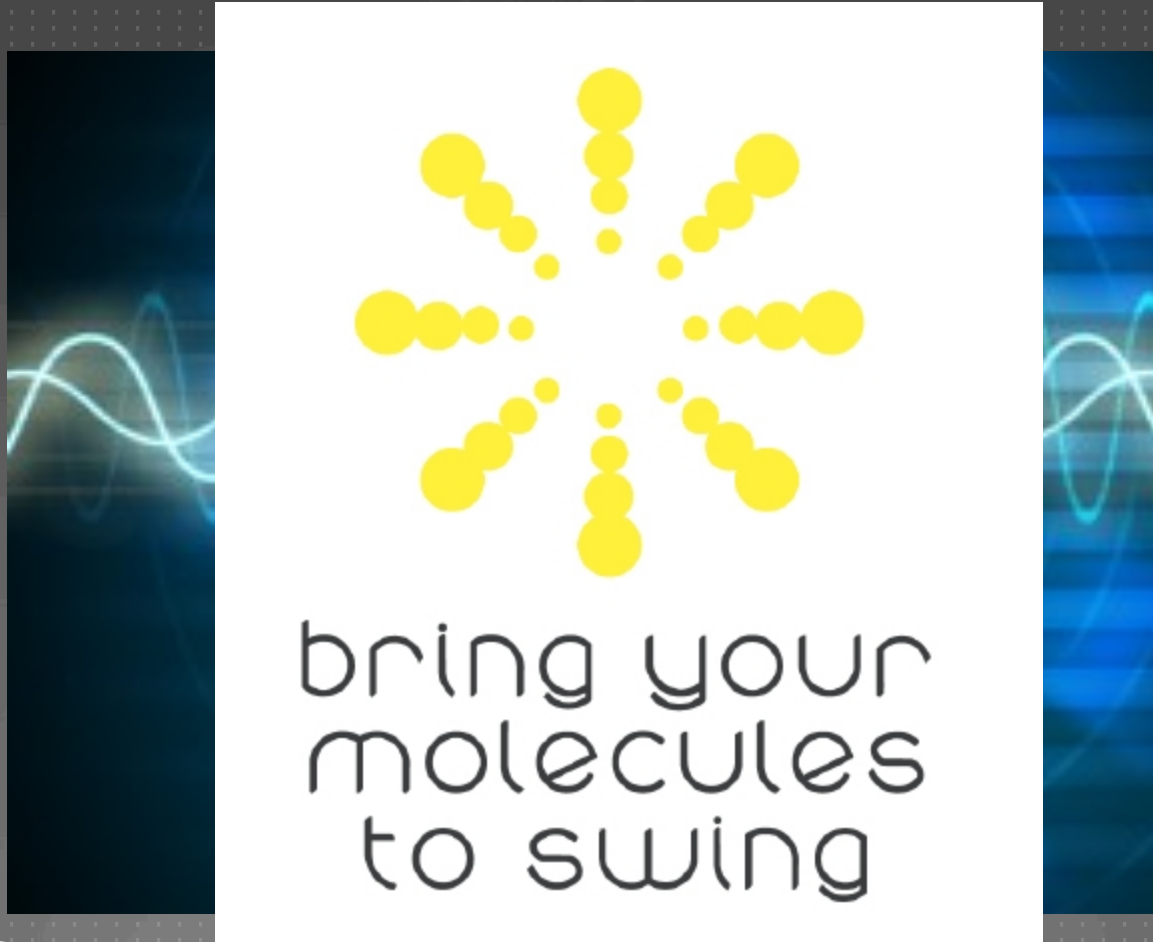
durch das Antidepressivum Amitriptylin zumindest mit verursacht werden. Das Eindringen von psychoaktiven Substanzen in die komplizierten Schlafabläufe kann eine Vielzahl der bekannten Nebenwirkungen wie kognitive Defizite, Gewichtszunahme und morgendliche Apathie erklären“, sagt der Schlaf Forscher Kunz. Weiterhin betont er: „Die Entwicklung von neuen Substanzen, die nicht nur tagsüber das Befinden von depressiven Menschen verbessern, sondern auch deren Schlafqualität fördern, ist voranzutreiben.“

Vier Millionen Menschen mit Depression

Etwa fünf Prozent der deutschen Bevölkerung zwischen 18 und 65 Jahren leiden derzeit an einer behandlungsbedürftigen Depression – das sind etwa 3,1 Millionen Menschen. Zählt man die Menschen mit Depressionen außerhalb dieser Altersgruppe hinzu, beträgt ihre Anzahl etwa vier Millionen. Etwa drei bis vier Mal so groß ist aber die Zahl derjenigen, die irgendwann im Laufe des Lebens an einer Depression erkranken, Frauen dabei doppelt so häufig wie Männer. Man nimmt an, dass die Neigung zur Depression zum Teil vererbbar ist. Wer einmal eine Depression durchlebt hat, hat ein erhöhtes Risiko, dass die Krankheit erneut auftritt.

Kunz, D. et al.: „Differential effect of an anticholinergic antidepressant on sleep – dependent memory consolidation“, Sleep, Mai 2014, Doi: 10.5665/sleep.3674

INS GLEICHGEWICHT BRINGEN



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STRESS UND NUTRITIVE MEDIZIN ALTBEKANNTE ÜBERLEGUNGEN NEU AUFGELEBT



NEUOTRANSMITTER MANGEL BEIM BURNOUT?

Neuropsychobiology, 2007;55(3-4):143-50. Epub 2007 Jul 18.

The psychobiology of burnout: are there two different syndromes?

Tops M¹, Boksem MA, Wijers AA, van Duinen H, Den Boer JA, Meijman TF, Korf J.

Abstract

BACKGROUND: Plasma prolactin levels are sensitive to dopamine and serotonin function, and fatigue. Low cortisol, dopamine and/or serotonin may be involved in burnout and detachment.

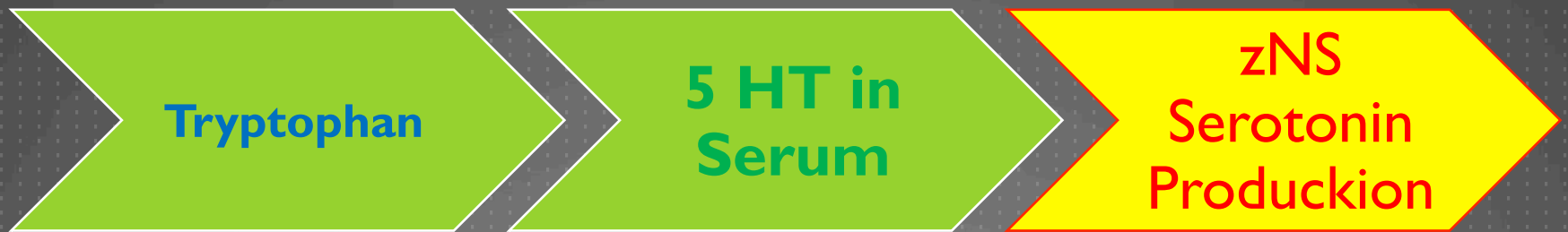
METHODS: In this double-blind within-subject study, we treated 9 female burnout subjects and 9 controls with 35 mg cortisol and placebo orally. We measured state affect and plasma prolactin, oxytocin, cortisol and adrenocorticotrophic hormone levels, and administered an attachment questionnaire.

RESULTS: The burnout subjects displayed an extreme distribution of basal prolactin levels, displaying higher or lower levels compared to the controls. The low prolactin burnouts had profoundly low attachment scores and tended to have low oxytocin levels. The high prolactin burnout subjects tended to show cortisol-induced decreased prolactin and fatigue, and increased vigor.

CONCLUSION: Results are consistent with the hypothesis that burnout subjects are either characterized by low serotonergic function or by low dopaminergic function, and that the latter group benefits from cortisol replacement. These preliminary results suggest that differentiating between two syndromes may resolve inconsistencies in research on burnout, and be necessary for selecting the right treatment strategy.

(c) 2007 S. Karger AG, Basel.

5 HT UND ZENTRALE SEROTONIN- WIRKUNG

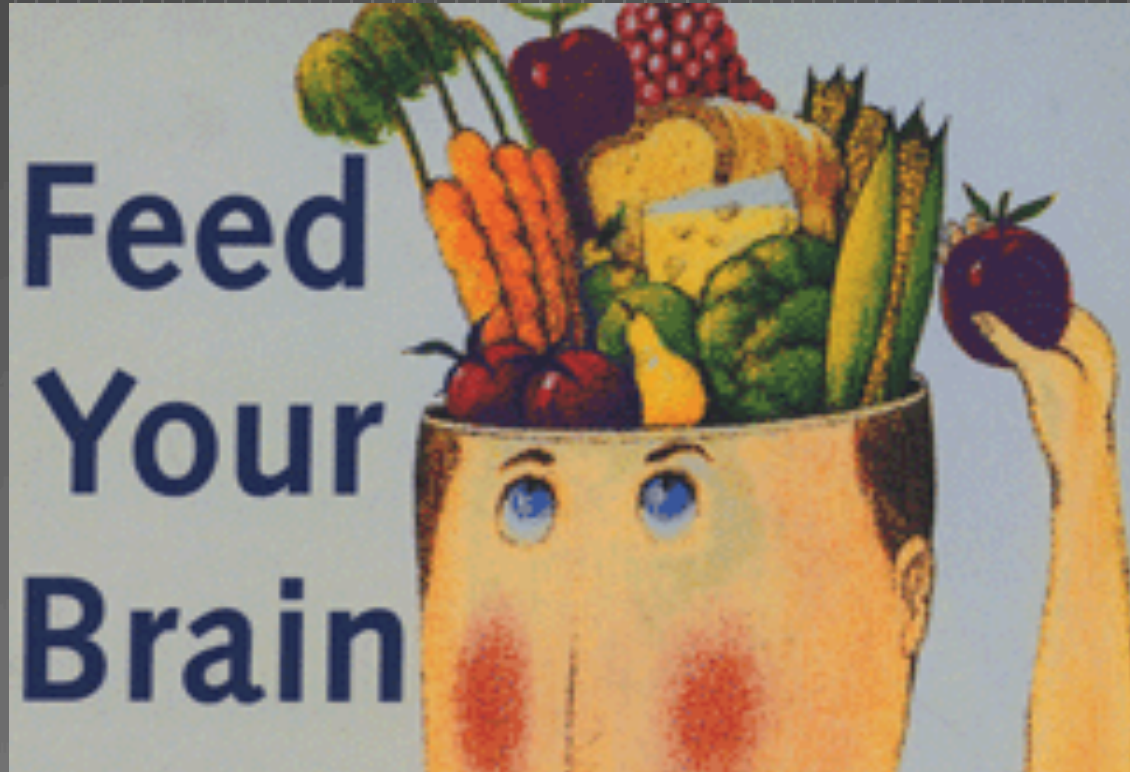


SEROTONIN PERIPHERIE UND ZENTRAL

- Sythesis rate of Serotonin in Cerebrum depends on nutrional Tryptophan supply
- CH consumption -> Insulin release-> Increase of metabolte Tryptophan ↑ (= Serotonin Precursor) -> Serotonin synthesis ↑

R. J. Wurtman, J. J. Wurtman: *Brain serotonin, carbohydrate-craving, obesity and depression.* In: *Obesity Research.* 3 Suppl 4, 1995, S. 477S–480S,

ANTI-STRESS-ERNÄHRUNG?



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TRYPTOPHAN REICHE ERNÄHRUNG FÜHRT ZU SEROTONINANSTIEG IM TIERVERSUCH

Serotonin (5HT) expression in rat pups treated with high-tryptophan diet during fetal and early postnatal development.

Musumeci G, Loreto C, Trovato FM, Giunta S, Imbesi R, Castrogiovanni P.

Department of Bio-Medical Sciences, Human Anatomy and Histology Division, University of Catania, Italy. Electronic address: g.musumeci@unicat.it.

Abstract

Serotonin (5HT) is a neurotransmitter synthesized in serotonergic neurons of the central nervous system and in the enterochromaffin cells of the gastrointestinal tract. 5HT regulates growth and maturation of some cerebral regions in the developing brain as well as the secretion of pituitary growth hormone. This hormone is necessary for development and growth through the stimulation of insulin-like growth factor synthesis. The precursor of 5HT, tryptophan (Trp), is an essential amino acid, since the human organism is unable to synthesize it and it is assumed only through diet. The aim of our study was to analyze how a high-tryptophan diet in pregnant rats affects growth and survival of pups until weaning. We monitored the number and weight of pups until weaning. Then, we detected serotonin and growth hormone levels in whole blood by ELISA of surviving pups at the end of the lactation period. We also analyzed by means of immunohistochemistry and Western blot the expression of serotonin in rat gastric tissue and the morphological structure of skeletal muscle tissue of both control and experimental pups. Hyperserotonemia and very low levels of growth hormone were detected in experimental pups compared to controls. Immunohistochemistry demonstrated a strong serotonin expression in stomach samples confirming that a high intake of tryptophan increases the production of serotonin in enterochromaffin cells, thereby resulting in hyperserotonemia in pups. These data were also strengthened by Western blot analysis. Histological alterations of skeletal muscle fibers in experimental pups were found and showed that in experimental samples the muscle tissue demonstrated deleterious alterations, being less developed and defined. Our data suggest that a high-tryptophan diet in pregnant rats induces hyperserotonemia in the fetus. Hyperserotonemia results in an excess of serotonin in the brain where it has a negative influence on development of serotonergic neurons and consequently on growth hormone production.

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Acta Histochem. 2013 Sep 23

TRYPTOPHAN SUPPLEMENTIERUNG UND EMOTIONEN

[Psychopharmacology \(Berl\)](#). 2006 Jul;187(1):121-30. Epub 2006 May 4.

Tryptophan supplementation induces a positive bias in the processing of emotional material in healthy female volunteers.

[Murphy SE](#), [Longhitano C](#), [Ayres RE](#), [Cowen PJ](#), [Harmer CJ](#).

Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford, OX3 7JX, UK.

Abstract

RATIONALE: The serotonin precursor L-tryptophan (TRP) is available as a nutritional supplement and is licensed as an antidepressant in a number of countries. However, evidence of its efficacy as the primary treatment for depression is limited, and the direct action of TRP on the symptoms of depression and anxiety has not been well-characterised.

OBJECTIVES: The present study assessed whether TRP induces cognitive changes opposite to the negative biases found in depression and characteristic of those induced by serotonergic antidepressants in healthy volunteers.

MATERIALS AND METHODS: Thirty eight healthy volunteers were randomised to receive 14 days double-blind intervention with TRP (1 g 3x a day) or placebo. On the final day, emotional processing was assessed using four tasks: facial expression recognition, emotion-potentiated startle, attentional probe and emotional categorisation and memory.

RESULTS: TRP increased the recognition of happy facial expressions and decreased the recognition of disgusted facial expressions in female but not male, volunteers. TRP also reduced attentional vigilance towards negative words and decreased baseline startle responsivity in the females.

CONCLUSIONS: These findings provide evidence that TRP supplementation in women induces a positive bias in the processing of emotional material that is reminiscent of the actions of serotonergic antidepressants. This highlights a key role for serotonin in emotional processing and lends support to the use of TRP as a nutritional supplement in people with mild depression or for prevention in those at risk. Future studies are needed to clarify the effect of tryptophan on these measures in men.

PERIPHERE TRYPTOPHANVERSORGUNG UND NERVENSYSTEM

Adv Exp Med Biol. 1981;133:207-19.

Influence of plasma tryptophan on brain 5HT synthesis and serotonergic activity.

Curzon G.

Abstract

Studies are described on the effect of plasma tryptophan changes on brain 5HT synthesis in man and rat. Results show that human brain 5HT synthesis is influenced by the supply of tryptophan to the brain. This is indicated by: (a) significant correlations between plasma free tryptophan and CSF 5HIAA concentrations; (b) raised cortical 5HT concentrations after infusing tryptophan. In rat experiments, determinations of brain tryptophan uptake from a bolus of plasma injected into the carotid artery showed: (a) increased uptake when bolus free tryptophan was raised and total tryptophan kept constant; (b) unchanged uptake when bolus free tryptophan was kept constant and total tryptophan decreased. Brain tryptophan uptake from a buffer bolus was decreased by large neutral amino acids. Plasma total tryptophan could be rapidly decreased and free tryptophan increased by briefly disturbing food deprived rats. When free tryptophan concentration rose markedly there was an associated increase of brain tryptophan and 5HT turnover. Studies of shock provoked analgesia in rats and cortical evoked potentials in man both suggest that physiological variations of serotonergic activity are sufficient to influence these measures. This raises the possibility that moderate changes of tryptophan supply to the brain could, in some circumstances, alter serotonergic activity.

TRYPTOPHAN REICHES ESSEN?

- ▶ Die Umwandlung von Tryptophan in 5-Hydroxytryptophan und schließlich in 5-Hydroxytryptamin (Serotonin) im ZNS ist durch exogene Zufuhr von Tryptophan stimulierbar.
- ▶ Notwendige Voraussetzung für eine ausreichende Serotoninsynthese im Gehirn scheint ein stetiges Angebot von freiem Tryptophan an der Blut-Hirnschranke zu sein.

Walderhaug et al. 2007, Schweighofer et al. 2008

AMINOSÄUREN AUSWAHL WICHTIG FÜR DIE SEROTOINSYNTHESE

- Für die Auswahl von Tryptophanreichen Lebensmitteln ist nicht die absolute Inhaltsmenge entscheidend sondern das **Verhältnis von Tryptophan zu anderen Aminosäuren** wie den verzweigkettigen AS und Leucin und Phenylalanin...

TRYPTOPHAN REICHE LEBENSMITTEL

| Food | Protein [g/100 g of food] | Tryptophan [g/100 g of food] | Tryptophan/Protein [%] |
|----------------------|------------------------------|---------------------------------|------------------------|
| Egg, white, dried | 81.10 | 1.00 | 1.23 |
| Spirulina, dried | 57.47 | 0.93 | 1.62 |
| Cod, atlantic, dried | 62.82 | 0.70 | 1.11 |
| Soybeans, raw | 36.49 | 0.59 | 1.62 |
| Pumpkin seed | 33.08 | 0.57 | 1.72 |
| Cheese, Parmesan | 37.90 | 0.56 | 1.47 |
| Caribou | 29.77 | 0.46 | 1.55 |
| Sesame seed | 17.00 | 0.37 | 2.17 |
| Cheese, cheddar | 24.90 | 0.32 | 1.29 |
| Sunflower seed | 17.20 | 0.30 | 1.74 |
| Pistachio | 21.00 | 0.28 | 1.3 |
| Cashew | 17.00 | 0.25 | 1.47 |

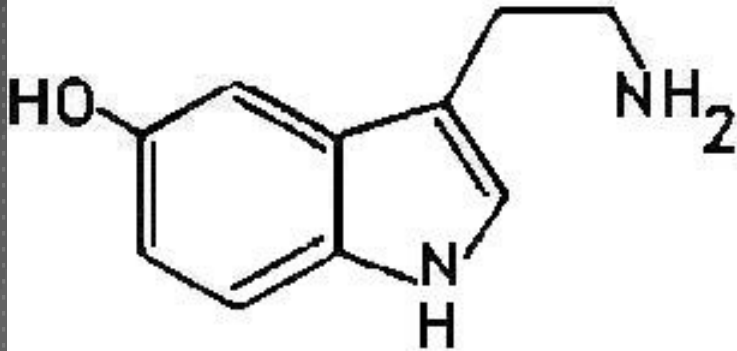
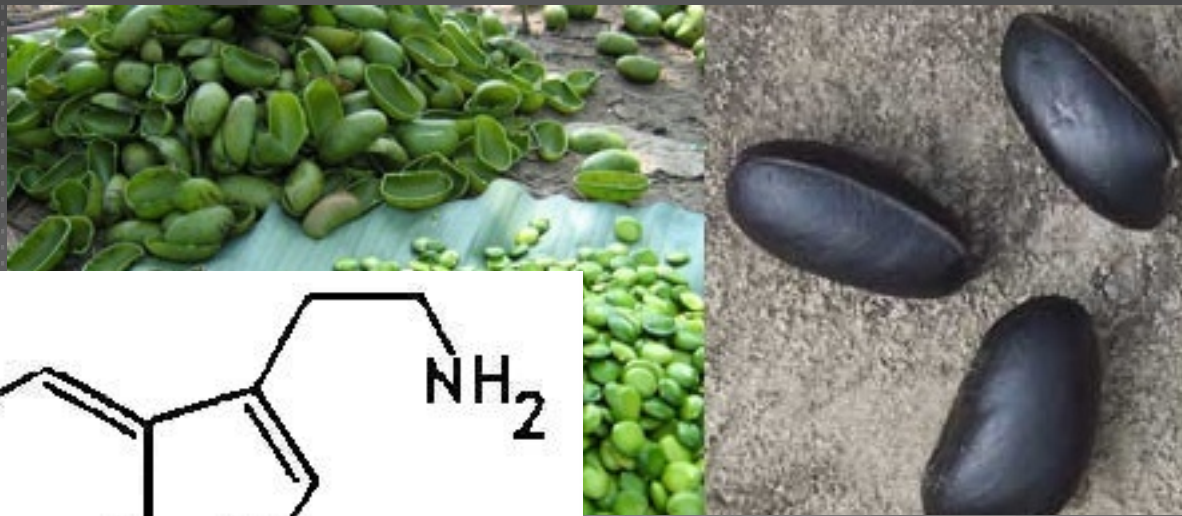
Joanne Holton, Nutrient Data Laboratory, Agricultural Research Service. "USDA National Nutrient Database for Standard Reference, Release 22 United States Department of Agriculture. 2009. Source Wikipedia

TRYPTOPHANGEHALT IN LEBENSMITTEL

| Food | Protein [g/100 g of food] | Tryptophan [g/100 g of food] | Tryptophan/Protein [%] |
|----------------------------------|------------------------------|---------------------------------|------------------------|
| almond | 21.00 | 0.21 | 1.00 |
| egg | 12.58 | 0.17 | 1.33 |
| wheat flour, white | 10.33 | 0.13 | 1.23 |
| baking chocolate, unsweetened | 12.9 | 0.13 | 1.23 |
| milk | 3.22 | 0.08 | 2.34 |
| rice, white | 7.13 | 0.08 | 1.16 |
| oatmeal, cooked | 2.54 | 0.04 | 1.16 |
| potatoes, russet | 2.14 | 0.02 | 0.84 |
| banana | 1.03 | 0.01 | 0.87 |

Joanne Holden, Nutrient Data Laboratory, Agricultural Research Service. "USDA National Nutrient Database for Standard Reference, Release 22 United States Department of Agriculture. 2009. Source Wikipedia

TRYPTOPHAN RICH FOOD



SEROTONIN

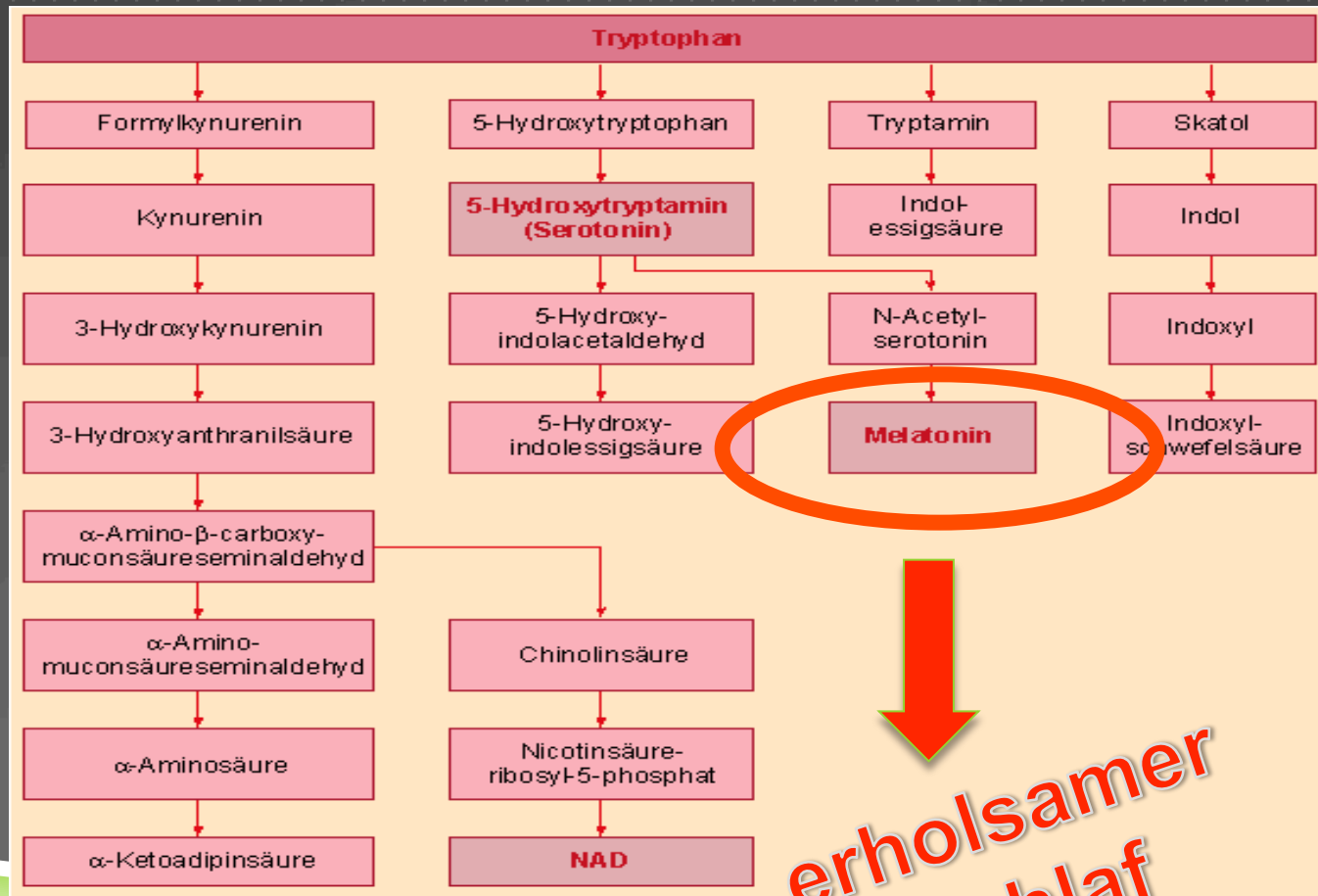
Griffonia simplicifolia

GRIFFONIA PHARMAKOLOGISCHE DATEN

- ▶ Nach oraler Verabreichung wird L-5-Hydroxytryptophan zu 50-85 % in den systemischen Kreislauf aufgenommen.
- ▶ Hier liegt es zu etwa 60 % an Plasmaproteine gebunden vor.
- ▶ Es wird fast vollständig zu Serotonin metabolisiert und in Form von 5-Hydroxyindolylessigsäure über den Urin ausgeschieden.
- ▶ Plasmahalbwertszeit beträgt ca. 2 bis 7 Stunden.

Westenberg HG, Gerritsen TW, Meijer BA, van Praag HM: *Kinetics of L-5-hydroxytryptophan in healthy subjects*. In: *Psychiatry Res.* 7, Nr. 3, Dezember 1982, S. 373–385

5 HT stärkt den Parasympathikus



STOLPERSTEINE TRYPTOPHANTHERAPIE



EIWEISS SHAKES IM FITNESS CENTRUM NICHT BEI DEPRESSIONEN



➤ Der Konsum von zusätzlichen Eiweissnahrung führt möglicherweise anteilig zu erhöhten **Phenylalanin und Leucinspiegeln** die in Wechselwirkung mit Tryptophan treten können.

PHENYLALANIN UND SEROTONIN

- Die Aminosäure **Phenylalanin blockiert** Serotonin Produktion, durch Behinderung der 5-Hydroxy-L-Tryptophan Decarboxylase (macht aus 5HT-→ Serotonin)
- **Steigerung der Proteinzufuhr erhöht** anteilig den Phenylalalinspiegel im **Blut!!!**

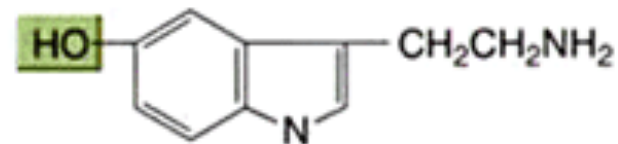
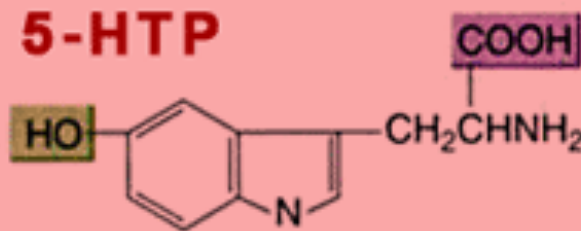
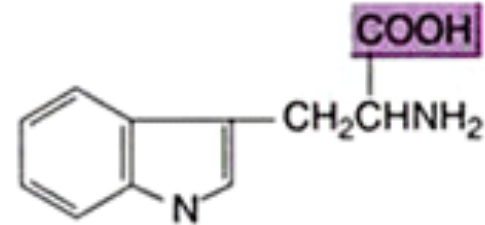
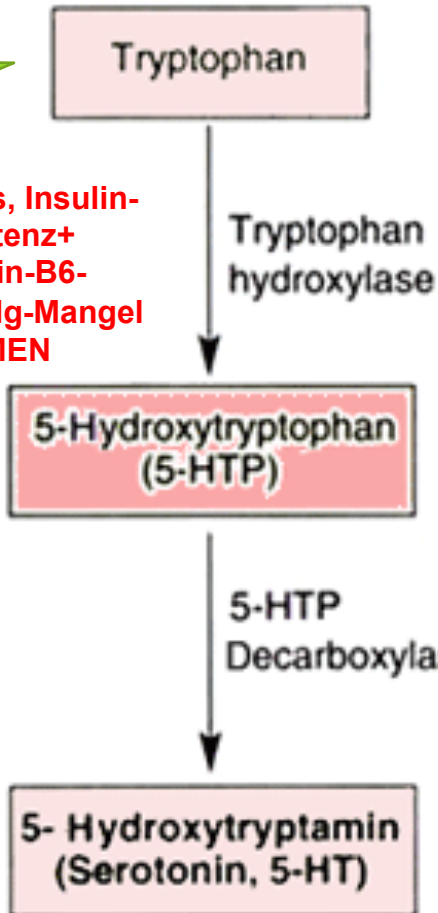
LEUCIN UND SEROTONIN

- ▶ Erhöhter Proteinverzehr erhöht den **Leucinspiegel im Blut.**
- ▶ Leucin steigert die Tryptophanpyrrolase, **welche Tryptophan irreversibel abbaut.**
- ▶ Leber kann Leucin nicht abbauen, dies kann nur die Muskulatur

SEROTONIN SYNTHESE

Darm

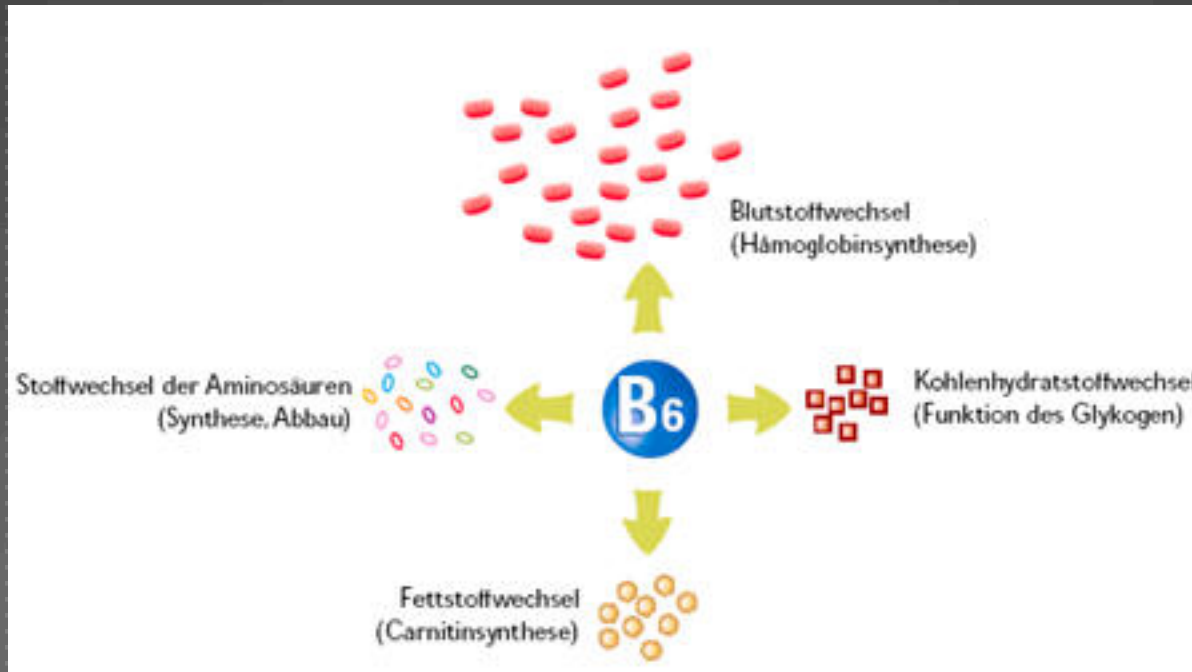
Stress, Insulin-
resistenz+
Vitamin-B6-
und Mg-Mangel
HEMMEN



STRESS REDUZIERENDE WIRKSTOFFE?

| | Wirkstoff | Wirkung |
|------------|----------------------|--|
| Rhodiola | Tyrosol und Rosavin | Entspannend |
| Catuaba | Catuabine A, B und C | Anregend, Antidepressiv |
| Yamswurzel | Diosgenin | Progesteronähnlich |
| Tyrosin | L-Tyrosin | Katecholaminsynthese: Dopamin, Adrenalin, Noradrenalin, Thyroxin |
| Vitamin B6 | Pyridoxin 5 Phosphat | Aufbau Serotonin Abbau Histamin |
| Vitamin B3 | Niacin | NADPH Vorstufe, Hemmung des Tryptophanabbaus |

PYRIDOXIN UND STOFFWECHSEL

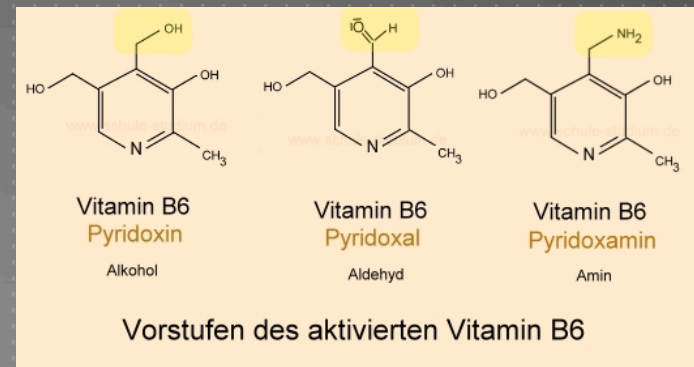


PYRIDOXIN 5 PHOSPHAT

P-5-P (Pyridoxal-5-Phosphate)

Die Abkürzung P-5-P steht für die Bezeichnung **Pyridoxal-5-Phosphat**. Dahinter verbirgt sich die aktive Coenzymform **von** Vitamin B 6, die einen entscheidenden **Vorteil** hat: Sie muss **von** der Leber nicht mehr umgewandelt werden, sondern kann in dieser Form direkt in den Stoffwechsel übergehen. Die übliche Form **von** Vitamin B 6 (Pyridoxin) muss, um Wirksamkeit entfalten zu können, immer erst in P-5-P umgewandelt werden. Klinische Studien haben ergeben, dass P-5-P bis zu 10 x wirksamer ist als Pyridoxin **HCl**.

Hinrichs, D. Handbuch der Nähr-und Vitalstoffe Constantia Verlag 2005 4. Auflage

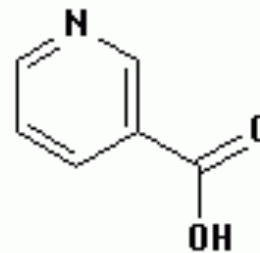


URSACHEN FÜR EINEN B6-MANGEL

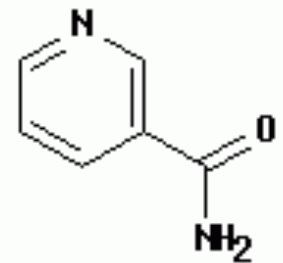
- ▶ Verschiedene Medikamente wie z.B. die oralen Kontrazeptiva —, Antihypertensiva (z.B. Hydralazin), und Penicillamin reduzieren Vitamin B6 im Körper
- ▶ **Cage Effekt:** Ausscheidung von Vitamin B6 über die Nieren wird durch die ansonsten empfohlene Aufnahme von Belaststoffen zusätzlich verstärkt. Ballaststoffe können nämlich Vitamin B6 als Gel „cage effect“ vermehrt binden und es zur Nierenausscheidung forcieren.

NIACIN UND TRYPTOPHAN

- ▶ Niacin hemmt den Tryptophanabbau (Enzym Tryptophanpyrrolase) und trägt damit zur Stabilisierung des Tryptophanpools im Körper bei.



nicotinic acid
(niacin)



nicotinamide
(niacinamide)

DIFFERENTIALDIAGNOSE CFS/ME

- ▶ Ausschlussdiagnose
- ▶ Komplexe körperlich lähmende Erschöpfung, Verschlimmerung nach Anstrengung, Schmerzen und kognitive Prozessen.

Carruthers BM et al. Chronic Fatigue Syndrome: Clinical Working Definition, Diagnostic and Treatment Protocols J

CFS 2003 11 (1) 7-116

CHRONISCHES ERSCHÖPFUNGSSYNDROM (CFS/ME)

[Int J Clin Exp Med](#). 2012;5(3):208-20. Epub 2012 Jun 15.

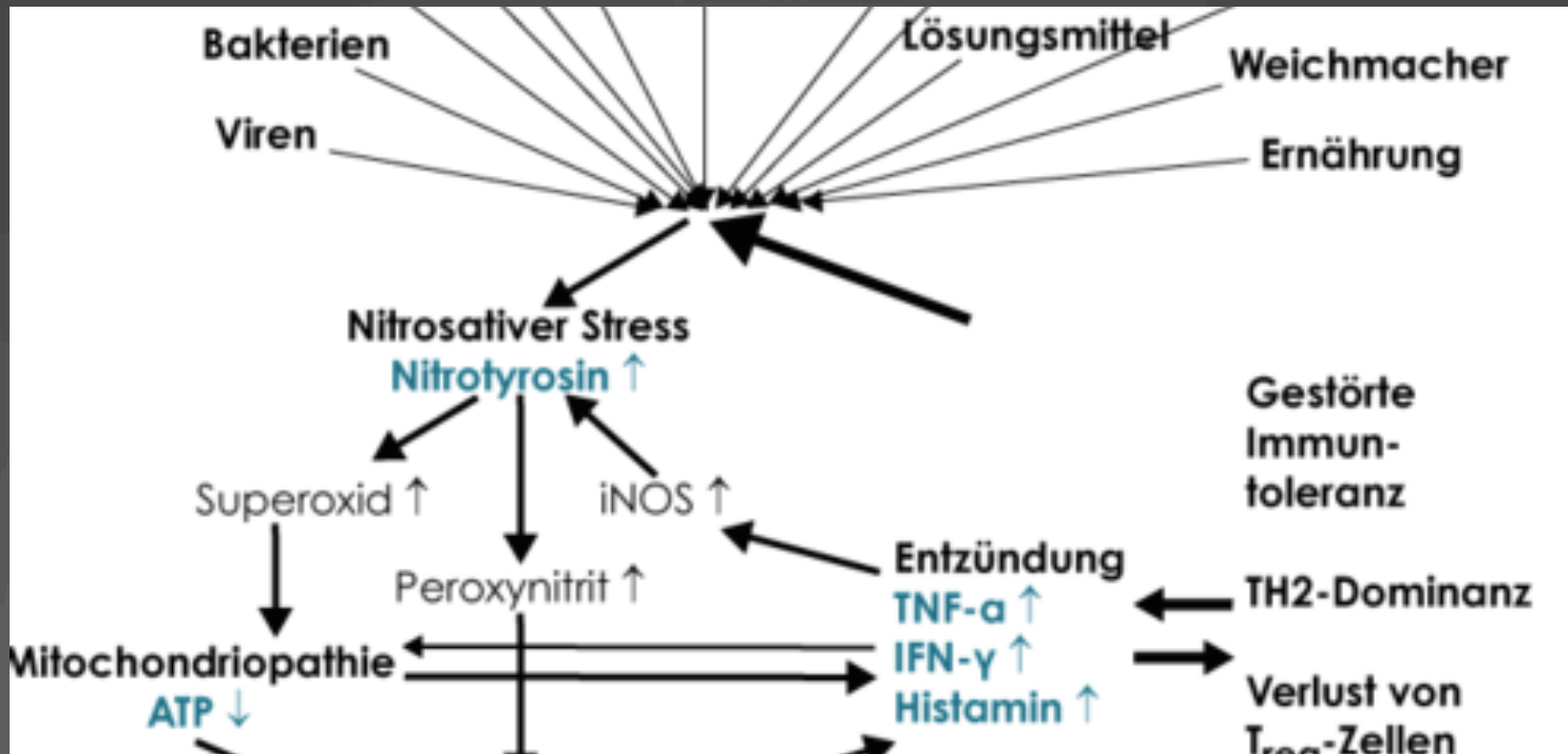
Mitochondrial dysfunction and the pathophysiology of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).

[Booth NE](#), [Myhill S](#), [McLaren-Howard J](#).

Abstract

The objectives of this study are to test the hypothesis that the fatigue and accompanying symptoms of Chronic Myalgic Encephalomyelitis/Fatigue Syndrome are in part due to defects in energy provision at the cellular level, and to understand the pathophysiology of the defects so that effective medical intervention can be implemented. We performed an audit of 138 patients (ages 18-65) diagnosed with ME/CFS and attending a private practice. The patients and 53 normal, healthy controls had the ATP Profile test carried out on neutrophils from a 3-ml venous blood sample. This test yields 6 numerical factors that describe the availability of ATP and the efficiency of oxidative phosphorylation in mitochondria. Other biomedical measurements, including the concentration of cell-free DNA in plasma, were made. The results of the audit are compared with the controls and a previous cohort of 61 patients. We find that all patients tested have measurable mitochondrial dysfunction which correlates with the severity of the illness. The patients divide into two main groups differentiated by how cellular metabolism attempts to compensate for the dysfunction. Comparisons with exercise studies suggest that the dysfunction in neutrophils also occurs in other cells. This is confirmed by the cell-free DNA measurements which indicate levels of tissue damage up to 3.5 times the normal reference range. The major immediate causes of the dysfunction are lack of essential substrates and partial blocking of the translocator protein sites in mitochondria. The ATP Profile is a valuable diagnostic tool for the clinical management of ME/CFS.

NITROSATIVER STRESS UND MITOCHONDRIOPATHIE



CFS/ME

EMPFOHLENE WIRKSTOFFE

| | Wirkstoff | Wirkung |
|---------------------------|--|--|
| Curcuma Coenzym 10 | Diferuloylmethan; pflanzliche Polyphenole. | Antiinflammativ und Hämoxxygenase-I (HO-I) bildend Elektronen- und Protonen- Überträger zwischen dem Komplex I bzw. Komplex II und dem Komplex III der Atmungskette. Coenzym der oxidativen Phosphorylierung, |
| Methyl B12 | Methylcobalamin | Reduziert Nitrostress |
| Vitamin B5 | Pantothensäure Pantoinsäure und β -Alanin | Aufbau Acetyl COA und Acetylcholin (Vagus) |
| Acetyl-Carnithin | Carnithin | β -Oxidation der Fettsäuren in Mitochondrien |

CURCUMIN UND MITOCHODRIOPATHIE

[Free Radic Biol Med.](#) 2013 Mar 30;61C:119-129. doi: 10.1016/j.freeradbiomed.2013.03.017. [Epub ahead of print]

Curcumin maintains cardiac and mitochondrial function in chronic kidney disease.

[Correa F¹](#), [Buelna-Chontal M](#), [Hernández-Reséndiz S](#), [R García-Niño W](#), [J Roldán F](#), [Soto V](#), [Silva-Palacios A](#), [Amador A](#), [Pedraza-Chaverrí J](#), [Tapia E](#), [Zazueta C](#).

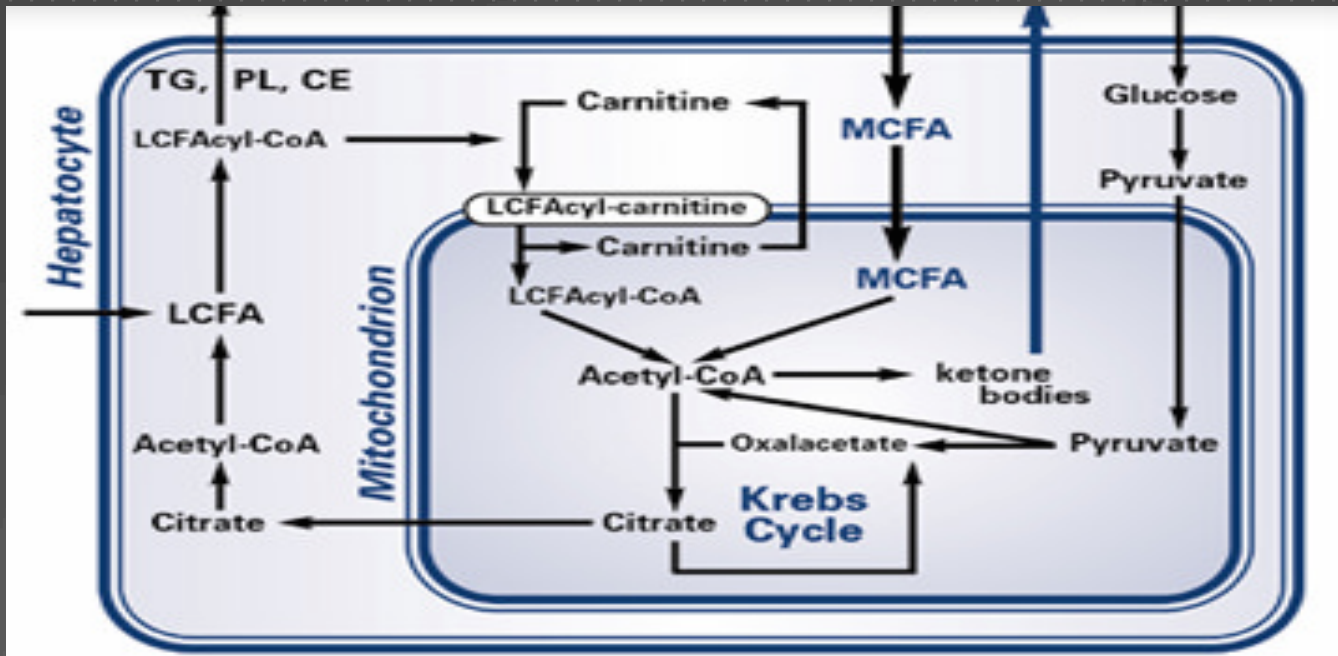
Author information



Abstract

Curcumin, a natural pigment with antioxidant activity obtained from turmeric and largely used in traditional medicine, is currently being studied in the chemoprevention of several diseases for its pleiotropic effects and nontoxicity. In chronic renal failure, the pathogenic mechanisms leading to cardiovascular disorders have been associated with increased oxidative stress, a process inevitably linked with mitochondrial dysfunction. Thus, in this study we aimed at investigating if curcumin pretreatment exerts cardioprotective effects in a rat model of subtotal nephrectomy (5/6Nx) and its impact on mitochondrial homeostasis. Curcumin was orally administered (120mg/kg) to Wistar rats 7 days before nephrectomy and after surgery for 60 days (5/6Nx+curc). Renal dysfunction was detected a few days after nephrectomy, whereas changes in cardiac function were observed until the end of the protocol. Our results indicate that curcumin treatment protects against pathological remodeling, diminishes ischemic events, and preserves cardiac function in uremic rats. Cardioprotection was related to diminished reactive oxygen species production, decreased oxidative stress markers, increased antioxidant response, and diminution of active metalloproteinase-2. We also observed that curcumin's cardioprotective effects were related to maintaining mitochondrial function. Aconitase activity was significantly higher in the 5/6Nx + curc (408.5±68.7nmol/min/mg protein) than in the 5/6Nx group (104.4±52.3nmol/min/mg protein, P<0.05), and mitochondria from curcumin-treated rats showed enhanced oxidative phosphorylation capacities with both NADH-linked substrates and succinate plus rotenone (3.6±1 vs 1.1±0.9 and 3.1±0.7 vs 1.2±0.8, respectively, P<0.05). The mechanisms involved in cardioprotection included both direct antioxidant effects and indirect strategies that could be related to protein kinase C-activated downstream signaling.

ACETYL L-CARNITHIN



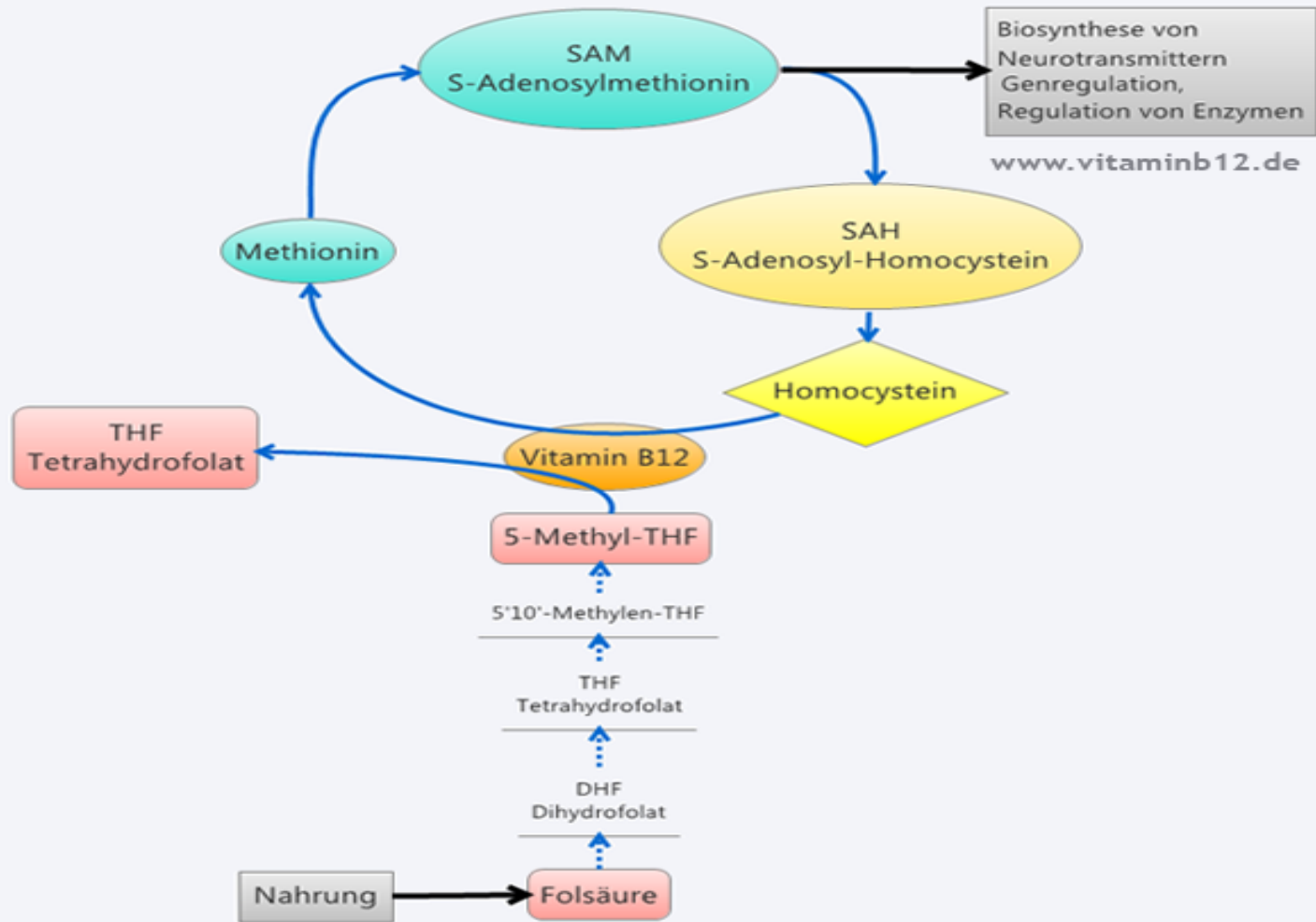
Acetyl-L-Carnitin fördert während der Fettsäureoxidation die Aufnahme von Acetyl-CoA in die Mitochondrien, es steigert die Acetylcholin-Produktion

METHYL-COBALAMIN UND NITROSATIVER STRESS

- ▶ Methylcobalamin ist eine der beiden bioaktiven Coenzym-Formen von Vitamin B12, die unser Körper wirklich benötigt.
- ▶ Nur Methylcobalamin und Adenosylcobalamin können direkt eine gesundheitliche Wirkung entfalten – alle anderen Formen von Vitamin B12 müssen vom Körper erst in Methylcobalamin oder Adenosylcobalamin umgewandelt werden, um als Coenzyme im Körper aktiv werden zu können.

WIRKUNG METYL-COBALAMIN

- ▶ Es reaktiviert die Folsäure,
- ▶ macht das gefährliche Homocystein unschädlich und
- ▶ bildet eine Vorstufe des wichtigen S-Adenosylmethionin.



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