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Psychische Aspekte bei der Hashimoto Thyreoiditis

E. Petnehazy

SCHILDDRÜSEN INSTITUT

Acta Med Scand. 1976;199(3):233-6.

Myxedematous madness without myxedema. Selective defect of TSH release on TRF loading in a young woman with a history of severe depressive illness cured with thryoid hormone replacement therapy.

Nordgren L, von Schéele C.

Klinik

BARMHERZIGE BRÜDER
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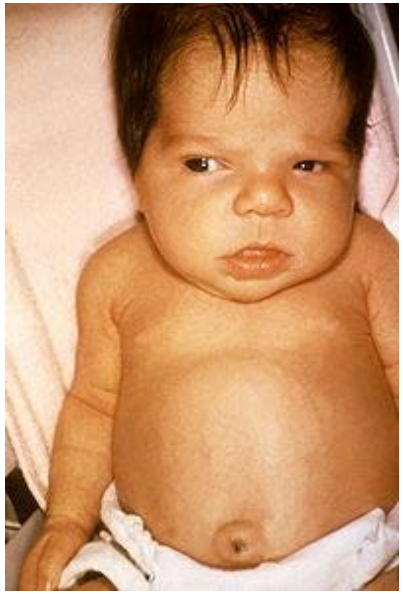
- Makroglossie
- Nabelhernie
- Trinkfaulheit
- Obstipation
- Bradykardie
- Muskelhypotonie
- Bewegungsarmut
- Ikterus neonatorum prolongatus
- Wachstumsrückstand
- **Mentale Retardierung**
- **Verzögerte motorische Entwicklung**



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Neuropsychiatrische Symptome

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kognitive Beeinträchtigung

(Gedanken, Denkleistung, Konzentration, Merkfähigkeit)

affektive Beeinträchtigung

(Emotionen, Stimmung, Gefühle, soziales Verhalten)

von milder Beeinträchtigung bis ausgeprägten Störungen (Depression, Pseudodemenz)

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Zusammenhang Schilddrüse und Psyche ?

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Schilddrüsenfunktionsstörung per se ?

Fehlregulation lokal im Gehirn ?

Schilddrüsenantikörper per se ?

Übergeordneter immunologischer Prozess?

Unabhängig von der Schilddrüse ?

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Hashimoto und Psyche

BARMHERZIGE BRÜDER
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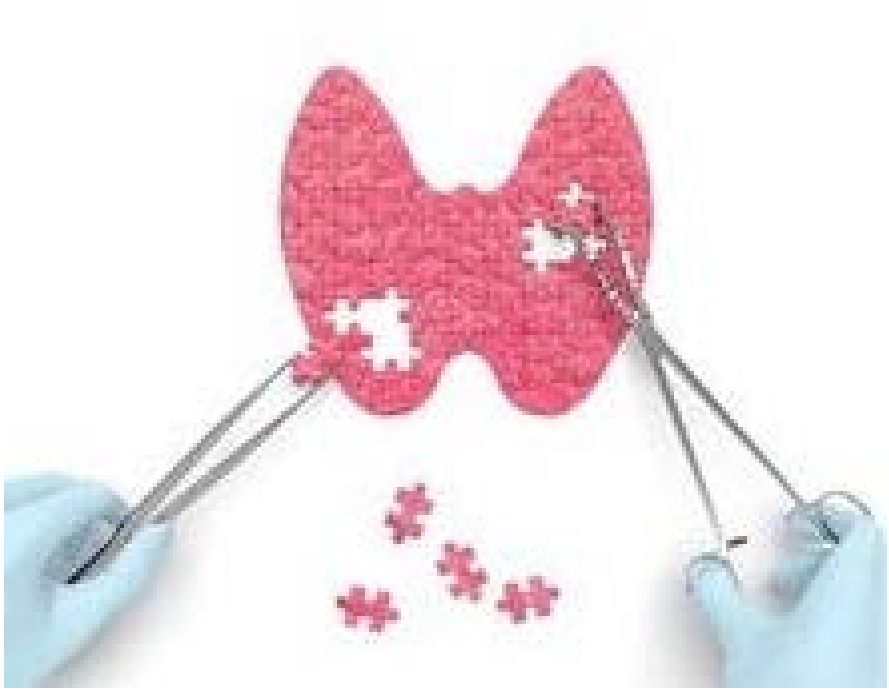

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Hypothyroidism and Depression

Colin M. Dayan[a] Vijay Panicker[b]

Eur Thyroid J 2013;2:168–179
DOI: 10.1159/000353777

BARMHERZIGE BRÜDER KRANKENHAUS GRAZ-EGGENBERG

Table 1. Studies investigating the relationship between thyroid function and depression/psychological well-being

Study	n	Thyroid measure	Psychiatric measure	Analysis	Association	Direction	p
Engum et al. [14]	30,589	TSH	HADS	abnormal vs. euthyroid	no		–
Forman-Hoffman and Philibert [16]	6,869	free T4/TSH	DIS	continuous	yes	↓ ↓	0.001 TSH 0.03 free T4
Roberts et al. [18]	5,857	free T4/TSH	HADS	continuous	no (depression)		–
Almeida et al. [19]	3,932	free T4/TSH	GDS, ICD depression	continuous	no		
Grabe et al. [74]	3,790	free T4/T3/TSH	Zersson Complaint Scale	abnormal vs. euthyroid	no		
Williams et al. [17]	2,269	total T4	GHQ-30	continuous	yes		
Philibert et al. [24]	1,555	free T4/TSH	lifetime MD	continuous	no		
Guimaraes et al. [20]	1,298	free T4/TSH	PRIME-MD	abnormal vs. euthyroid	TSH >10 yes Clin Hypo yes SC Hypo no	↑ ↑ –	
de Jongh et al. [75]	1,219	TSH +/– T4/T3	CES-D	abnormal vs. euthyroid	ns		
van de Ven et al. [23]	1,125	free T4/TSH	BDI, current/ever depression	groups of thyroid	ns		
Kritz-Silverstein et al. [76]	1,110	TSH	BDI	continuous	men yes women no	↓ –	
Gussekloo et al. [77]	599	free T4/TSH	GDS	continuous	no		–
Pop et al. [25]	538	free T4/TSH	EDS	abnormal vs. euthyroid	no		–
Kim et al. [78]	495	TSH	GMS	continuous	ns		
Jorde et al. [38]	243	free T4/TSH	GHQ-30	SC hypothyroid vs. euthyroid	yes	↓	<0.01
Gulseren et al. [21]	160	free T4/T3/TSH	HDRS, SF-36	abnormal vs. euthyroid	yes	↑	0.001
Frey et al. [79]	121	free T4/T3/TSH	NEO depressive trait	continuous	TSH & neuro	↓	0.0002 TSH
van Boxtel et al. [80]	120	TSH	SCL	continuous	no		–
Bono et al. [22]	36	free T4/T3/TSH	HDRS	SC hypothyroid vs. treated	yes	↑	<0.05

HADS = Hospital anxiety and depression scale; DIS = diagnostic interview schedule; GDS = geriatric depression scale; ICD = international classification of diseases; GHQ = general health questionnaire; PRIME-MD = primary care evaluation of mental disorders; CES-D = centre for epidemiological studies-depression scale; BDI = becks depression index; EDS = edinburgh depression scale; GMS = geriatric mental scale; HDRS = hamilton depression rating scale; SF-36 = short form 36; NEO = neurotism, extraversion, openness personality inventory; SCL = symptomatic check list; SC = subclinical; ↑ = positive association; ↓ = inverse association.

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Controversial studies

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Association between postpartum thyroid dysfunction and thyroid antibodies and depression.

B. Harris, S. Othman, J. A. Davies, G. J. Weppner, C. J. Richards, R. G. Newcombe, J. H. Lazarus, A. B. Parkes, R. Hall, and D. I. Phillips

BMJ. 1992 Jul 18; 305(6846): 152–156.

Conclusion—Depressive symptoms are associated with positive thyroid antibody status in the postpartum period.

Transient post-partum thyroid dysfunction and postnatal depression.

Harris B[1], Fung H, Johns S, Kologlu M, Bhatti R, McGregor AM, Richards CJ, Hall R.

J Affect Disord. 1989 Nov-Dec;17(3):243-9.

The presence of autoantibodies showed little association with depressed mood

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Hypothyroidism and Depression

Colin M. Dayan[a] Vijay Panicker[b]

Eur Thyroid J 2013;2:168–179
DOI: 10.1159/000353777

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Conclusion:

Despite the large number of studies, the relationship between thyroid function and depression remains poorly defined (many conflicting studies)

Subjects on thyroxine even if biochemically euthyroid have poorer psychological well-being than subjects with no thyroid disease

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Thyroxine & poorer psychological well being

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Acta Psychiatr Scand. 2002 Jul;106(1):27-34.

An association between depression, anxiety and thyroid function--a clinical fact or an artefact?

Engum A[1], Bjøro T, Mykletun A, Dahl AA.

Clin Endocrinol (Oxf). 2009 Oct;71(4):574-80. doi: 10.1111/j.1365-2265.2008.03521.x.

A paradoxical difference in relationship between anxiety, depression and thyroid function in subjects on and not on T4: findings from the HUNT study.

Panicker V[1], Evans J, Bjøro T, Asvold BO, Dayan CM, Bjerkeset O.

Clin Endocrinol (Oxf). 2002 Nov;57(5):577-85.

Psychological well-being in patients on 'adequate' doses of l-thyroxine: results of a large, controlled community-based questionnaire study.

Saravanan P[1], Chau WF, Roberts N, Vedhara K, Greenwood R, Dayan CM.

Eur J Endocrinol. 2005 Dec;153(6):747-53.

Cognitive functioning and well-being in euthyroid patients on thyroxine replacement therapy for primary hypothyroidism.

Wekking EM[1], Appelhof BC, Fliers E, Schene AH, Huyser J, Tijssen JG, Wiersinga WM.

Thyroid. 2007 Mar;17(3):249-58.

Health status, psychological symptoms, mood, and cognition in L-thyroxine-treated hypothyroid subjects.

Samuels MH[1], Schuff KG, Carlson NE, Carello P, Janowsky JS.

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Thyroxine & poorer mental health

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Mis-attribution of symptoms – overlap of both depression and hypothyreoidism in older women

Depressive symptoms mostly unrelated to thyroid disease

Genetic variants

Comorbidities , chronic disease and longlife medication are associated with poorer mental health

Hypothyroidism and Depression

Eur Thyroid J 2013;2:168–179
DOI: 10.1159/000353777

Colin M. Dayan[a] Vijay Panicker[b]

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Hypothyroidism and Depression

Colin M. Dayan[a] Vijay Panicker[b]

Eur Thyroid J 2013;2:168–179
DOI: 10.1159/000353777

BARMHERZIGE BRÜDER KRANKENHAUS GRAZ-EGGENBERG

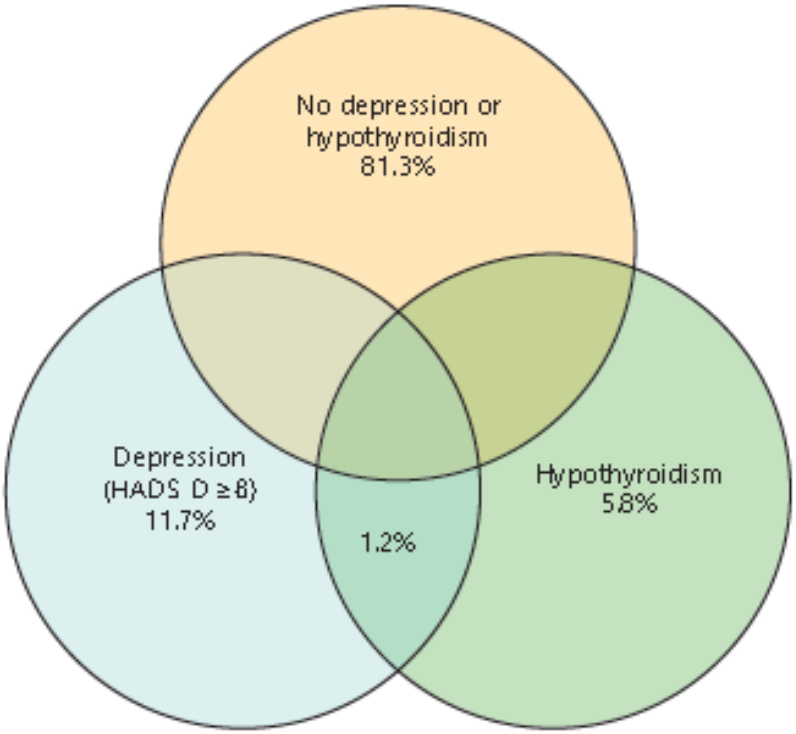

Fig. 3. Overlap of subjects with both depression and raised TSH in the HUNT 2 cohort.

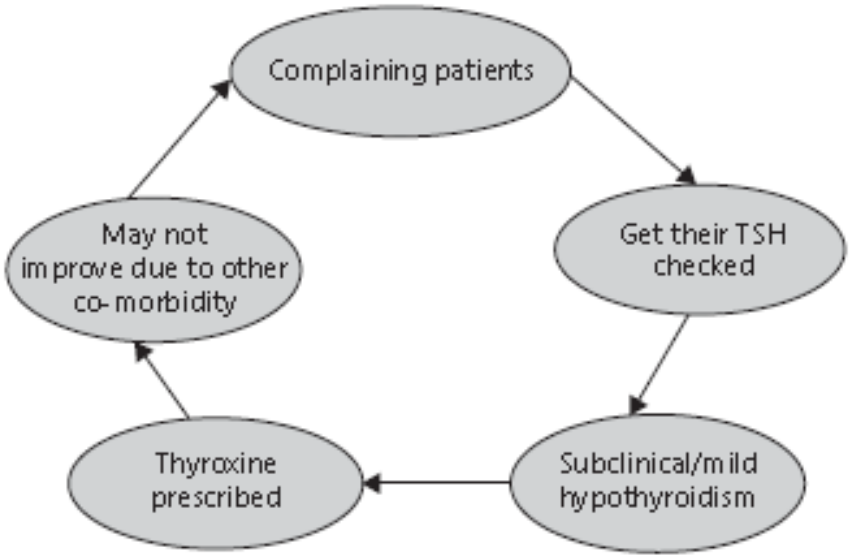

Fig. 2. Cycle of mis-attribution of symptoms to thyroid disease and continued symptoms. Proposed mechanism to explain why many subjects do not respond to thyroid hormone replacement despite adequate levels of TSH.

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More antidepressant medication under thyroxine

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Eur J Endocrinol. 2009 Dec;161(6):917-21. doi: 10.1530/EJE-09-0606. Epub 2009 Sep 15.

Treated hypothyroidism, cognitive function, and depressed mood in old age: the Rancho Bernardo Study.

Kramer CK[1], von Mühlen D, Kritz-Silverstein D, Barrett-Connor E.

treated hypothyroidism group had more frequent antidepressant medication use (19.5 vs 8.5%, P<0.001)

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Hashimoto Thyreoiditis

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Latent

Manifeste Hypothyreose

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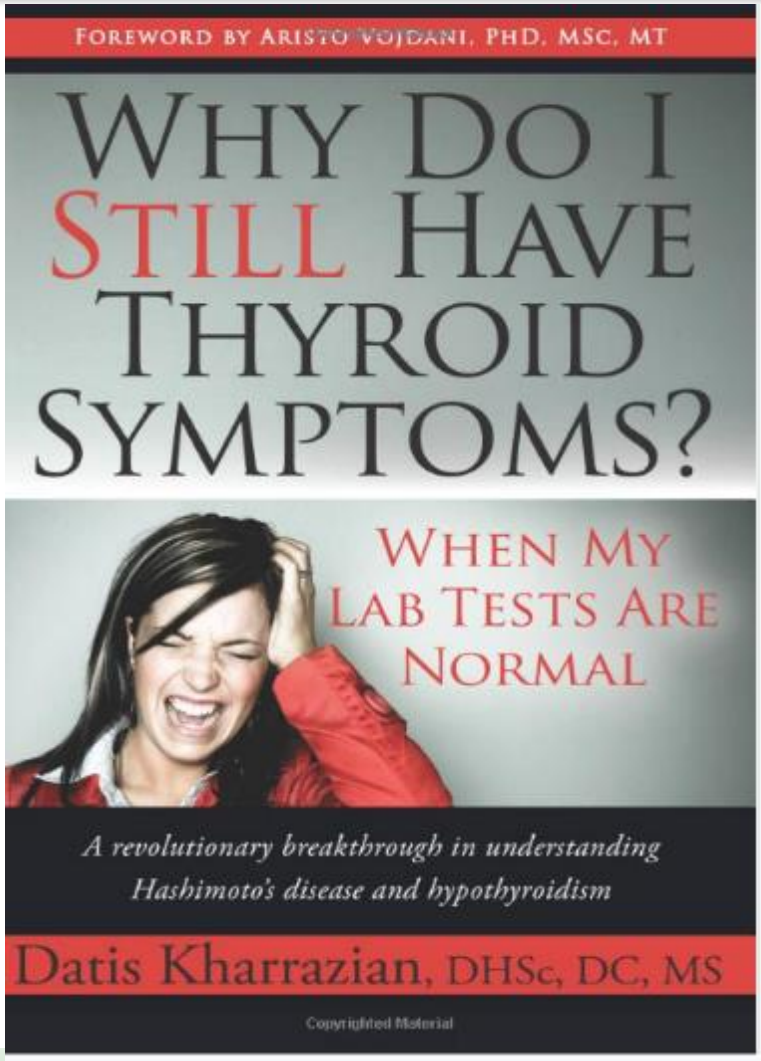
Hashimoto


FOREWORD BY ARISTO VOJDANI, PHD, MSC, MT
WHY DO I STILL HAVE THYROID SYMPTOMS?
WHEN MY LAB TESTS ARE NORMAL
A revolutionary breakthrough in understanding Hashimoto's disease and hypothyroidism
Datis Kharrazian, DHSc, DC, MS
Copyrighted Material

Leben mit Hashimoto

„Quality of life“

Libido

Regelmäßiger Zyklus

Vitalität, Leistungsfähigkeit

Ausgeglichenheit, stabile Stimmung

Aussehen (Gewicht, Haut, Haare)

Selbstbestimmung bei Kinderwunsch

Hashimoto Thyreoiditis und Quality of Life

BARMHERZIGE BRÜDER
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GRAZ-EGGENBERG

Autoimmunity affects health-related quality of life in patients with Hashimoto's thyroiditis

Hilal Bektas Uysal [a,*], Mediha Ayhan [b]

Kaohsiung Journal of Medical Sciences (2016) xx, 1–

Am J Surg. 2014 Jun;207(6):974-9. doi: 10.1016/j.amjsurg.2013.05.005. Epub 2013 Sep 24.

Quality of life after thyroid surgery in women with benign euthyroid goiter: influencing factors including Hashimoto's thyroiditis.

Promberger R[1], Hermann M[2], Pallikunnel SJ[2], Seemann R[3], Meusel M[2], Ott J[4].

Thyroid. 2011 Feb;21(2):161-7. doi: 10.1089/thy.2010.0191. Epub 2010 Dec 27.

Hashimoto's thyroiditis affects symptom load and quality of life unrelated to hypothyroidism: a prospective case-control study in women undergoing thyroidectomy for benign goiter.

Ott J[1], Promberger R, Kober F, Neuhold N, Tea M, Huber JC, Hermann M.

J Neuroendocrinol. 2008 Oct;20(10):1101-14. doi: 10.1111/j.1365-2826.2008.01774.x. Epub 2008 Jul 30.

The thyroid-brain interaction in thyroid disorders and mood disorders.

Bauer M[1], Goetz T, Glenn T, Whybrow PC.

Clin Endocrinol (Oxf). 2016 Jun;84(6):925-31. doi: 10.1111/cen.12956. Epub 2015 Oct 19.

Sexual function and depressive symptoms in young women with thyroid autoimmunity and subclinical hypothyroidism.

Krysiak R[1], Drosdzol-Cop A[2], Skrzypulec-Plinta V[2], Okopien B[1].

Nord J Psychiatry. 2015 Jan;69(1):73-8. doi: 10.3109/08039488.2014.929741. Epub 2014 Jul 1.

Well-being and depression in individuals with subclinical hypothyroidism and thyroid autoimmunity - a general population study.

Fjaellegaard K[1], Kvetny J, Allerup PN, Bech P, Ellervik C.

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SF36- Gesundheitsfragebogen

BARMHERZIGE BRÜDER
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Krankheitsunspezifisches Messinstrument zur Erhebung der gesundheitsbezogenen Lebensqualität

Beschreibung des individuellen Gesundheitszustandes von Patienten und krankheitsbedingte Belastungen

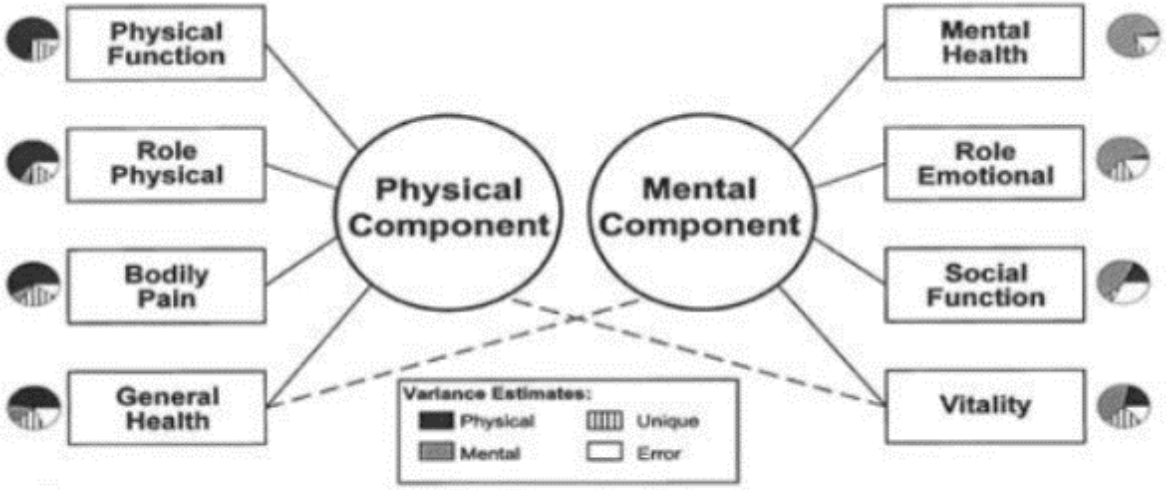

Abbildung 6: Repräsentation physischer und psychischer Komponenten der Gesundheit durch die verschiedenen Subskalen des SF-36 (Ware, 2000).

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SF-36 Fragebogen

BARMHERZIGE BRÜDER
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ORIGINAL ARTICLE

Autoimmunity affects health-related quality of life in patients with Hashimoto's thyroiditis

Hilal Bektas Uysal [a,*], Mediha Ayhan [b]

…our study revealed that higher thyroid antibody levels were negatively correlated with life quality scores. Thus, patients who had higher anti-TPO and anti-Tg levels had significantly lower quality of life domain scores!

Kaohsiung Journal of Medical Sciences (2016), http://dx.doi.org/10.1016/j.kjms.2016.06.006

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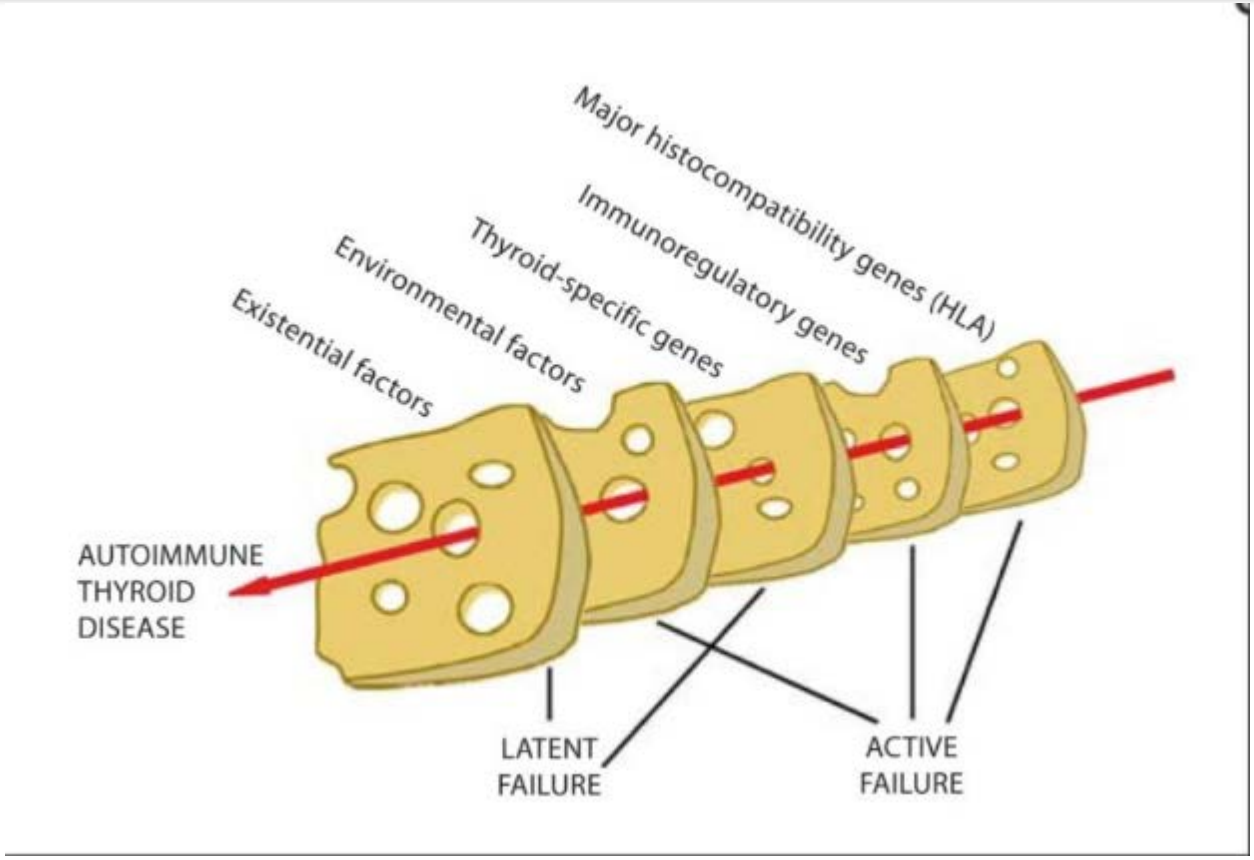
Immunpathogenese



Eur Thyroid J. 2013 Jan;1(4):243-50. doi: 10.1159/000343834. Epub 2012 Nov 2.

The immunopathogenesis of chronic autoimmune thyroiditis one century after hashimoto.

Weetman AP[1].

Immunpathogenese

BARMHERZIGE BRÜDER
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Genetische Faktoren:

Major Histokombatibilitätsgene (HLA)

Immunregulatorische Gene (CTLA4, PTPN22,FOXP3,CD40,CD25)

Schilddrüsenspezifische Gene (TSHR, Tg)

Umwelteinflüße:

Jodzufuhr, Nikotin, Alkohol, Infektionen, Stress, Medikamente, Selen, Zink, Eisen, Vitamin D3, Coenzym Q10, Omega 3-Fettsäuren

Existentielle Faktoren:

Weibliches Geschlecht (X-Chromosom, Frauenhormone),Parität, Alter

SCHILDDRÜSEN INSTITUT

Clinical Relevance of Environmental Factors in the Pathogenesis of Autoimmune Thyroid Disease

Wilmar M. Wiersinga Endocrinol Metab (Seoul). 2016 Jun; 31(2): 213–222.

Was tun ?

BARMHERZIGE BRÜDER
KRANKENHAUS
GRAZ-EGGENBERG

Genetische Faktoren

Major Histokombtibilitätsgene (HLA)

Immunregulatorische Gene (CTLA4, PTPN22,FOXP3,CD40,CD25)

Schilddrüsenspezifische Gene (TSHR, Tg)

Umwelteinflüße

Jodzufuhr, Nikotin, Alkohol, Infektionen, Stress, Medikamente, Selen, Zink, Eisen, Vitamin D3, Coenzym Q10, Omega 3, Sexualsteroide

Existentielle Faktoren

Weibliches Geschlecht (X-Chromosom, Frauenhormone),Parität, Alter

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Risikoprävention

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Modulation of Exposure to Environmental Factors in Order to Decrease the Risk of Developing Autoimmune Thyroid Disease

Preventive intervention	Risk of TPO-Ab	Risk of Hashimoto hypothyroidism	Risk of Graves hyperthyroidism
Stop smoking	Increase	Increase	Decrease
Use alcohol	No change	Decrease	Decrease
Use selenium	?	?	?
Use vitamin D	?	?	?
Avoid pregnancy	Decrease	Decrease	Decease
Avoid stress	No change	No change	Decrease

Eur J Endocrinol. 2014 Jun;170(6):R241-52. doi: 10.1530/EJE-14-0047. Epub 2014 Mar 7.

Mechanisms in endocrinology: autoimmune thyroid disease: old and new players.

Effraimidis G[1], Wiersinga WM[2].

Endocrinol Metab (Seoul). 2016 Jun; 31(2): 213–222. PMCID: PMC4923404
Published online 2016 May 13. doi: 10.3803/EnM.2016.31.2.213

Clinical Relevance of Environmental Factors in the Pathogenesis of Autoimmune Thyroid Disease

Wilmar M. Wiersinga

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Personalisierte Medizin

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Regulation des Immunsystems („Immunbalanz“)

Bei Mangel Ausgleich von Vitaminen/Spurenelementen

„lifestyle modification“

Gesunde Ernährung (mediterane Kost)

Ausdauersport

Ausreichende Schlaf- und Erholungsphasen

Psychosoziale Hygiene

Schilddrüsenhormonwirkung

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Adäquate Produktion/ Substitution

Transport Zielorgane

Aufnahme Zielzelle (Resistenz)

Konversion in aktives Hormon

Störungen

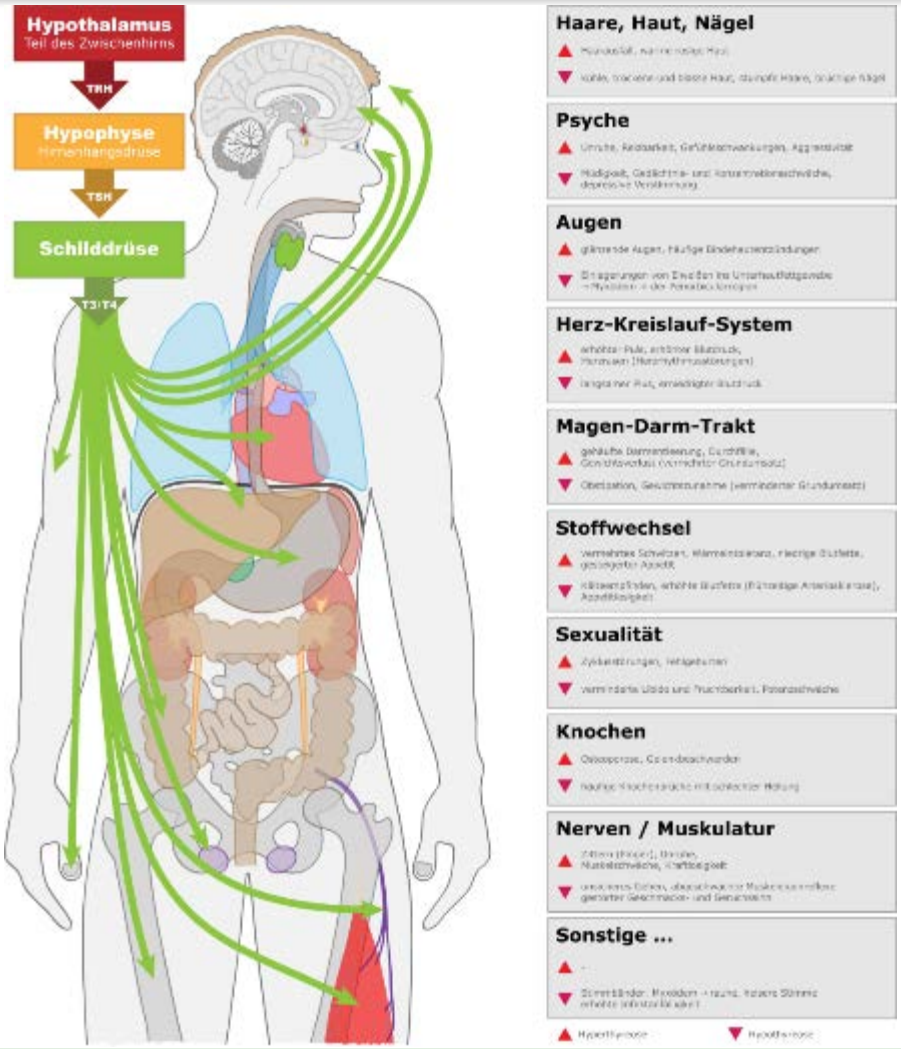
angeboren

bei Insulinresistenz

Nebenniereninsuffizienz

Depression

chron. Infektionen



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Schilddrüsenhormonmetabolismus Gehirn

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- Transporterproteine

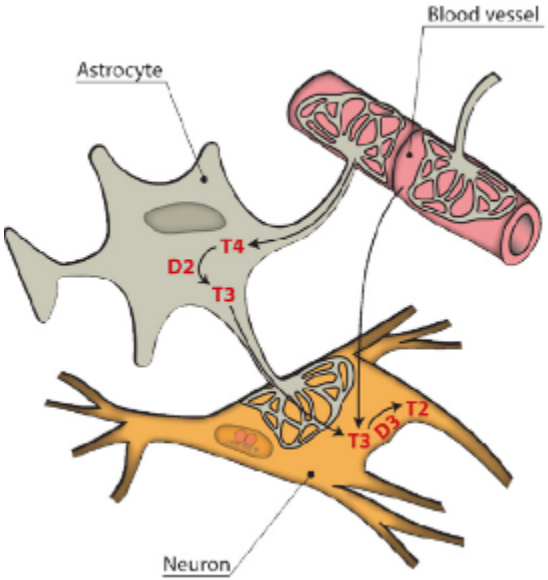
  Transthyretin, organic anion transporter polypeptid 1 (OATP1C1), monocarboxylase transporter 8 (MCT8)

- Dejodination

  Dejodinase Typ 2 (D2)

- Rezeptoren

  THR alpha



Thyroid Hormones in Brain Development and Function

Juan Bernal, M.D., Ph.D.
Professor of Research Instituto de Investigaciones Biomedicas, Consejo Superior de Investigaciones Científicas (CSIC) and Universidad Autónoma de Madrid (UAM), and Center for Biomedical Research in Rare Diseases (CIBERER), Madrid, Spain

Last Update: September 2, 2015

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Schilddrüsenhormonwirkung im Gehirn

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genomisch/ nichtgenomisch

TH-Rezeptor =Transkriptionsfaktor

Glukosemetabolismus (Insulin)

Neuronale Aktivität/ Neurotransmitter

Oxidativen Mitochondrienmetabolismus

Thyroid hormone's role in regulating brain glucose metabolism and potentially modulating hippocampal cognitive processes

V Jahagirdar[1] and EC McNay[1]

Metab Brain Dis. 2012 Jun; 27(2): 101–111.

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Schilddrüsenhormonwirkung im Gehirn

BARMHERZIGE BRÜDER KRANKENHAUS GRAZ-EGGENBERG

Thyroid hormone's role in regulating brain glucose metabolism and potentially modulating hippocampal cognitive processes

V Jahagirdar[1] and EC McNay[1]

Metab Brain Dis. 2012 Jun; 27(2): 101–111.

Thyroid hormone is a good candidate to be a modulator of memory processes

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J Thyroid Res. 2012;2012:590648. doi: 10.1155/2012/590648. Epub 2011 Dec 14.

BARMHERZIGE BRÜDER
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GRAZ-EGGENBERG

The Link between Thyroid Function and Depression.

Hage MP[1], Azar ST.

Schilddrüsenfunktionsstörungen können zu neuropsychiatrischen Alterationen führen

Depression kann zu Veränderungen der Schilddrüsenhormonkonstellation und TSH-Tagesrhythmik führen

Die antidepressive Therapie kann zu Veränderungen der Schilddrüsenhormonkonstellation führen

Scheinbare Assoziation postpartale Depression und Thyreoiditis

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Hashimoto und Psyche

BARMHERZIGE BRÜDER
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GRAZ-EGGENBERG

Curr Opin Psychiatry. 2010 Jul;23(4):363-8. doi: 10.1097/YCO.0b013e3283387b50.

Thyroid disease and mental disorders: cause and effect or only comorbidity?

Bunevicius R[1], Prange AJ Jr.

Thyroid autoimmunity itself, even in the absence of a change in thyroid state, may contribute to mental symptoms in vulnerable patients. Thus, the brain may be more involved in autoimmune processes than previously realized.

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Hashimoto und Psyche

BARMHERZIGE BRÜDER
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Endocr J. 2017 Apr 29;64(4):425-429. doi: 10.1507/endocrj.EJ16-0418. Epub 2017 Mar 4.

Is thyroid autoimmunity itself associated with psychological well-being in euthyroid Hashimoto's thyroiditis?

Yalcin MM[1], Altinova AE[1], Cavnar B[2], Bolayir B[1], Akturk M[1], Arslan E[1], Ozkan C[1], Cakir N[1], Balos Toruner F[1].

In conclusion, HRQoL is impaired in patients with HT independent of levothyroxine replacement. Also, depression and anxiety scores of these patients are higher than euthyroid subjects without HT. Therefore, our results indicate that thyroid autoimmunity *per se* may have an impact on psychological well-being in euthyroid patients with HT.

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Immunbalance

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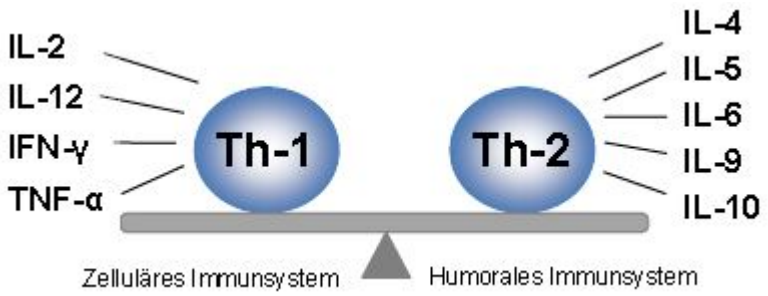
Schlüsselrolle T-Helferzellen (CD4)



Th1 - Dominanz	Th2 - Dominanz
Organspezifische Auto-immunerkrankungen (z.B. Diabetes mellitus Typ I, Hashimoto-Thyreoiditis, M. Basedow, multiple Sklerose)	**allergische Reaktionen** Typ I-Allergien: Rhinitis, Konjunktivitis, Asthma bronchiale, atop. Dermatitis, Nahrungsmittelallergien der Typen I und III
Kontaktdermatitis (z.B. Nickel)	Mykosen
LKN-Tuberkulose	Miliare Tuberkulose

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Cytokine-Associated Emotional and Cognitive Disturbances in Humans

Abraham Reichenberg, PhD; Raz Yirmiya, PhD; Andreas Schuld, MD; Thomas Kraus, MD; Monika Haack, MA; Abraham Morag, MD†; Thomas Pollmächer, MD

Arch Gen Psychiatry. 2001;58:445-452

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T3/T4 Kombinationstherapie ?

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Overall studies have not shown any benefits

But some subjects feel better under T4/T3 combination

genetic polymorphism in deiodinases or thyroid hormone transporters

J Clin Endocrinol Metab. 2009 May;94(5):1623-9. doi: 10.1210/jc.2008-1301. Epub 2009 Feb 3.

Common variation in the DIO2 gene predicts baseline psychological well-being and response to combination thyroxine plus triiodothyronine therapy in hypothyroid patients.

Panicker V[1], Saravanan P, Vaidya B, Evans J, Hattersley AT, Frayling TM, Dayan CM.

or placebo effect

J Clin Endocrinol Metab. 2005 Feb;90(2):805-12. Epub 2004 Dec 7.

Partial substitution of thyroxine (T4) with tri-iodothyronine in patients on T4 replacement therapy: results of a large community-based randomized controlled trial.

Saravanan P[1], Simmons DJ, Greenwood R, Peters TJ, Dayan CM.

?

Hypothyroidism and Depression

Colin M. Dayan[a] Vijay Panicker[b]

Eur Thyroid J 2013;2:168–179
DOI: 10.1159/000353777

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Thyroxin liquid ?

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Endocrine. 2017 Jan;55(1):51-59. doi: 10.1007/s12020-016-1003-9. Epub 2016 Jul 7.

Comparative study between the effects of replacement therapy with liquid and tablet formulations of levothyroxine on mood states, self-perceived psychological well-being and thyroid hormone profile in recently thyroidectomized patients.

Lombardi CP[1], Bocale R[2], Barini A[3], Barini A[3], D'Amore A[1], Boscherini M[1], Bellantone R[1].

Our data indicate a greater efficacy of liquid formulation of levothyroxine in ameliorating mood states and self-perception of mental well-being and thyroid hormone profile after 2 months of replacement therapy in recently thyroidectomized patients.

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Postpartale Thyreoiditis und Depression

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Postpartum Mood Disorders and Thyroid Autoimmunity

Maria Le Donne,[1,*] Carmela Mento,[2] Salvatore Settineri,[3] Alessandro Antonelli,[4] and Salvatore Benvenga[5,6]
Front Endocrinol (Lausanne). 2017;
Published online 2017 May 4. doi: 1

Mögliche Assoziation bei SD AK (TPO) pos. Schwangeren (10% aller Schwangeren) mit postpartaler Thyreoiditis und postpartaler Depression

Neuropsychologische Evaluierung wäre sinnvoll

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Hashimoto Enzephalopathie

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Steroidresponsive Encephalopathie assoziiert mit Autoimmunthyreoiditis (SREAT)

Ausschlußdiagnose

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Hashimoto Enzephalopathie

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Ähnlich Vielzahl an neurologischen und psychiatrischen Erkrankungen

Leichte kognitive Beeinträchtigung bis zum Status epilepticus

Wesensveränderung, sozialer Rückzug, Verwirrtheit

Kognitive Defizite bis zu Demenz

Krampfanfälle und Bewegungsstörung

Psychiatrische Symptome wie Halluzinationen, Wahn und Depression

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Mögliche Pathogenese

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Autoimmunbedingte Vaskulitis des ZNS

Immunkomplexablagerungen

Autoimmunreaktion auf Antigene

Toxische Wirkung von TRH im ZNS

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Diagnosekriterien

BARMHERZIGE BRÜDER
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Vorhandensein SD AK (Anti TPO und/oder AntiTg)

Leichte bis mittelschwere Proteinerhöhung im Liquor

Unspezifische Veränderungen im EEG

Im MRT unspezifische fokale oder konfluierende Hyperintensitäten der weißen Substanz

Globale oder fokale Hypoperfusion SPECT bzw. Hypometabolismus im FDG-PET

Hashimoto Enzephalopathie

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First-line Therapie: Cortison

Second-line Therapie: Immuntherapie wie
Azathioprin
Methotrexat
Rituximab
Mycophenolat
Immunglobuline
Plasmapherese

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Zusammenhang Schilddrüse und Psyche ?

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Schilddrüsenfunktionsstörung per se ?

Fehlregulation lokal im Gehirn ?

Schilddrüsenantikörper per se ?

Übergeordneter immunologischer Prozess?

Unabhängig von der Schilddrüse ?

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Danke für Ihre Aufmerksamkeit !

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