S1: Chronische vermoeidheid: onderzoek naar kwetsbaarheid

Drs. Maud De Venter

Drs. Jela Illegems

Prof. dr. Filip Van Den Eede

9e Vlaams Geestelijke Gezondheidscongres

Universiteit Antwerpen / UZA

S1: Chronische vermoeidheid: onderzoek naar kwetsbaarheid

Inleiding

Filip Van Den Eede

9e Vlaams Geestelijke Gezondheidscongres

Universiteit Antwerpen / UZA

Allemaal anders: terugblik op VGGC 2008

UA (2008)

CHRONISCH VERMOEIDHEIDSSYNDROOM EN MAJEURE DEPRESSIE: EEN PAAR APART?

Samenwerking CAPRI UA en KUL

Voorzitter: Dr. Van Den Eede F (UZA/CAPRI UA)

Programma:

0-15 min:	Depressie bij chronisch vermoeidheidssyndroom: oorzaak? gevolg? Of beide? Spreker: Van Houdenhove B. (KUL)
15-30 min:	De affectieve spectrum hypothese als mogelijke verklaring voor de relatie tussen functioneel somatische syndromen en depressie Spreker: Kempke S. (KUL)
30-45 min:	Chronisch vermoeidheidssyndroom versus majeure depressie: een neurobiologische invalshoek Spreker: Van Den Eede F. (UZA/CAPRI UA)
45-60 min:	Psychomotorische vertraging in het chronisch vermoeidheidssyndroom en in de majeure depressie: een vergelijkende studie Spreker: Schrijvers D. (CAPRI UA)
60-90 min:	Interactieve discussie Moderator: Van Houdenhove B. (KUL)

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CVS: omschrijving

Casusdefinitie Chronisch Vermoeidheidssyndroom
CDC - Fukuda et al. (1994)

Minstens 6 maanden aanhoudende of steeds terugkerende vermoeidheid waarvoor geen lichamelijke verklaring is gevonden +

- Rust biedt onvoldoende herstel
- Geen gevolg van voortdurende inspanning
- Functionele beperkingen

4

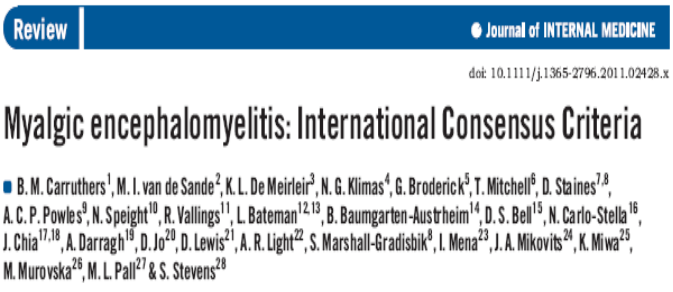
CVS: omschrijving

In combinatie met **vier of meer** van de volgende symptomen, gedurende **6 maanden** aanhoudend of regelmatig terugkerend en die er niet waren voor de vermoeidheid begon:

- Zelfgerapporteerde verslechtering van geheugen of concentratievermogen
- Keelpijn
- Gevoelige hals- of okselklieren
- Spierpijn
- Gewrichtspijnen
- Hoofdpijn
- Niet-verfrissende slaap
- Na inspanning: gevoel van uitputting (malaise) gedurende 24 uur of langer

5

Nieuwe criteria in ontwikkeling



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Nieuwe criteria in ontwikkeling: SEID

VIEWPOINT

Beyond Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome
An IOM Report on Redefining an Illness

Ellen Wright Clayton, MD, JD
Center for Biomedical Ethics and Society, Vanderbilt University, Nashville, Tennessee.

JAMA March 17, 2015 Volume 313, Number 11

"Systemic exertion intolerance disease"

Exertion : physical, cognitive, emotional

7

Nosologische discussies

Journal of Psychosomatic Research 97 (2017) 127–130

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

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

Short communication

Syndromes of bodily distress or functional somatic syndromes - Where are we heading. Lecture on the occasion of receiving the Alison Creed award 2017

Per Fink

The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Denmark

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Nosologische discussies

Table 1
Differences and similarities in criteria and concepts between different diagnostic constructs.

Bodily distress syndrome[a]	Somatic symptom disorder DSM-V[b]	Somatoform disorders DSM-IV or ICD-10	Functional somatic syndromes
Defined by physical symptom pattern	Defined by emotional and behavioural symptoms/characteristic	Defined by physical symptom pattern including emotional and behavioural symptoms/characteristics and exclusion of organic basis	Defined by a primary symptom, or a symptom pattern or/and assumed attribution (depending on the FSS)
Organic (CNS) based bodily symptoms	Bodily symptoms of any aetiology	Symptoms without organic basis (medically unexplained)	Organic based (CNS or peripheral)
Emotional or behavioural symptoms not necessary for the diagnosis but are prevalent and may be important for the treatment	Emotional or behavioural symptoms are crucial for the diagnosis	Includes worrying and preoccupation with physical health and bodily sensations	Emotional or behavioural symptoms not necessary for the diagnosis but are prevalent and are assumed secondary to physical ailment
Medical and psychiatric differential diagnoses have to be excluded	No requirement of exclusion of a medical diagnosis, but of psychiatric differential diagnosis	Organic explanations and other mental disorders have to be excluded	Unclear relations to differential diagnoses, multiple FFS diagnoses possible
Suffering from symptoms of BDS	Suffering from emotional and behavioural trouble related to bodily symptoms or sensations	Suffering from medical unexplained symptoms and emotional/behavioural trouble	Suffering from symptoms of FSS
Cause unknown but emotional or physical stress and dysfunction in the CNS likely to be involved	Health anxiety and misinterpretation of bodily symptoms	Stress, emotional conflicts etc.	In some cause is unknown. Some FFS are defined by an assumed cause, (like Multiple chemical sensitivity)
Challenge the mental/physical dichotomy thinking of medicine	A mental disorder	A mental disorder	A non-psychiatric disorder
Based on empirical studies	Consensus driven	Poor empiric basis, most consensus driven	Consensus driven, poor empiric basis with a few exceptions

[a] May apply to the ICD-11 PC Bodily Stress Disorder draft as well.
[b] May apply to the ICD-11 (psychiatric chapter) Bodily Distress Disorder as well.

Fink, 2017

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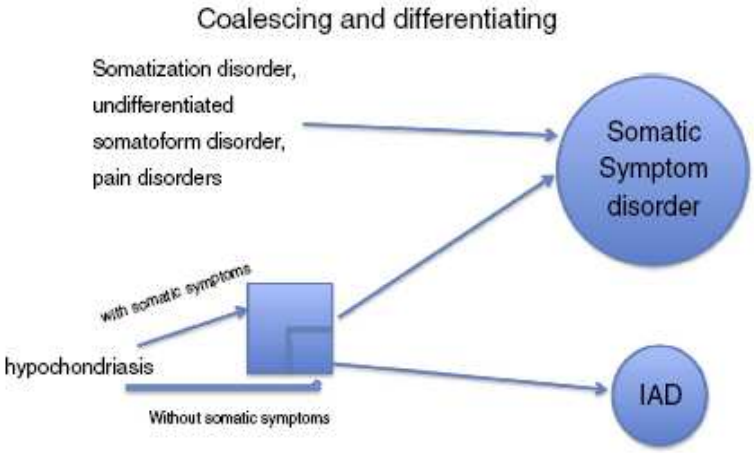
DSM-5



Dimsdale et al., 2013

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Somatisch-symptoomstoornis (DSM-5)

- A: Een of meer lichamelijke klachten waar de betrokkene onder lijdt, of die het dagelijks leven in significante mate verstoren.
- B: Excessieve gedachten, gevoelens of gedragingen samenhangend met de lichamelijke klachten of de hiermee gepaard gaande zorgen over de gezondheid, tot uiting komend in minstens één van de volgende kenmerken:
  - 1. Disproportionele en persisterende gedachten over de ernst van de klachten.
  - 2. Een persisterende hoge mate van ongerustheid over de gezondheid of de klachten.
  - 3. Het excessief veel tijd en energie besteden aan deze klachten of aan de zorgen over de gezondheid.
- C: Persisterend klachtenpatroon (> 6m)

DSM-IV, APA 1994
DSM-5, APA 2013

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Nosologische verwarring

Letter to the Editor

Psychotherapy and Psychosomatics

Received: May 21, 2018
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Psychother Psychosom 2018;87:234–235
DOI: 10.1159/000490731

The Need to Distinguish between Bodily Distress Disorder and Somatic Symptom Disorder

Filip Van Den Eede[a, b] *Christina van der Feltz-Cornelis*[c, d]

[a]University Department of Psychiatry, Antwerp University Hospital, Edegem, Belgium; [b]Collaborative Antwerp Psychiatric Research Institute, University of Antwerp, Antwerp, Belgium; [c]Tranzo Department, Tilburg School of Behavioral and Social Sciences, Tilburg University, Tilburg, The Netherlands; [d]Department of Health Science, HYMS, University of York, York, UK

Dear Editor,

We read the article entitled "Management of Functional Somatic Syndromes and Bodily Distress" by Henningsen et al. [1] with great interest. The authors state that they intend to develop a unifying perspective on the understanding and management of functional somatic syndromes and bodily distress, while also providing an update on current concepts and their aetiologies as well as evidence-based recommendations for treatment, thereby concentrating on developments in the last decade. However, we feel that, for several reasons, rather than offering clarification, the paper creates conceptual confusion.

Firstly, it is important to differentiate between functional somatic syndromes (FSS) or bodily distress disorder (BDD) (both mainly characterized by medically unexplained symptoms) on the one hand and somatic symptom disorder (SSD) on the other. In their "terminology, classification and overlap" section, the authors refer to SSD as an arbitrary DSM-5 alternative to FSS (or BDD), thus sharing the view Fink takes [2]. Although this may seem understandable from a historical perspective, considering the poor conceptualization of somatoform disorders in the DSM-IV, we would like to point out that in the DSM-5 the criteria for SSD are based on a very different conceptualization and incorporate an important change [3]. More precisely, the persistent, explained or unexplained, somatic symptoms have to be associated with disproportionate thoughts, feelings and behaviours related to these symptoms. In our view, future DSM editions should adopt a more dimensional approach to the diagnosis of SSD, placing less emphasis on health anxiety and incorporating the Diagnostic Criteria for Psychosomatic Research [4]. This system has merit as it showed its clinical utility in predicting treatment outcomes. Also, it takes subthreshold syndromes and the heterogeneity of psychological problems affecting a sizable number of patients suffering from a medical illness into account [5], such as allostatic overload and demoralization. In DSM-5, these conditions are too vaguely being described as "psychological factors affecting other medical conditions."

Second, regarding the differentiation between FSS/BDD and SSD, empirical research has shown that not all patients with FSS fulfil the criteria of SSD. In their study of patients with fibromyalgia, Häuser et al. [6] find that merely 25.6% of a sample of 156 patients met the SDD criteria. Furthermore, a recent latent-class analysis of chronic fatigue syndrome revealed important differences in between-group scores on the Cognitive Behavioural Responses Questionnaire [7]. More precisely, the largest subgroup (33%) mainly reported features associated with FSS, showing the lower scores, and the smallest subgroup (11%) showed high scores particularly on behaviour avoidance and damage beliefs. In keeping with this, the latter group was also more likely to believe that their symptoms were physical in nature. Hence, only a proportion of patients with FSS show characteristics of SSD. Moreover, as Henningsen et al. [1] mention themselves, the number of bodily symptoms is a strong predictor of disability and health care use, but with health anxiety being an additional and independent predictor.

Third, in their schematic model of the aetiology of bodily distress, the authors mainly adopt insights from cognitive and behavioural theories and do not include evidence on physiological disturbances in FSS. For instance, chronic fatigue syndrome has been associated with hypothalamic-pituitary-adrenal axis dysfunction, which seems clinically relevant as it is linked to severer symptoms and/or disability and poorer outcomes to standard treatments [8]. As to irritable bowel syndrome, the evidence strongly suggests that it is a systems disease that not only involves complex individual systems (i.e., the nervous, immune, digestive and microbiota systems and the environment), but also their complex reciprocal interactions [9]. Moreover, it has been pointed out earlier that the so-called unexplained symptoms will eventually stop being unexplained once the underlying pathogenic mechanisms are unveiled [10]. Adhering to the concept of FSS or BDD as a concept excluding somatic explanations does not help research and clinical practice further, as it hampers taking such developments into account. Thus, an approach that continues to focus on so-called unexplained symptoms misses the opportunity to advance research and clinical care in this domain.

KARGER

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Onderzoek naar fenotypes (symptomen CVS)

Journal of Psychosomatic Research 81 (2016) 14–23

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

Chronic fatigue syndrome (CFS) symptom-based phenotypes in two clinical cohorts of adult patients in the UK and The Netherlands

Simon M. Collin [a,*], Stephanie Nikolaus [b], Jon Heron [a], Hans Knoop [b], Peter D. White [c], Esther Crawley [a]

[a] School of Social and Community Medicine, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS8 2BN, UK
[b] Expert Centre for Chronic Fatigue, Radboud University Medical Centre Nijmegen, The Netherlands
[c] Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK

Onderzoek naar fenotypes (symptomen CVS)

Psychological Medicine (2017), 47, 1454–1465. © Cambridge University Press 2017
doi:10.1017/S0033291716003615

ORIGINAL ARTICLE

Heterogeneity in chronic fatigue syndrome – empirically defined subgroups from the PACE trial

T. E. Williams[1], T. Chalder[2], M. Sharpe[3] and P. D. White[1]*

[1] *Centre for Psychiatry, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine, Queen Mary University of London, London, UK*
[2] *Academic Department of Psychological Medicine, King's College London, Weston Education Centre, London, UK*
[3] *Department of Psychiatry, Psychological Medicine Research, University of Oxford, Oxford, UK*

Onderzoek naar fenotypes (symptomen CVS)

Fig. 2. Subgroups – five-class solution. Diagrammatic representation of the five-class solution, highlighting the key features used to identify each subgroup. FSS, Functional somatic syndromes; CBRQ, Cognitive Behavioural Responses Questionnaire; CFS, chronic fatigue syndrome.

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Etiologie

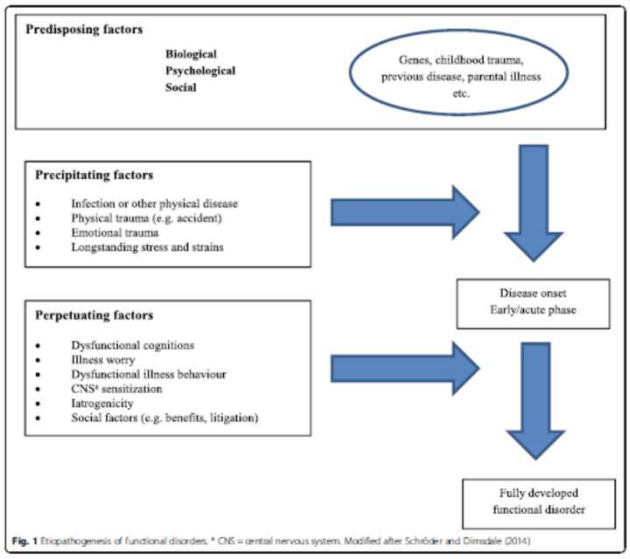

Fig. 1 Etiopathogenesis of functional disorders. * CNS = central nervous system. Modified after Schröder and Dimsdale (2014)

Budtz-Lilly et al., 2015

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Etiologie en behandeling

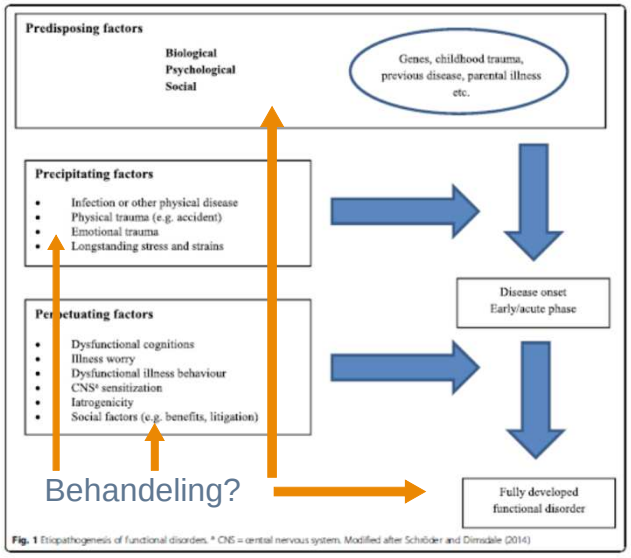

Fig. 1 Etiopathogenesis of functional disorders. * CNS = central nervous system. Modified after Schröder and Dimsdale (2014)

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Behandeling

Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial

P D White, K A Goldsmith, A L Johnson, L Potts, R Walwyn, J C DeCesare, H L Baber, M Burgess, L V Clark, D L Cox, J Bavinton, B J Angus, G Murphy, M Murphy, H O'Dowd, D Wilks, P McCrone, T Chalder*, M Sharpe*, on behalf of the PACE trial management group†

Summary

Background Trial findings show cognitive behaviour therapy (CBT) and graded exercise therapy (GET) can be effective treatments for chronic fatigue syndrome, but patients' organisations have reported that these treatments can be harmful and favour pacing and specialist health care. We aimed to assess effectiveness and safety of all four treatments.

Lancet 2011; 377: 823-36
Published Online February 18, 2011

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Behandeling

Journal of Psychosomatic Research 97 (2017) 45–51

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

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

Long-term follow-up after cognitive behaviour therapy for chronic fatigue syndrome☆

Anthonie Janse[a,b], Stephanie Nikolaus[a], Jan F. Wiborg[a], Marianne Heins[a], Jos W.M. van der Meer[c], Gijs Bleijenberg[d], Marcia Tummers[e], Jos Twisk[f], Hans Knoop[a,b,*]

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Behandeling

Psychotherapy and Psychosomatics

Regular Article

Psychother Psychosom 2015;84:368–376
DOI: 10.1159/000438867

Received: March 21, 2015
Accepted after revision: July 20, 2015
Published online: September 25, 2015

Randomised Controlled Trial of Cognitive Behaviour Therapy Delivered in Groups of Patients with Chronic Fatigue Syndrome

Jan F. Wiborg Jose van Bussel Agaat van Dijk Gijs Bleijenberg Hans Knoop

Expert Centre for Chronic Fatigue, Radboud University Medical Center, Nijmegen, The Netherlands

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Behandeling

Letter to the Editor

Psychotherapy and Psychosomatics

Received: February 29, 2016
Accepted: March 1, 2016
Published online: August 12, 2016

Psychother Psychosom 2016;85:308
DOI: 10.1159/000445166

Group Cognitive Behaviour Therapy for Chronic Fatigue Syndrome

Jelo Illegems[a, b], *Greta Moorkens*[a, b], *Filip Van Den Eede*[a, c, d]

[a]Behaviour Therapy Division for Fatigue and Functional Symptoms, [b]Department of Internal Medicine, and [c]University Department of Psychiatry, Antwerp University Hospital, Edegem, and [d]Collaborative Antwerp Psychiatric Research Institute, University of Antwerp, Antwerp, Belgium

reported. Moreover, the authors did not elaborate on the fact that exclusively participants who were willing to receive group therapy were included in the trial, which may likewise have positively affected the outcomes. The participants in the group interventions may have been a highly motivated subgroup, while the participants allocated to the waiting list for individual therapy may have become demotivated. We also wonder whether personality might have been of influence on the patients' readiness to participate in group therapy. As to this, we are planning to conduct a study on the effects of personality dimensions on the short- and longer-term outcomes of group CBT. In that respect, it has recently been found that high levels of neuroticism at baseline were associated with a larger improvement in mental quality of life after group CBT for

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Agenda voor wetenschappelijk onderzoek

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 14 May 2018
doi: 10.3389/fpsyt.2018.00151

A European Research Agenda for Somatic Symptom Disorders, Bodily Distress Disorders, and Functional Disorders: Results of an Estimate-Talk-Estimate Delphi Expert Study

OPEN ACCESS

Christina M. van der Feltz-Cornelis[1,2*], *Iman Elfeddali*[1,2], *Ursula Werneke*[3], *Ulrik F. Malt*[4,5], *Omer Van den Bergh*[6], *Rainer Schaefert*[7,8], *Willem J. Kop*[9], *Antonio Lobo*[10,11], *Michael Sharpe*[12], *Wolfgang Söllner*[13], *and Bernd Löwe*[14] *On Behalf of EAPM*[†]

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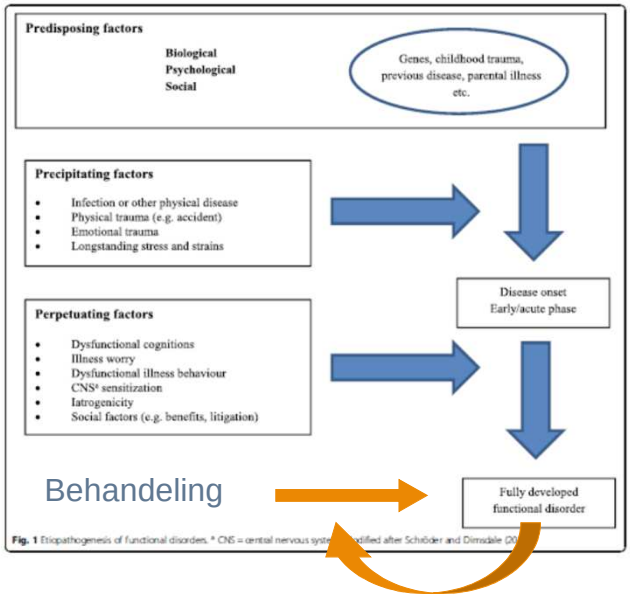
Onderzoek naar voorspellers van behandeluitkomst



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Onderzoek naar voorspellers van behandeluitkomst

Journal of Psychosomatic Research 81 (2016) 14–23

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Journal of Psychosomatic Research

Chronic fatigue syndrome (CFS) symptom-based phenotypes in two clinical cohorts of adult patients in the UK and The Netherlands

Simon M. Collin [a,*], Stephanie Nikolaus [b], Jon Heron [a], Hans Knoop [b], Peter D. White [c], Esther Crawley [a]

[a] School of Social and Community Medicine, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS8 2BN, UK
[b] Expert Centre for Chronic Fatigue, Radboud University Medical Centre Nijmegen, The Netherlands
[c] Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK

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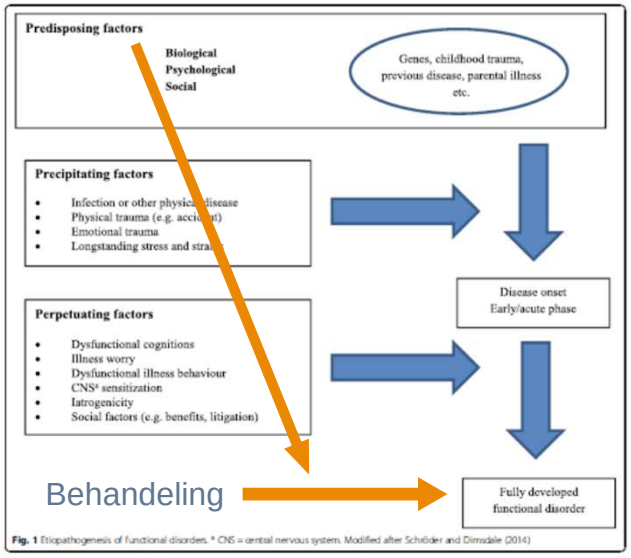
Onderzoek naar voorspellers van behandeluitkomst



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Programma S1

Inleiding: chronische vermoeidheid en uitputting: allemaal anders
Spreker: Filip Van Den Eede (UZP campus UZA / CAPRI UA)

Chronische vermoeidheid: neuro-endocriene correlaten en kwetsbaarheidsfactoren
Spreker: Filip Van Den Eede (UZP campus UZA / CAPRI UA)

Chronische vermoeidheid: voorbeschikkende rol van jeugdtrauma en het effect ervan op de behandeling
Spreker: Maud De Venter (UZP campus UZA / CAPRI UA)

Chronische vermoeidheid: voorbeschikkende rol van persoonlijkheidsdimensies en het effect ervan op de behandeling
Spreker: Jela Illegems (CGVF algemeen inwendige ziekten UZA . CAPRI UA)

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S1: Chronische vermoeidheid: onderzoek naar kwetsbaarheid

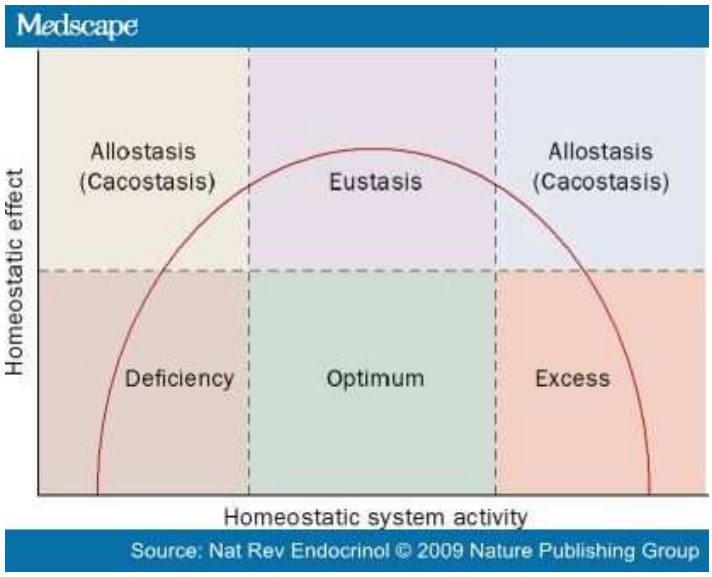
Neuro-endocriene correlaten en kwetsbaarheidsfactoren

Filip Van Den Eede

9e Vlaams Geestelijke Gezondheidscongres

Universiteit Antwerpen / UZA

Stressbiologie



Chrousos, 2009

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Chronische stress

Psychological Bulletin
2007, Vol. 133, No. 1, 25–45

0033-2909/07/$12.00 DOI: 10.1037/0033-2909.133.1.25

If It Goes Up, Must It Come Down? Chronic Stress and the Hypothalamic-Pituitary-Adrenocortical Axis in Humans

Gregory E. Miller, Edith Chen, and Eric S. Zhou
University of British Columbia

The notion that chronic stress fosters disease by activating the hypothalamic-pituitary-adrenocortical (HPA) axis is featured prominently in many theories. The research linking chronic stress and HPA function is contradictory, however, with some studies reporting increased activation, and others reporting the opposite. This meta-analysis showed that much of the variability is attributable to stressor and person features. Timing is an especially critical element, as hormonal activity is elevated at stressor onset but reduces as time passes. Stressors that threaten physical integrity, involve trauma, and are uncontrollable elicit a high, flat diurnal profile of cortisol secretion. Finally, HPA activity is shaped by a person's response to the situation; it increases with subjective distress but is lower in persons with posttraumatic stress disorder.

Keywords: stress, trauma, cortisol, HPA axis

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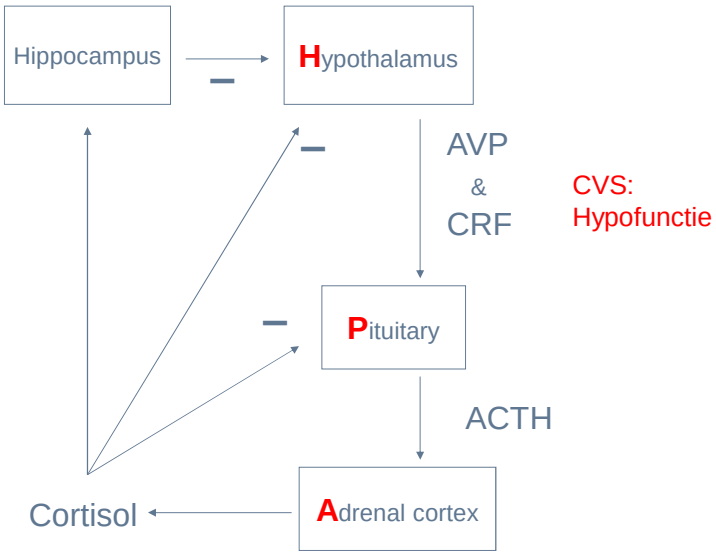
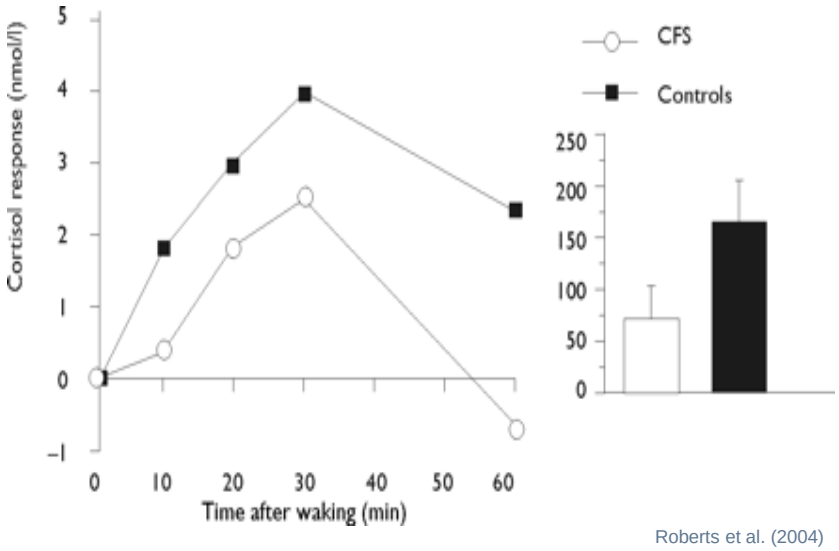


Ontregeling van de HPA-as in CVS



Roberts et al. (2004)

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Ontregeling van de HPA-as in CVS

Psychoneuroendocrinology (2013) 38, 2405—2422

Available online at www.sciencedirect.com

SciVerse ScienceDirect

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

REVIEW

Unstimulated cortisol secretory activity in everyday life and its relationship with fatigue and chronic fatigue syndrome: A systematic review and subset meta-analysis☆

Daniel J.H. Powell[a,*], Christina Liossi[a], Rona Moss-Morris[a,b], Wolff Schlotz[a,c]

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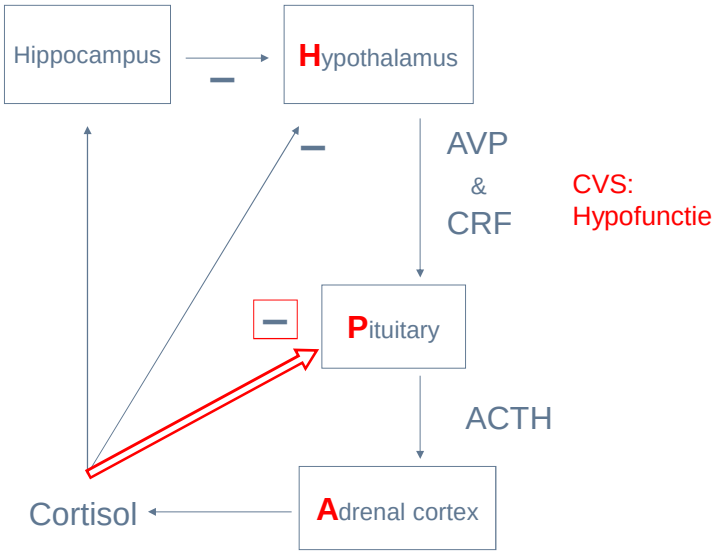
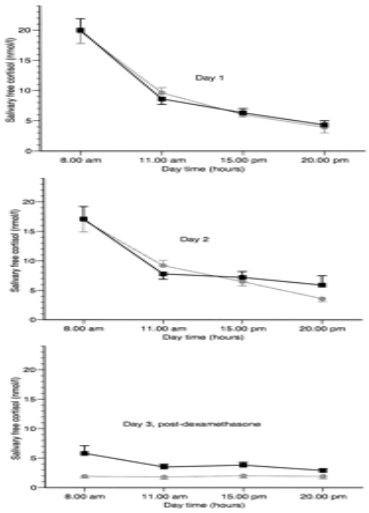


Ontregeling van de HPA-as in CVS



Gaab et al. (2008)

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Ontregeling van de HPA-as in CVS

Psychological Medicine (2008), **38**, 963–973. © 2007 Cambridge University Press
doi:10.1017/S0033291707001444 Printed in the United Kingdom

ORIGINAL ARTICLE

Combined dexamethasone/corticotropin-releasing factor test in chronic fatigue syndrome

F. Van Den Eede[1,2,3], G. Moorkens[4], W. Hulstijn[3], B. Van Houdenhove[5], P. Cosyns[1,2], B. G. C. Sabbe[3,6] and S. J. Claes[3,5*]

Ontregeling van de HPA-as in CVS

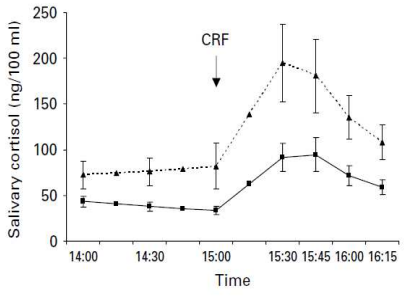

Fig. 1. Mean salivary (free) cortisol values (ng/100 ml) ± S.E.M. at seven time-points during the combined low-dose dexamethasone/corticotropin-releasing factor (CRF) test in CFS patients (■, $n = 34$) and in control subjects (▲, $n = 25$). Participants took 0.5 mg dexamethsone orally at 23:00 hours on the evening before neuroendocrine testing. Human CRF (100 μg) was administered 16 h later at 15:00 hours.

Van Den Eede et al., 2008

Ontregeling van de HPA-as in CVS

Basale hormonale veranderingen en cortisol na ontwaken:

- Lagere concentratie van cortisol in bloed, speeksel en urine
- Lagere concentratie van ACTH in bloed
- Verlaagde cortisolconcentratie na ontwaken

Gestoorde functietesten:

- Lagere ACTH-respons na toediening van CRF, insuline of naloxone
- Lagere ACTH-respons na inspanningsproef
- Lagere ACTH-respons na psychologische stress
- Verhoogde gevoeligheid voor negatieve terugkoppeling van cortisol
- Lagere cortisolrespons na toediening van ACTH

Van Den Eede et al., 2007

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Ontregeling van de HPA-as in CVS

Neuropsychobiology

Original Paper

Neuropsychobiology 2007;55:112–120
DOI: 10.1159/000104468

Hypothalamic-Pituitary-Adrenal Axis Function in Chronic Fatigue Syndrome

Filip Van Den Eede[a, c, d] Greta Moorkens[b] Boudewijn Van Houdenhove[e]
Paul Cosyns[a, c] Stephan J. Claes[d, e]

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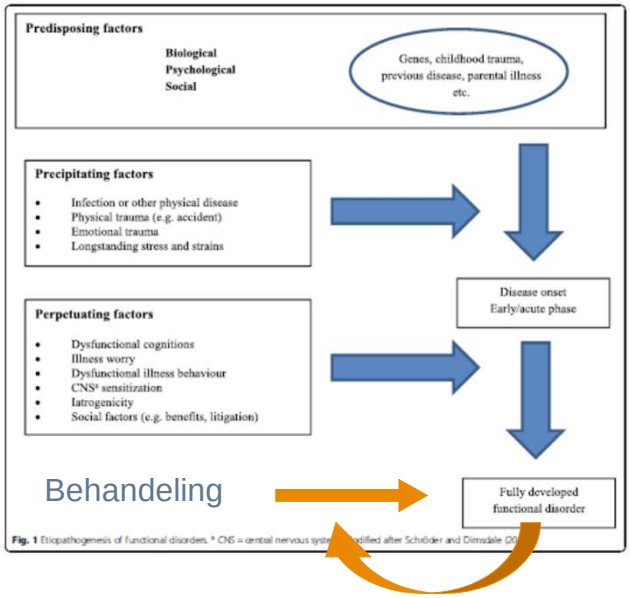
Onderzoek naar voorspellers van behandeluitkomst



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Onderzoek naar voorspellers van behandeluitkomst

Psychological Medicine (2010), **40**, 515–522. © Cambridge University Press 2009
doi:10.1017/S0033291709990390

ORIGINAL ARTICLE

Does hypocortisolism predict a poor response to cognitive behavioural therapy in chronic fatigue syndrome?

A. D. L. Roberts[1,2], M.-L. Charler[2], A. Papadopoulos[3], S. Wessely[1,2,3], T. Chalder[1,2] and A. J. Cleare[1,2,3]*

[1] *King's College London, Institute of Psychiatry, Department of Psychological Medicine, London, UK*
[2] *Chronic Fatigue Syndrome Research and Treatment Unit, Maudsley Hospital, London, UK*
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Rol HPA-as in de pathogenese?

Hypothalamic–pituitary–adrenal axis dysfunction in chronic fatigue syndrome

Andrew S. Papadopoulos and Anthony J. Cleare

Abstract | The weight of current evidence supports the presence of the following factors related to hypothalamic–pituitary–adrenal (HPA) axis dysfunction in patients with chronic fatigue syndrome (CFS): mild hypocortisolism; attenuated diurnal variation of cortisol; enhanced negative feedback to the HPA axis; and blunted HPA axis responsiveness. Furthermore, HPA axis changes seem clinically relevant, as they are associated with worse symptoms and/or disability and with poorer outcomes to standard treatments for CFS. Regarding etiology, women with CFS are more likely to have reduced cortisol levels. Studies published in the past 8 years provide further support for a multifactorial model in which several factors interact to moderate HPA axis changes. In particular, low activity levels, depression and early-life stress appear to reduce cortisol levels, whereas the use of psychotropic medication can increase cortisol. Addressing these factors—for example, with cognitive behavioral therapy—can increase cortisol levels and is probably the first-line approach for correcting HPA axis dysfunction at present, as steroid replacement is not recommended. Given what is now a fairly consistent pattern of findings for the type of HPA axis changes found in CFS, we recommend that future work focuses on improving our understanding of the cause and relevance of these observed changes.

Papadopoulos, A. S. & Cleare, A. J. *Nat. Rev. Endocrinol.* 8, 22–32 (2012); published online 27 September 2011; doi:10.1038/nrendo.2011.153

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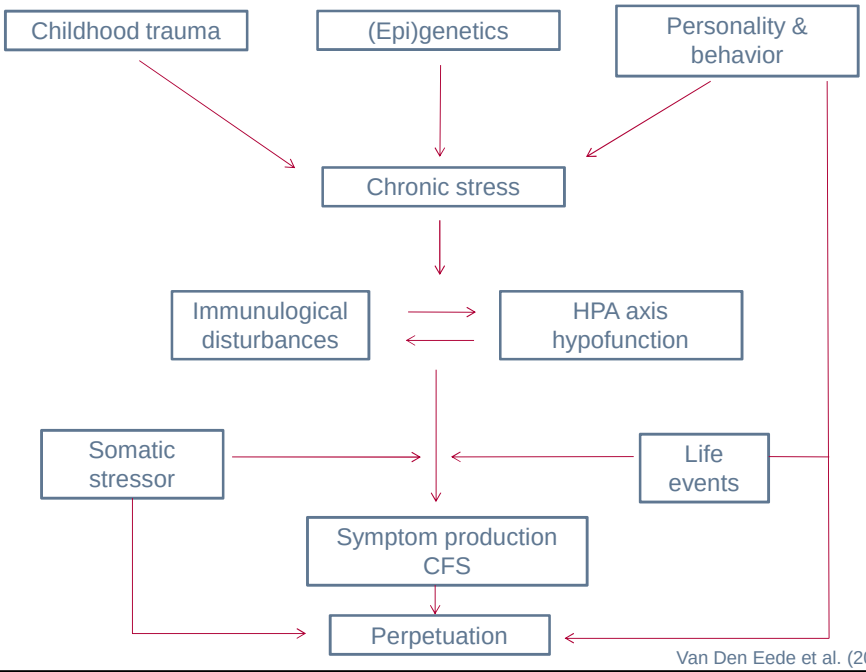
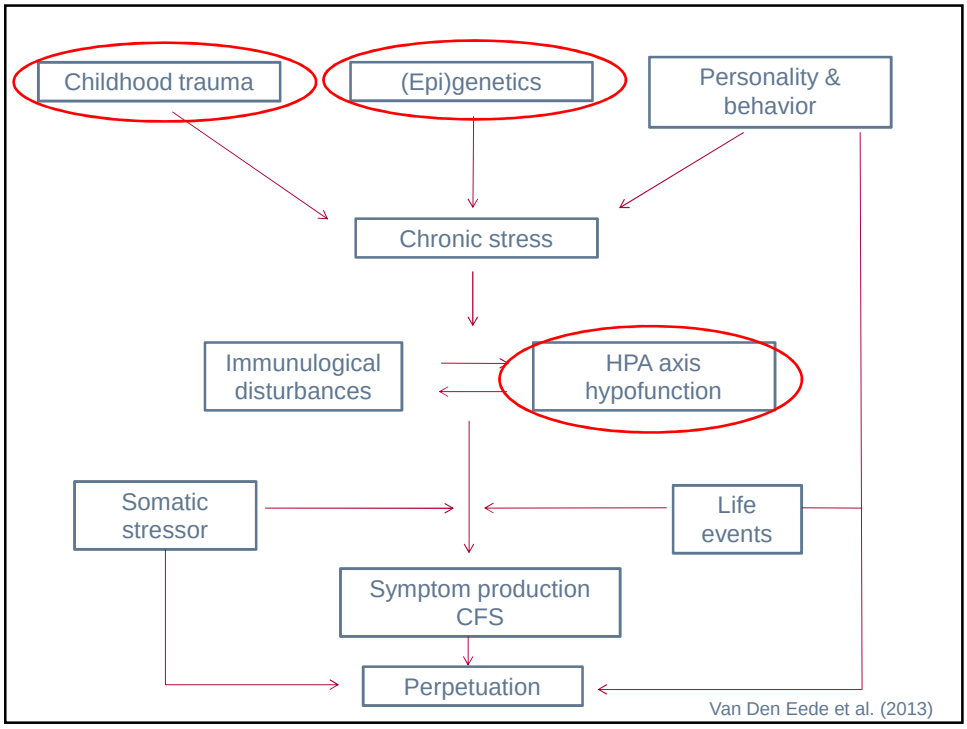


Van Den Eede et al. (2013)



Van Den Eede et al. (2013)

Jeugdtrauma en hypofunctie HPA-as (CVS)

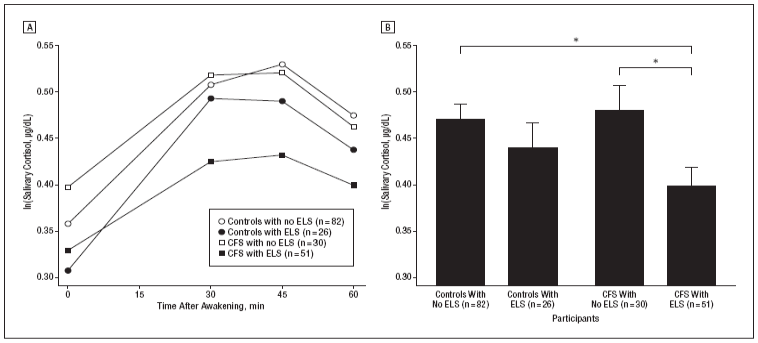


Figure. Logarithm-transformed mean salivary cortisol concentrations in response to awakening (A) and mean (SE) areas under the curve (B) in individuals with chronic fatigue syndrome (CFS) and well control subjects randomly identified from the general population in Georgia and stratified by the presence or absence of histories of childhood trauma (early-life stress [ELS]). There were significant main effects for group indicating decreased cortisol response and areas under the curve in individuals with CFS and childhood trauma but not in individuals with CFS without childhood trauma relative to control subjects and individuals with CFS with no childhood trauma. *$P < .05$.

Heim et al., 2009

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Jeugdtrauma en hypofunctie HPA-as (CVS)

Psychoneuroendocrinology (2015) 52, 14–21

Available online at www.sciencedirect.com

ScienceDirect

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

Effects of early childhood trauma on hypothalamic–pituitary–adrenal (HPA) axis function in patients with Chronic Fatigue Syndrome

Stefan Kempke[a,*,1], Patrick Luyten[a,b], Sarah De Coninck[c], Boudewijn Van Houdenhove[d], Linda C. Mayes[e], Stephan Claes[d]

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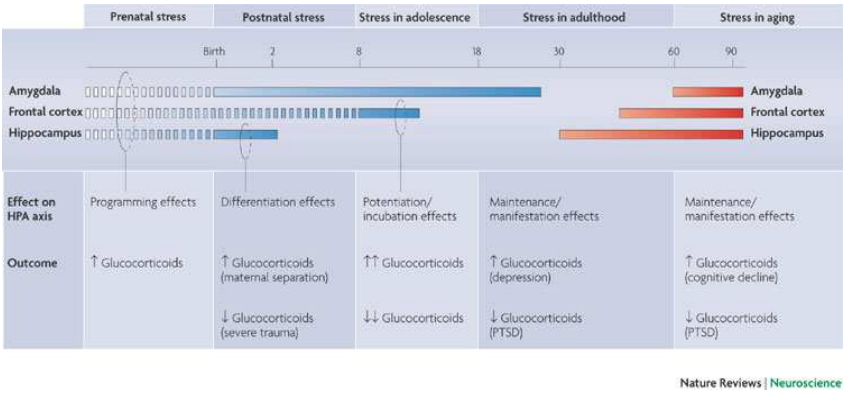
Jeugdtrauma: ontwikkelingsperspectief



Lupien et al., 2009

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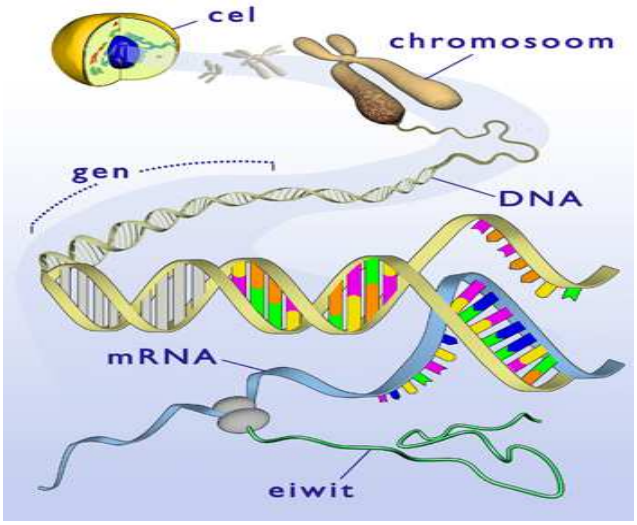
Genetica



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Genetica

A Twin Study of Chronic Fatigue

DEDRA BUCHWALD, MD, RICHARD HERRELL, PHD, SUZANNE ASHTON, BS, MEGAN BELCOURT, BS, KAREN SCHMALING, PHD, PATRICK SULLIVAN, MD, MICHAEL NEALE, PHD, AND JACK GOLDBERG, PHD

Objective: The etiology of chronic fatigue syndrome is unknown, but genetic influences may be important in its expression. Our objective was to assess the role of genetic and environmental factors in unexplained chronic fatigue. **Methods:** A classic twin study was conducted using 146 female-female twin pairs, of whom at least one member reported ≥6 months of fatigue. After completing questionnaires on symptoms, zygosity, physical health, and a psychiatric interview, twins were classified using three increasingly stringent definitions: 1) chronic fatigue for ≥6 months, 2) chronic fatigue not explained by exclusionary medical conditions, and 3) idiopathic chronic fatigue not explained by medical or psychiatric exclusionary criteria of the chronic fatigue syndrome case definition. Concordance rates in monozygotic and dizygotic twins were calculated for each fatigue definition along with estimates of the relative magnitude of genetic and environmental influences on chronic fatigue. **Results:** The concordance rate was higher in monozygotic than dizygotic twins for each definition of chronic fatigue. For idiopathic chronic fatigue, the concordance rates were 55% in monozygotic and 19% in dizygotic twins (p = .042). The estimated heritability in liability was 19% (95% confidence interval = 0–56) for chronic fatigue ≥6 months, 30% (95% confidence interval = 0–81) for chronic fatigue not explained by medical conditions, and 51% (95% confidence interval = 7–96) for idiopathic chronic fatigue. **Conclusions:** These results provide evidence supporting the familial aggregation of fatigue and suggest that genes may play a role in the etiology of chronic fatigue syndrome. **Key words:** chronic fatigue, twins, concordance, genetics.

Psychosomatic Medicine 63:936–943 (2001)

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Genetica

Genes, Brain and Behavior (2007) 6: 167–176

Glucocorticoid receptor polymorphisms and haplotypes associated with chronic fatigue syndrome

M. S. Rajeevan*,†, A. K. Smith†, I. Dimulescu†, E. R. Unger†, S. D. Vernon†, C. Heim‡ and W. C. Reeves†

†Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, and ‡Emory University School of Medicine, Atlanta, GA,

alleles: one protective and the other conferring risk of CFS. These results demonstrate *NR3C1* as a potential mediator of chronic fatigue, and implicate variations in the 5′ region of *NR3C1* as a possible mechanism through which the alterations in HPA axis regulation and behavioural characteristics of CFS may manifest.

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Genetica

Tijdschr. voor Geneeskunde, 67, nr. 4, 2011
doi: 10.2143/TVG.67.04.2000913

OVERZICHT

Genetica van het chronischevermoeidheidssyndroom: een neuro-endocriene invalshoek

W. VAN DAELE[1], J. DE BUCK[1], T. DE JONG[1], S.J. CLAES[2], G. MOORKENS[3], F. VAN DEN EEDE[1, 4, 5]

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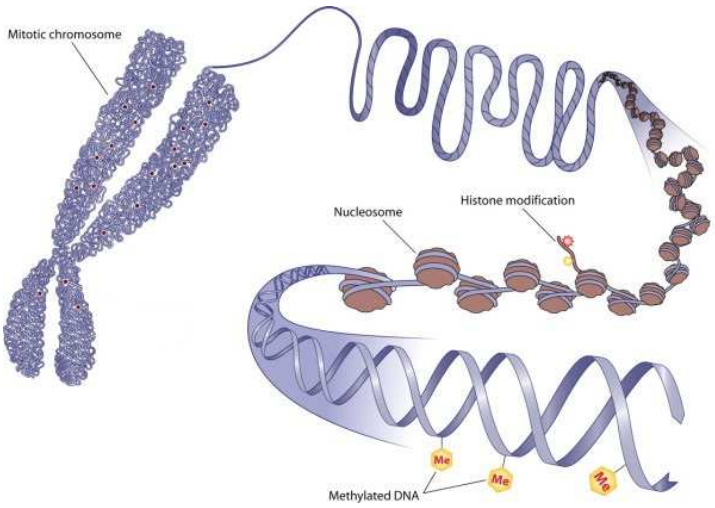
Epigenetica



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CVS en epigenetica

OPEN ACCESS Freely available online

PLOS ONE

DNA Methylation Modifications Associated with Chronic Fatigue Syndrome

Wilfred C. de Vega[1,2,3], Suzanne D. Vernon[4], Patrick O. McGowan[1,2,3]*

1 Centre for Environmental Epigenetics and Development, University of Toronto, Scarborough, ON, Canada, 2 Department of Biological Sciences, University of Toronto, Scarborough, ON, Canada, 3 Department of Cell and Systems Biology, University of Toronto, Toronto, ON, Canada, 4 CFIDS Association of America, Charlotte, North Carolina, United States of America

August 2014 | Volume 9 | Issue 8 | e104757

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CVS, HPA-as en epigenetica

de Vega *et al. BMC Medical Genomics* (2017) 10:11
DOI 10.1186/s12920-017-0248-3

BMC Medical Genomics

RESEARCH ARTICLE Open Access

Epigenetic modifications and glucocorticoid sensitivity in Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS)

Wilfred C. de Vega[1,2], Santiago Herrera[1,6], Suzanne D. Vernon[5,7] and Patrick O. McGowan[1,2,3,4*]

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CVS, HPA-as en epigenetica

Chronic Fatigue Syndrome and DNA Hypomethylation of the Glucocorticoid Receptor Gene Promoter 1F Region: Associations With Hypothalamic-Pituitary-Adrenal Axis Hypofunction and Childhood Trauma

Elise Vangeel, MSc, Filip Van Den Eede, MD, PhD, Titia Hompes, MD, PhD, Benedetta Izzi, PhD, Jurgen Del Favero, PhD, Greta Moorkens, MD, PhD, Diether Lambrechts, PhD, Kathleen Freson, PhD, and Stephan Claes, MD, PhD

Psychosomatic Medicine 2015

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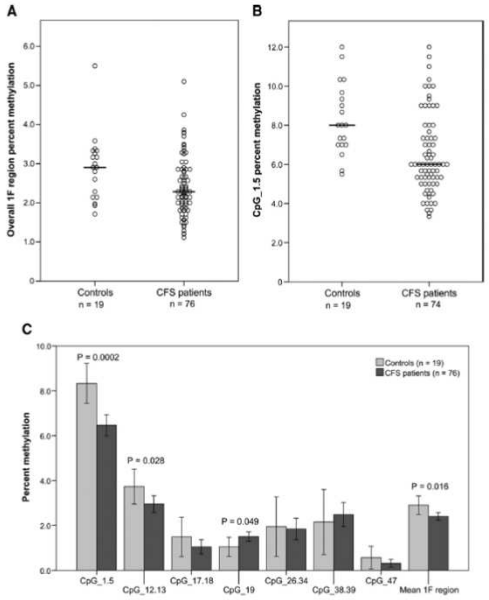
CVS, HPA-as en epigenetica



Vangeel et al., 2015

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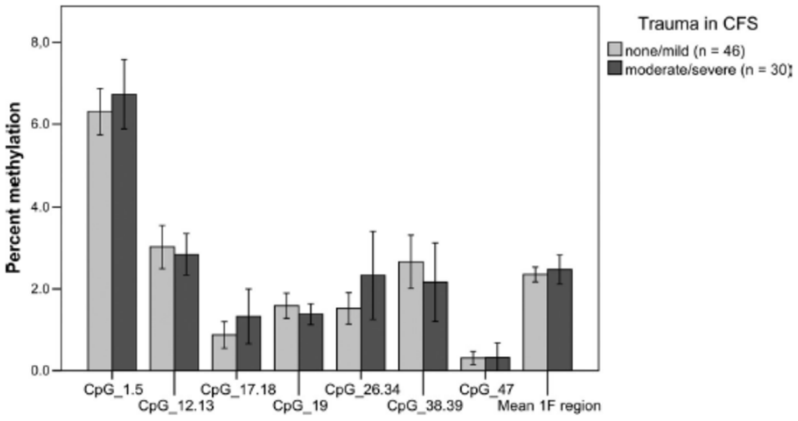
Jeugdtrauma en epigenetica

McGowan et al. (2009)

CVS, jeugdtrauma en epigenetica



Vangeel et al., 2015

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CVS, jeugdtrauma en epigenetica

Journal of Psychosomatic Research 104 (2018) 55-60

Contents lists available at ScienceDirect

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

Glucocorticoid receptor DNA methylation and childhood trauma in chronic fatigue syndrome patients

Elise Beau Vangeel[a,b,*], Stefan Kempke[a], Jelena Bakusic[c], Lode Godderis[c,d], Patrick Luyten[e,f], Leen Van Heddegem[g], Veerle Compernolle[g], Philippe Persoons[a], Diether Lambrechts[i,j], Benedetta Izzi[k], Kathleen Freson[b], Stephan Claes[a,h]

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CVS: epigenetische subtypes?

EPIGENOMICSVOL. 10, NO. 5RESEARCH ARTICLE

Integration of DNA methylation & health scores identifies subtypes in myalgic encephalomyelitis/chronic fatigue syndrome

Wilfred C de Vega, Lauren Erdman, Suzanne D Vernon, Anna Goldenberg
&
Patrick O McGowan

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Besluit: CVS: heterogeniteit (allemaal anders)

- Verschillende fenotypes (gebaseerd op symptomen)
- Psychiatrische comorbiditeit
  - Somatisch-symptoomstoornis
  - Affectieve stoornissen
- Biologische correlaten:
  - Neuro-endocrien (HPA-as): hypofunctie
  - (Epi)genetische verschillen
- Psychologische kwetsbaarheid
  - Jeugdtrauma ⟹ Maud De Venter
  - Persoonlijkheidsdimensies ⟹ Jela Illegems
- Voorspellende waarde op behandeluitkomst?

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