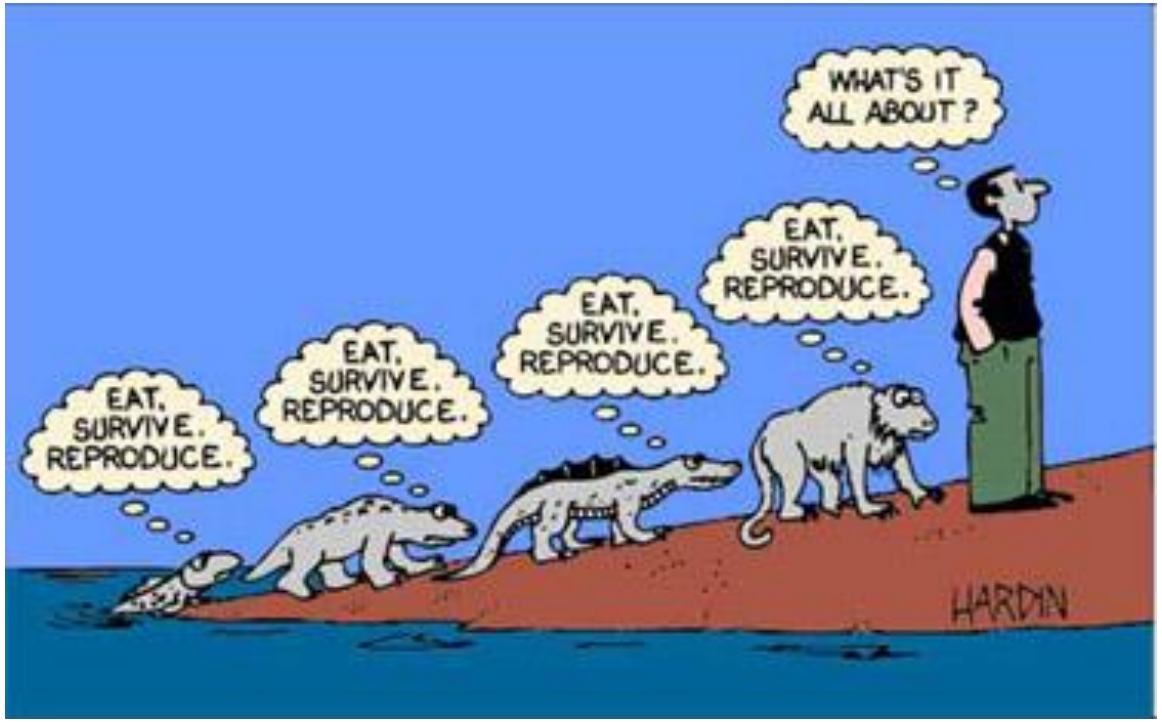
Green care evoluutiopsykologisesta näkökulmasta

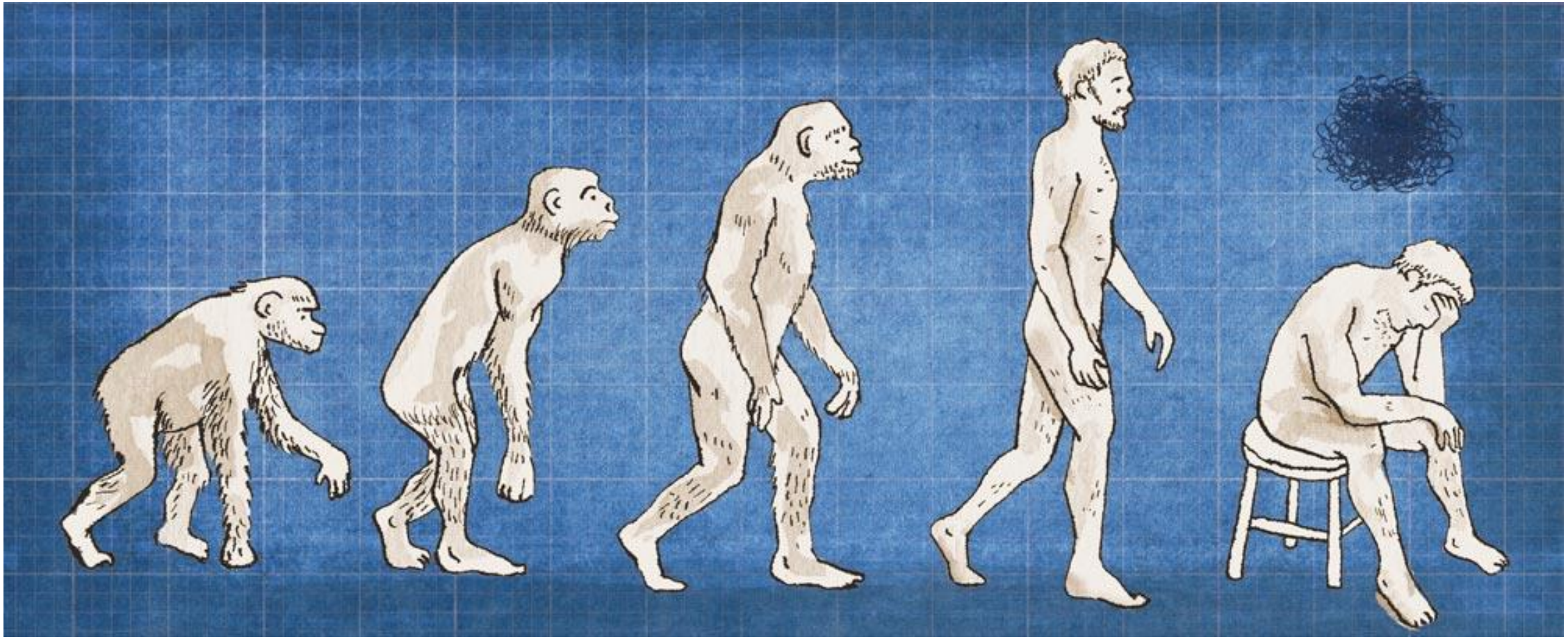
Markus J Rantala

Turun yliopisto



Evolutiivien psykiatria ja masennus

(*Terra Cognita*, painossa)



Masennus ei ole yksi sairaus vaan on olemassa 12 eri masennustyyppiä

Hoito pitää suunnata masennustyypin mukaan!

- Rantala, MJ, Luoto, S., Krams I. & Karlsson H. (2018)Depression subtyping based on evolutionary psychiatry: proximate mechanisms and ultimate functions. *Brain, Behavior, and Immunity*.

Metsästäjä-keräilijöillä kliininen masennus on harvinaista!

NIH Public Access
Author Manuscript
J Affect Disord. Author manuscript; available in PMC 2013 November 01.

Published in final edited form as:
J Affect Disord. 2012 November ; 140(3): 205–214. doi:10.1016/j.jad.2011.12.036.

Depression as a disease of modernity: explanations for increasing prevalence

Brandon H Hidaka, B.A. [MD/PhD Candidate]
Department of Dietetics and Nutrition, University of Kansas Medical Center, 2116 W 47th Terr, Westwood, KS 66205, Phone: (913) 636-8095, Fax: (913) 945-6848

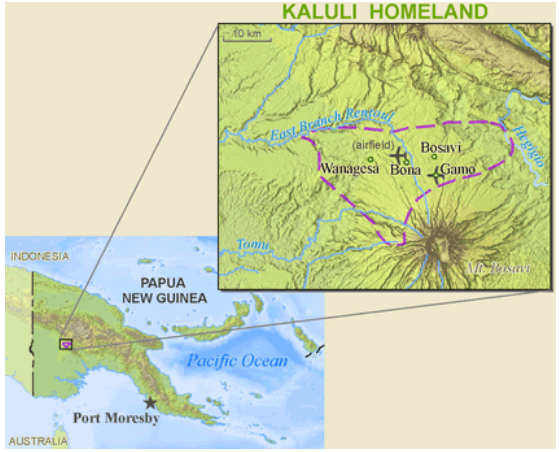
Brandon H Hidaka: bhidaka@kumc.edu

NIH-PA Author Manuscript

Metsästäjä-keräilijöiltä saattaa löytyä ratkaisu masennuksen yleistymisen selittämiseksi

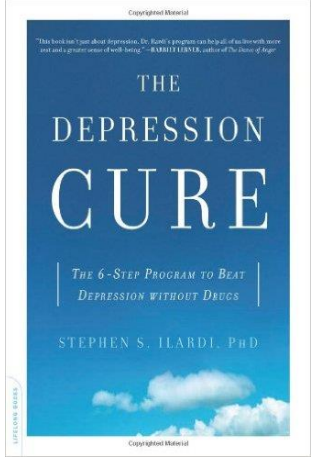
- Vain 1/2000 tutkitusta Kaluli-kansan jäsenestä kärsii masennuksesta. (Ainoa löydetty tapaus sai vain lievän masennuksen diagnoosin)

- Schieffelin EL. The cultural analysis of depressive affect: An example from New Guinea. In: Kleinman AM, Good B, editors. Culture and depression: Studies in the anthropology and cross-cultural psychiatry of affect and disorder. University of California Press; 1986. pp. 101–133.



Tansanian Hadzoilla ei tavata masennusta

(Appicella et al, unpublished)



Toraja kansa ei kärsi masennuksesta

- Hollan, D. W. & Wellenkamp, J. C. *Contentment and suffering : culture and experience in Toraja*. (Columbia University Press, 1994).
- Hollan, D. W. & Wellenkamp, J. C. *The thread of life : Toraja reflections on the life cycle*. (University of Hawaii Press, 1996).

- Kiinalaiset jotka ovat syntyneet vuoden 1966 jälkeen on **22.4X** suurempi todennäköisyys sairastua masennukseen elämänsä aikana kuin ennen vuotta 1937 syntyneillä.

NIH Public Access
Author Manuscript
Psychol Med. Author manuscript; available in PMC 2007 September 12.

NIH-PA Author Manuscript

Published in final edited form as:
Psychol Med. 2007 January ; 37(1): 61–71.

Lifetime Prevalence and Inter-cohort Variation in DSM-IV Disorders in Metropolitan China

Sing Lee, MB, BS, FRCPsych,
Department of Psychiatry, The Chinese University of Hong Kong, HKSAR, PRC

Adley Tsang, BSocSci,
Hong Kong Mood Disorders Center, The Chinese University of Hong Kong, HKSAR, PRC

Ming-Yuan Zhang, MD,
Shanghai Mental Health Center, PRC.

Yue-Qin Huang, MD, MPH, PhD,
Peking University Institute of Mental Health, PRC.

Yan-Ling He, MD,
Shanghai Mental Health Center, PRC.

Zhao-Rui Liu, MD, MPH,
Peking University Institute of Mental Health, PRC.

Yu-cun Shen, and **Ronald C. Kessler, PhD**
Department of Health Care Policy, Harvard Medical School, MA, USA.

Mitä länsimaalaisempi elämäntyyli sitä yleisempää on masennus

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J Affect Disord. Author manuscript; available in PMC 2013 November 01.

Published in final edited form as:
J Affect Disord. 2012 November ; 140(3): 205–214. doi:10.1016/j.jad.2011.12.036.

Depression as a disease of modernity: explanations for increasing prevalence

Brandon H Hidaka, B.A. [MD/PhD Candidate]
Department of Dietetics and Nutrition, University of Kansas Medical Center, 2116 W 47th Terr, Westwood, KS 66205, Phone: (913) 636-8095, Fax: (913) 945-6848

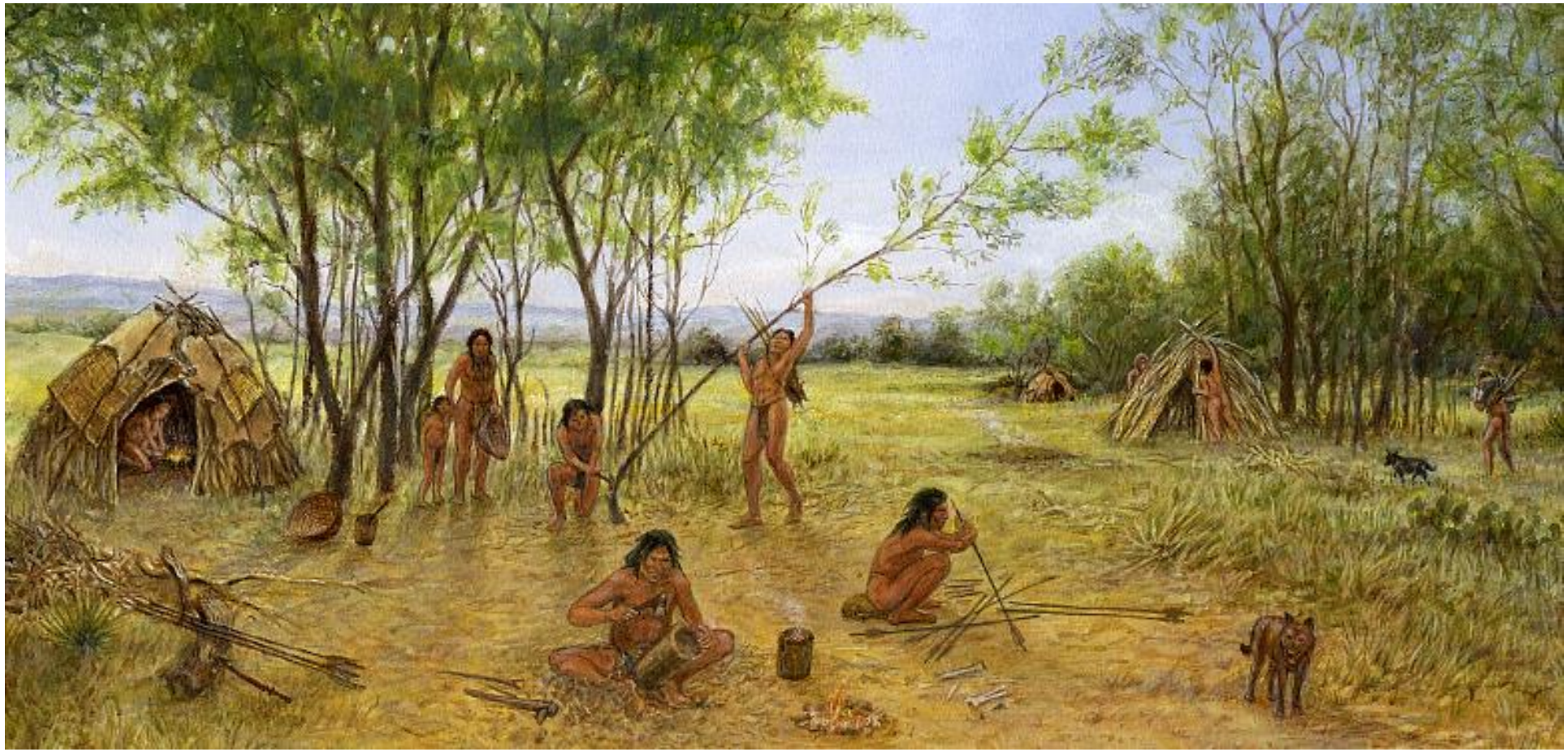
Brandon H Hidaka: bhidaka@kumc.edu

Amishit eivät kärsi masennusepidemiasta?

Masennuksen yleisyys vain 1%

Egeland & Hostetter (1983). American Journal of Psychiatry 140, 56-61

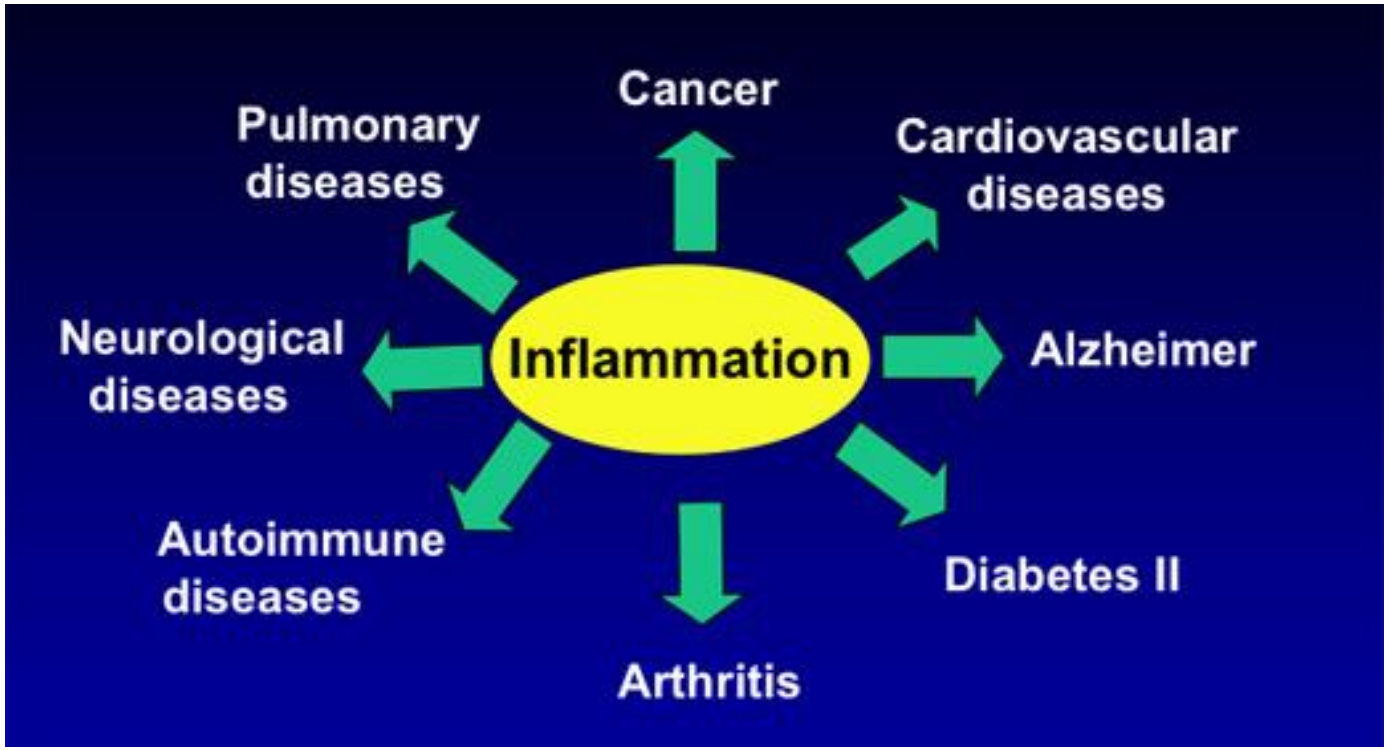
Miksi mielialan lasku johtaa kliiniseen masennukseen länsimaissa, mutta ei metsästäjä-keräilijöillä tai amisheilla?



405 NORTH
Sacramento

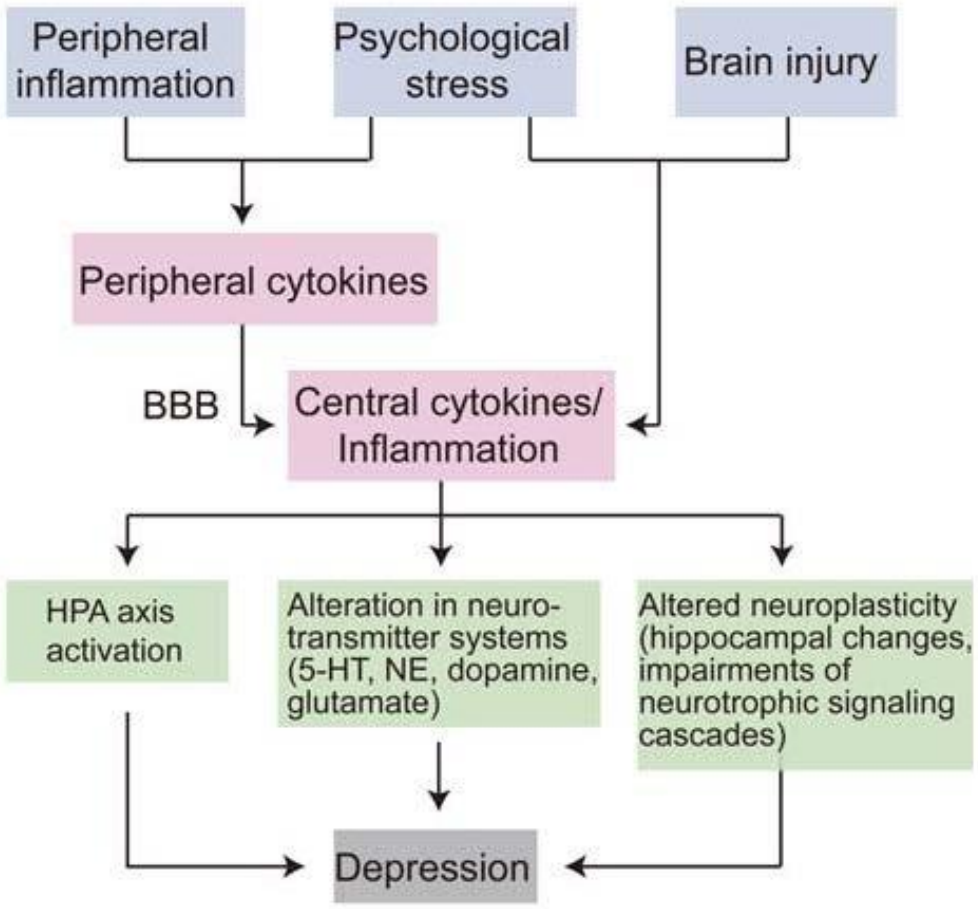
Ympäristö muuttui mutta ihmismieli ja keho eivät muuttuneet

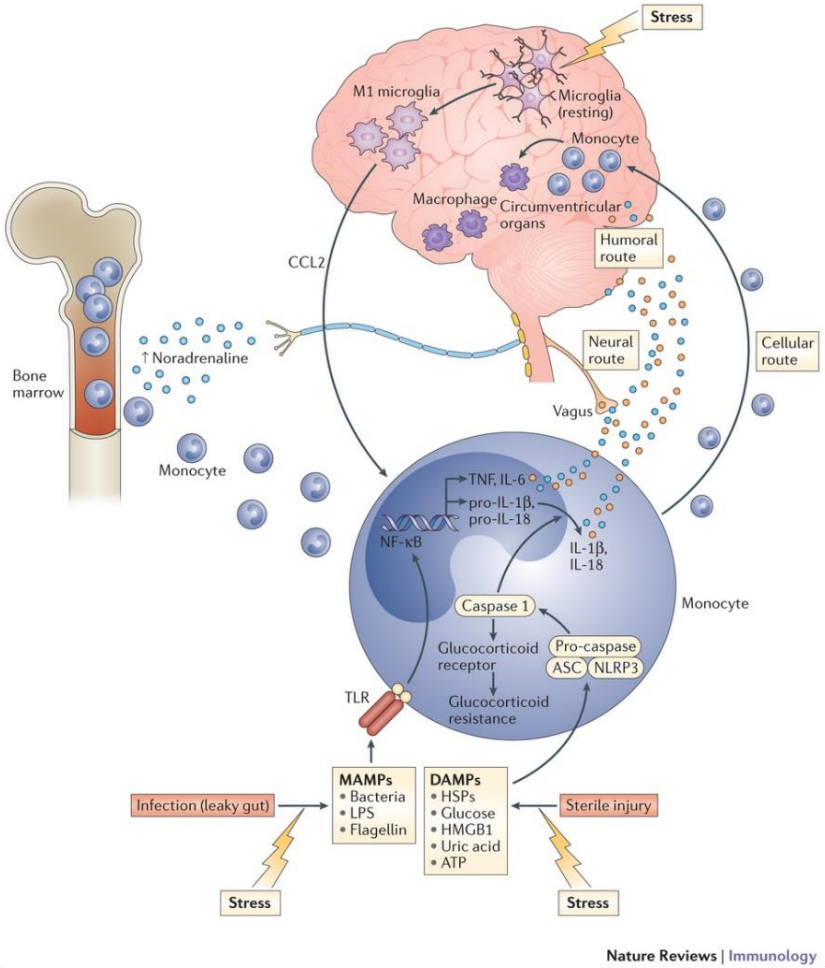
Monet nykyajan terveys ongelmat liittyvät kehon matala-aktiiviseen tulehdukseen



Entäs jos kliininen masennus ei olekaan sairaus vaan oire?

Suuri osa kliinisistä masennuksista on yhteydessä matala-aktiiviseen tulehdukseen!





REVIEWS

Nature Reviews Immunology 16, 22-34. (2016)

The role of inflammation in depression: from evolutionary imperative to modern treatment target

Andrew H. Miller[1] and Charles L. Raison[2]

Masennukselle altistavat geenit ovat yhteydessä immuunijärjestelmän toimintaan

Table 2 Immune/host defense functions of single-nucleotide polymorphisms (SNPs) associated with major depression based on the largest meta-analysis of genome-wide association studies (GWASs) conducted to date for major depression (MDD)

Gene ID	*Gene name*	*SNP with minimum P-value*	*Immune/host defense function of gene*
SEL1L2	*Sel-1 suppressor of lin-12-like 2*	rs17226852	No specific immune or host defense functions identified for *SEL1L2*. However, the other member of the sel1 gene family, *SEL1L*, has been shown to be important for quality control of IgM,[100] and the infectious capacity of several viruses,[101] including human cytomegalovirus,[102] a microsatellite polymorphism of *SEL1L*, is associated with autoimmune thyroid diseases[103]
ADCY3	*Adenylate cyclase 3*	rs2384061	*ADCY3* is integral to a rapid, NF-κB-independent, signaling cascade initiated by microbial stimulation of TLR4.[104] *ADCY3* also regulates crosstalk between FP prostanoid and prostaglandin E2 receptors.[105] This crosstalk regulates expression of *SAT1* gene, which has been reported to be underexpressed in prefrontal cortex of suicide completers.[106]
UNC93A	*Unc-93 homolog A*	rs2076008	No specific immune or host defense functions identified for *UNC93A*, but a closely related homolog, UNC93B, plays a crucial role in antigen presentation and TLR functioning, and deficiency in its expression reduces TNF-α production and increases vulnerability to a number of infections.[107–109] Blockade of *UNC93B* may protect against autoimmunity.[110]
TEX10	*Testis expressed 10*	rs1930243	No specific immune or host defense functions identified.
TTLL2	*Tubulin tyrosine ligase-like family, member 2*		No specific immune or host defense functions identified for *TTLL2*; however, other TTLL family members have been shown to be essential for proper cilliary structure and function and with this ability to clear pathogens and other harmful substances from the airway.[111]
GAL	*Galanin*	rs2156464	Signaling through either type 1 or type 2 receptors, *GAL* has numerous anti-inflammatory effects;[112–115] Consistent with PATHOS-D, multiple lines of evidence indicate *GAL* signaling is reduced in MDD;[116–118] GMAP, which is produced by cleavage of the same precursor as galanin, has direct antifungal activity[119]
PDK4	*Pyruvate dehydrogenase kinase, isozyme 4*	rs11531570	*PDK4* gene expression is upregulated by IFN-α and by LPS and contributes to muscle glycogen breakdown and lactate accumulation;[120,121] conversely, *PDK4* is inhibited by TNF-α via p38 MAPK and NF-κB signaling, leading to increased glucose oxidation;[122] anti-inflammatory omega-3 fatty acids increase *PDK4* in immature dendritic cells via enhanced PPAR-γ signaling[123]
NPM1	*Nucleophosmin*	rs11134697	Functions as an endogenous 'alarmin' that activates proinflammatory cytokines;[124–126] identified as a host virulence factor in viral infection;[127,128] may aid in HIV and HSV1 virus dispersal within cells;[129,130] complexes with, and inhibits, PKR, which has important antiviral properties[131]
USP3	*Ubiquitin-specific peptidase 3*	rs7183892	Embedding of *USP* genes in the copy number variable β-defensin cluster on chromosome 8p23.1 suggests a close tie with innate immunity;[132] *USP3* is activated by IL-4 and IL-6 and has antiproliferative and apoptotic properties;[133] highly homologous *USP17* necessary for type I IFN production in response to virus infection;[134]
ASB4	*Ankyrin repeat and SOCS box-containing 4*	rs11531570	No specific immune or host defense functions identified.

Open

Molecular Psychiatry (2013) 18, 15–37
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www.nature.com/mp

HYPOTHESIS

The evolutionary significance of depression in Pathogen Host Defense (PATHOS-D)

CL Raison[1,2] and AH Miller[3]

[1]*Department of Psychiatry, College of Medicine, University of Arizona, Tucson, AZ, USA;* [2]*John and Doris Norton School of Family and Consumer Sciences, University of Arizona, Tucson, AZ, USA and* [3]*Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA*

Miten laskea kehon matala-aktiivista tulehdusta?

Tulehduslääkkeet helpottavat masennuksen oireita

- Eivät vielä yleisessä käytössä.
- Eivät ole kuitenkaan pitkäaikainen ratkaisu, sillä ne helpottavat oireita, mutta eivät hoida syytä joka aiheuttaa matala-aktiivisen tulehduksen!

OPEN

Molecular Psychiatry (2016) 00, 1–9

www.nature.com/mp

ORIGINAL ARTICLE

Antidepressant activity of anti-cytokine treatment: a systematic review and meta-analysis of clinical trials of chronic inflammatory conditions

N Kappelmann[1], G Lewis[2], R Dantzer[3], PB Jones[1,4,5] and GM Khandaker[1,4,5]

Inflammatory cytokines are commonly elevated in acute depression and are associated with resistance to monoaminergic treatment. To examine the potential role of cytokines in the pathogenesis and treatment of depression, we carried out a systematic review and meta-analysis of antidepressant activity of anti-cytokine treatment using clinical trials of chronic inflammatory conditions where depressive symptoms were measured as a secondary outcome. Systematic search of the PubMed, EMBASE, PsycINFO and Cochrane databases, search of reference lists and conference abstracts, followed by study selection process yielded 20 clinical trials. Random effect meta-analysis of seven randomised controlled trials (RCTs) involving 2370 participants showed a significant antidepressant effect of anti-cytokine treatment compared with placebo (standardised mean difference (SMD) = 0.40, 95% confidence interval (CI), 0.22–0.59). Anti-tumour necrosis factor drugs were most commonly studied (five RCTs); SMD = 0.33 (95% CI; 0.06–0.60). Separate meta-analyses of two RCTs of adjunctive treatment with anti-cytokine therapy and eight non-randomised and/or non-placebo studies yielded similar small-to-medium effect estimates favouring anti-cytokine therapy; SMD = 0.19 (95% CI, 0.00–0.37) and 0.51 (95% CI, 0.34–0.67), respectively. Adalimumab, etanercept, infliximab and tocilizumab all showed statistically significant improvements in depressive symptoms. Meta-regression exploring predictors of response found that the antidepressant effect was associated with baseline symptom severity ($P = 0.018$) but not with improvement in primary physical illness, sex, age or study duration. The findings indicate a potentially causal role for cytokines in depression and that cytokine modulators may be novel drugs for depression in chronically inflamed subjects. The field now requires RCTs of cytokine modulators using depression as the primary outcome in subjects with high inflammation who are free of other physical illnesses.

Molecular Psychiatry advance online publication, 18 October 2016; doi:10.1038/mp.2016.167

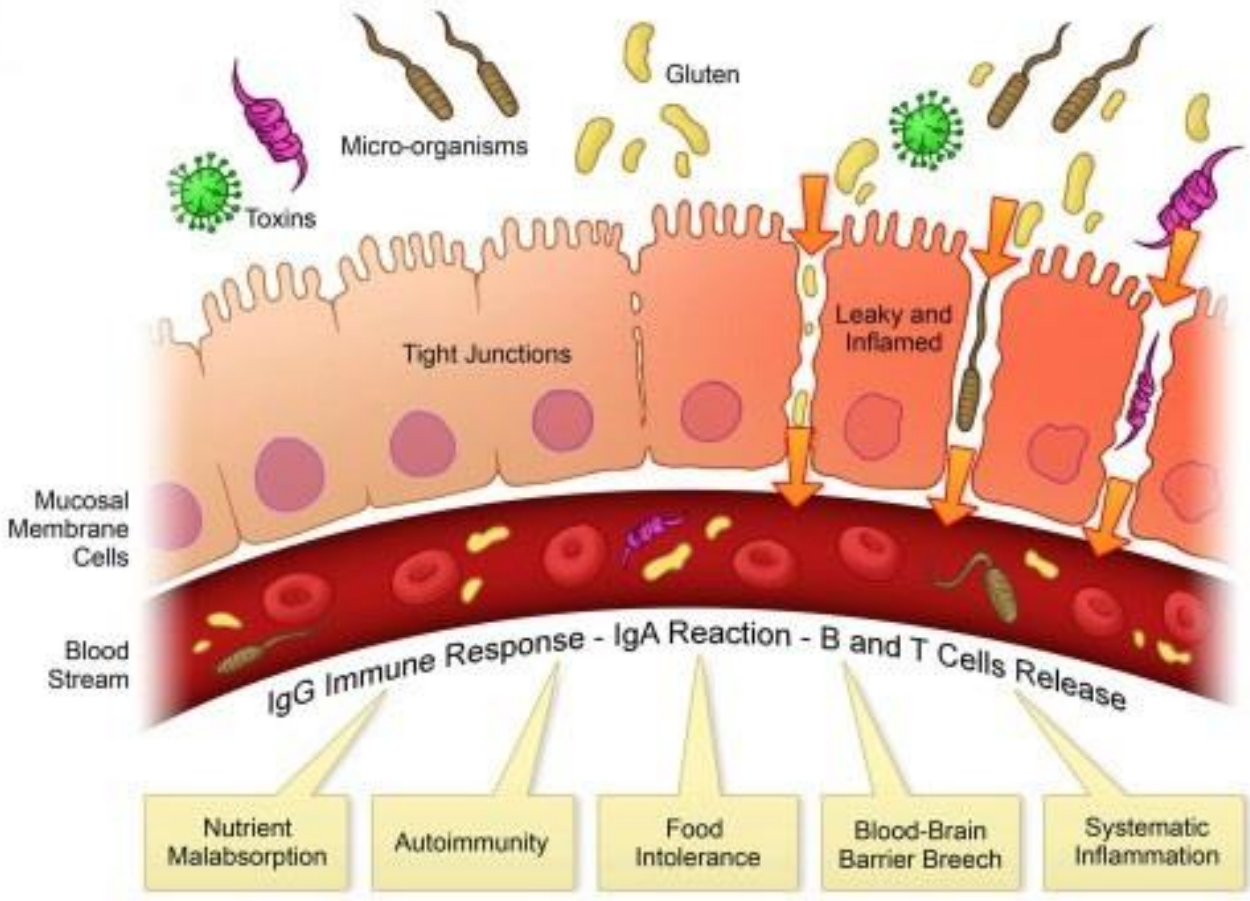
Masennuksen hoidossa pitäisi keskittyä oireiden hoitamisen sijasta hoitamaan myös masennuksen laukaisseita syitä ja vähentämään sille altistavia tekijöitä .

- Masennuksen laukaisevat tekijät

- Masennukselle altistavat tekijät

"My doctor told me to avoid any unnecessary stress, so I didn't open his bill."

Krooninen stressi aiheuttaa matala-aktiivista tulehdusta



Krooninen työstressi aiheuttaa masennusta

Ennen harjoittelua vain 3.9 % lääketieteenopiskelijoista ylitti kliinisesti masentuneen kriteerit, mutta harjoitteluajan loppupuolella jo 25.7%

Psykomotoristen ongelmat	+217%
Anhedonian	+217%.
Keskittymisongelmat	+204%.
Uupumuksen tunne	+145%,
Syömisongelmat	+ 164.4%,
Itsemurha ajatukset	+146%
Uniongelmat	+52%.

ORIGINAL ARTICLE

A Prospective Cohort Study Investigating Factors Associated With Depression During Medical Internship

Srijan Sen, MD, PhD; Henry R. Kranzler, MD; John H. Krystal, MD; Heather Speller, MD; Grace Chan, PhD; Joel Gelernter, MD; Constance Guille, MD

Arch Gen Psychiatry. 2010;67(6):557-565

Vuorotyö pitää yllä kroonista stressiä

Pyri välttämään kroonista stressiä!

Traumaattinen lapsuus heikentää stressinsietokykyä ja altistaa siten myöhemmin masennukselle ja monille muille mielenterveysongelmalle

Encyclopedia on Early Childhood Development

BRAIN

Childhood Trauma and Adult Stress Responsiveness

Christine Heim, PhD
Emory University, USA
June 2009

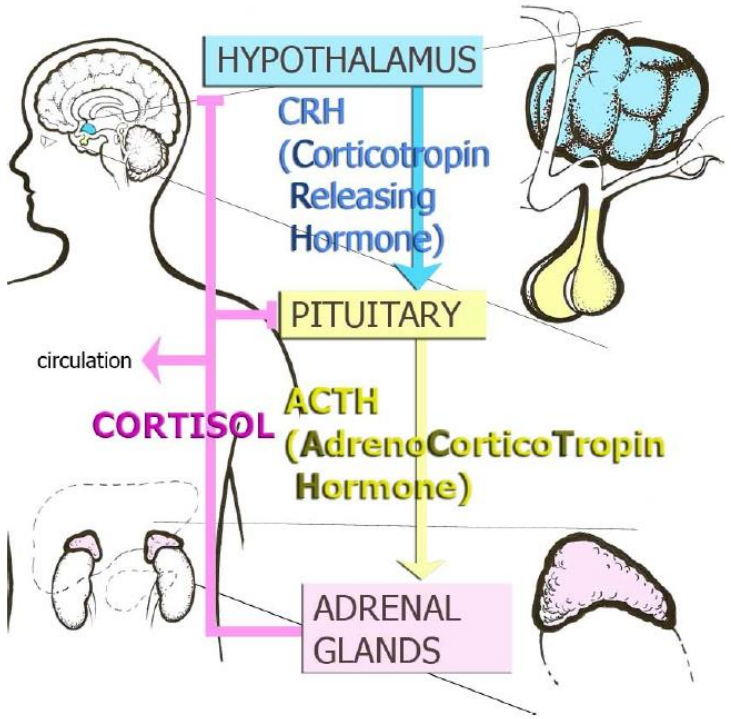


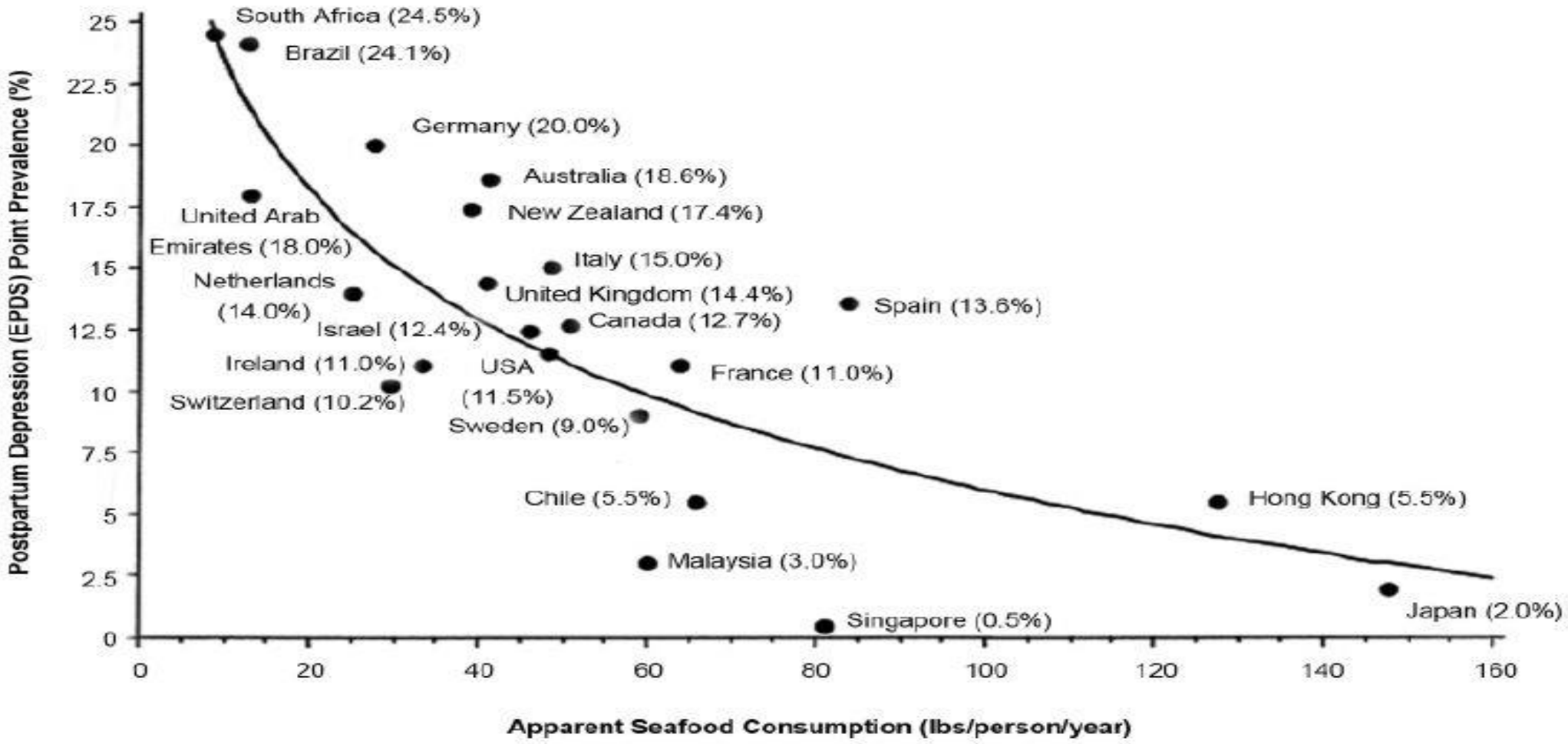
Figure 1. Hypothalamic-Pituitary Adrenocortical Axis or Stress Hormone Axis

Miksi stressi aiheuttaa nukkumisongelmia?

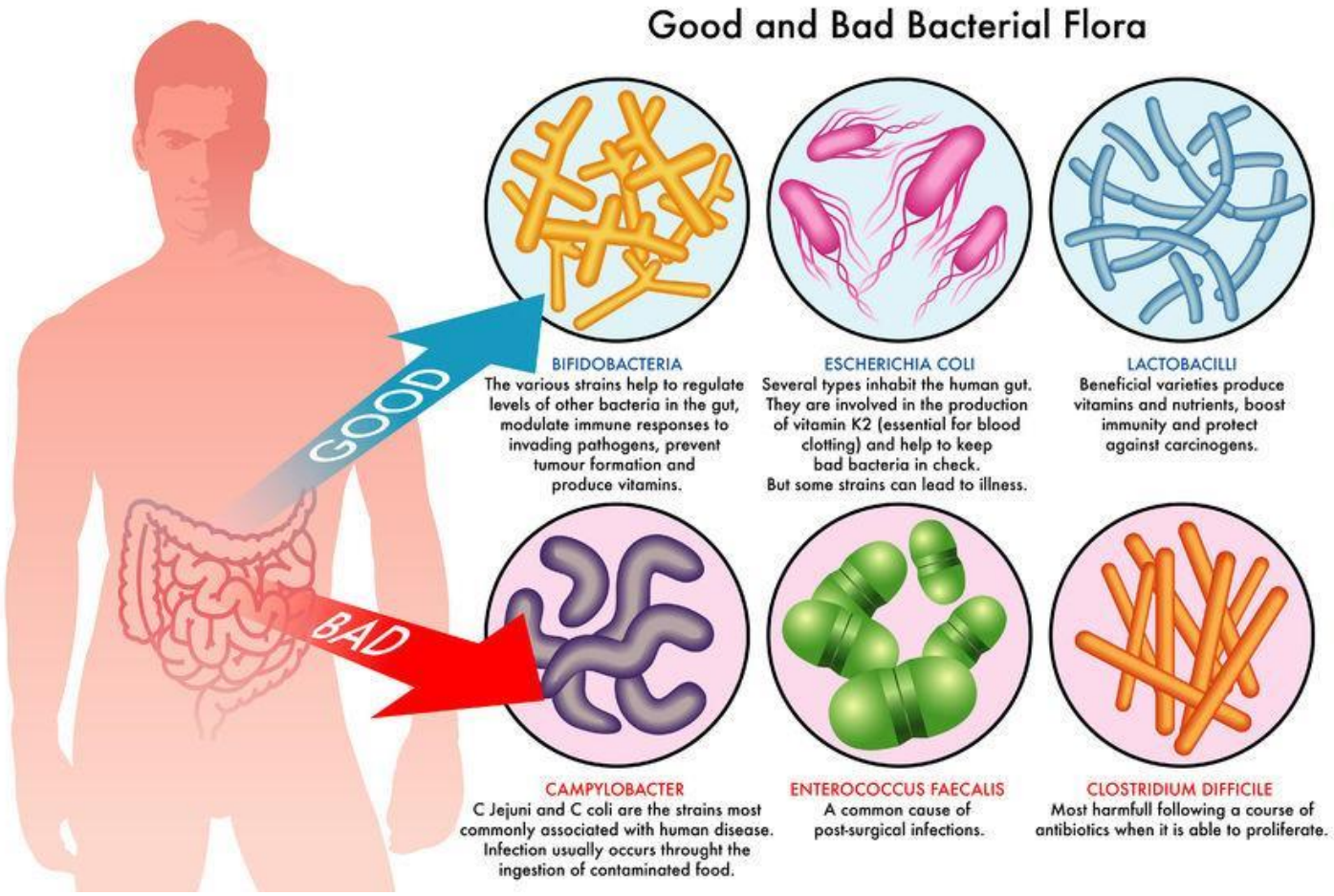
Ruokavalio vaikuttaa matala-aktiiviseen tulehdukseen

Meren elävien syönti ja synnytyksen jälkeinen masennus

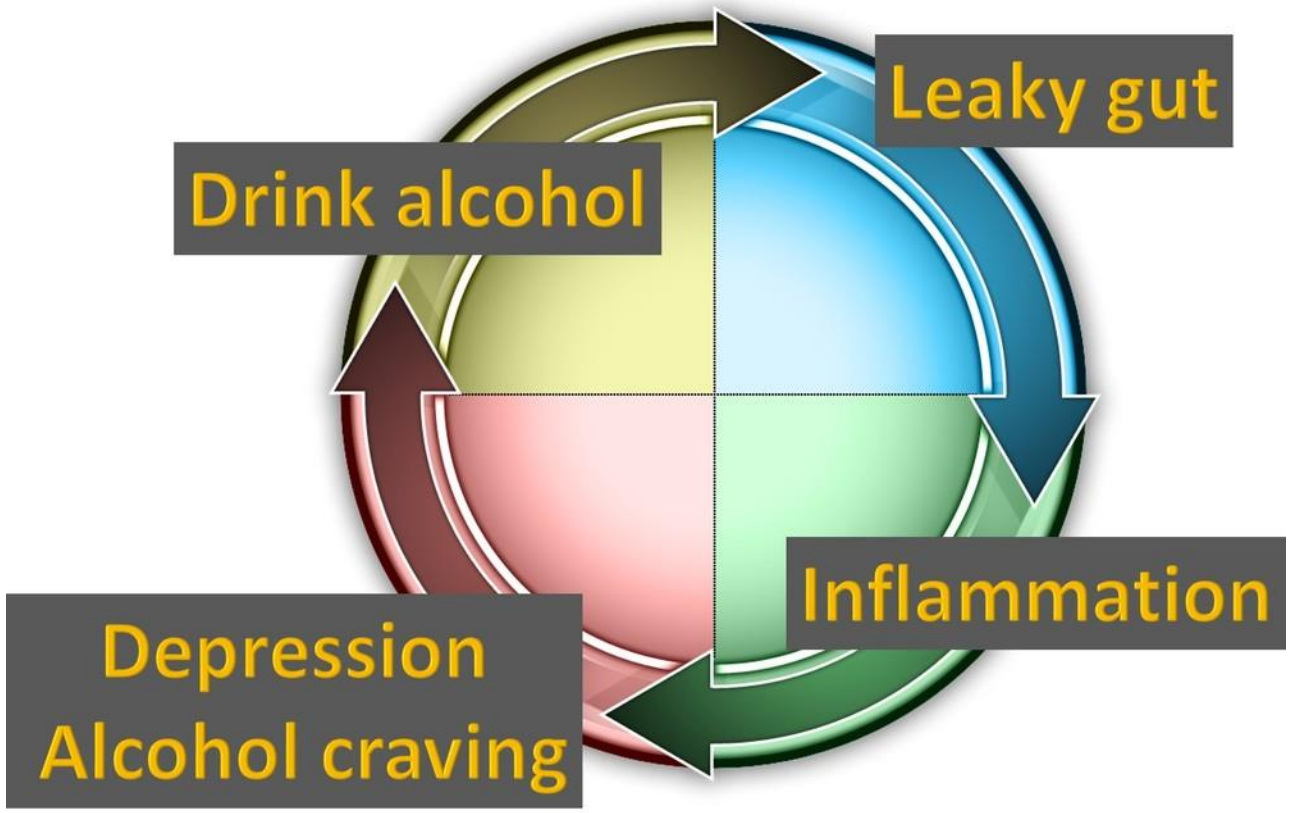
Hibbel et al. 2002. *Journal of Affective Disorders*.



Suolistobakteerit vaikuttavat mielialaan



Vältä alkoholia



Bjarnason et al. 1984. THE LEAKY GUT OF ALCOHOLISM - POSSIBLE ROUTE OF ENTRY FOR TOXIC COMPOUNDS. Lancet 1, 179-182.

D-vitamiinilisä on puutteesta kärsivälle vähintään yhtä tehokas hoitokeino kuin masennuslääkkeet!

Spedding, S. Vitamin D and Depression: A Systematic Review and Meta-Analysis Comparing Studies with and without Biological Flaws. *Nutrients* **6**, 1501-1518, doi:10.3390/nu6041501 (2014).

Kotimaa

Uusi suositus: Liikunta tehoaa masennukseen kuin lääkkeet tai terapia

Suositus huomauttaa myös, että masennuksen oireet hälvenevät sitä enemmän mitä raskaampaa ja useammin toistuvaa liikunta on.

Hiihtäjiä Helsingin Paloheinässä torstaina. (KUVA: JUSSI NUKARI LEHTIKUVA)

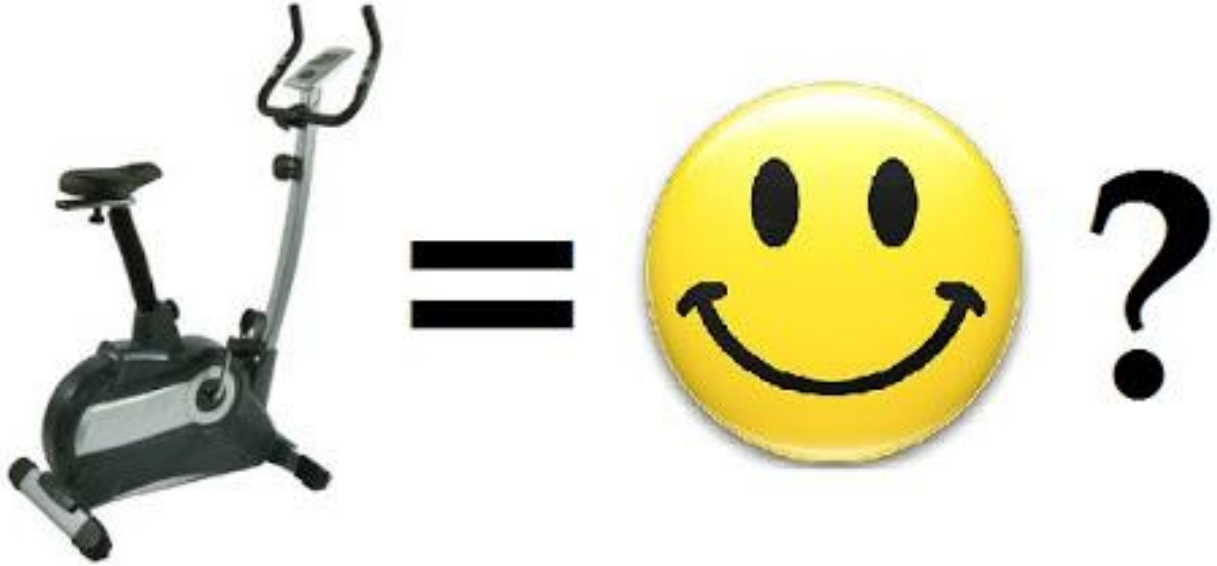
Päivi Repo HS
Julkaistu: 16.1.2016 2:00

Luetuimmat

JUURI NYT | PÄIVÄ › | VIIKKO ›

1. **Kolumni:** Uusi Vain elämää -osallistujalista on pöyristyttävä – eikä se ole edes tulevan kauden pahin ongelma
2. **Nyt.fi:** Tämän opin seksityöntekijöiden arjesta Suomessa kun katsoin uuden kotimaisen dokumentin
3. Nimimerkki Musta Pekka mielipidesivulla: Työttömyyteni jatkuessa tunnen vihaa päättäjiä ja yhteiskuntaa kohtaan
4. Vieraiden miesten treffipyyntöjä, uhkailua ja savukaasupanos työpaikalla – kostoa hautonut asiakas vainosi vuosia Marjo Oinosta
5. Berner kaavailee kaikkien puolueiden parlamentaarista komiteaa hoitamaan liikenneuudistusta – "Nyt tarvitsen kolme minuuttia ajatusten kasaamiseksi"

Miksi liikunta on tehokkaampaa kuin masennuslääkkeet ja terapia?



Miten saada ihmiset liikkumaan enemmän?

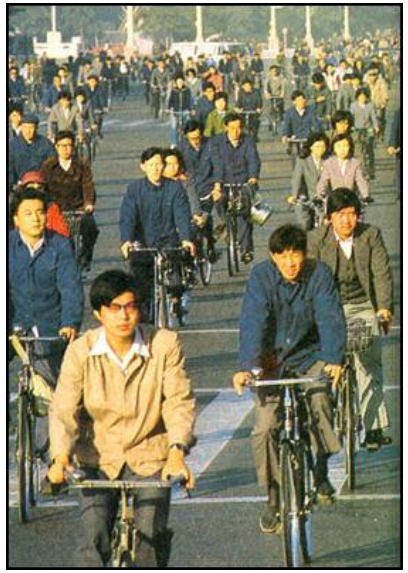
Ihmiset eivät ole adaptoituneet harrastamaan liikuntaa!

Kaikki tietävät liikunnan hyödyt mutta harva liikkuu riittävästi!

Syy: Luonnonvalinta on aiemmin suosinut ihmisiä jotka ovat säästäneet energiaa silloin kuin mahdollista, välttämällä turhaa liikkumista!

Ratkaisu: Suurimmalle osalle meistä pitää olla mielekäs syy liikkua!

Mitkä ovat mielekkäitä syitä liikkua?



Miten saada masentuneet liikkumaan?

Luonnon merkitys henkiselle terveydelle

Luonnon näkeminen laskee stressiä

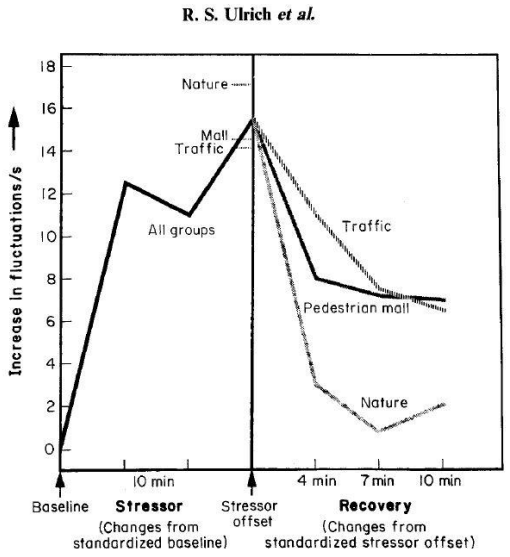


FIGURE 1. Changes in skin conductance (SCR) during stress and recovery.

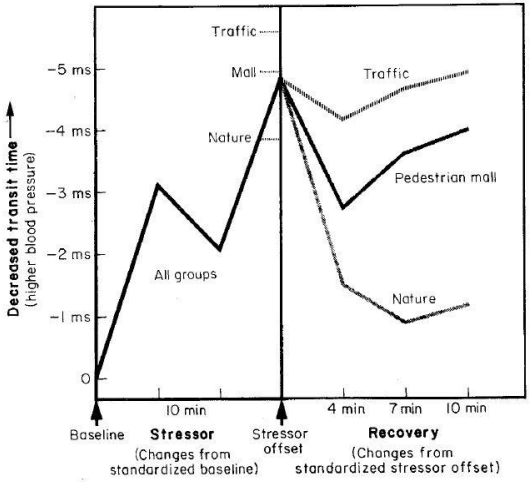


FIGURE 2. Changes in pulse transit time (PTT) during stress and recovery.

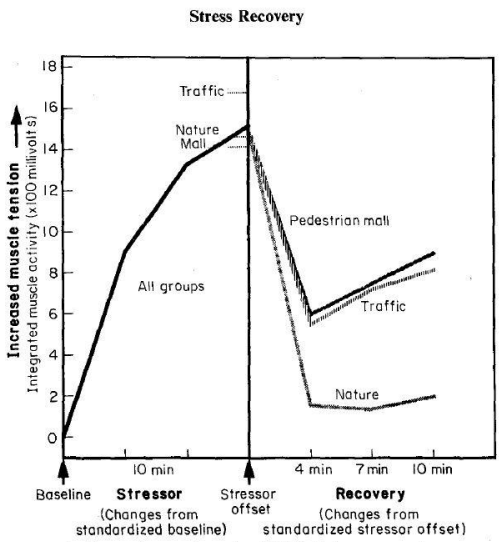


FIGURE 3. Changes in muscle tension (EMG) during stress and recovery.

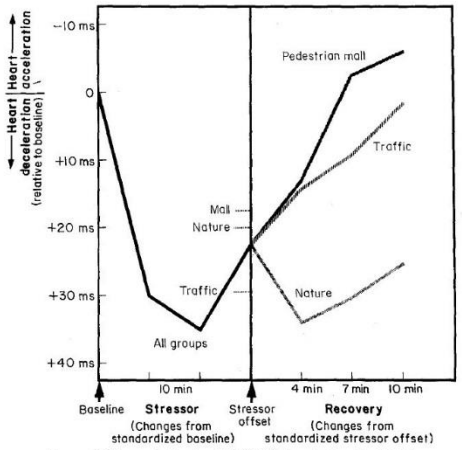


FIGURE 4. Changes in heart period (HP) during stress and recovery.

Ulrich et al 1991. Stress recovery during exposure to natural and urban environments. *Journal of Environmental Psychology* 11, 201-230.

Potilaat jotka näkevät luontoa sairaalan ikkunasta paranee nopeammin.

Ulrich, R.S. 1984. View through a window may influence recovery from surgery. *Science*, *224*, 420–421.

Sellin ikkunan maisema vaikuttaa vankien mielenterveyteen

- Moore, E.O. (1982). A prison environment's effect on health care service demands. *Journal of Environmental Systems*, 11, 17-34.

Pelkkä maisemakuva seinällä riittää laskemaan stressiä

Heerwagen (1990). Psychological aspects of windows and window design. Pp.269-280.

Kirkasvalohoito

Kirkasvalohoito on yhtä tehokasta hoitoa kaikkiin masennustyyppeihin kuin masennuslääkkeet

Reviews and Overviews

The Efficacy of Light Therapy in the Treatment of Mood Disorders: A Review and Meta-Analysis of the Evidence

Robert N. Golden, M.D.

Bradley N. Gaynes, M.D., M.P.H.

R. David Ekstrom, M.A., M.P.H.

Robert M. Hamer, Ph.D.

Frederick M. Jacobsen, M.D., M.P.H.

Trisha Suppes, M.D., Ph.D.

Katherine L. Wisner, M.D.

Charles B. Nemeroff, M.D., Ph.D.

Objective: The purpose of this study was to assess the evidence base for the efficacy of light therapy in treating mood disorders.

Method: The authors systematically searched PubMed (January 1975 to July 2003) to identify randomized, controlled trials of light therapy for mood disorders that fulfilled predefined criteria. These articles were abstracted, and data were synthesized by disease and intervention category.

Results: Only 13% of the studies met the inclusion criteria. Meta-analyses revealed that a significant reduction in depression symptom severity was associated with bright light treatment (eight studies, having an effect size of 0.84 and 95% confidence interval [CI] of 0.60 to 1.08) and dawn simulation in seasonal affective disorder (five studies; effect size=0.73, 95% CI=0.37 to 1.08) and with bright light treatment in nonseasonal depression (three studies; effect size=0.53, 95% CI=0.18 to 0.89). Bright light as an adjunct to antidepressant pharmacotherapy for nonseasonal depression was not effective (five studies; effect size=–0.01, 95% CI=–0.36 to 0.34).

Conclusions: Many reports of the efficacy of light therapy are not based on rigorous study designs. This analysis of randomized, controlled trials suggests that bright light treatment and dawn simulation for seasonal affective disorder and bright light for nonseasonal depression are efficacious, with effect sizes equivalent to those in most antidepressant pharmacotherapy trials. Adopting standard approaches to light therapy's specific issues (e.g., defining parameters of active versus placebo conditions) and incorporating rigorous designs (e.g., adequate group sizes, randomized assignment) are necessary to evaluate light therapy for mood disorders.

(Am J Psychiatry 2005; 162:656–662)

Matala-aktiivinen tulehdus sotkee biologisen kellon toiminnan.

Review

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Systems Biology of Circadian-Immune Interactions

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Suurperheet ovat kadonneet

Evolutiivisessa historiassa äidit eivät kasvattaneet lapsia yksin vaan lähisukulaiset osallistuivat lastenhoitoon (ja koko kylä).

Synnytyksen jälkeinen masennus yleistynyt

- Synnytyksen jälkeinen masennus vaivaa 10-15 prosenttia synnyttäneistä!
- Altistavat tekijät ovat riittämätön sosiaalinen tuki, talousvaikeudet ja synnytyskomplikaatiot*.
- Psykologinen adaptaatio!
- Synnytyksen jälkeiseen masennukseen ei liity matala-aktiivista tulehdusta!

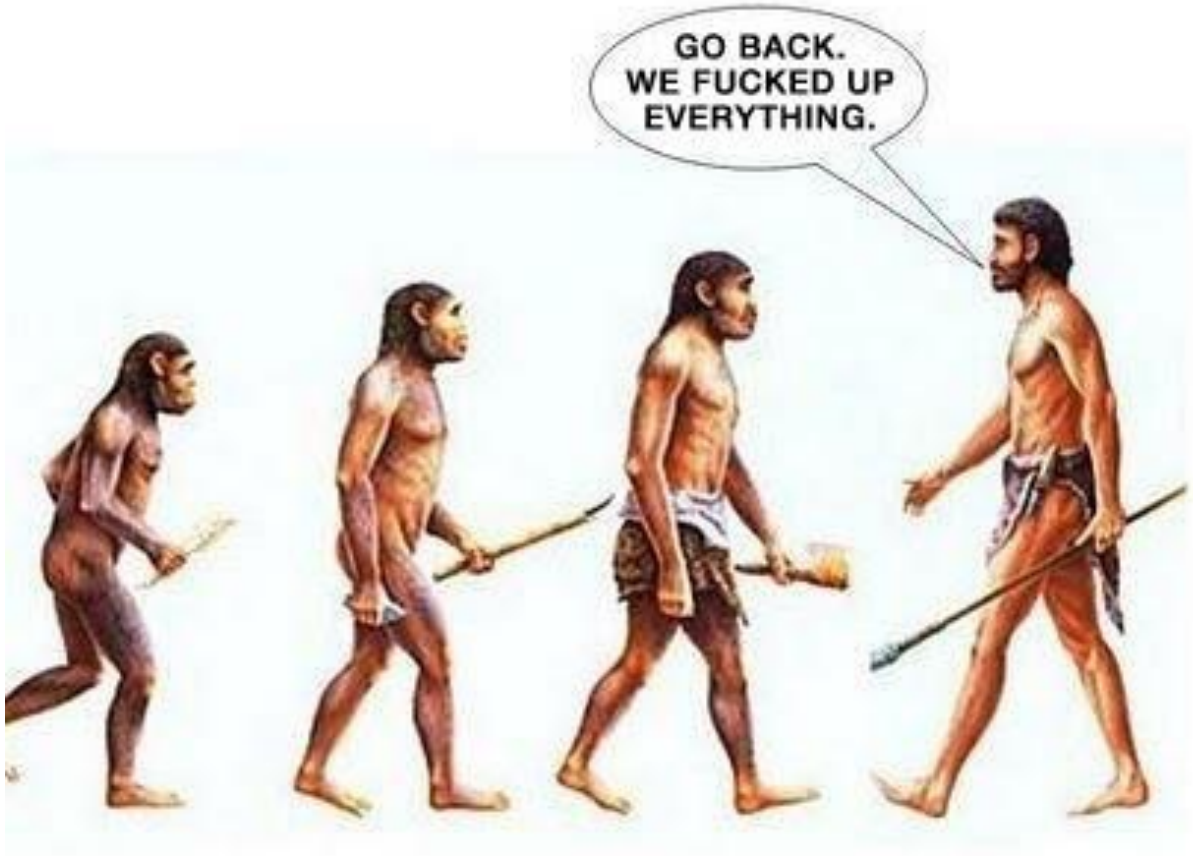
*Robertson et al 2004. Antenatal risk factors for postpartum depression: a synthesis of recent literature. Gen Hosp Psychiatry. 2004;26:289–295.

Mitä hamsteriäiti tekee jos se kokee ettei pysty kasvattamaan poikasiian isoiksi?

Yhteisöllisyys on kadonnut

Masennusta pystyy hoitamaan ja välttämään elämällä elämää mihin olemme sopeutuneet

- Kroonisen stressin välttäminen
- Liikunta
- Terveellinen ruokavalio
- Alkoholin ja muiden huumeiden välttäminen
- Kirkasvalo altistus
- Riittävä nukkuminen
- Luontokontaktin lisääminen
- Yhteisöllisyys (sosiaalinen elämä)
- Media-altistuksen vähentäminen

+Mindfulness

Kiitos mielenkiinnostanne!