Theories and Concepts in Psychoneuroimmunology: What is at Stake?

Robert Dantzer
Department of Symptom Research
The University of Texas MD Anderson Cancer Center
Houston TX

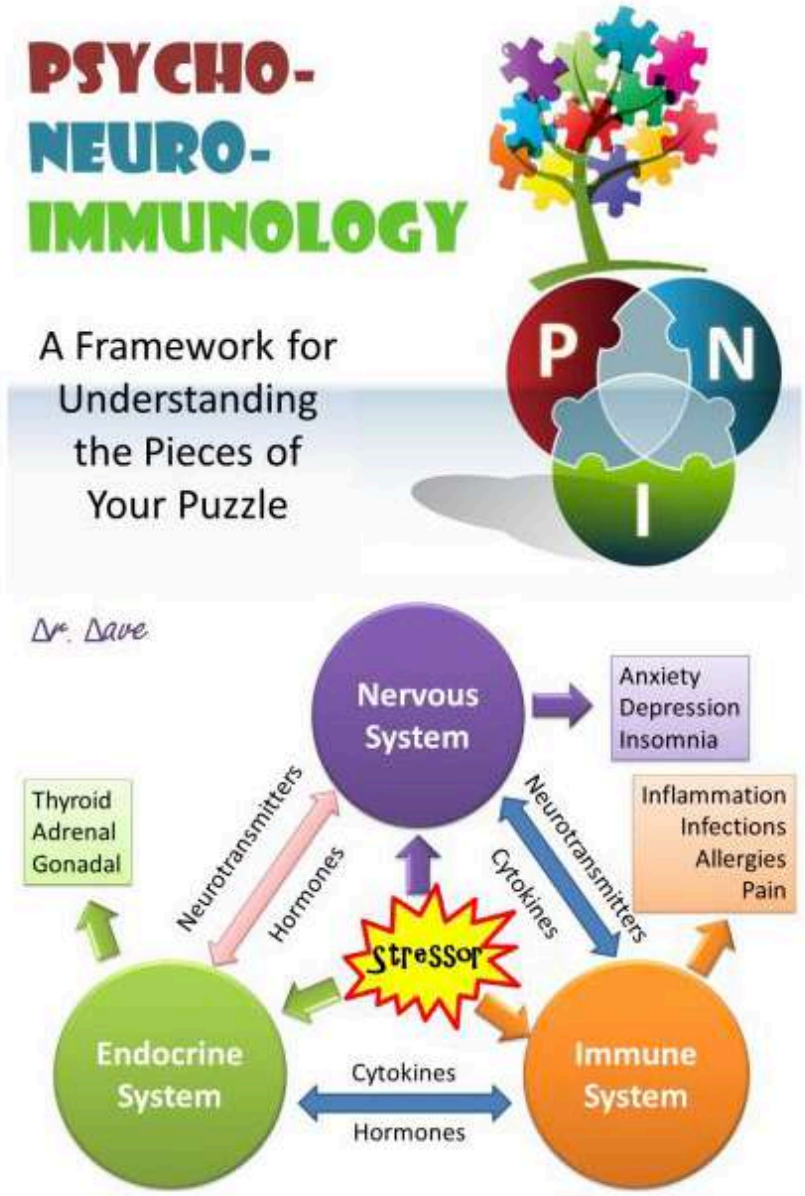


Table 1. *The early decades of research that shaped the field of neuroimmune interactions*

Early Neuroimmune Research
1. The psychosomatic approach:
Psychological factors and emotions influence disease onset and progression (allergies, peptic ulcer, cancer, autoimmune diseases, infectious diseases)
2. The biobehavioral approach:
Experimental stressors impact immune functions (1964: Solomon proposes the term "psychoimmunology")
The immune system can be modulated by conditioned stimuli (Metalnikov and Chorine, 1926; Ader, 1974)
3. The cellular communication approach:
Immune cells express neurotransmitter receptors (Szentivanyi, 1958; Hadden, 1970–5; Pert, 1985)
Immune cells produce brain and pituitary peptides (Blalock, 1980)
4. The neuroanatomical approach:
Innervation of the spleen and other lymphoid organs by the autonomic nervous system (Felten, 1980)
5. The effect of immune factors on the neuroendocrine system:
Interleukin-1 activates the hypothalamic-pituitary-adrenal axis by acting in the brain (Besedovsky and Del Rey, 1975)

Ddave.com

Dantzer, Physiol Rev, 2018

What I would like to discuss:

1. PNI and theories of cellular communication

2. PNI and the normal vs. the pathological

3. PNI and the opponent process theory

1/ Theories of cellular communication

- Cellular communication signals together with their signaling pathways can be found in most cells of the body and are not specific of a given organ

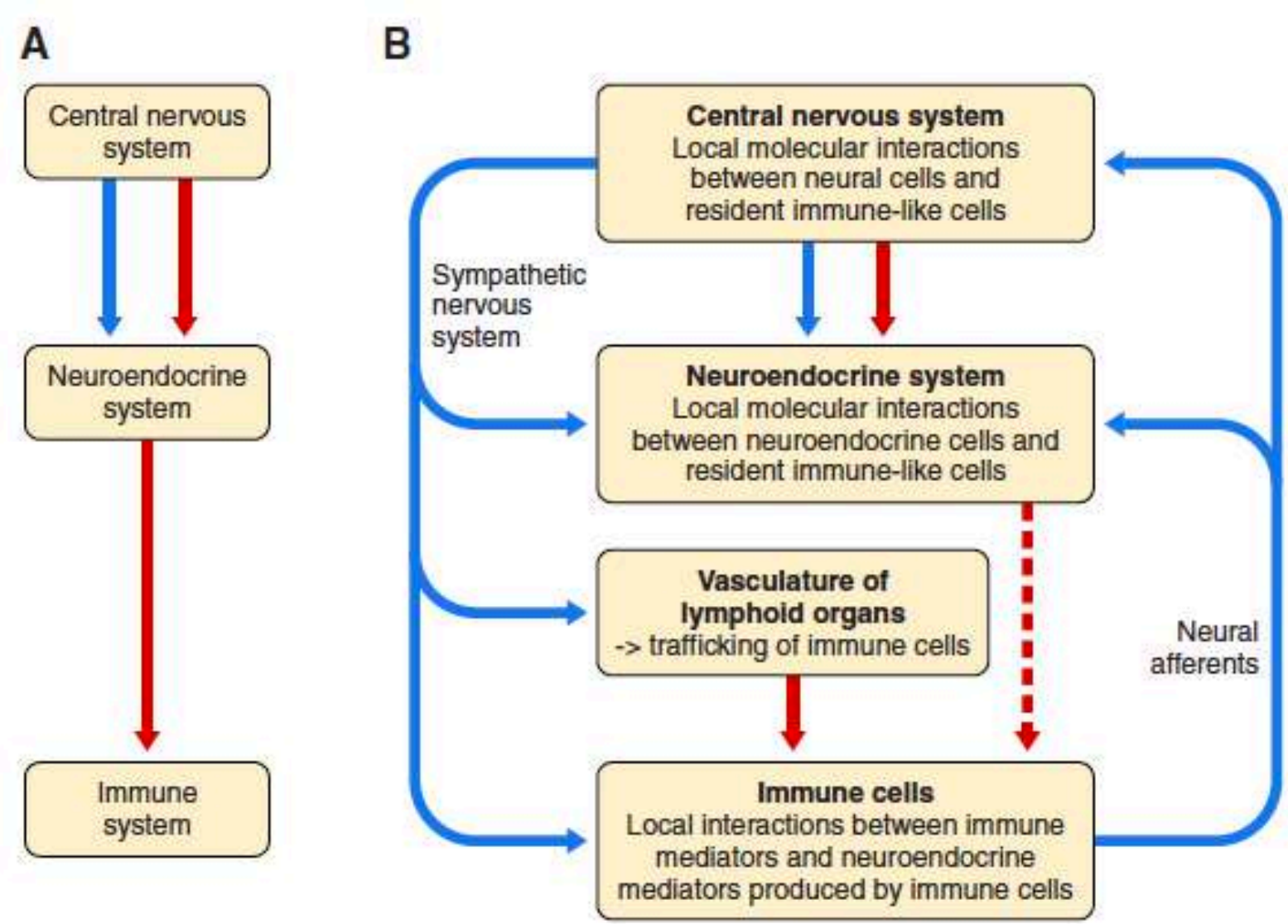
- Specificity of cellular communication comes from the way organs are functionally structured

- Organs that concur to the same function(s) must be able to coordinate their joint functions by reciprocal communication pathways

- In addition to specific organ diseases, there are diseases that affect communication signals and communication pathways

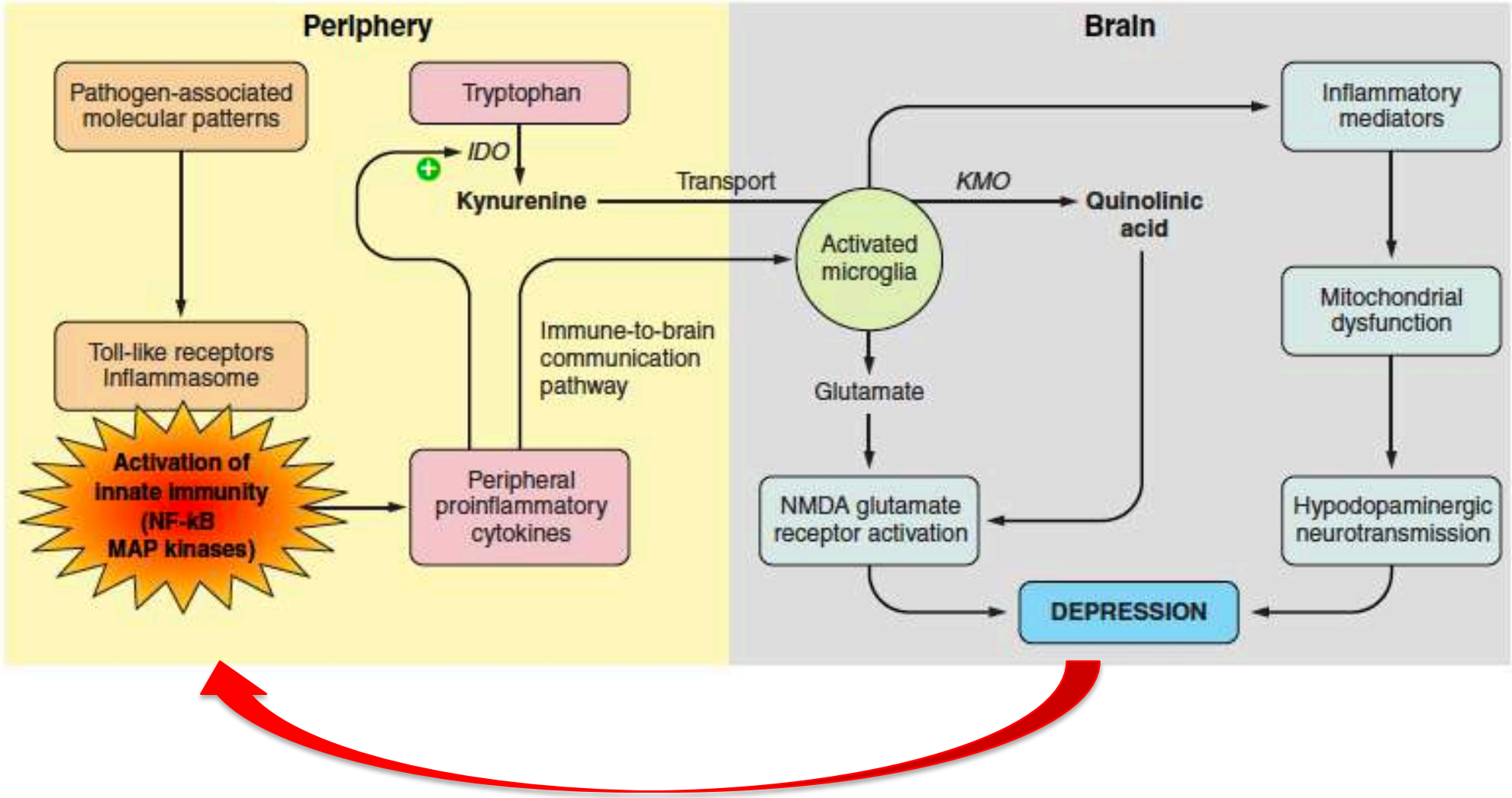
1991

Schematic representation of neuroimmune interactions



Dantzer, Physiol Rev, 2018

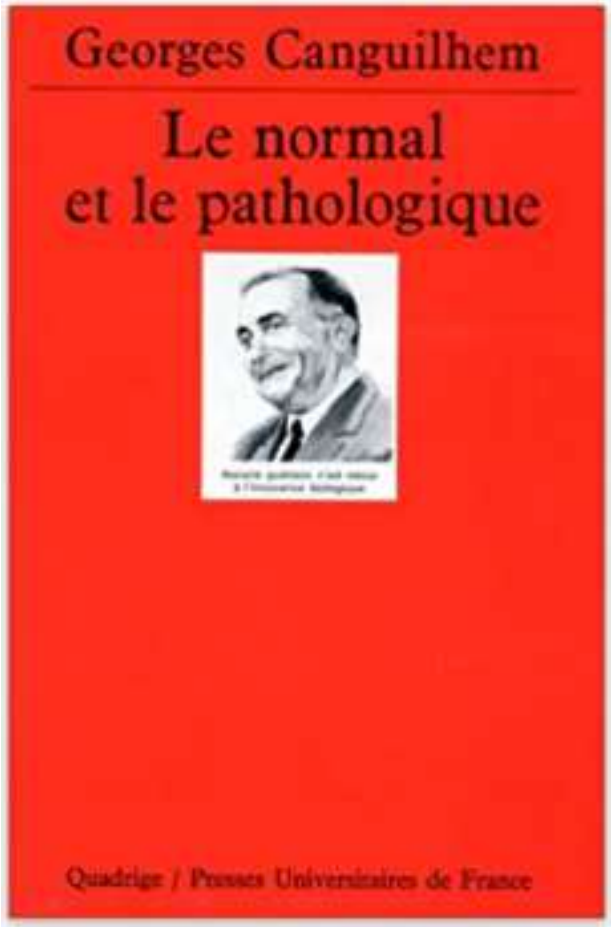
An example of intricate communication pathways: inflammation-induced depression

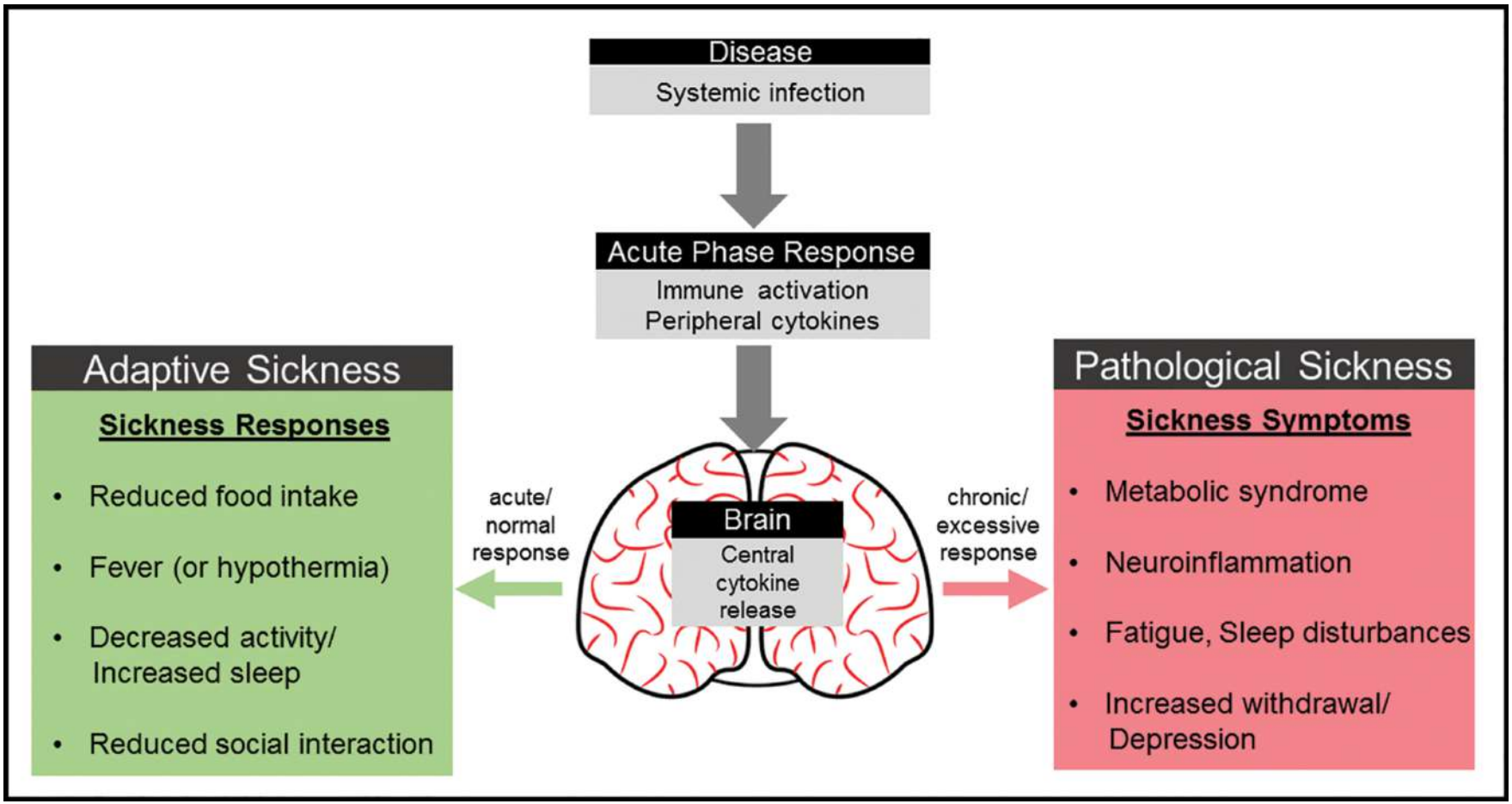


2. The normal and the pathological

2.1 Health as a reversible condition

Canguilhem: "*Ce qui caractérise la santé c'est la possibilité de tolérer des infractions à la norme habituelle et d'instituer des normes nouvelles dans des situations nouvelles. [...]*
La santé c'est une marge de tolérance des infidélités du milieu. [...]
[...] Etre en bonne santé c'est pouvoir tomber malade et s'en relever, c'est un luxe biologique. Inversement, le propre de la maladie c'est d'être une réduction de la marge de tolérance des infidélités du milieu. [...]'





KE Sylvia, GE Demas, A return to wisdom: using sickness behaviors to integrate ecological and translational research, Integr Comp Biol, 2017, 57, 1204-13

Cytokines Cause Reorganization of Host Priorities

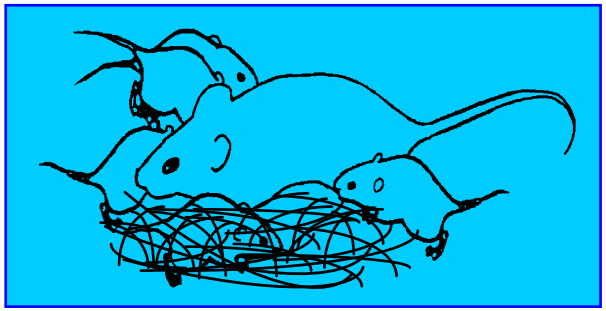
(Aubert et al., Brain Behav Immun 1997, 11:229-238)

Medical interpretation

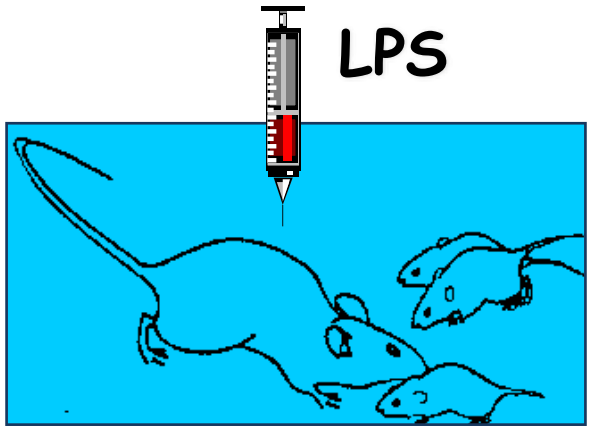
Cytokines → Internal state (weakness) → Behavioral alterations

Motivational interpretation

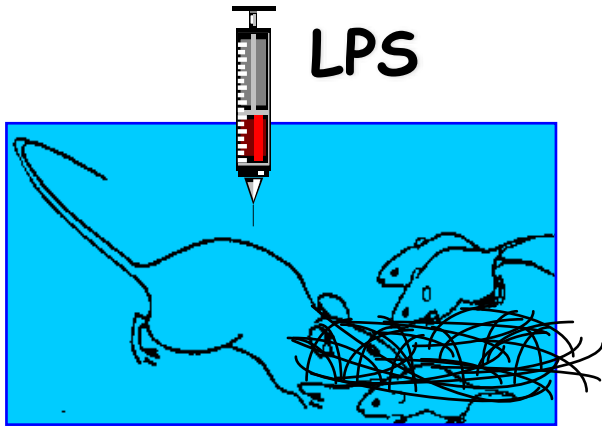
Cytokines → Internal state → Environmental contingencies → Behavioral alterations



24°C



24°C



6°C

MOTIVATIONAL INTERPRETATION OF SICKNESS

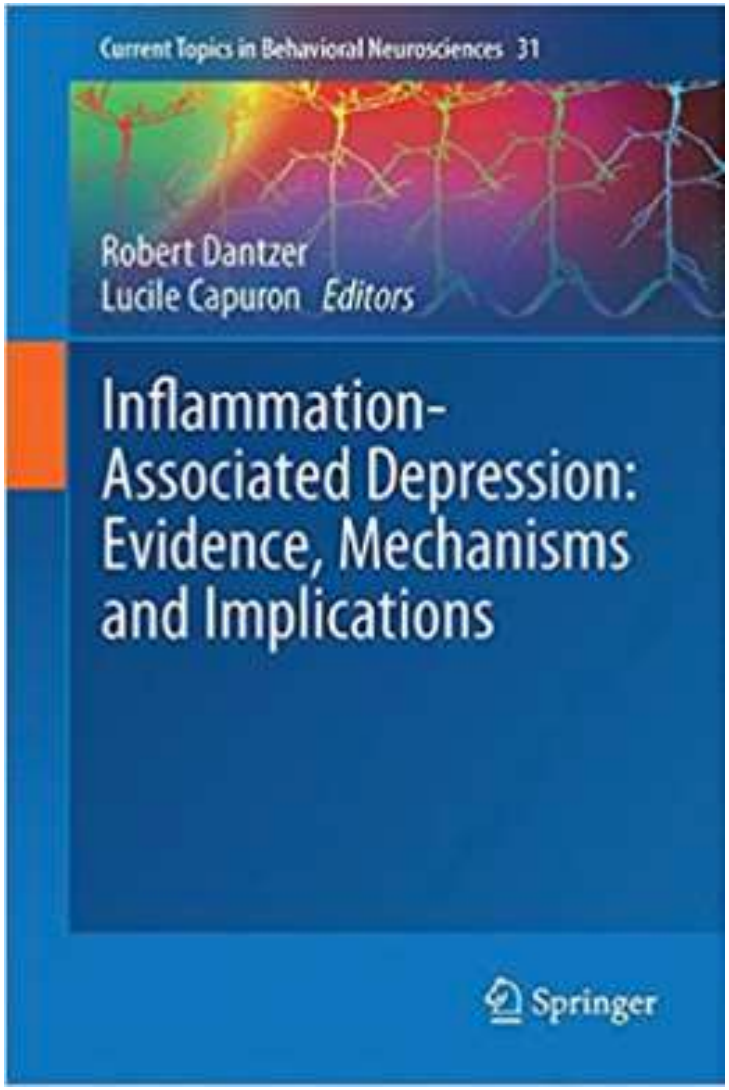
Threat → Fear →

- Fear feelings
- Fear behavior
- Visceral arousal

Pathogenic micro-organisms → Sickness →

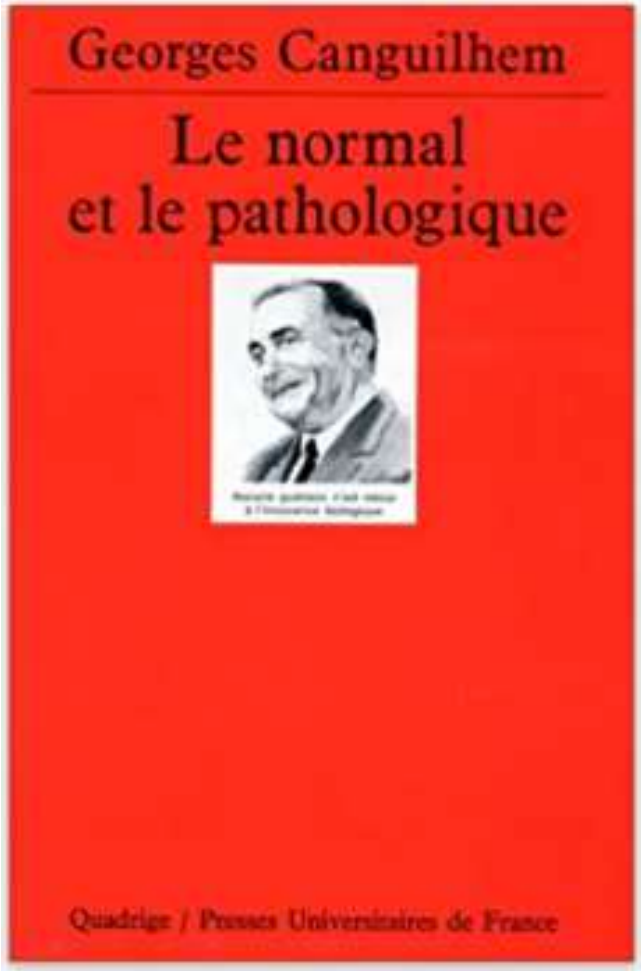
- Malaise
- Sickness behavior
- Visceral arousal

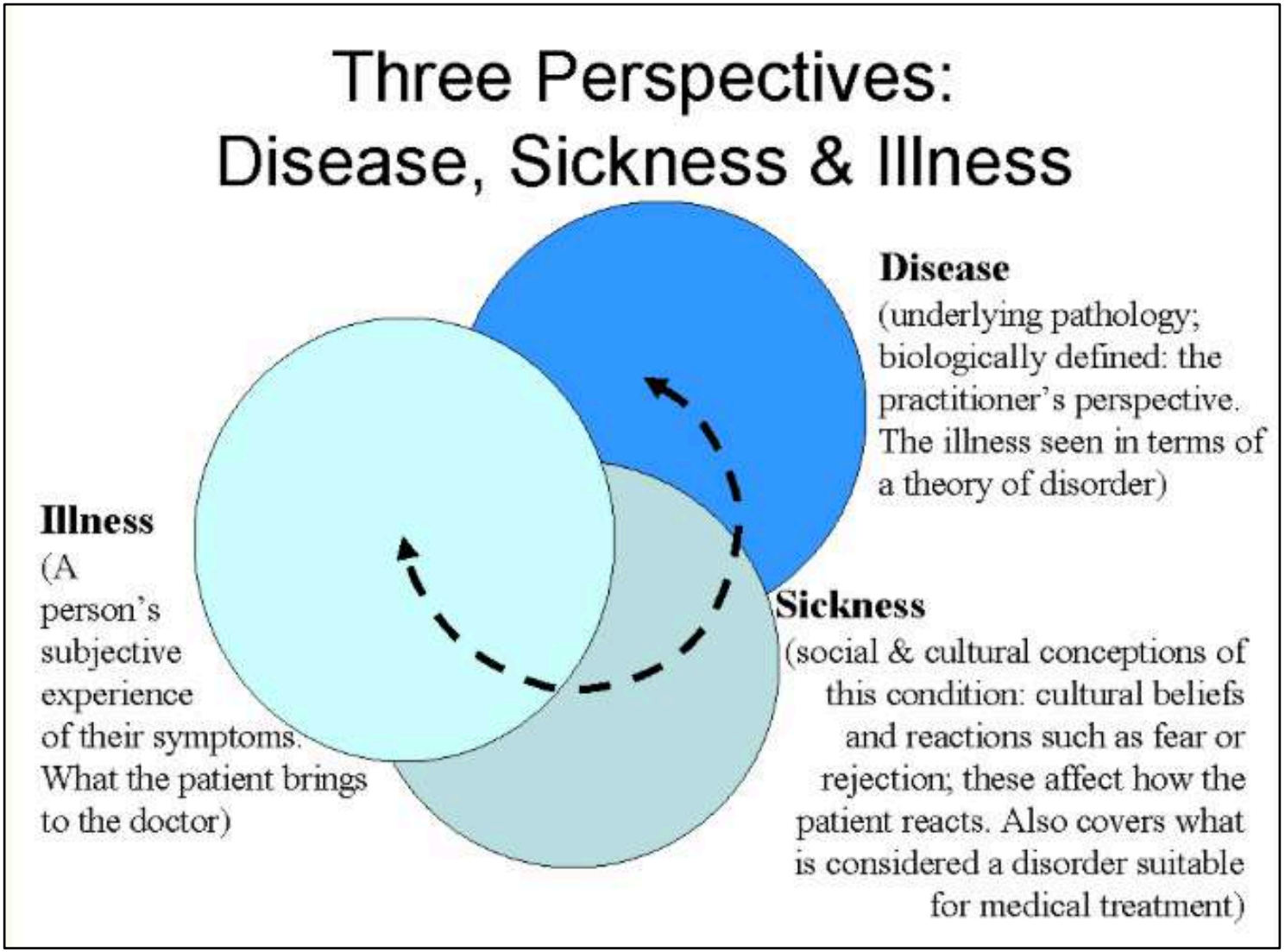
Major depressive disorder as a disease of immune-to-brain communication pathways?



2.2 What it means to be ill

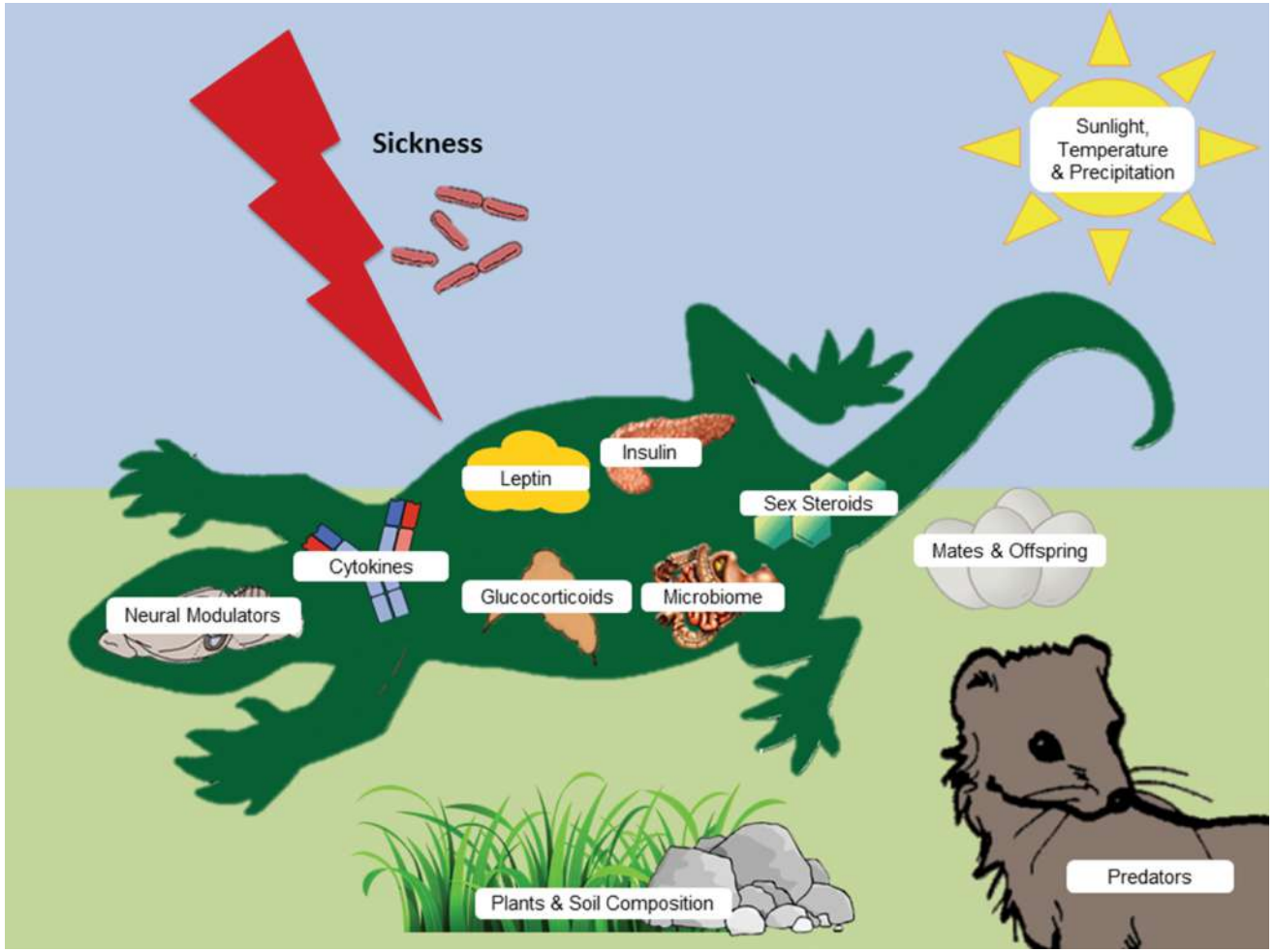
Canguilhem: "*Chercher la maladie au niveau de la cellule c'est confondre le plan de la vie concrète où la polarité biologique fait la différence de la santé et de la maladie et le plan de la science abstraite où le problème reçoit une solution. [...] nous voulons dire que la maladie d'un vivant ne loge pas dans des parties d'organisme. [...] Le même donné biologique peut être considéré comme partie ou comme tout. Nous proposons que c'est comme tout qu'il peut être dit ou non malade*"





Twaddle, A. (1994a). Disease, illness and sickness revisited. In: A. Twaddle & L. Nordenfelt. (Eds.) Disease, Illness and Sickness: Three Central Concepts in the Theory of Health (pp. 1–18). Linkoping: Studies on Health and Society, 18
Hofmann, B. (2002) On the triad disease, illness and sickness, J Med Philo, 27, 651-73

Ecoimmunology views sickness behavior as an integrated response to energetic, social, and environmental contexts



KE Sylvia, GE Demas, A return to wisdom: using sickness behaviors to integrate ecological and translational research, Integr Comp Biol, 2017, 57, 1204-13

Some examples of the adaptive value of sickness behavior

Journal of Experimental Biology

Log in

Search

Advanced search

Home Articles About us For authors Journal info Contacts

RESEARCH ARTICLE

Eating when ill is risky: immune defense impairs food detoxification in the caterpillar *Manduca sexta*

Laura E. McMillan, Dylan W. Miller, Shelley A. Adamo

Journal of Experimental Biology 2018 221: jeb173336 doi: 10.1242/jeb.173336 Published 7 February 2018

Article Figures & tables Supp info Info & metrics PDF PDF + SI

Previous Article Next Article

This Issue

Keywords

Illness-induced anorexia, Psychoneuroimmunology, Sickness behavior, Ecoimmunology, Pesticide

Article

Cell

Pathogen-Mediated Inhibition of Anorexia Promotes Host Survival and Transmission

Sheila Rao,[1] Alexandria M. Palaferri Schieber,[1] Carolyn P. O'Connor,[2] Mathias Leblanc,[3] Daniela Michel,[1] and Janelle S. Ayres[1,4,*]

[1]Nomis Center for Immunobiology and Microbial Pathogenesis

[2]Flow Cytometry Core Facility

[3]Gene Expression Laboratory

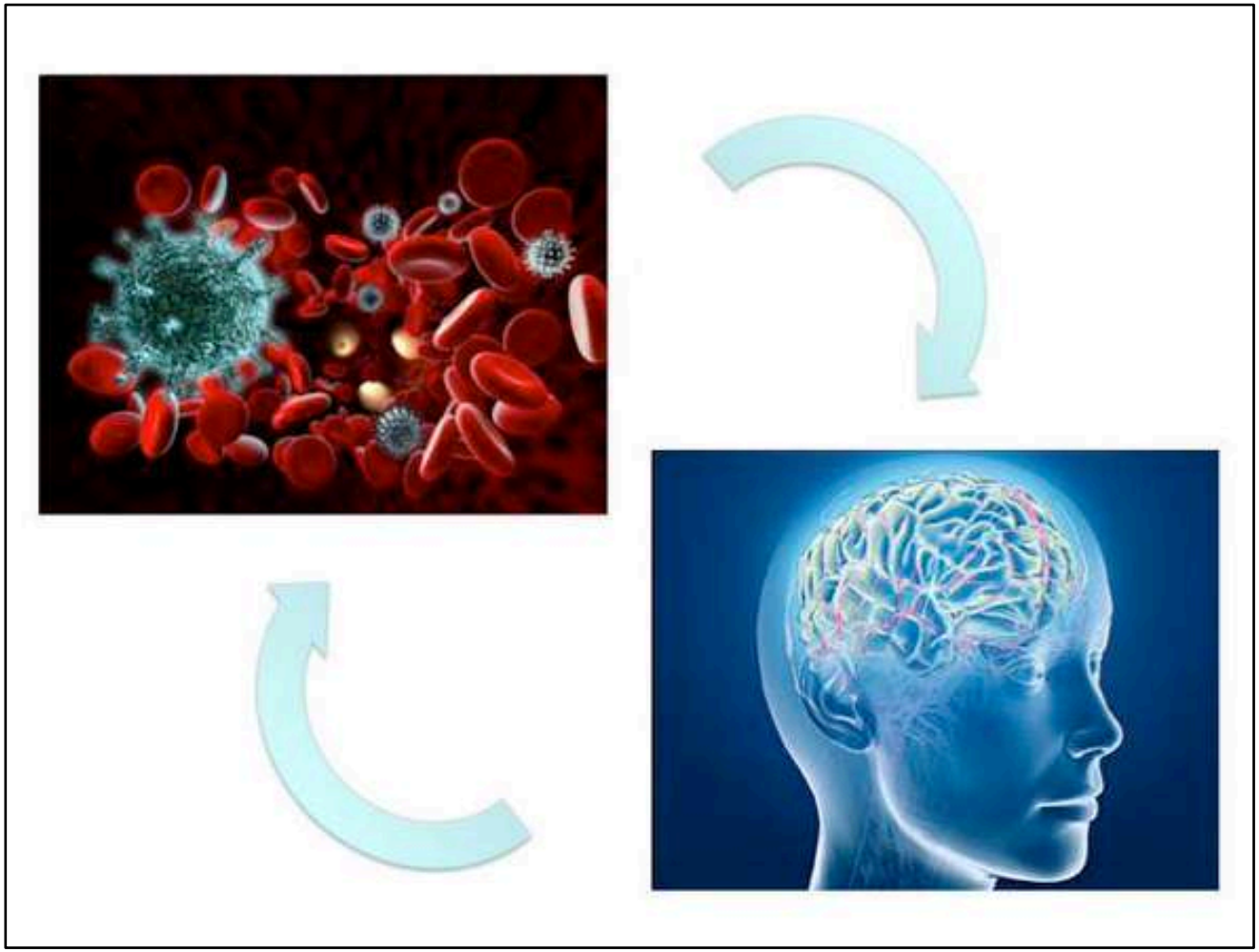
The Salk Institute for Biological Studies, La Jolla, CA 92037, USA

[4]Lead Contact

*Correspondence: jayres@salk.edu

http://dx.doi.org/10.1016/j.cell.2017.01.006

Is immunopsychiatry a useful concept?



Compared to *psychoneuroimmunology*, "the recent use of the term *immunopsychiatry* represents a hierarchical shift: it suggests that our brain no longer governs the immune system, but, on the contrary, that our behaviours and emotions are governed by peripheral immune mechanisms…. The introduction of the term *immunopsychiatry* has created the opportunity of managing psychiatric disorders through novel treatment approaches targeting the immune system" (Pariante, Lancet Psychiatry, 2015)

International Review of Neurobiology
Volume 26, 1985, Pages 249-314

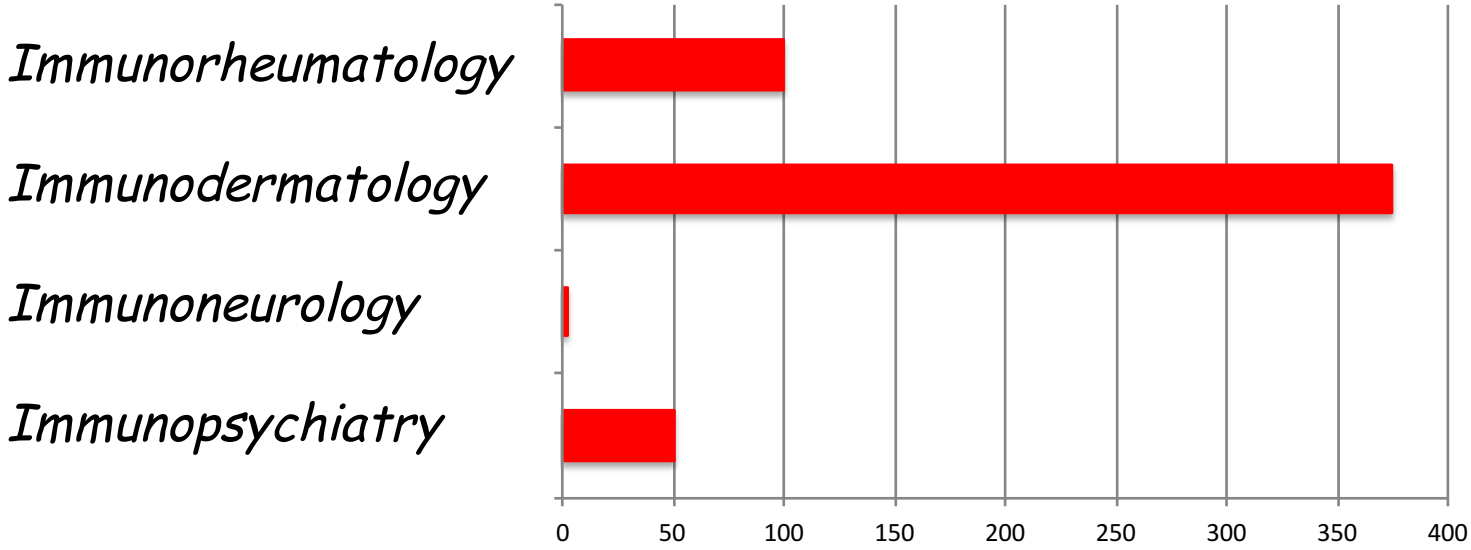
From Immunoneurology to Immunopsychiatry: Neuromodulating Activity of Anti-Brain Antibodies

Branislav D. Janković

Show more

https://doi.org/10.1016/S0074-7742(08)60076-8

Number of references in PubMed



Is depression really maladaptive?

Journal of Affective Disorders 172 (2015) 315–323

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Review

An adaptationist perspective on the etiology of depression

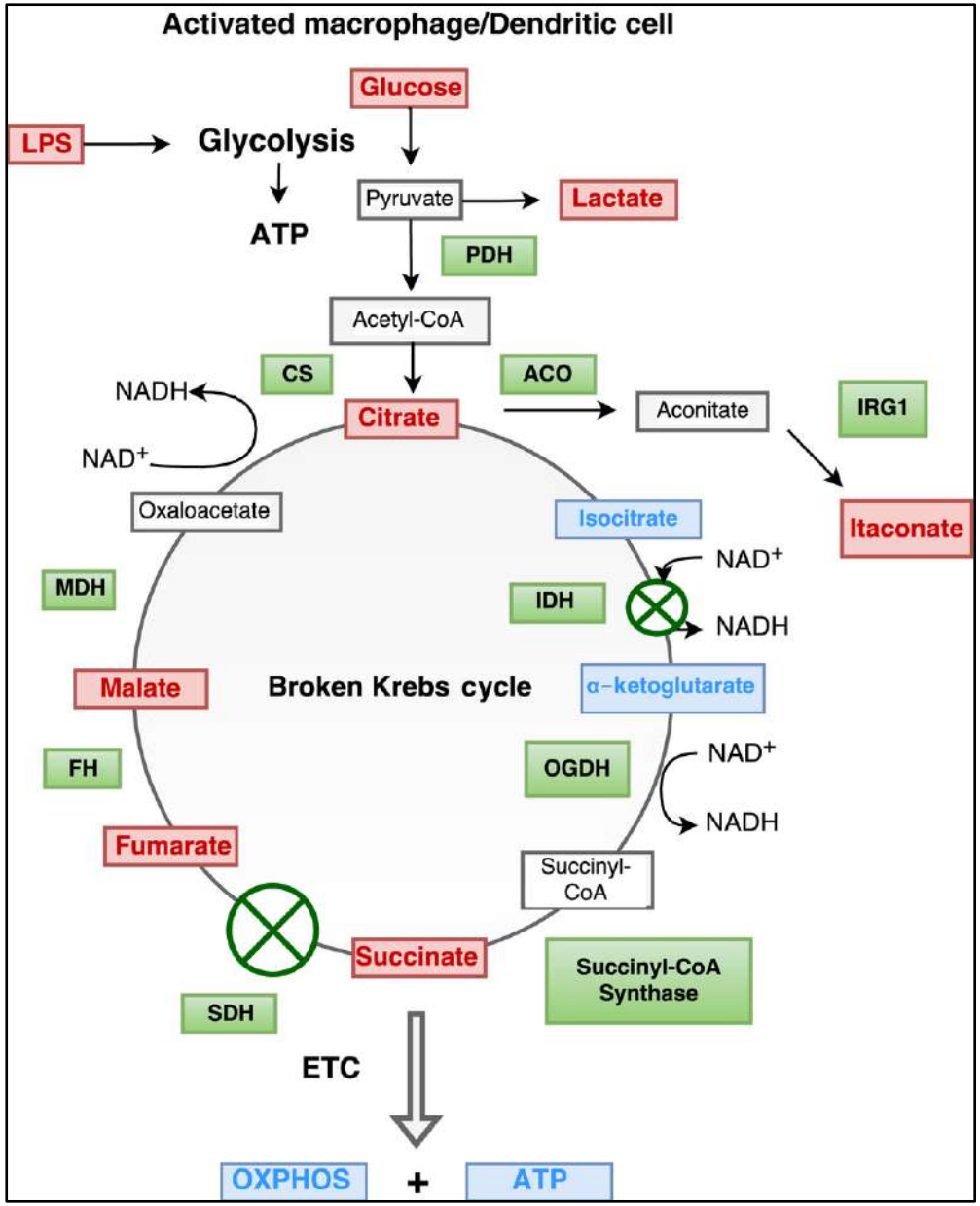
Zachary Durisko [a,b,*], Benoit H. Mulsant [c,d], Paul W. Andrews [b,*]

[a] Social Aetiology of Mental Illness (SAMI) CIHR Training Program, Centre for Addiction and Mental Health (CAMH), Suite 1111, 33 Russell Street, Toronto, Ontario, Canada M5S 3B1
[b] Evolutionary Ecology of Health Research Laboratories, Department of Psychology, Neuroscience & Behaviour, McMaster University, 1280 Main Street West, Hamilton, Ontario, Canada L8S 4K1
[c] Centre for Addiction and Mental Health (CAMH), 1001 Queen Street West, Toronto, Ontario, Canada M6J 1H4
[d] Department of Psychiatry, Faculty of Medicine, University of Toronto, 250 College Street, Toronto, Ontario, Canada M5T 1R8

Possible adaptive functions of depression:

- Biasing cognition to avoid losses
- Conserving energy
- Disengaging from unobtainable goals
- Signaling submission
- Soliciting resources
- Promoting analytical thinking

Does conservation of energy play a role in inflammation-induced depression?

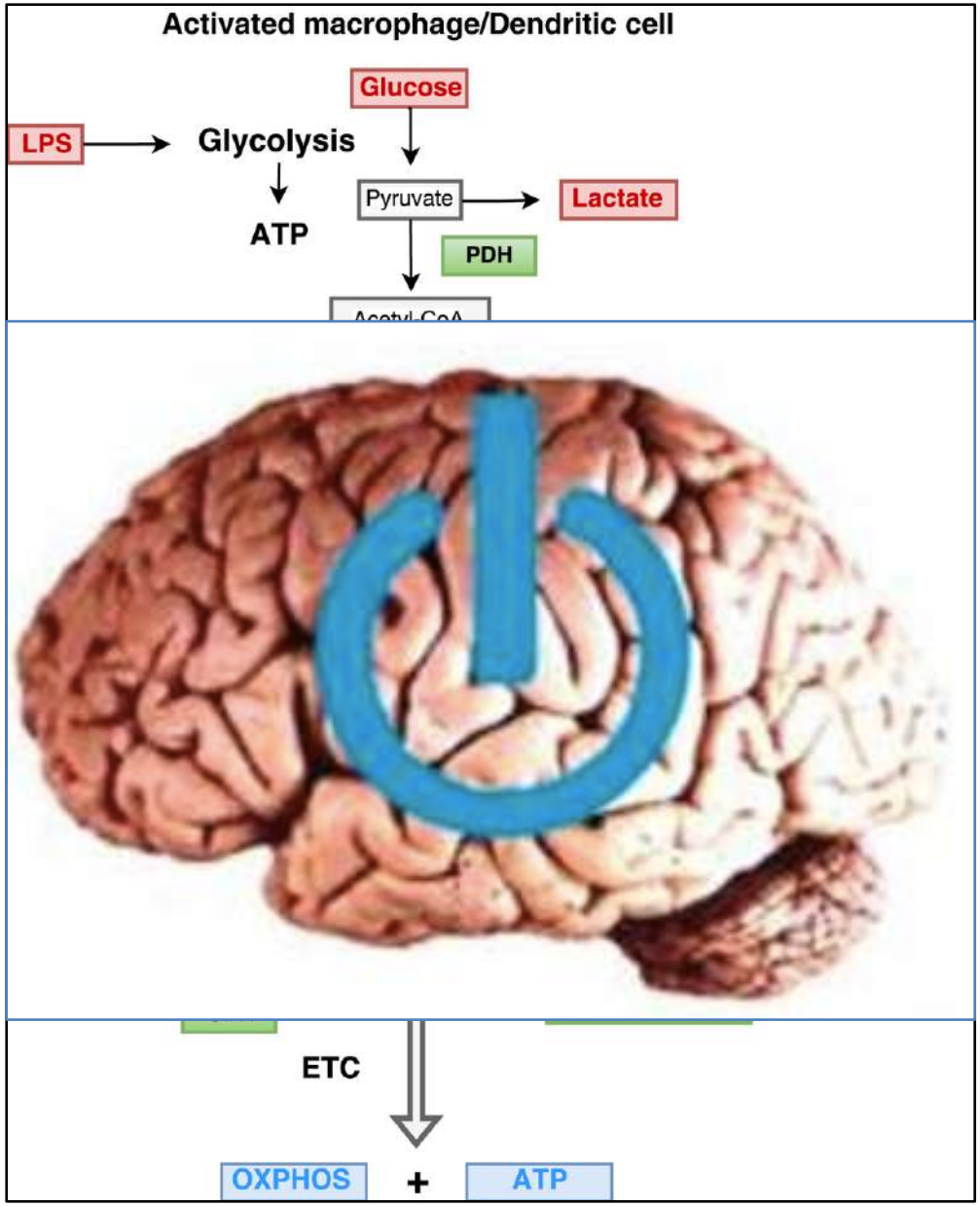


Metabolic features of inflammation:

- *Increased glycolysis*
- *Reduced OXPHOS and generation of ATP*

Ryan & O'Neill, Febs Lett, 2017

Does conservation of energy play a role in inflammation-induced depression?



Metabolic features of inflammation:

- *Increased glycolysis*
- *Reduced OXPHOS and generation of ATP*

The brain represents only 2% of the body weight but demands 20% of our resting metabolic rate

Ryan & O'Neill, Febs Lett, 2017

3/ Opponent process theory

(Cut because unpublished)