IMPACTO DEL ESTRÉS SOBRE EL SISTEMA INMUNITARIO

Matilde Medina Martel

¿Qué es estrés?

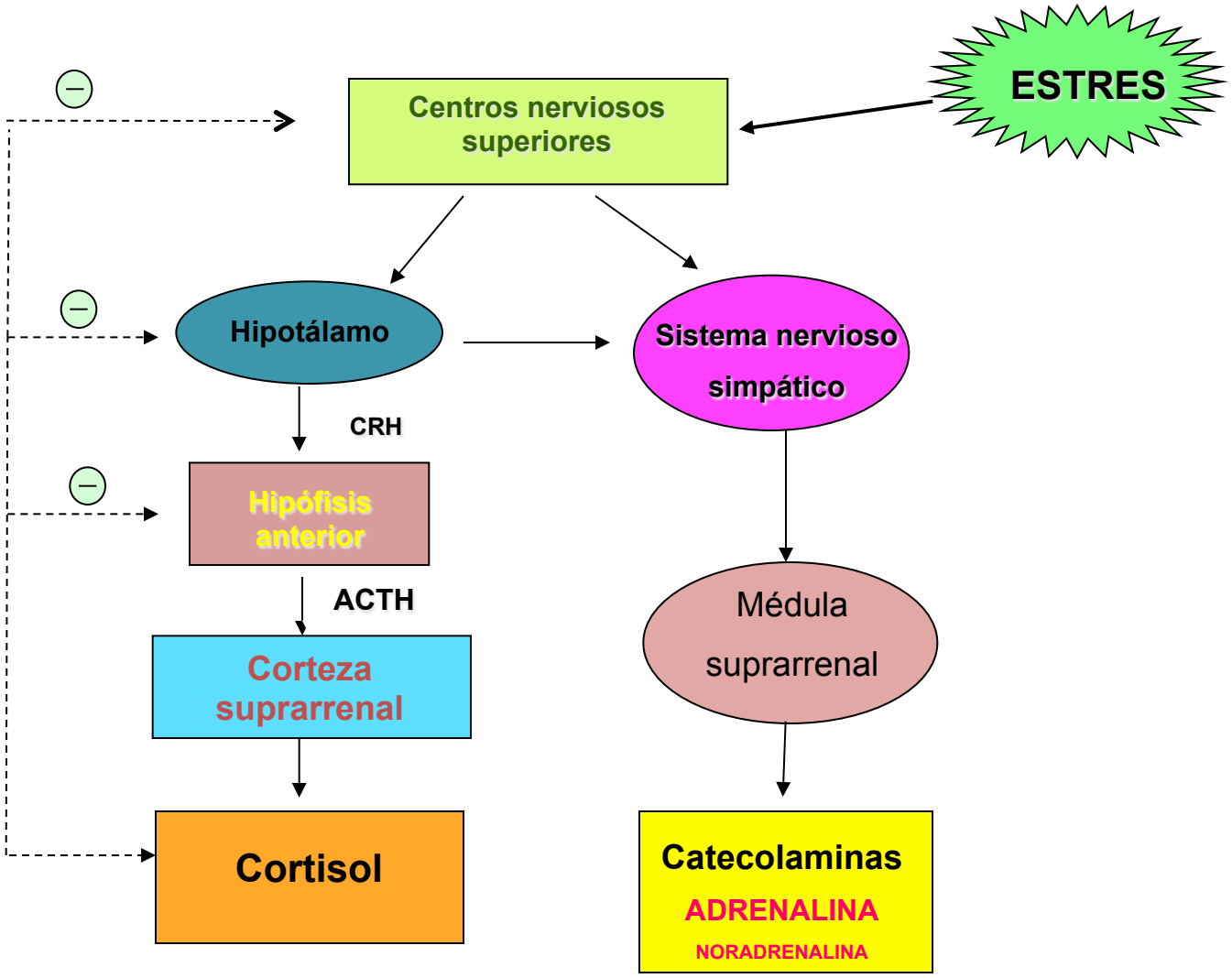
El estrés puede ser definido como una serie de eventos, los cuales incluyen en primer lugar un estímulo (estresor), que precipita una reacción en el cerebro (percepción de estrés), la cual activa los sistemas de respuesta fisiológica del organismo (respuesta al estrés).

Estresor

Cerebro

Respuesta

Respuesta al estrés



Pioneros en el estudio del estrés

1.- Walter Cannon (1871-1945):

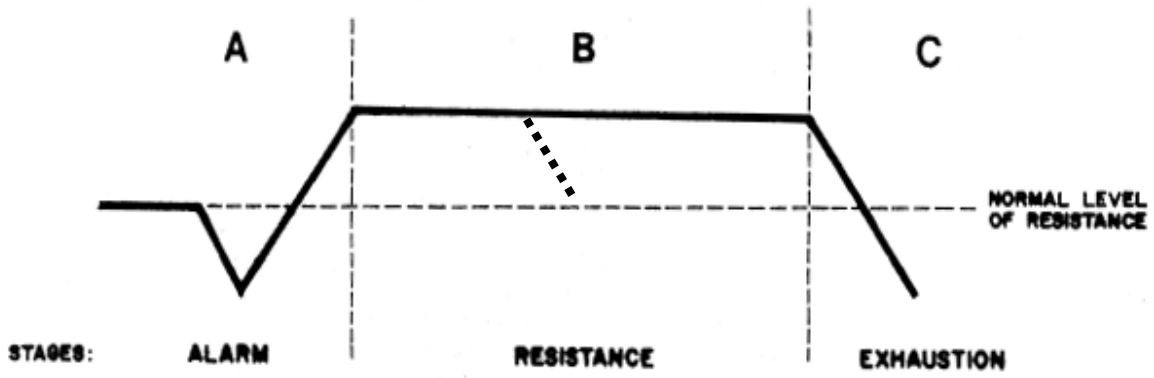
- **Homeostasis**
- **Estrés**
- Respuesta de **lucha o huída**

2.- Hans Selye (1907-1982):

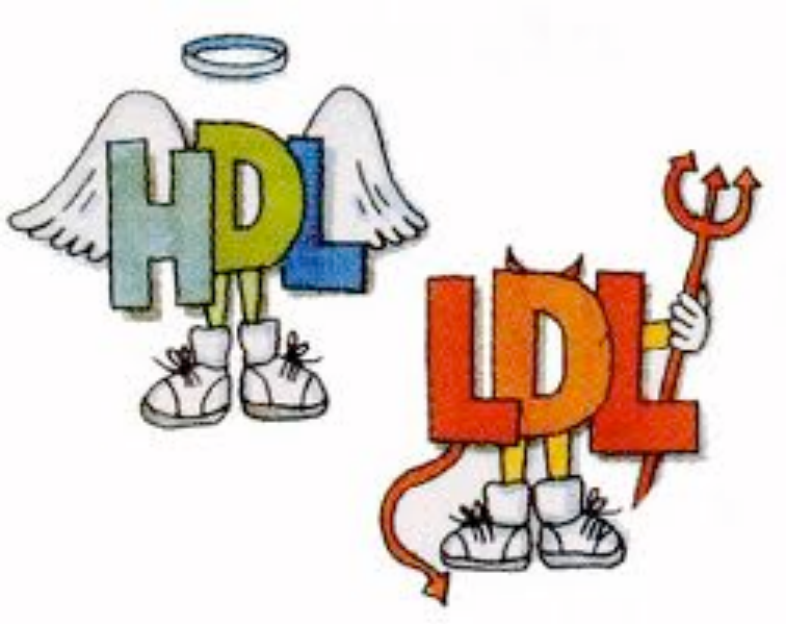
- **Síndrome general de adaptación**

H. Selye, 1936

Síndrome general de adaptación



¿El estrés es bueno o malo?

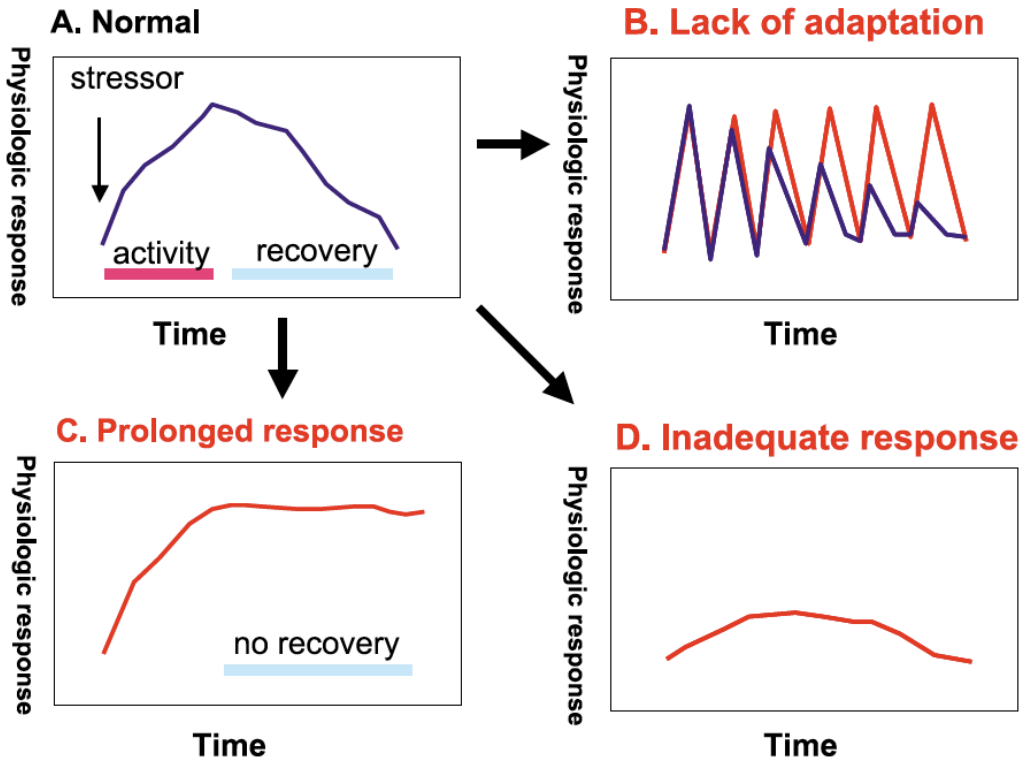


Eustrés (Selye, 1976)

Distrés (Selye, 1976)

Formas de respuesta al estrés

2 aspectos importantes de la respuesta al estrés son: **magnitud y duración.**



Tomado de Rokutan y col. (2005).

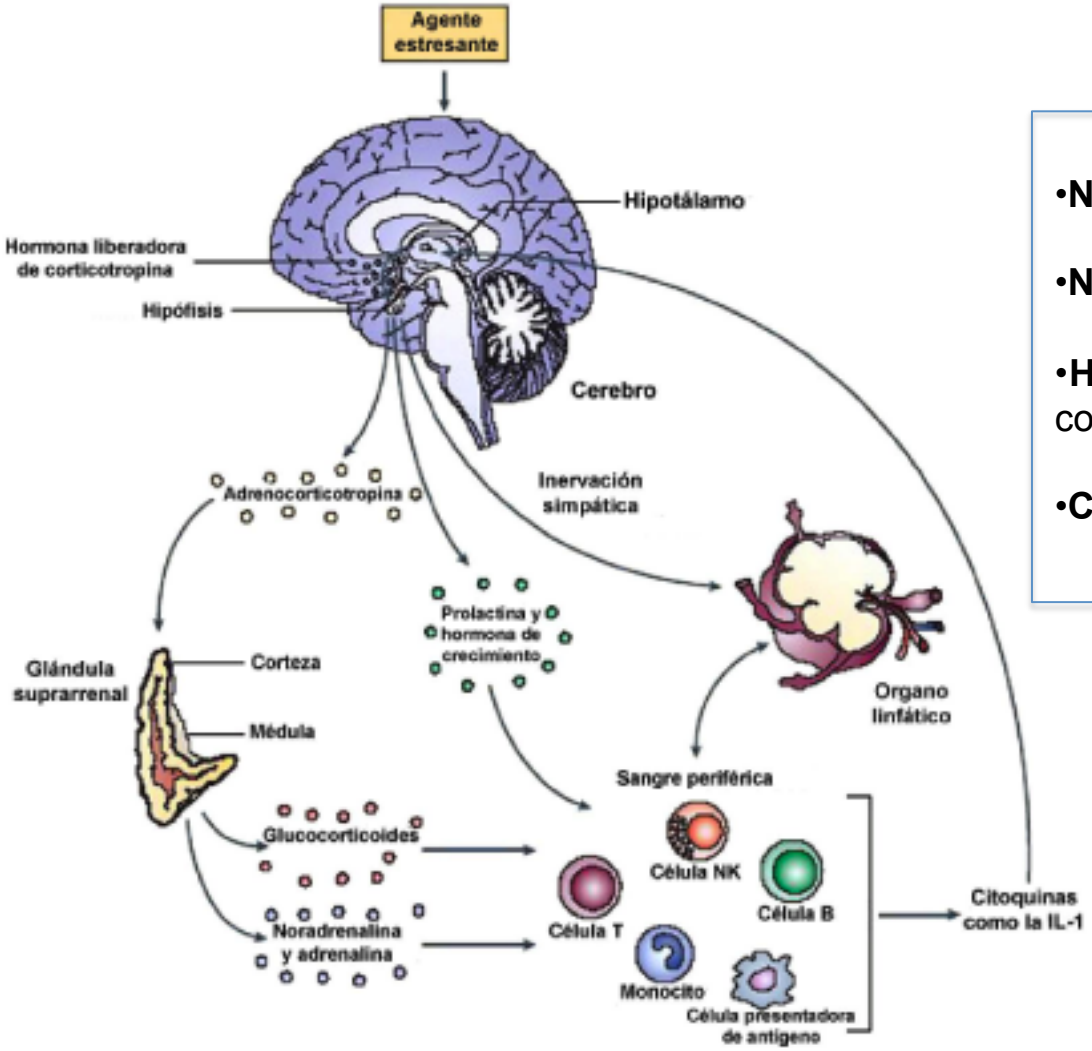
Estrés crónico
(Distrés, sobrecarga alostática)

Ha sido asociado a la fisiopatogenia de diversas enfermedades:

- Psiquiátricas (ansiedad y depresión).
- Metabólicas (DMT2)
- Cardiovasculares (hipertensión, ateroesclerosis, cardiopatía isquémica)
- Infecciosas (aumenta la suceptibilidad a infecciones)
- Autoinmunes (AR, LES, EM)
- Alérgicas (dermatitis atópica y asma alérgica)
- Gastrointestinales (s. de colon irritable, úlceras)
- Cáncer

Estrés e interacción neuroinmune

Neuroinmunomodulación



- **Neurotransmisores:** AD, NA, DA y 5-HT.
- **Neuropéptidos:** CRH, AVP, NPY, SP
- **Hormonas:** Prolactina, GH, ACTH, cortisol.
- **Citoquinas:** IL-1, IL-6, TNF-α.

Adaptado de Webster-Marketon y Glaser (2008).

Brain Behav Immun. 2008 January ; 22(1): 105–113.

Stressor-Specific Alterations in Corticosterone and Immune Responses in Mice

Stephanie L. Bowers[1], **Staci D. Bilbo**[1,*], **Firdaus S. Dhabhar**[2], and **Randy J. Nelson**[1,3]

1 *Departments of Psychology, Neuroscience, and Institute for Behavioral Medicine Research, The Ohio State University, Columbus, OH 43210 USA*

2 *Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA 94305 USA*

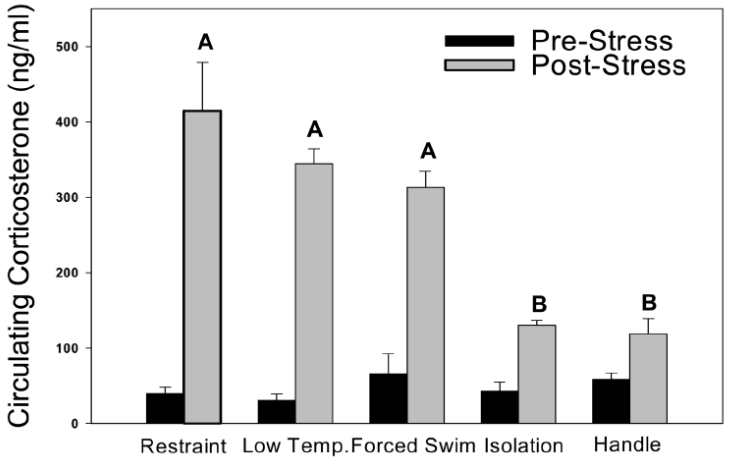


Figure 5.
Corticosterone concentrations after one (acute) session of treatment. All stressor treatments significantly elevated corticosterone concentrations compared to baseline. "A" is significantly different from "B".

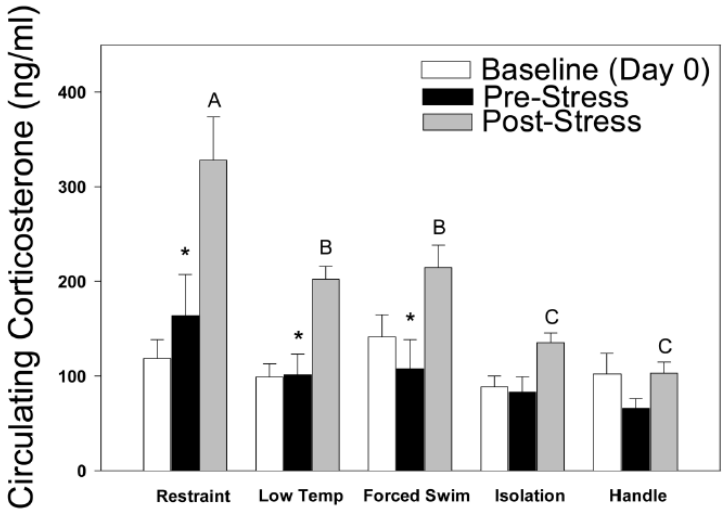


Figure 3.
Baseline (day 0), pre-, and post-stress (day 15) corticosterone concentrations. Restraint elicited higher corticosterone values than all other stressor treatments. Only restraint, forced swim, and low temperature induced significantly elevated corticosterone concentrations following stressor treatment compared to their respective day 15 baseline.
*Significant difference between pre- and post-stress; "A" is higher than all other groups, "B" higher than "C."

Brain Behav Immun. 2008 January ; 22(1): 105–113.

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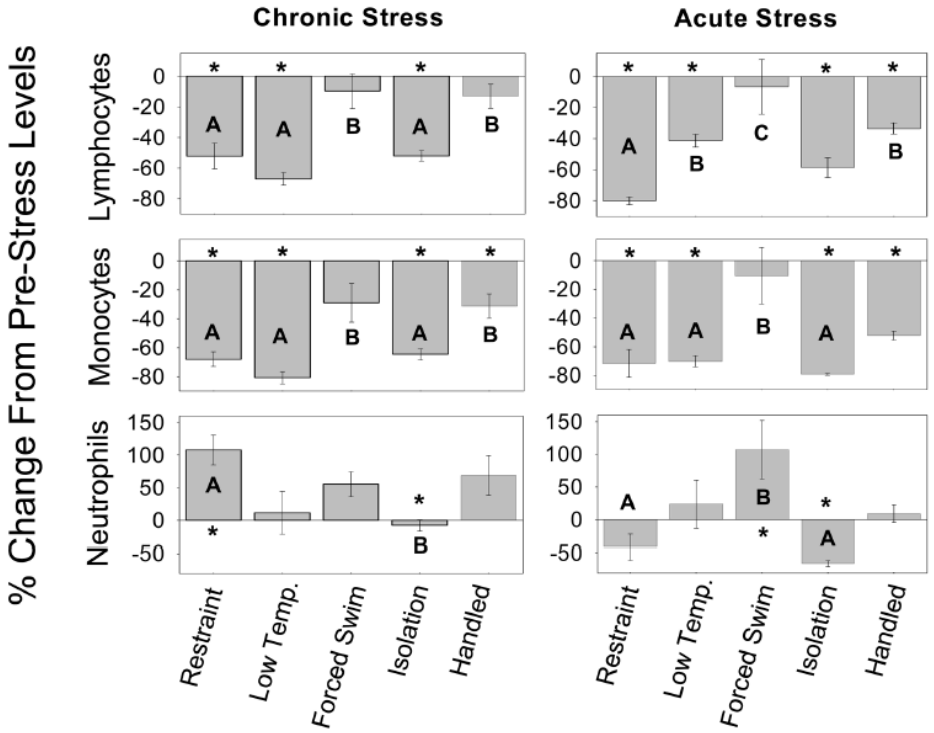


El estrés puede afectar diversos componentes del sistema inmunitario

Inmunidad natural

Celular:

- Fagocitos: PMN neutrófilos, monocitos-macrófagos.
- Células NK

Humoral:

- Defensinas
- Citoquinas: IFN-α, IFN-β, IL-1, TNF, IL-15, IL-12, IFN-γ, IL-6
- Complemento

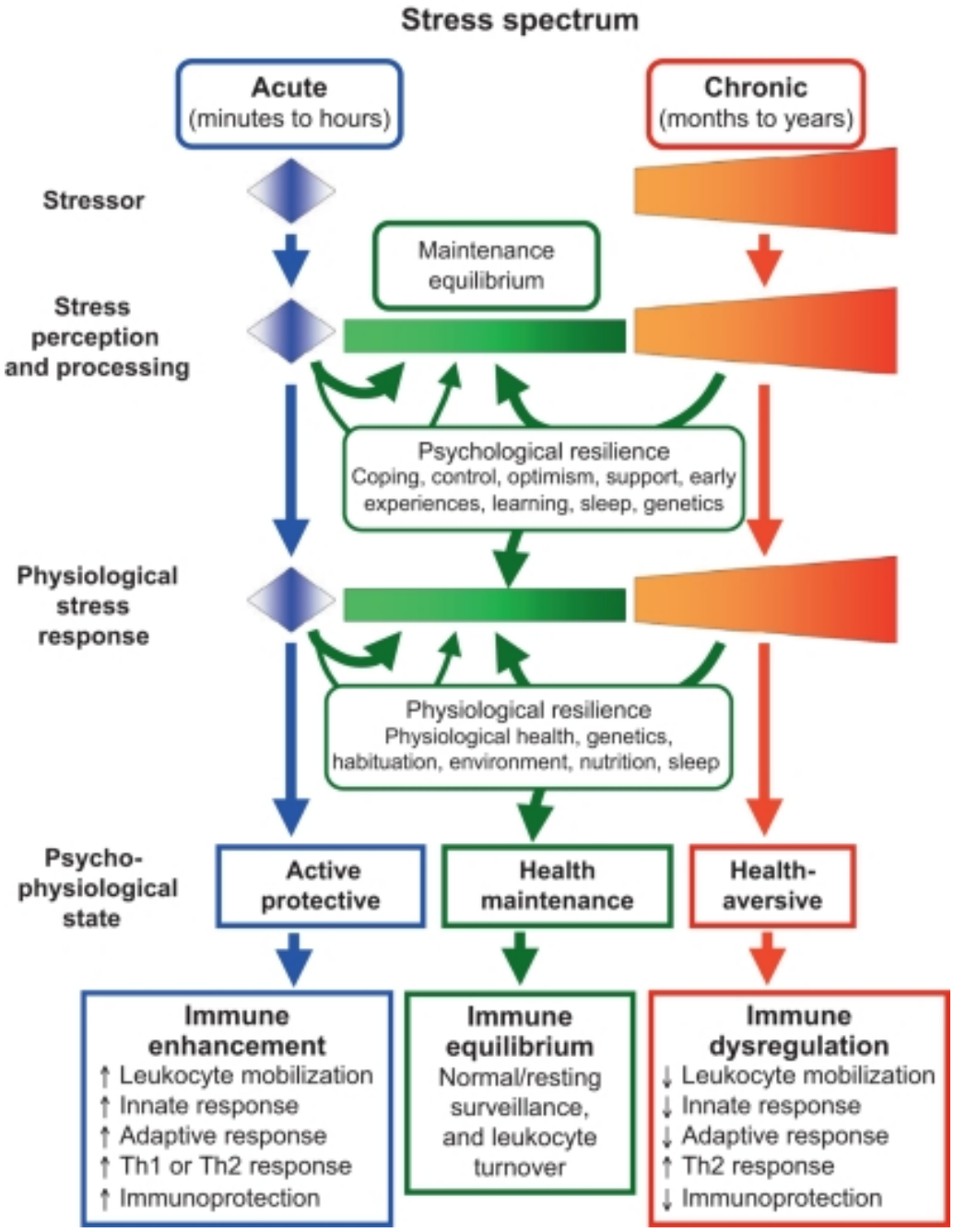
Inmunidad adquirida

Celular:

- LT CD_4+ (T_H y T_{reg})
- LT CD_8+
- LB

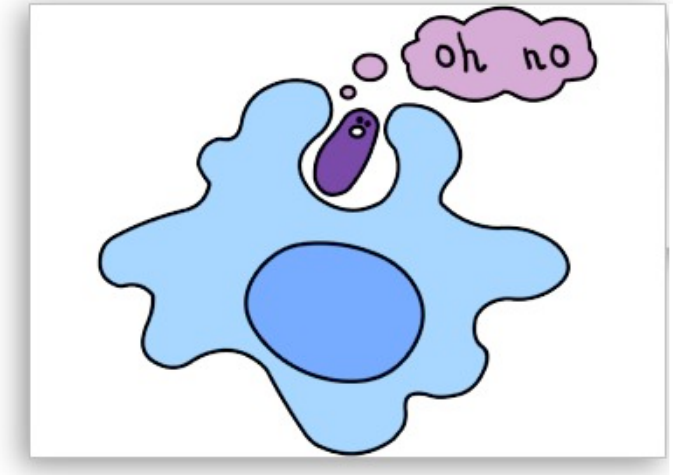
Humoral:

- Citoquinas:
  TH_1: IL-2, IFN-γ, TNF
  TH_2: IL-4, IL-5, IL-10, IL-13
- Anticuerpos: Ig A,Ig M, Ig G.



Tomado de Dhabhar, 2009

Estrés e inmunidad natural



Psychosomatic Medicine 69:225–234 (2007)

Immune Function Declines With Unemployment and Recovers After Stressor Termination

Frances Cohen, PhD, Margaret E. Kemeny, PhD, Leonard S. Zegans, MD, Paul Johnson, MPhil, Kathleen A. Kearney, PhD, and Daniel P. Stites, MD

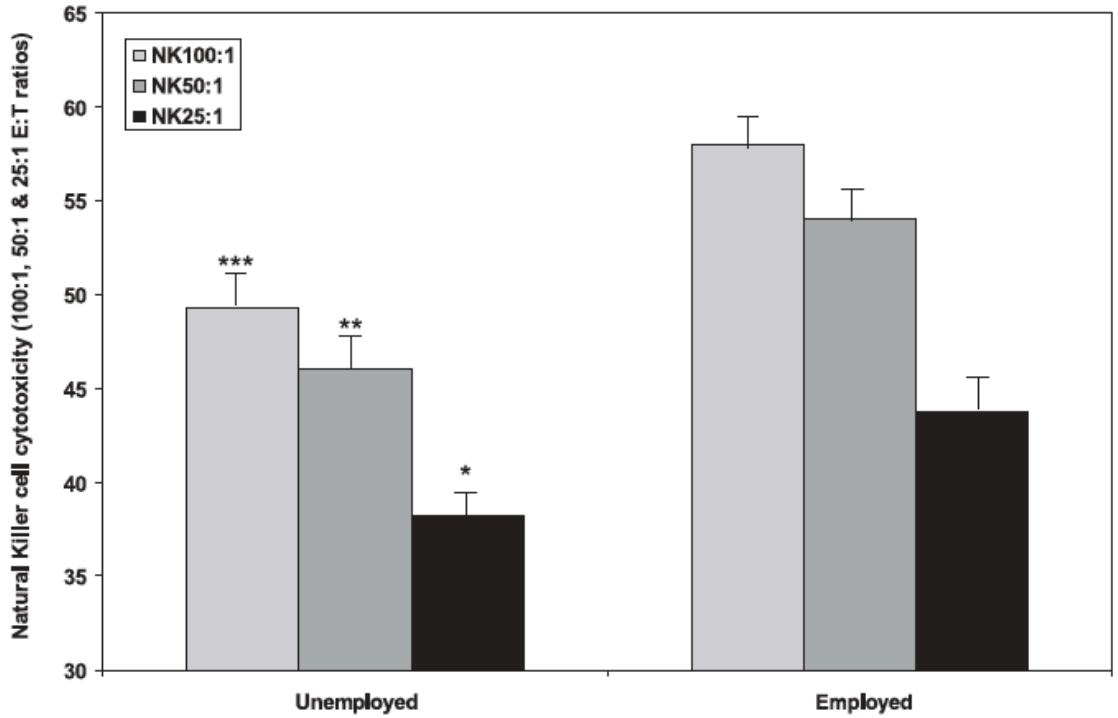


Figure 1. Mean natural killer cell cytotoxicity at 3 effector:target ratios for unemployed and employed participants averaged over 4-month study period; $n = 150$. Error bars represent standard errors of the mean. *$p < .05$ for unemployed versus employed sample; **$p < .01$ for unemployed versus employed sample; ***$p < .001$ for unemployed versus employed sample.

Psychosom Med. 2009 January ; 71(1): 57–62

Chronic Interpersonal Stress Predicts Activation of Pro- and Anti-Inflammatory Signaling Pathways Six Months Later

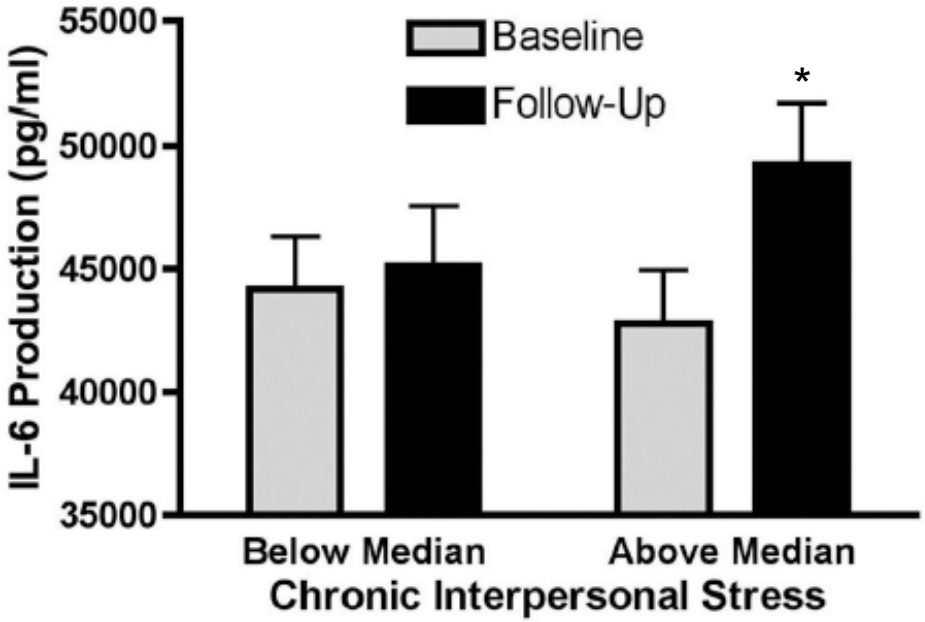
Gregory Miller, Ph.D.[1,*], **Nicolas Rohleder, Ph.D.**[1], and **Steve W. Cole, Ph.D.**[2,3,4]

[1]Department of Psychology, University of British Columbia

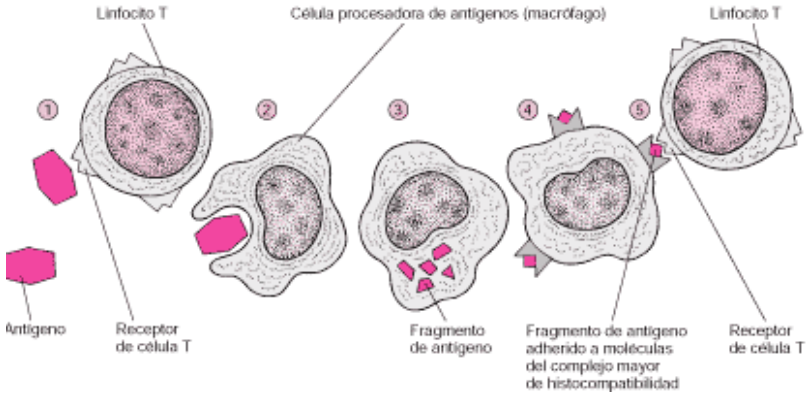
[2]Department of Medicine, Division of Hematology-Oncology, UCLA School of Medicine

[3]UCLA AIDS Institute, Molecular Biology Institute, & Jonsson Comprehensive Cancer Center

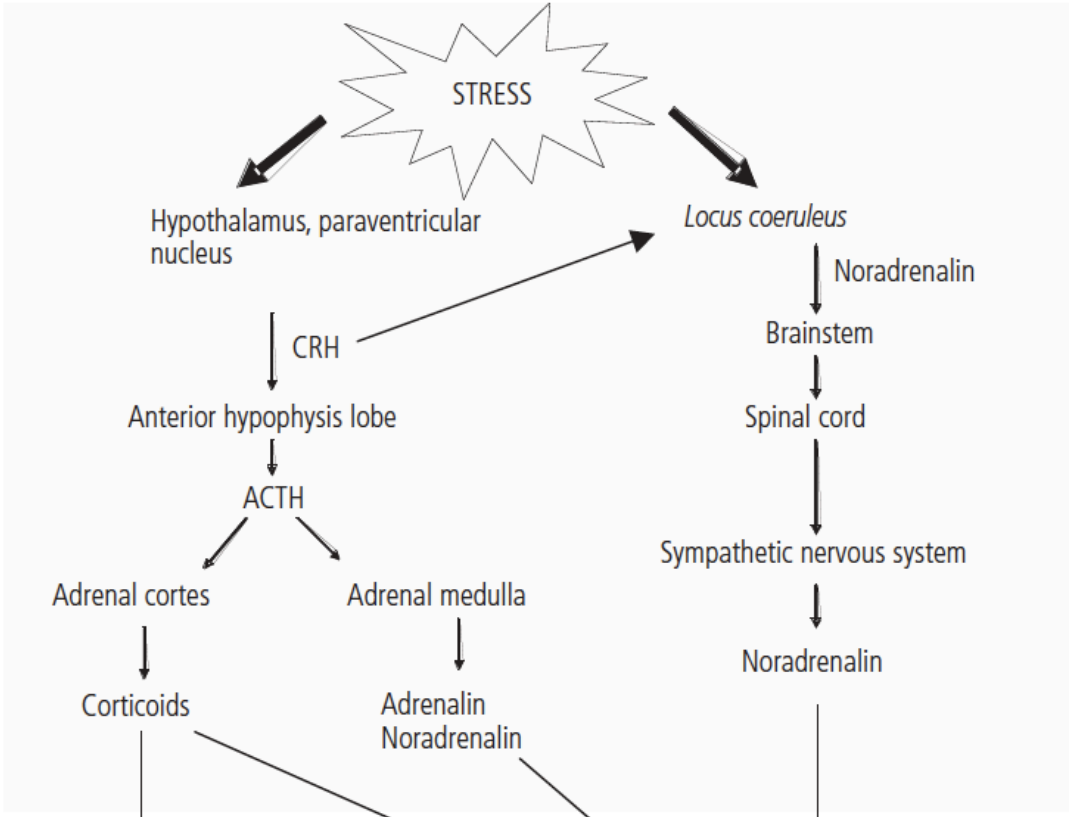
[4]Norman Cousins Center at UCLA



Estrés e inmunidad adquirida



Modificación del perfil de citoquinas



Aumento de la inmunidad humoral

Disminución de la inmunidad celular

Tomado de “Stress and allergy”, Montoro y col., 2009.

El aumento de la inmunidad humoral:

asociado al desarrollo de enfermedades alérgicas

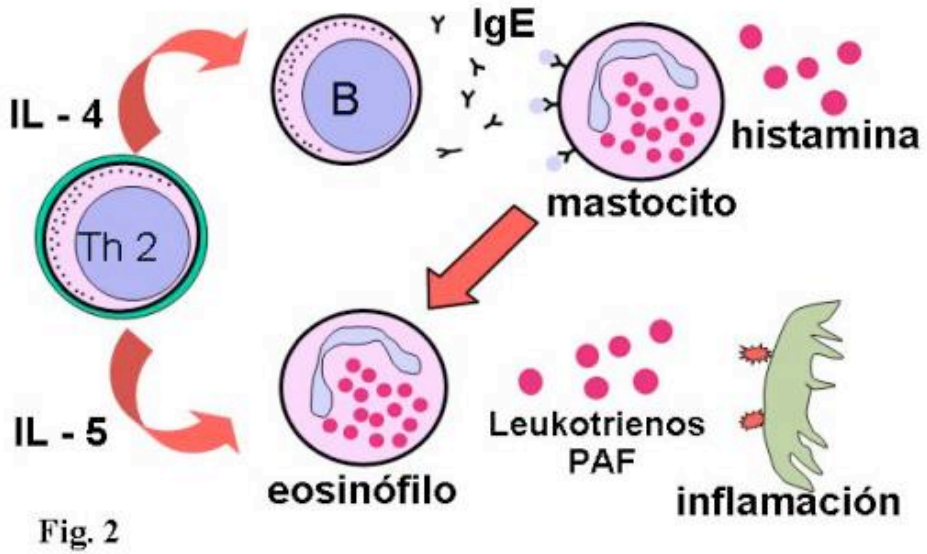
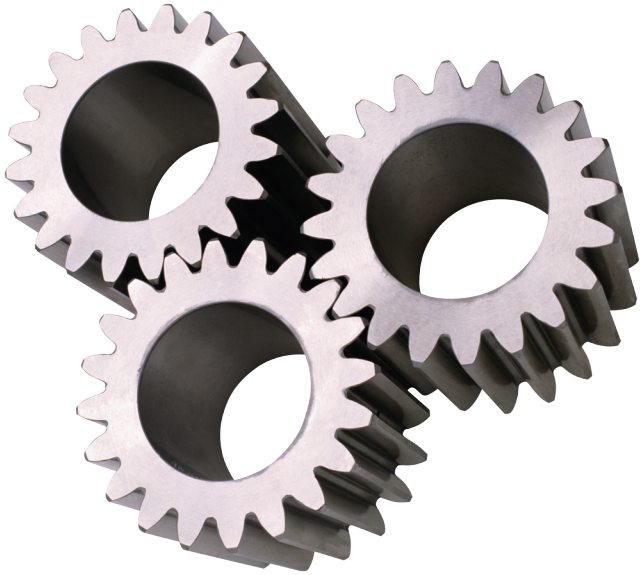


Fig. 2

Efectos generales del estrés crónico sobre la respuesta inmune

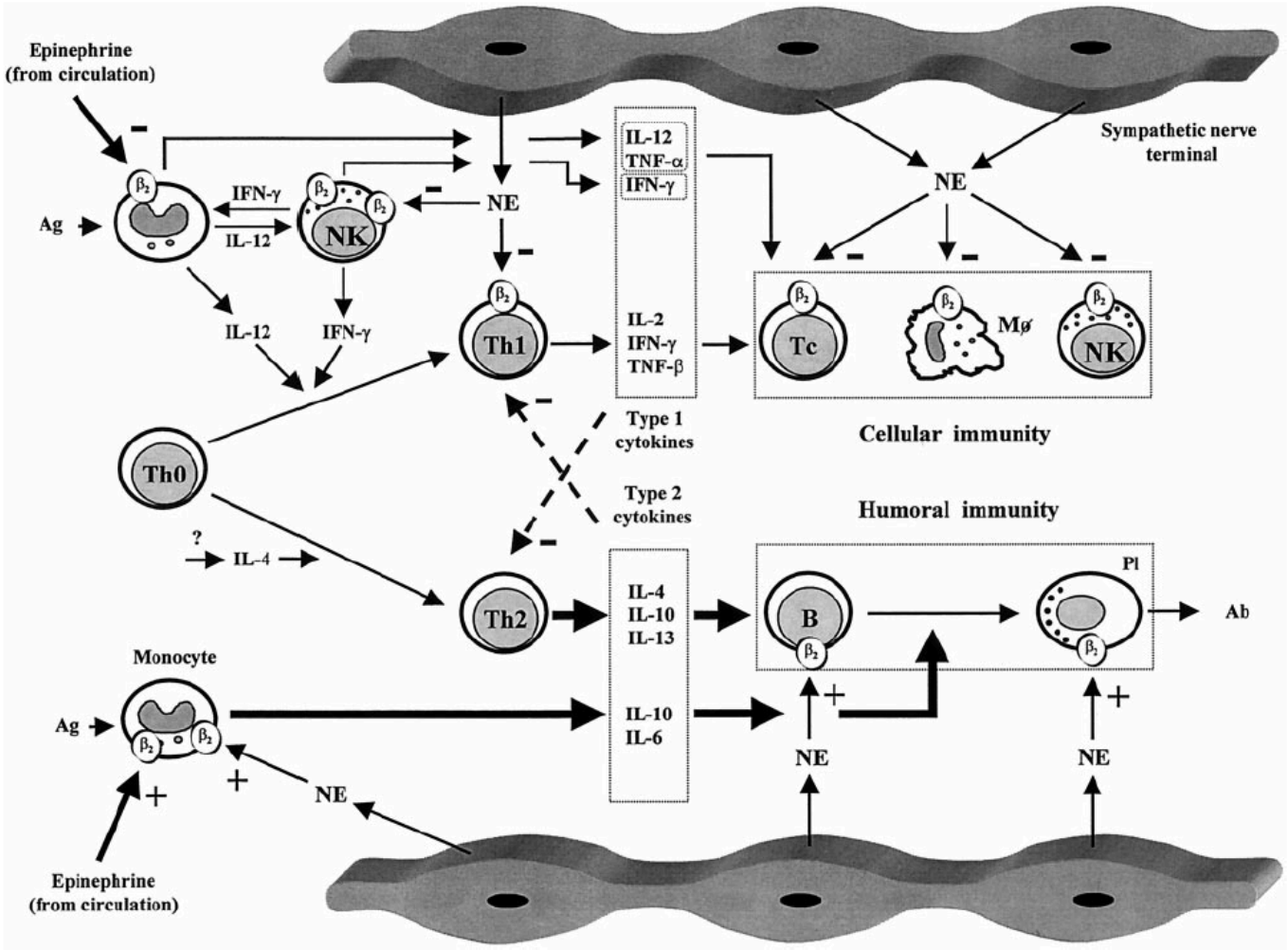
Modificado de “Stress hormones and immune function”, Webster Marketon y Glaser, 2008.

Algunos mecanismos involucrados



The Sympathetic Nerve—An Integrative Interface between Two Supersystems: The Brain and the Immune System

ILIA J. ELENKOV, RONALD L. WILDER, GEORGE P. CHROUSOS, AND E. SYLVESTER VIZI[1]

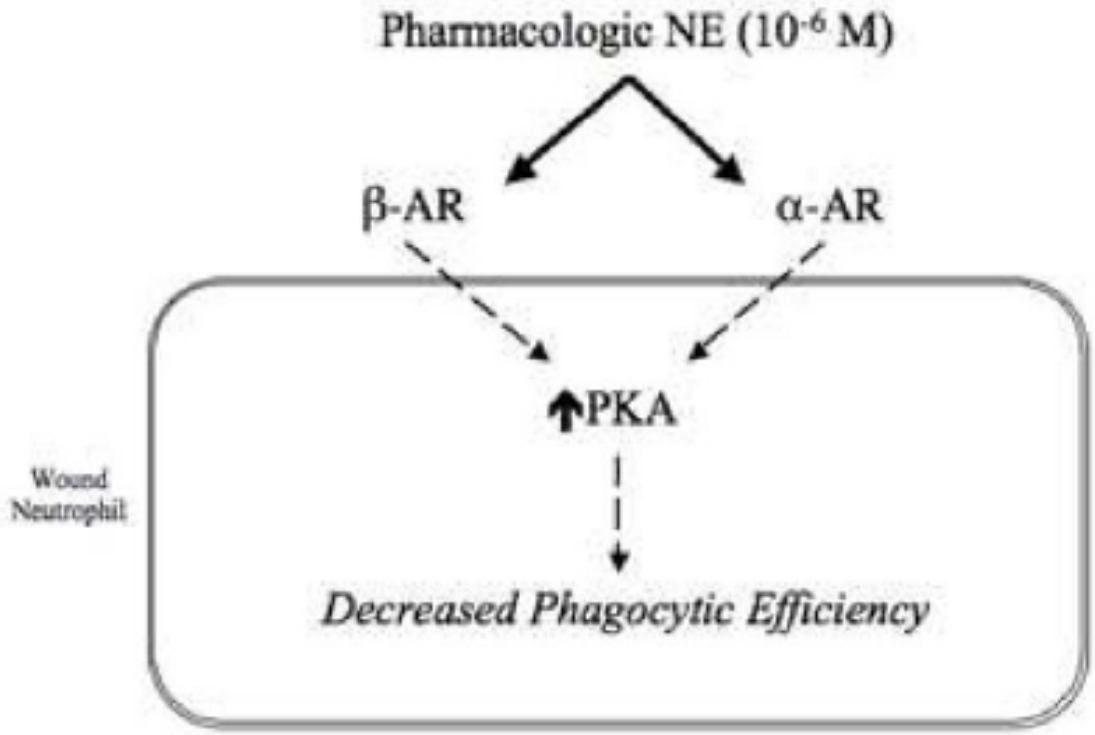


Pharmacol Rev 52:595–638, 2000

J Surg Res. 2009 April ; 152(2): 311–318. doi:10.1016/j.jss.2008.05.001.

Norepinephrine-mediated Suppression of Phagocytosis by Wound Neutrophils

Ankush Gosain, M.D., Ph.D.[1,2,3], Richard L. Gamelli, M.D.[1,3], and Luisa A. DiPietro, D.D.S., Ph.D.[4]



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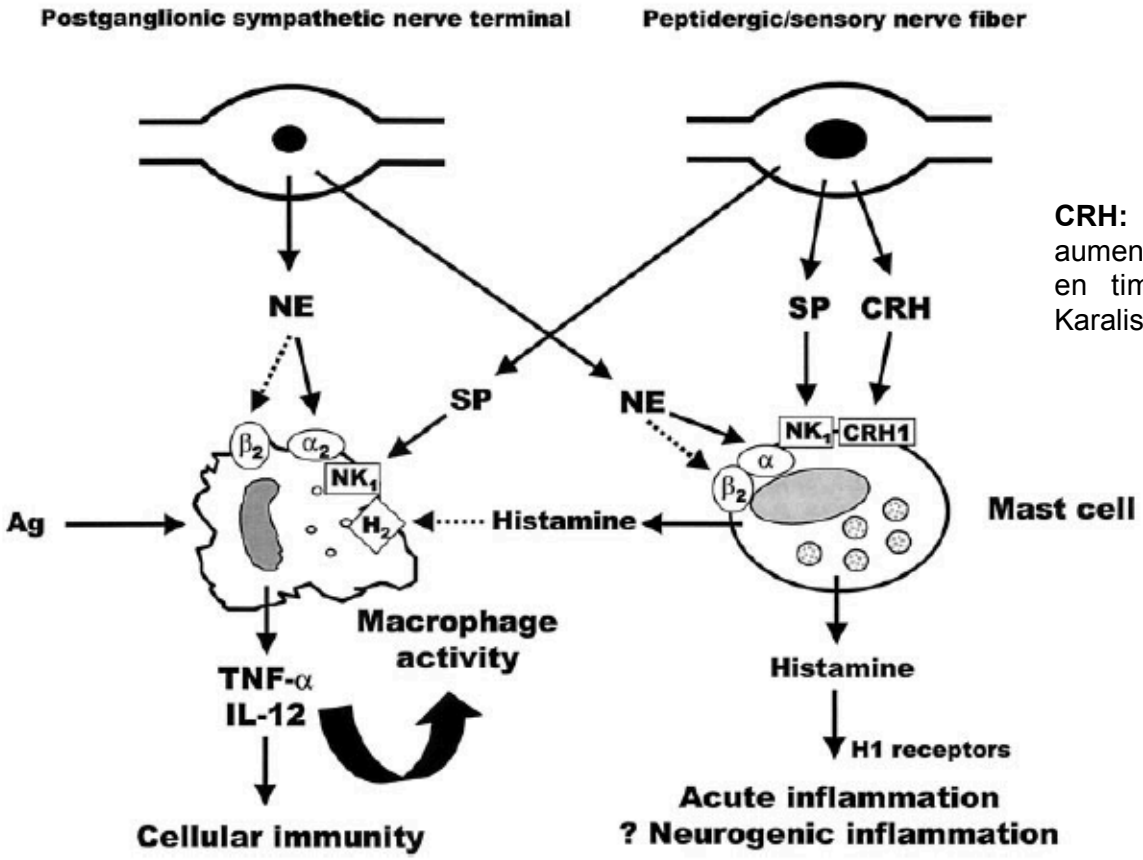
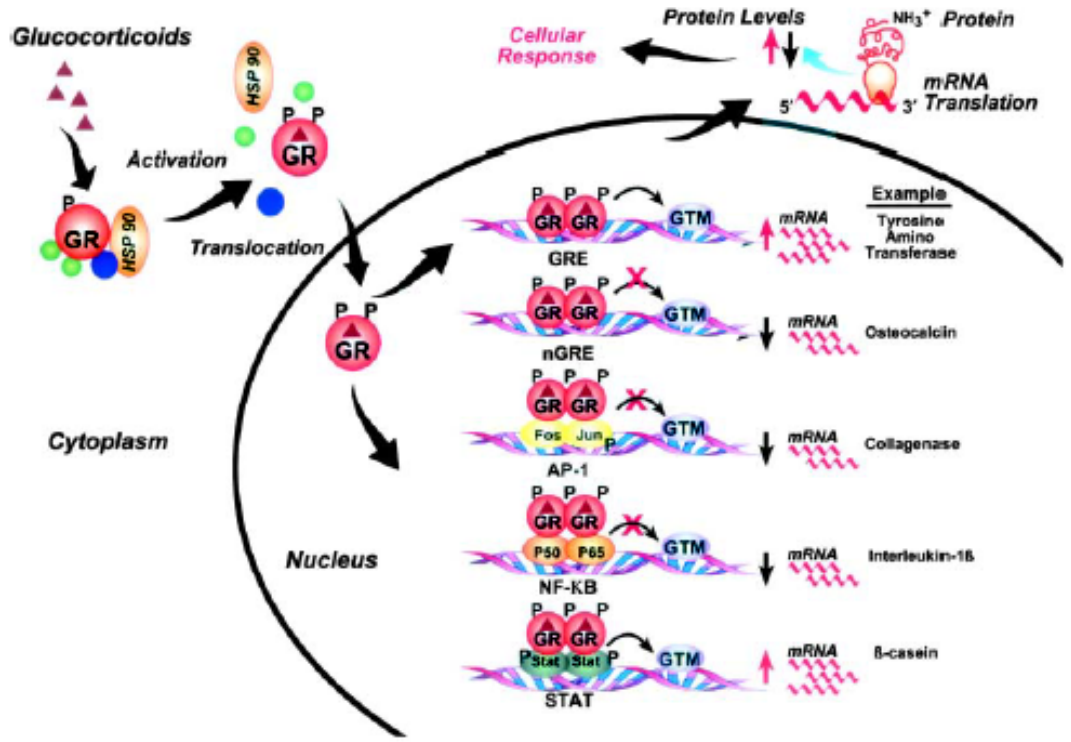


CRH: acciones pro-inflamatorias, aumenta la unión del NF-kB al ADN en timocitos de ratón (Zhao y Karalis, 2002)

Pharmacol Rev 52:595–638, 2000

Mecanismo de acción de los glucocorticoides

RGα y RGβ



Tomado de Necela y Cidlowsky, 2004

Brain, Behavior, and Immunity 25 (2011) 239–249

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

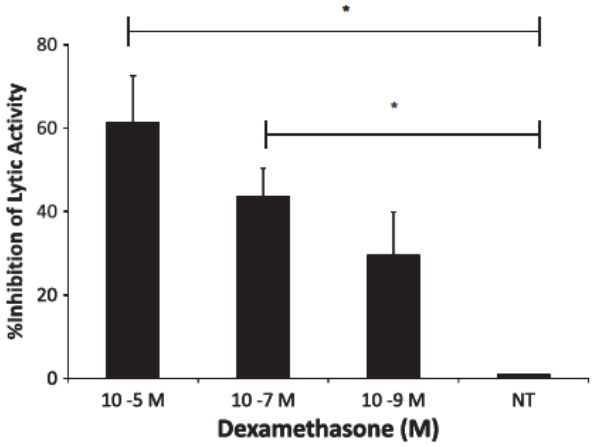
journal homepage: www.elsevier.com/locate/ybrbi

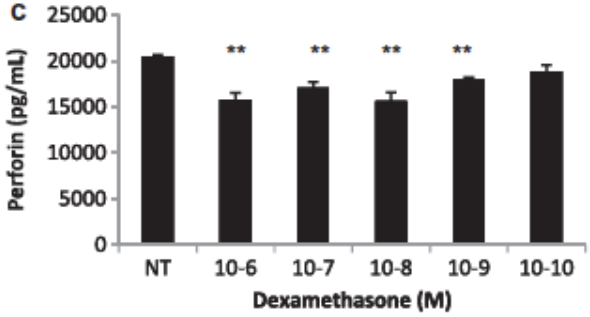
Named Series: Epigenetics, Brain, Behavior, and Immunity

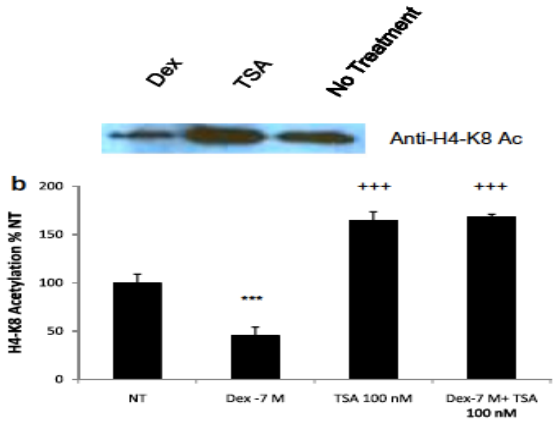
Glucocorticoid dysregulation of natural killer cell function through epigenetic modification ☆

Karen Krukowski [a,1], Justin Eddy [a,1], Kelly Loster Kosik [a], Teresa Konley [a], Linda Witek Janusek [b], Herbert L. Mathews [a,*]

[a] Department of Microbiology and Immunology, Stritch School of Medicine, Loyola University of Chicago, Maywood, IL 60153, USA
[b] Marcella Niehoff School of Nursing, Loyola University of Chicago, Maywood, IL 60153, USA



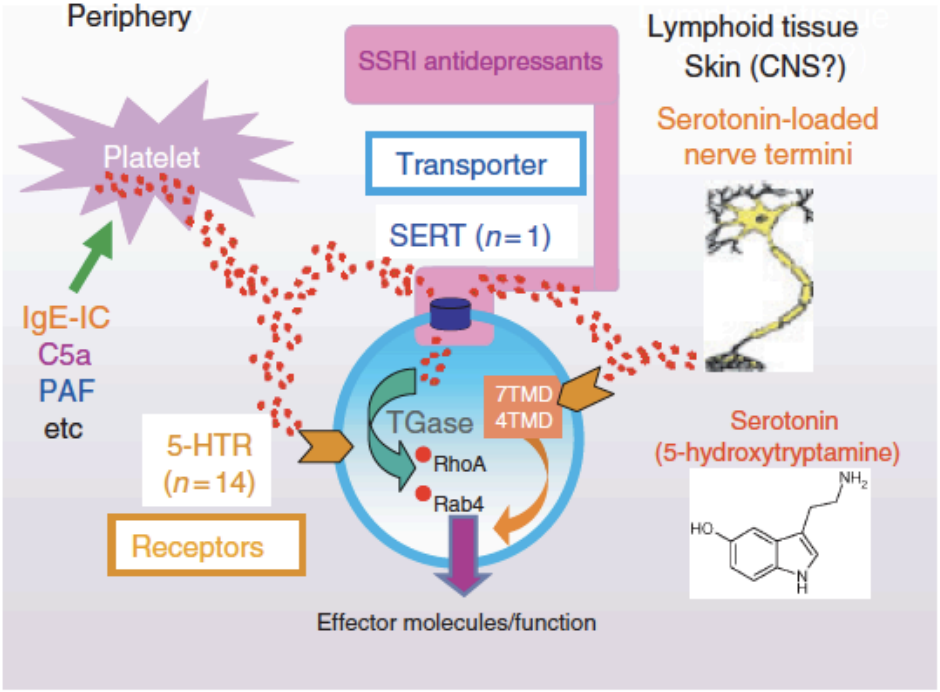




2005 Blackwell Publishing Ltd, *Immunology*, **115,** 289–295

Close encounters of the monoamine kind: immune cells betray their nervous disposition

Elizabeth J. Meredith,[1] Anita Chamba,[1] Michelle J. Holder,[1] Nicholas M. Barnes[2] and John Gordon[1]



Conclusiones

1. El estrés afecta la inmunidad **natural** y **adquirida** (**humoral** y **celular)**.

2. Sus efectos son complejos porque dependen de **múltiples factores**:
- tiempo de exposición al agente estresante
- naturaleza del mismo
- percepción de estrés
- capacidad de adaptación individual (asociada a factores genéticos, psicológicos, sociales, etc.)

3. Muchos de los mecanismos moleculares involucrados aún se desconocen

4. Un buen manejo del estrés podría disminuir el impacto del mismo sobre el sistema inmune, sobre todo en los individuos mas susceptibles

5. La identificación temprana de individuos susceptibles al estrés, permitiría intervenciones oportunas para evitar los efectos deletéreos del mismo sobre la salud


Gracias