

US EPA ARCHIVE DOCUMENT

# Protective and Damaging Effects of Mediators Of Stress and Adaptation:

Linking social and physical environments

Bruce S. McEwen, Ph.D.

Alfred E. Mirsky Professor  
Head, Harold and Margaret Milliken Hatch  
Laboratory of Neuroendocrinology

The Rockefeller University, NY



Family

Neighborhood

Work

Larger social environment

Subjective ladder

Toxic chemicals

Toxic social environment

## Standardized Mortality Ratio, by Occupational Status



Physical activity

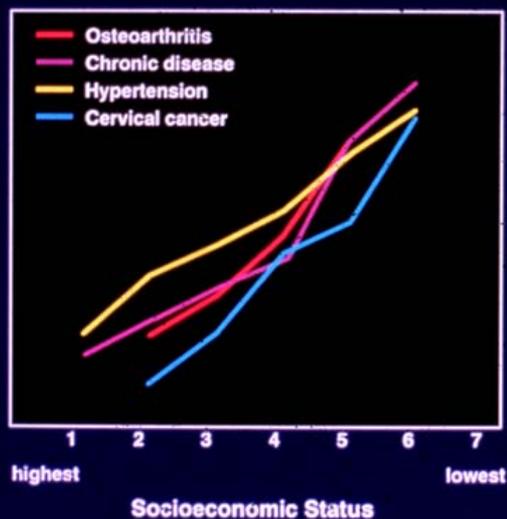
Sleep

Diet

Alcohol

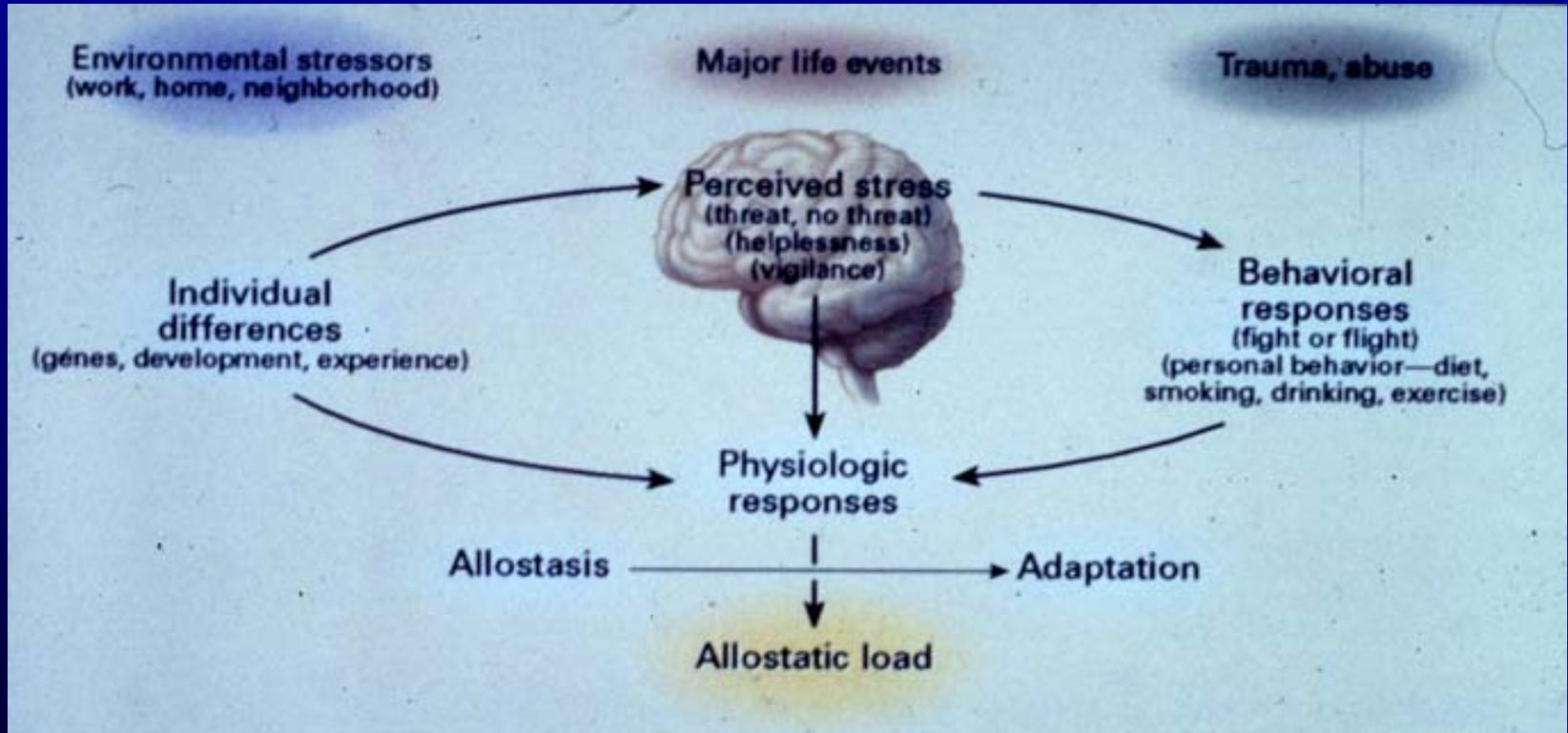
Smoking

## Morbidity Rate by Socioeconomic Status Level



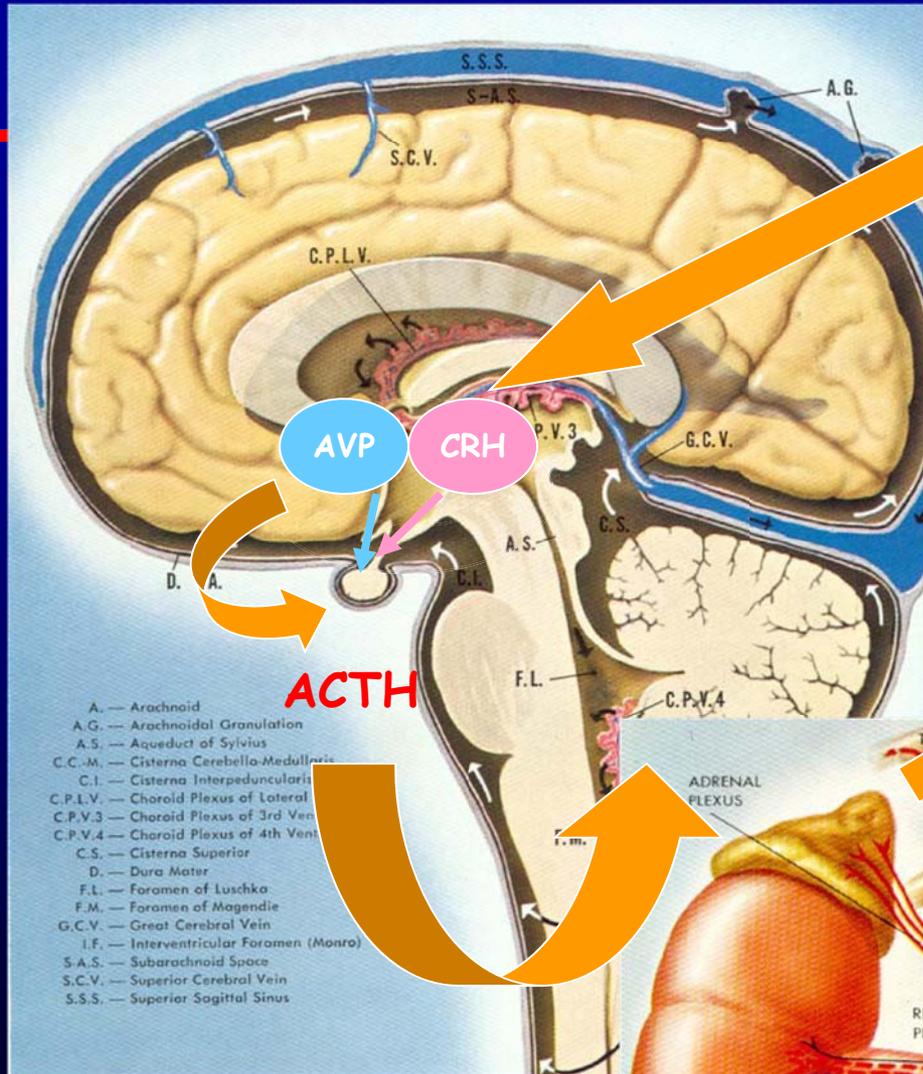
# Social environment and health

## Central Role of the Brain



McEwen B. New England J. Med. 1998

# ... and so what about stress?



**STRESS**

**Many targets  
for cortisol**

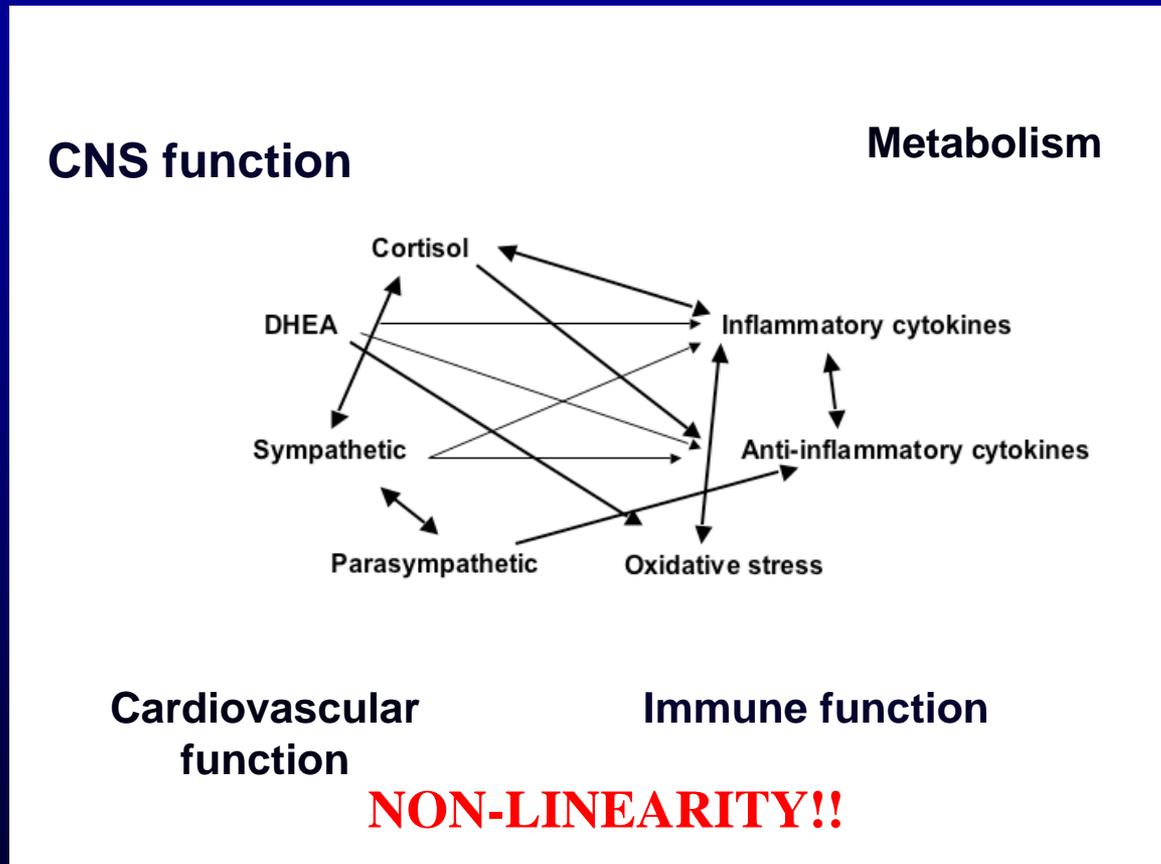
**Cortisol**

Acute - enhances immune,  
Memory, energy replenishment,  
Cardiovascular function

Chronic - suppresses immune,  
Memory, promotes bone  
Mineral loss, muscle wasting;  
Metabolic syndrome

# Mediators of stress and adaptation

## NETWORK OF ALLOSTASIS

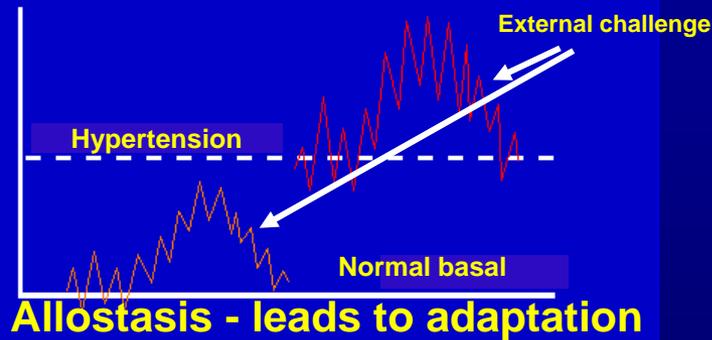


Each mediator has biphasic effects

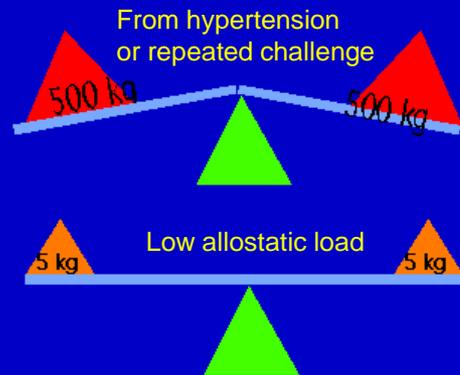
Mediators regulate other mediator systems

# Stress - a challenge to the body

## PROTECTION VS. DAMAGE



### ALLOSTATIC LOAD



Sterling and Eyer 1988; McEwen and Stellar 1993

# What we often mean by “stress” is being “stressed out”!

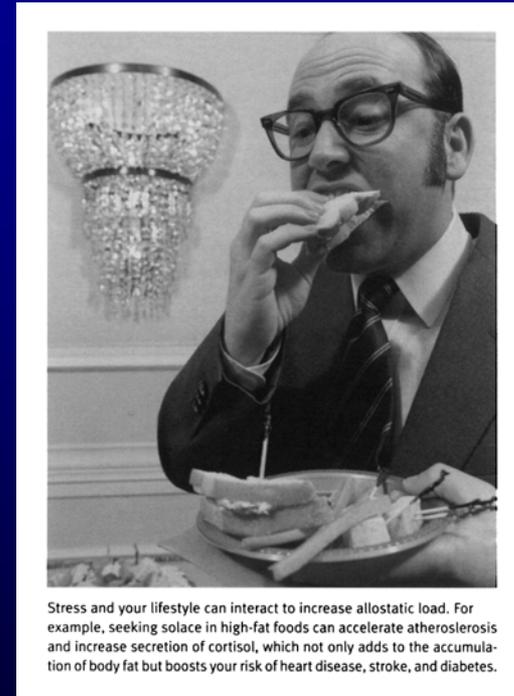
Feeling overwhelmed, out of control, exhausted, anxious, frustrated, angry

## What happens to us?

Sleep deprivation

Eating too much of wrong things,  
alcohol excess, smoking

Neglecting regular, moderate exercise



**All of these contribute to allostatic overload**  
**Psychosocial stress is a major factor**

# Sleep quality, social relationships and cytokines

## Social relationships, sleep quality, and interleukin-6 in aging women

Elliot M. Friedman<sup>\*†</sup>, Mary S. Hayney<sup>‡</sup>, Gayle D. Love<sup>§</sup>, Heather L. Urry<sup>¶</sup>, Melissa A. Rosenkranz<sup>¶</sup>, Richard J. Davidson<sup>¶</sup>, Burton H. Singer<sup>¶</sup>, and Carol D. Ryff<sup>§</sup>

<sup>\*</sup>Robert Wood Johnson Health & Society Scholars Program, Department of Population Health Sciences, <sup>†</sup>School of Pharmacy, <sup>§</sup>Institute on Aging, and <sup>¶</sup>Department of Psychology, University of Wisconsin, Madison, WI 53726; and <sup>¶</sup>Office of Population Research, Princeton University, Princeton, NJ 08544

Contributed by Burton H. Singer, October 24, 2005

This study examined the interplay of social engagement, sleep quality, and plasma levels of Interleukin-6 (IL-6) in a sample of aging women ( $n = 74$ , aged 61–90,  $M$  age = 73.4). Social engagement was assessed by questionnaire, sleep was assessed by using the NightCap in-home sleep monitoring system and the Pittsburgh Sleep Quality Index, and blood samples were obtained for analysis of plasma levels of IL-6. Regarding subjective assessment, poorer sleep (higher scores on the Pittsburgh Sleep Quality Index) was associated with lower positive social relations scores. Multivariate regression analyses showed that lower levels of plasma IL-6 were predicted by greater sleep efficiency ( $P < 0.001$ ), measured objectively and by more positive social relations ( $P < 0.05$ ). A significant interaction showed that women with the highest IL-6 levels were those with both poor sleep efficiency and poor social relations ( $P < 0.05$ ). However, those with low sleep efficiency but compensating good relationships as well as women with poor relationships but compensating high sleep efficiency had IL-6 levels comparable to those with the protective influences of both good social ties and good sleep.

social engagement

**Increased blood pressure;  
decreased parasympathetic tone.**

**Elevated evening cortisol, glucose, insulin.**

**Elevated inflammatory cytokines.**

**Increased appetite, which can increase 1-3  
after over-eating.**

**Depressed mood.**

**Impaired cognitive function.**

# Allostatic Load Battery (CARDIA)

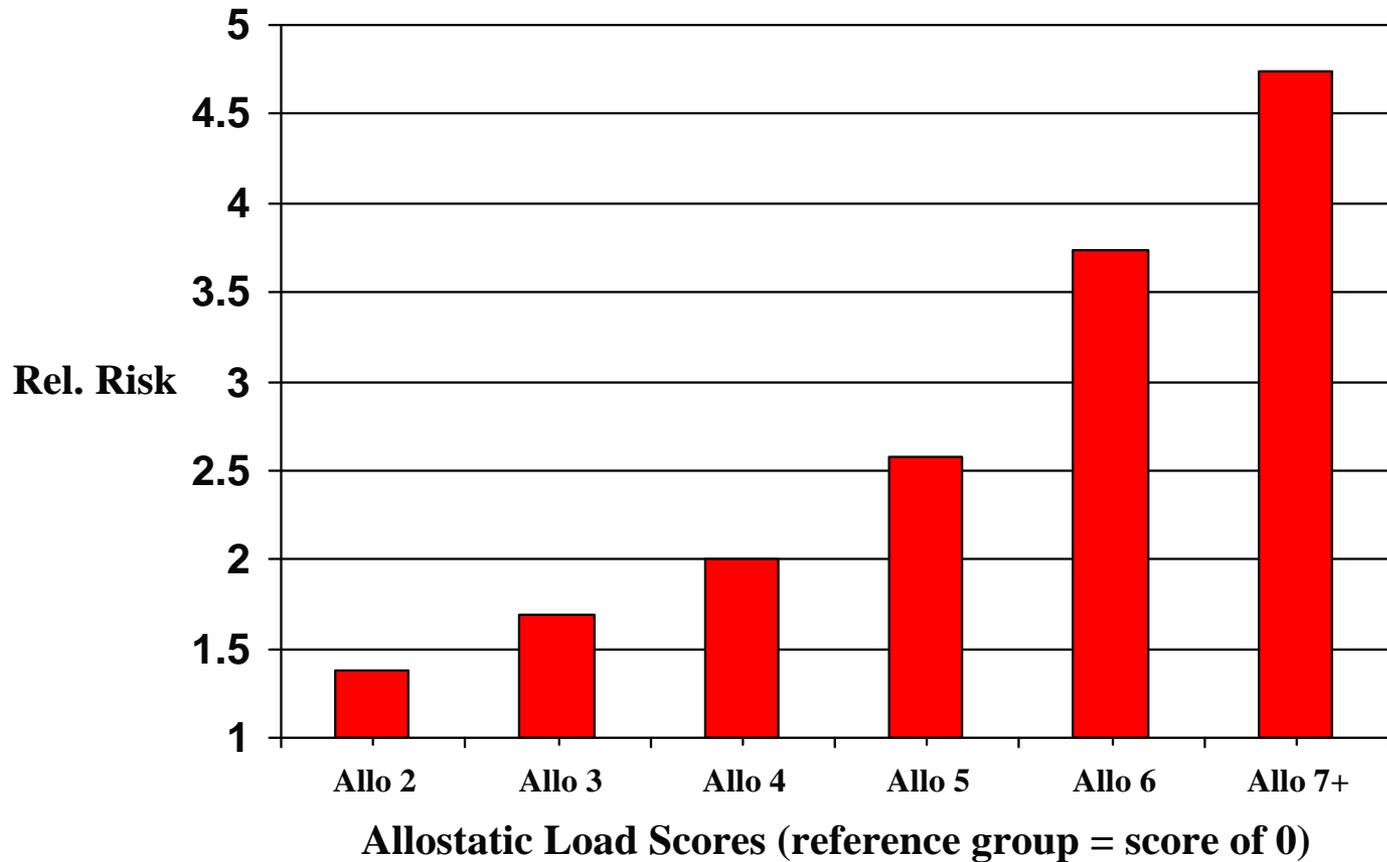
## Year 2000 Exam (n=769)

- **Cardiovascular**
  - SBP & DBP
  - Heart Rate Variability
    - Low Freq. Power
    - High Freq. Power
    - Heart rate
- **Metabolism**
  - HDL Cholesterol
  - LDL Cholesterol
  - Triglycerides
  - Fasting Insulin
  - Fasting Glucose
- **Waist circumference**
- **Inflammation**
  - Fibrinogen
  - CRP
  - IL-6
- **SNS**
  - Ur. Epinephrine
  - Ur. Norepinephrine
- **HPA**
  - Urinary Cortisol
  - Salivary Cortisol
    - Am rise
    - Pm decline

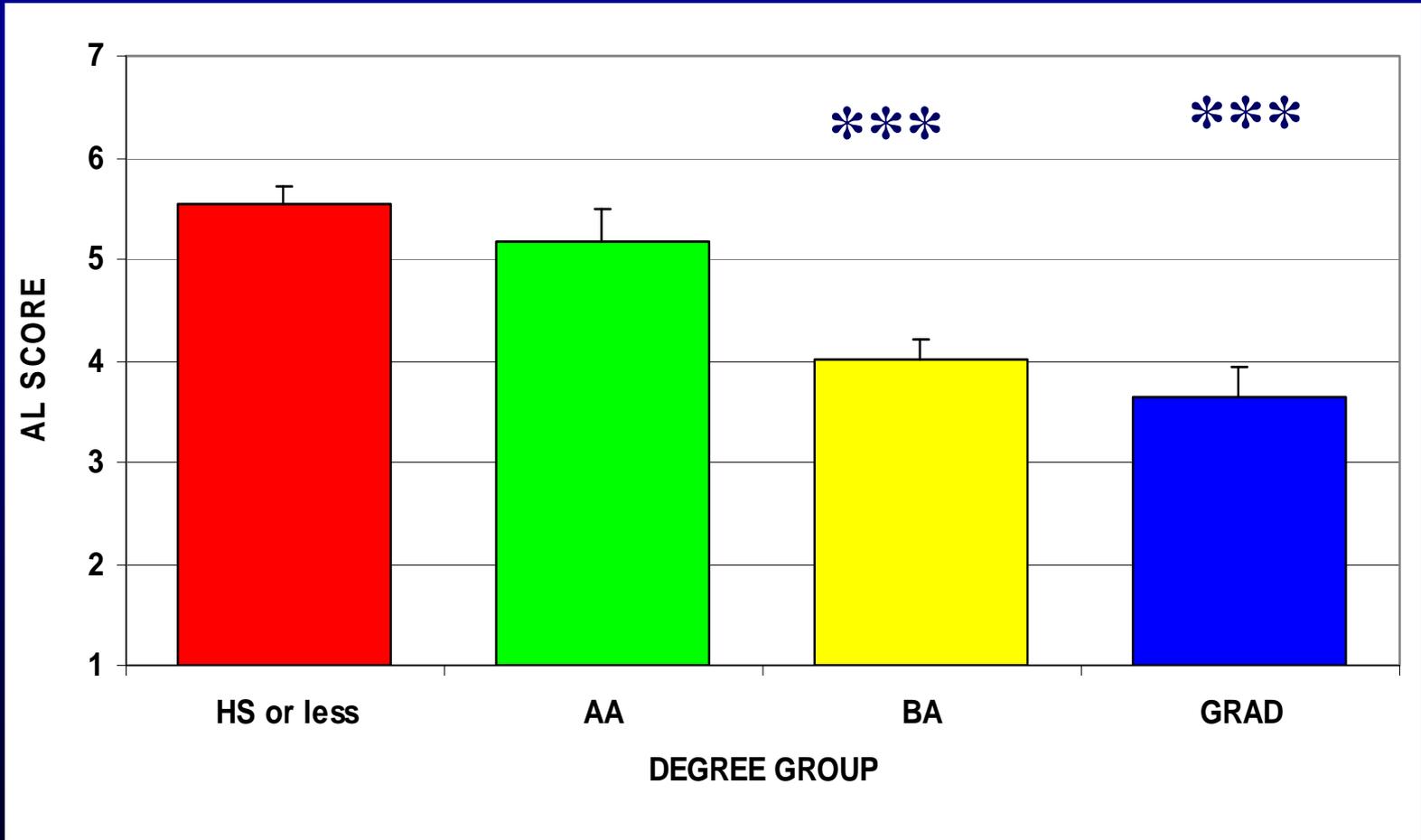
Prof. Teresa Seeman, UCLA

# Allostatic Load & 7-yr Mortality

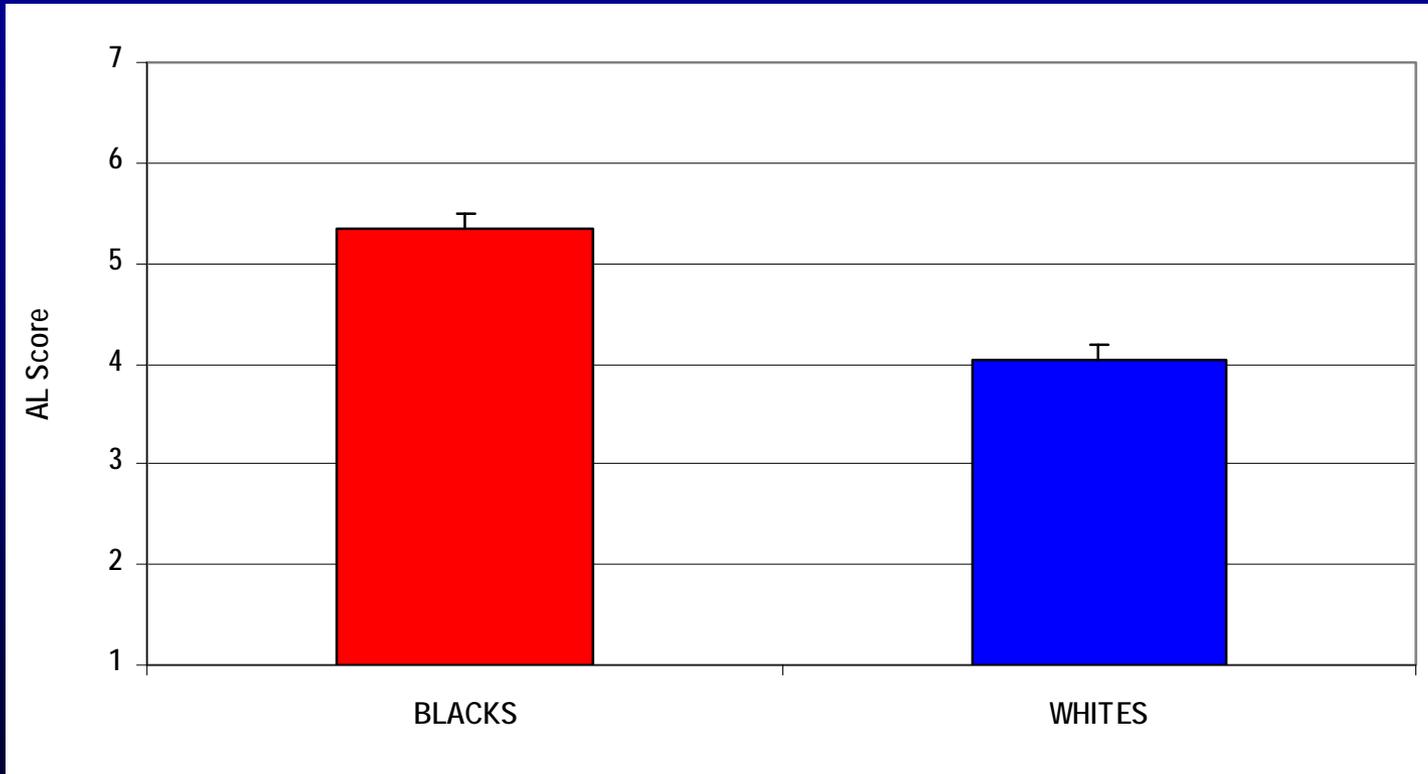
## MacAthur Successful Aging Study



# AL Score by Education

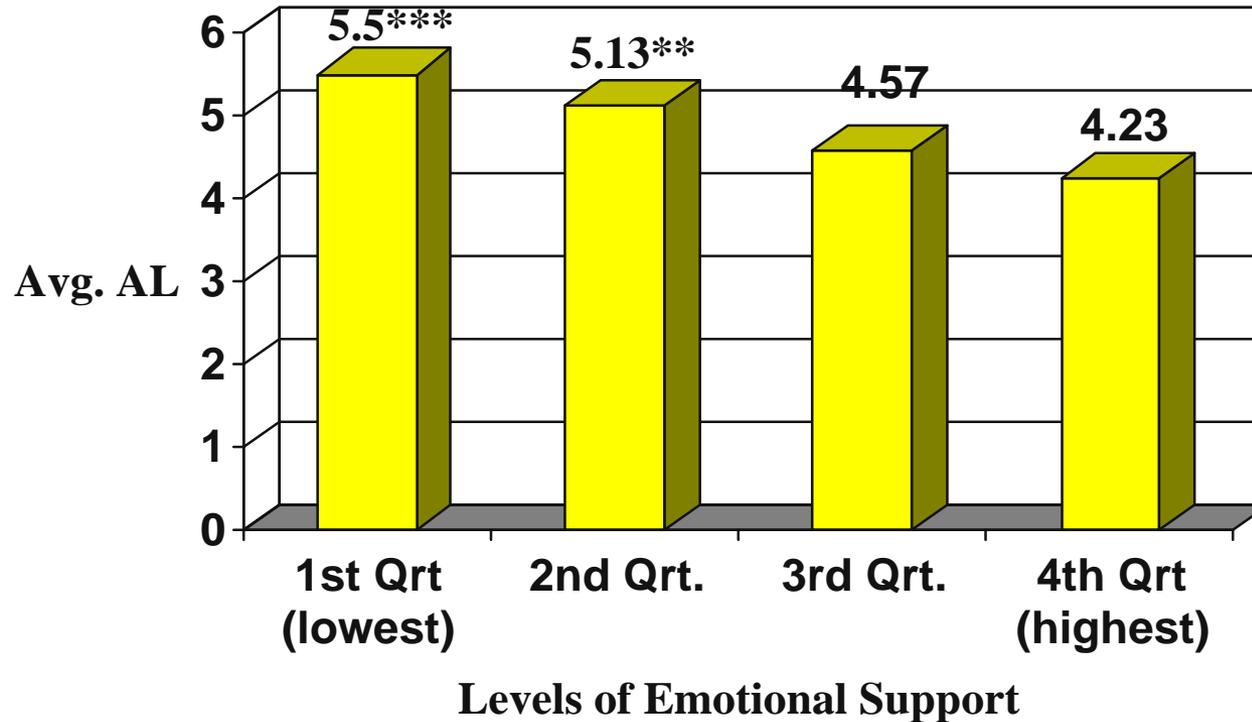


# AL by Race

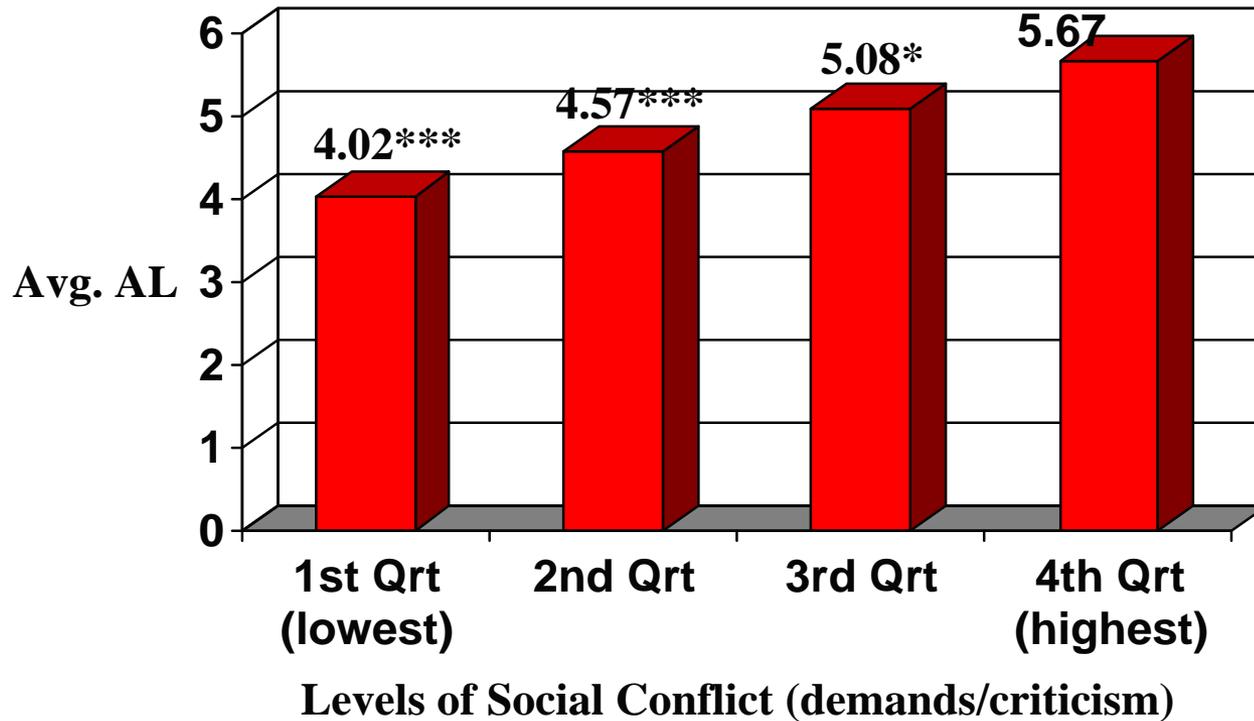


$p < 0.001$

# Social Support & Allostatic Load: CARDIA



# Social Conflict & Allostatic Load: CARDIA



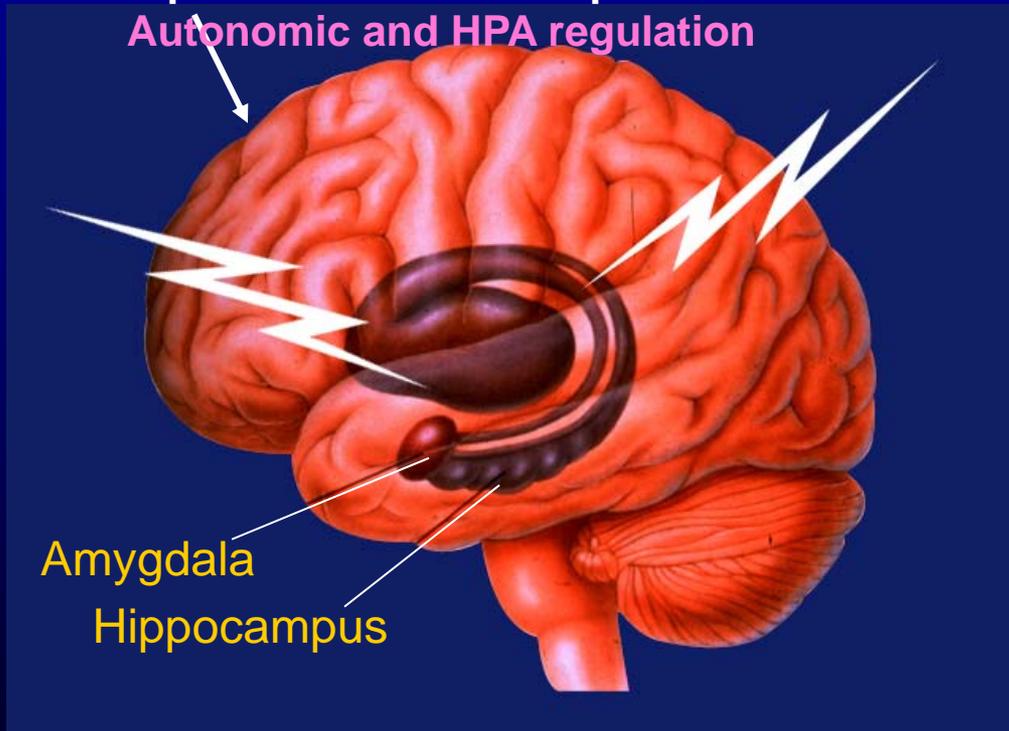
# Brain Under Stress:

Role in cognitive function, emotion,  
neuroendocrine and autonomic regulation

## Prefrontal cortex

Decision making, working memory,  
top down control of impulsive behavior

Autonomic and HPA regulation



## Hippocampus

Contextual, episodic, spatial  
memory

Shut off of HPA

## Amygdala

Emotion, fear, anxiety,

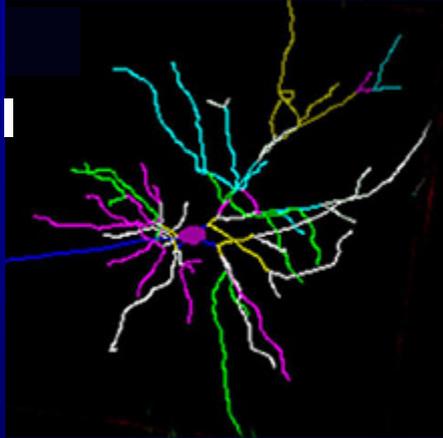
Aggression

Turns on HPA and  
autonomic response

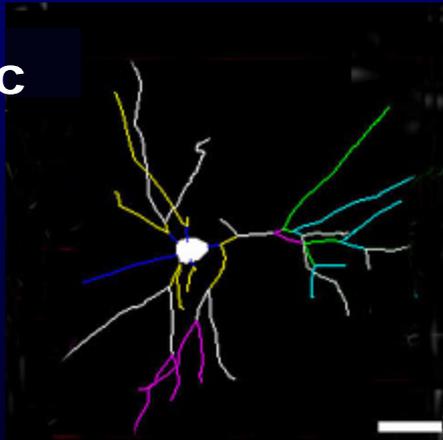
# Stress causes neurons to shrink or grow

....but not necessarily to die

Control

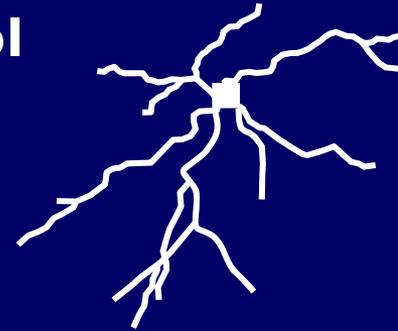


Chronic stress

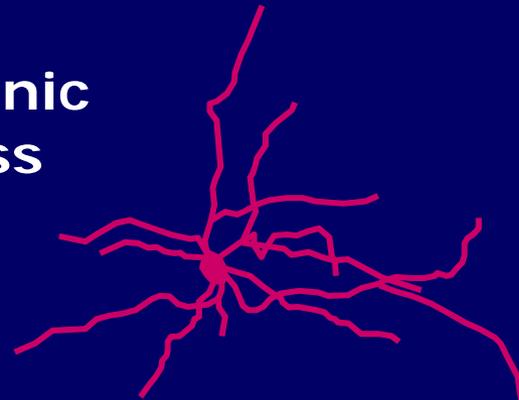


Prefrontal Cortex  
And Hippocampus

Control



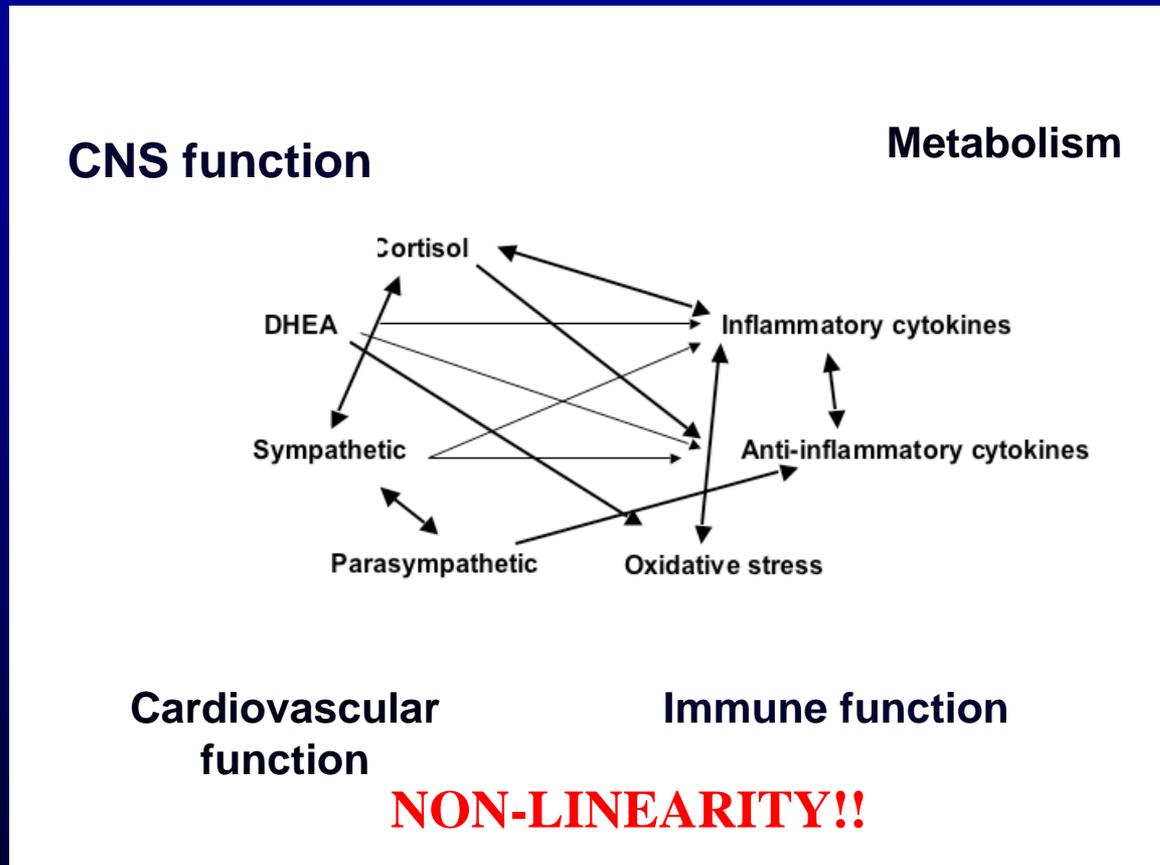
Chronic stress



Amygdala  
Orbitofrontal Ctx

# Mediators of stress and adaptation

## NETWORK OF ALLOSTASIS



Toxic chemicals (eg lead exposure, diesel exhaust)  
Feed into network of allostasis  
(eg elevated inflammation, cortisol)

# Neuroscience, Molecular Biology, and the Childhood Roots of Health Disparities

## Building a New Framework for Health Promotion and Disease Prevention

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Jack P. Shonkoff, MD

W. Thomas Boyce, MD

Bruce S. McEwen, PhD

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A scientific consensus is emerging that the origins of adult disease are often found among developmental and biological disruptions occurring during the early years of life. These early experiences can affect adult health in 2 ways—either by cumulative damage over time or by the biological embedding of adversities during sensitive developmental periods. In both cases, there can be a lag of many years, even decades, before early adverse experiences are expressed in the form of disease. From both basic research and policy perspectives, confronting the origins of disparities in physical and mental health early in life may produce greater effects than attempting to modify health-related behaviors or improve access to health care in adulthood.