Addressing Health Disparities through Neuroscience

Views by Two

September 19, 2011

Neuroscience Center (6001 Executive Blvd. Rockville, Maryland 20852) Room A from 2:00-3:30 pm

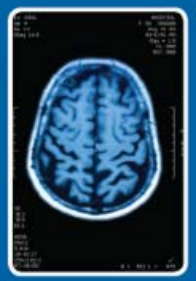
Speakers:

Bruce S. McEwen, Ph.D.
Alfred E. Mirsky Professor, Harold and Margaret Milliken Hatch Laboratory of Neuroendocrinology
Rockefeller University

Neuroscience Perspectives on Brain and Body Health: Importance of the Social Environment

James S. Jackson, Ph.D.
Director and Research Professor, Institute for Social Research, Daniel Katz Distinguished University Professor of Psychology
University of Michigan

The Affordances Framework for Understanding Population Disparities in Physical and Mental Health



NATIONAL INSTITUTES OF HEALTH

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Neuroscience Perspectives on Brain and Body Health

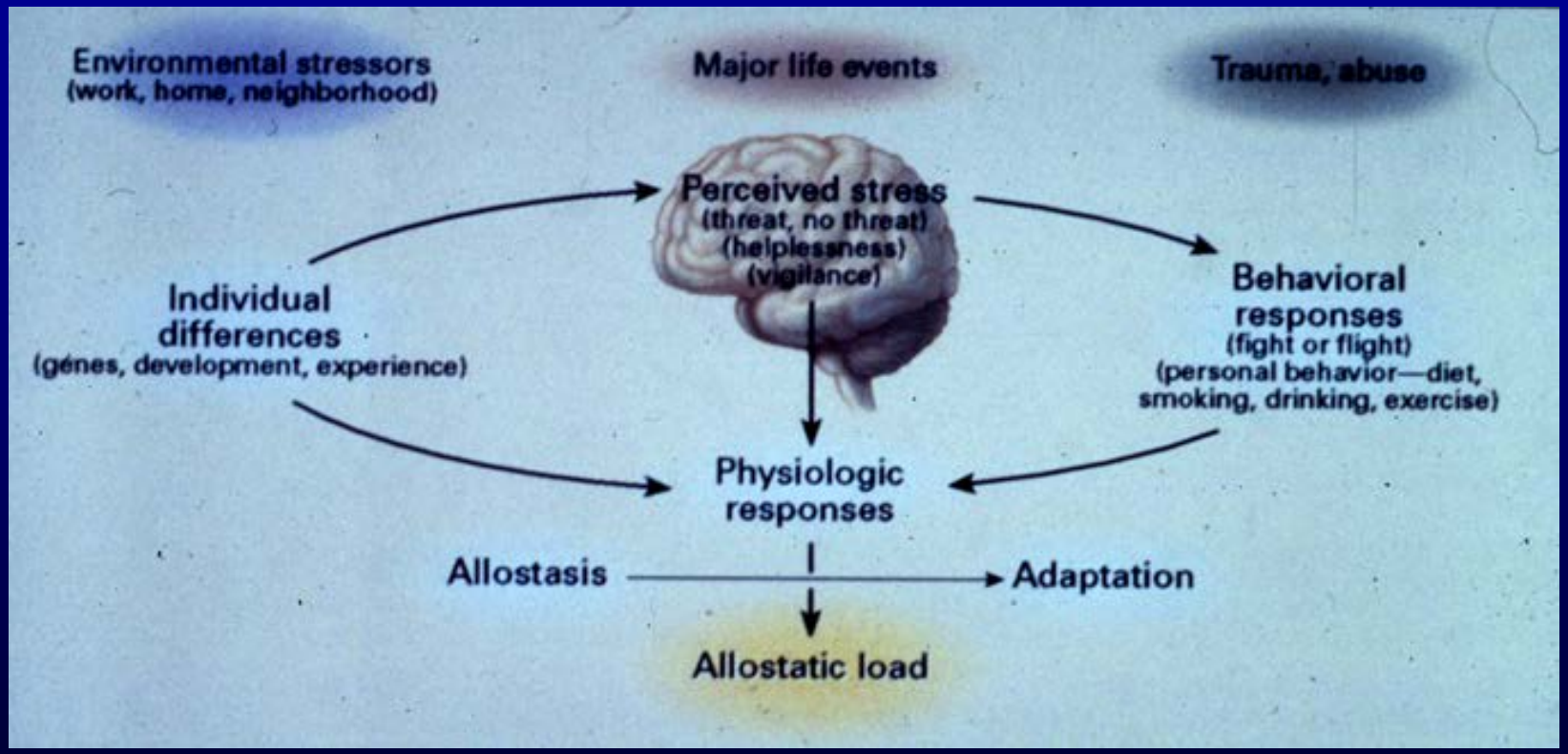
Importance of the Social Environment

Bruce S. McEwen, Ph.D.

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

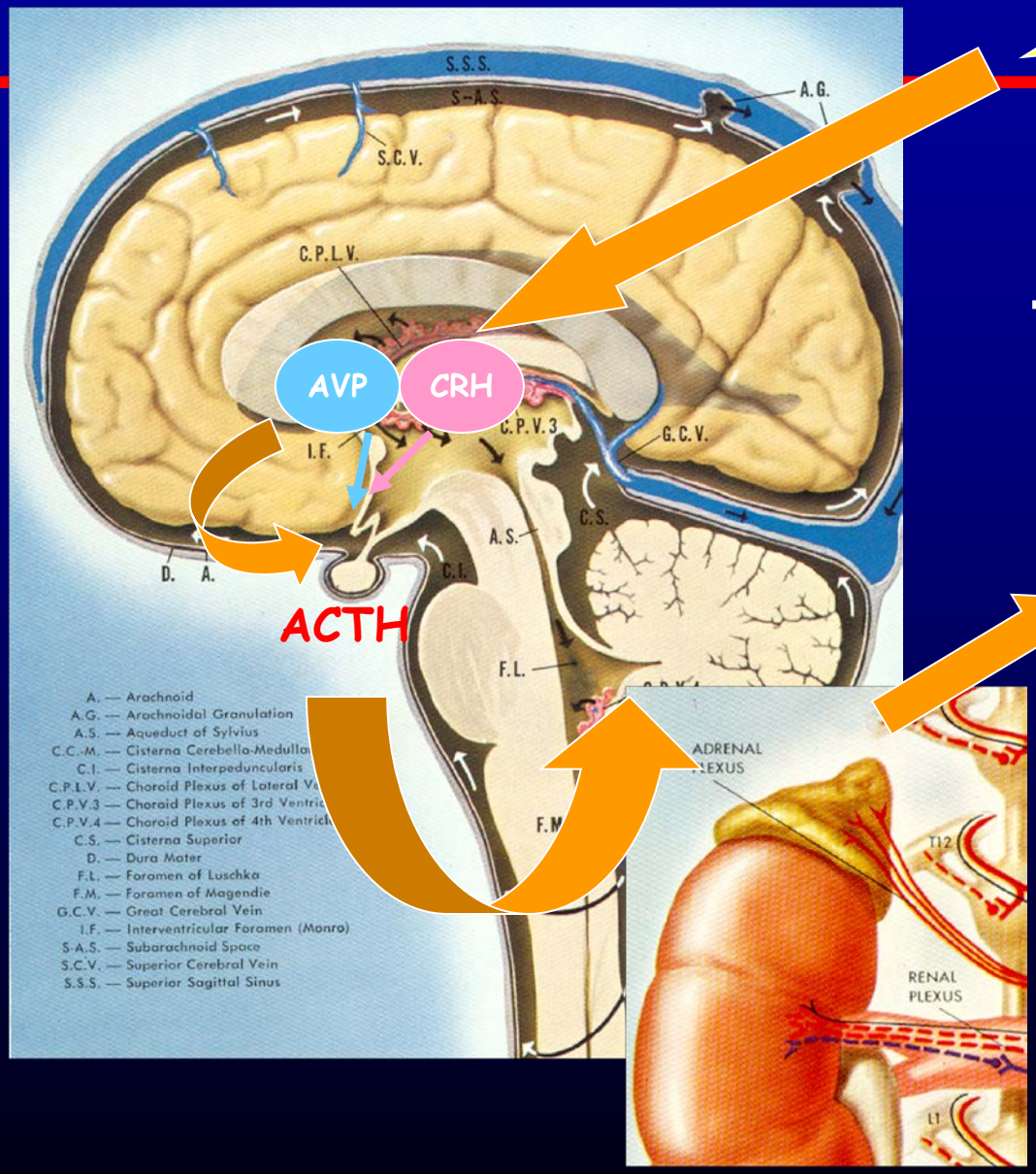
The Rockefeller University, NY

Social environment and health
Central Role of the Brain



McEwen BS, New England Journal of Medicine 1998

Stress, allostasis and allostatic load



STRESS

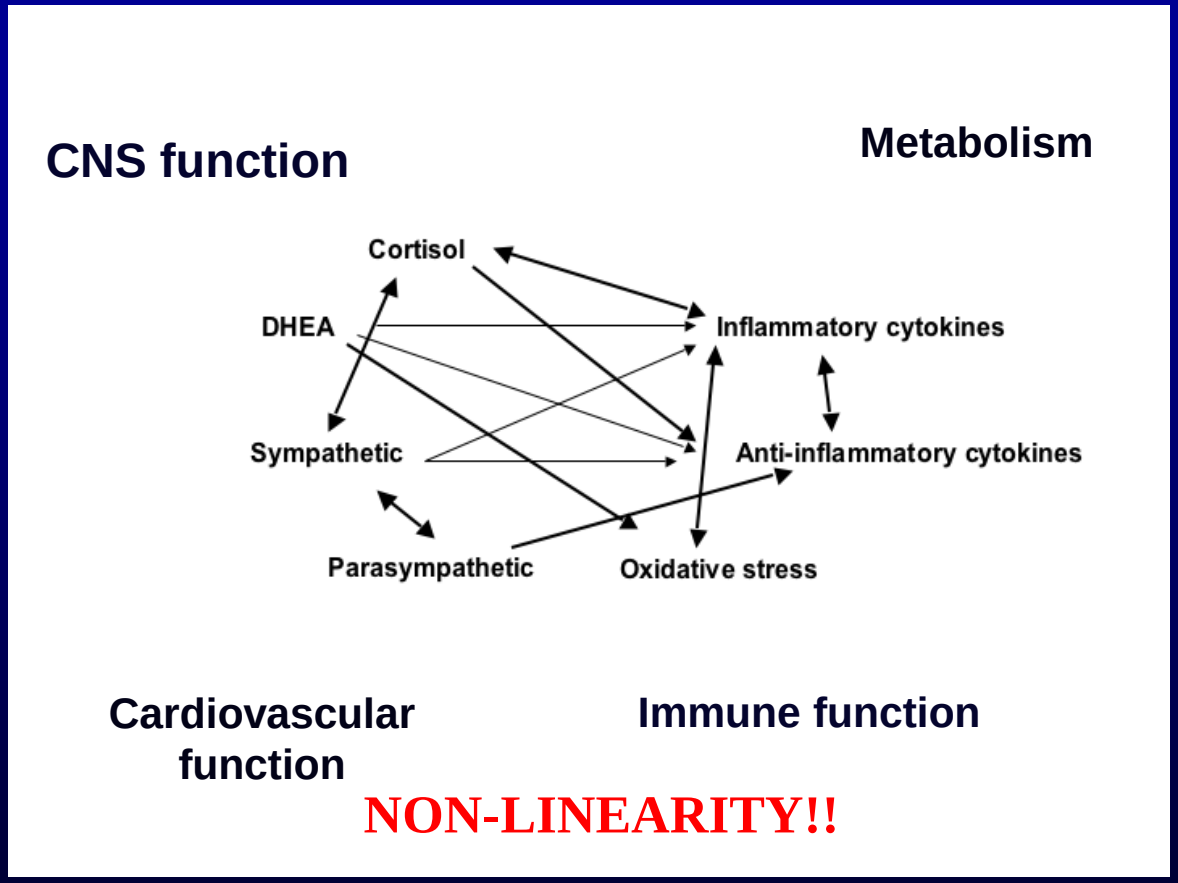
Many targets for cortisol

Cortisol

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

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

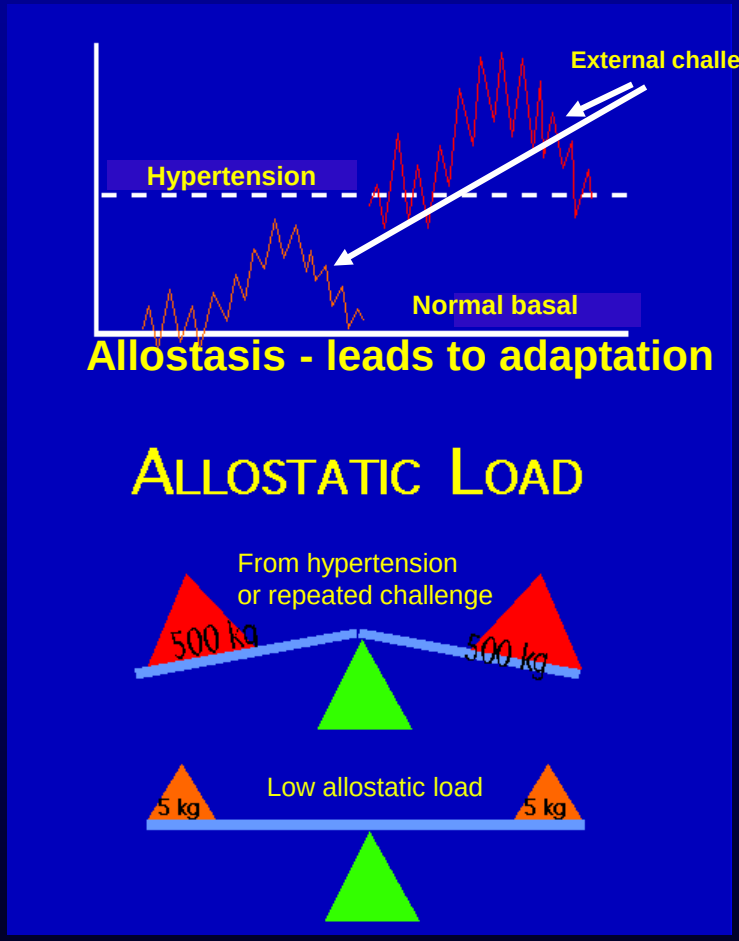
Mediators of stress and adaptation



Each mediator has biphasic effects

Mediators regulate other mediator systems

Stress - a challenge to the body
PROTECTION VS. DAMAGE



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

Stress and your lifestyle can interact to increase allostatic load. For example, seeking solace in high-fat foods can accelerate atheroslerosis and increase secretion of cortisol, which not only adds to the accumulation of body fat but boosts your risk of heart disease, stroke, and diabetes.

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*†, Mary S. Hayney‡, Gayle D. Love§, Heather L. Urry¶, Melissa A. Rosenkranz¶, Richard J. Davidson¶, Burton H. Singer‖, and Carol D. Ryff§

*Robert Wood Johnson Health & Society Scholars Program, Department of Population Health Sciences, ‡School of Pharmacy, §Institute on Aging, and ¶Department of Psychology, University of Wisconsin, Madison, WI 53726; and ‖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.

Coronary Artery Risk Development in Young Adults (CARDIA)

- Slides from Prof.Teresa Seeman, Ph.D. UCLA

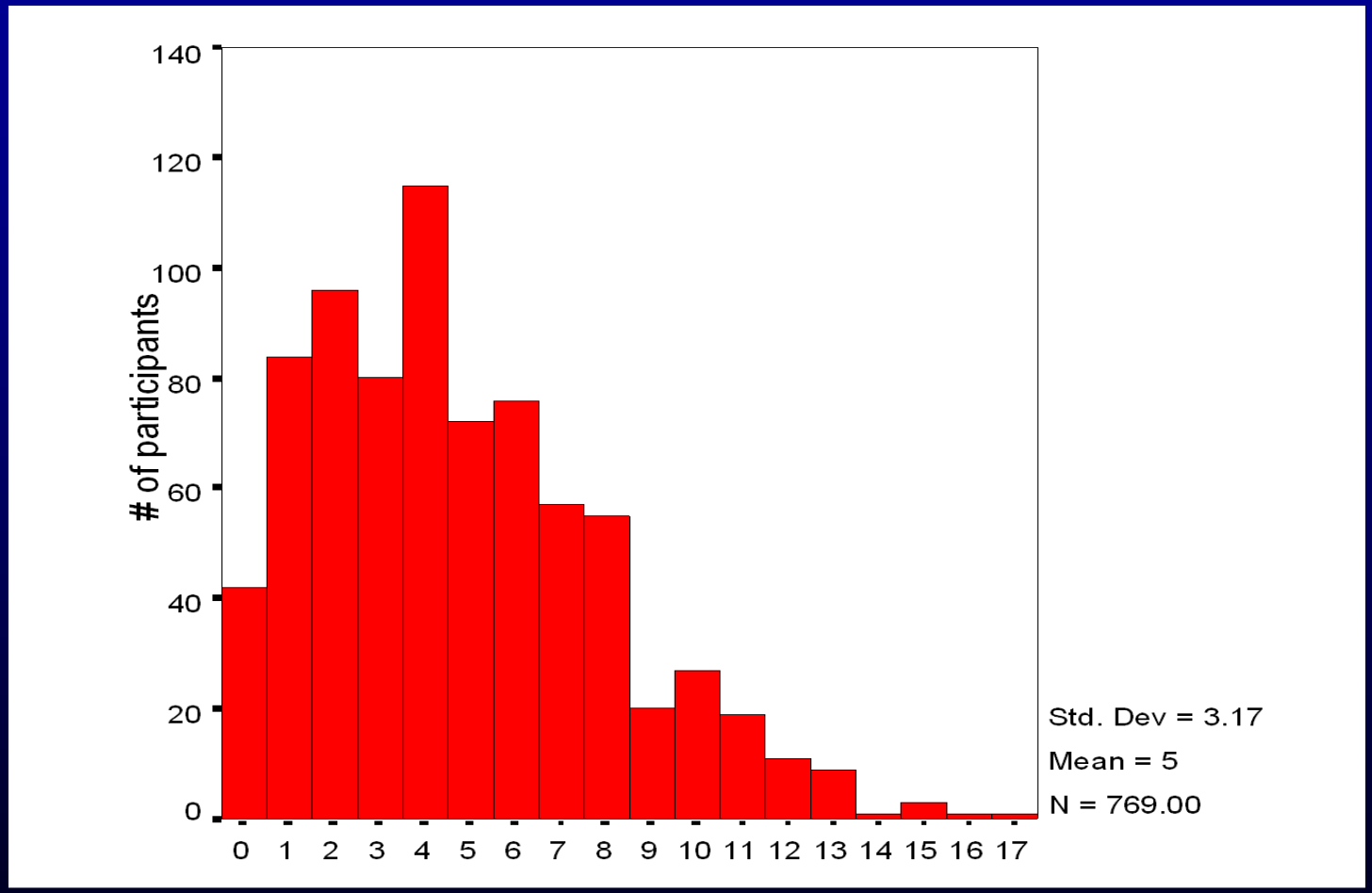
- N ~ 5,000, ages 18-30 in 1985
  - ages 33-45 at 15-yr follow-up in 2000
- 4 sites (Birmingham, AL; Chicago, IL; Minneapolis, MN; Oakland, CA)
- Stratified sampling - equal # by gender, ethnicity, age and education
- Followups = 1987, 1990, 1992, 1995, 2000

Allostatic Load Ancillary Study
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

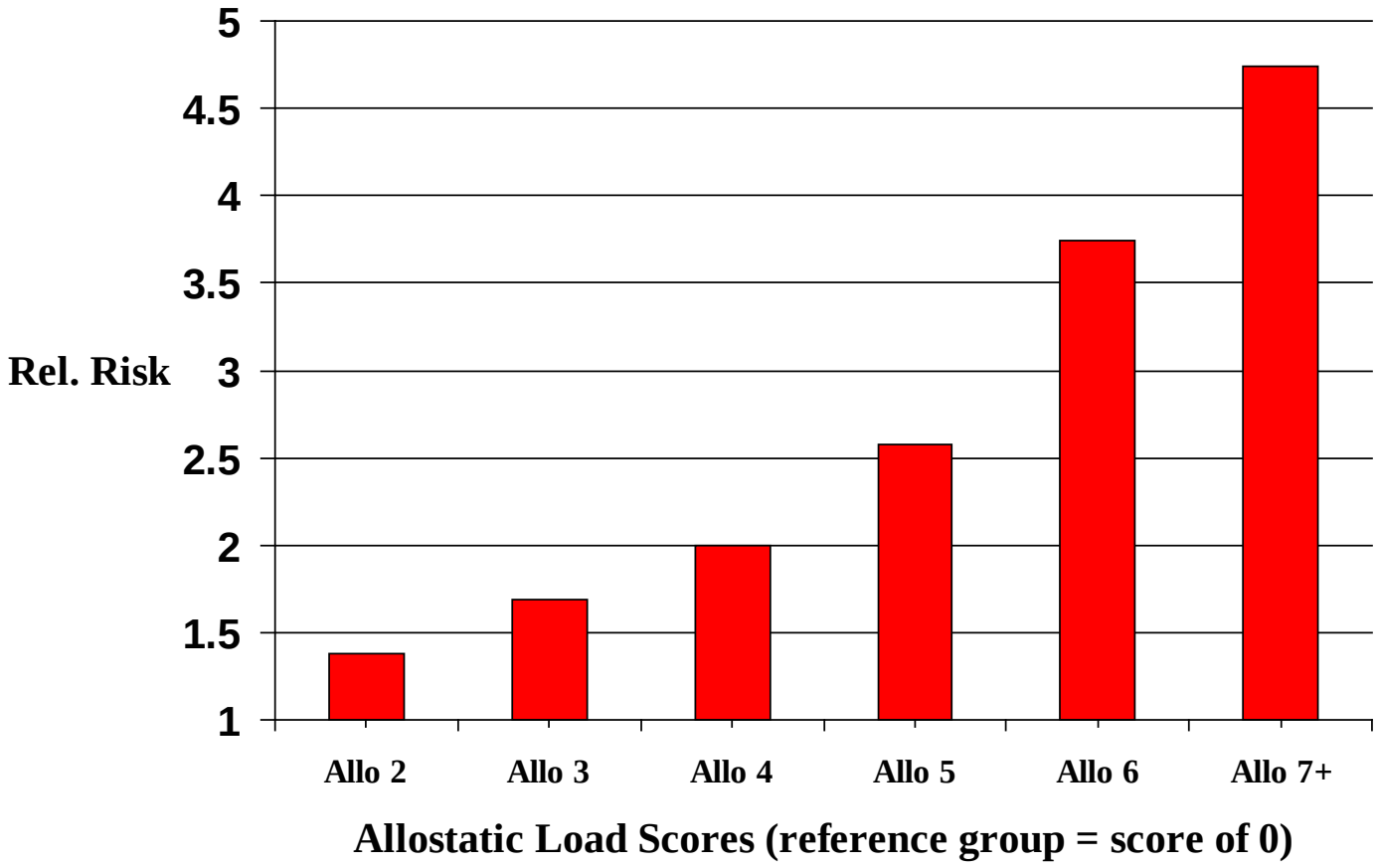
Distribution of AL

scored as being in extreme quartile of distribution of 1 or more of 17 parameters



Allostatic Load & 7-yr Mortality

MacAthur Successful Aging Study



What factors increase or decrease the allostatic load score?

Lower allostatic load:

-Education

-Social support and integration

Higher allostatic load:

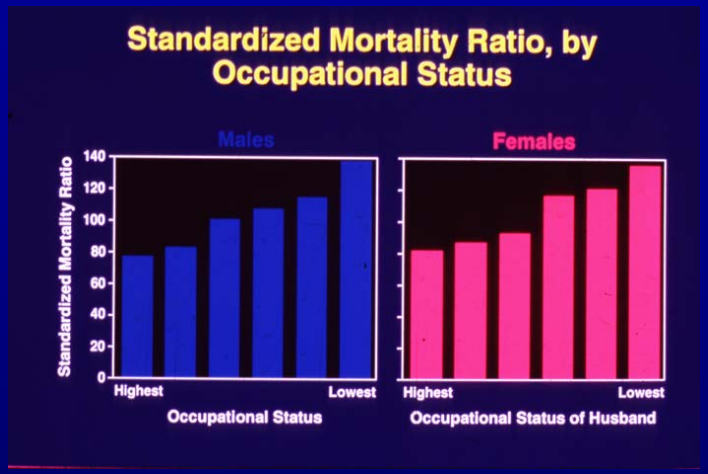
-Social conflict

-Race - discrimination?**

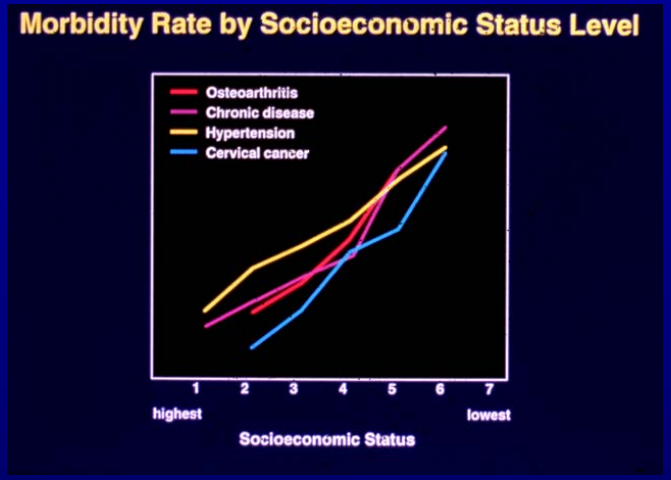
** NEEDS FURTHER DOCUMENTATION

Socioeconomic Status and Health

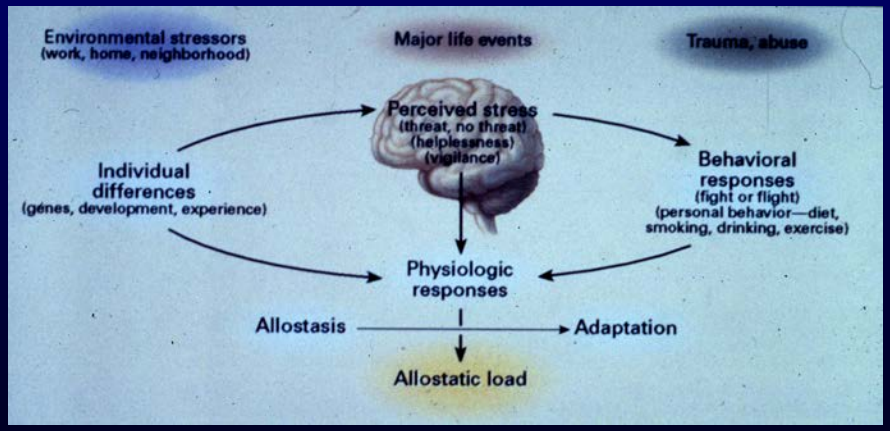
How does SES get under the skin to affect health?



Whitehall Study - UK

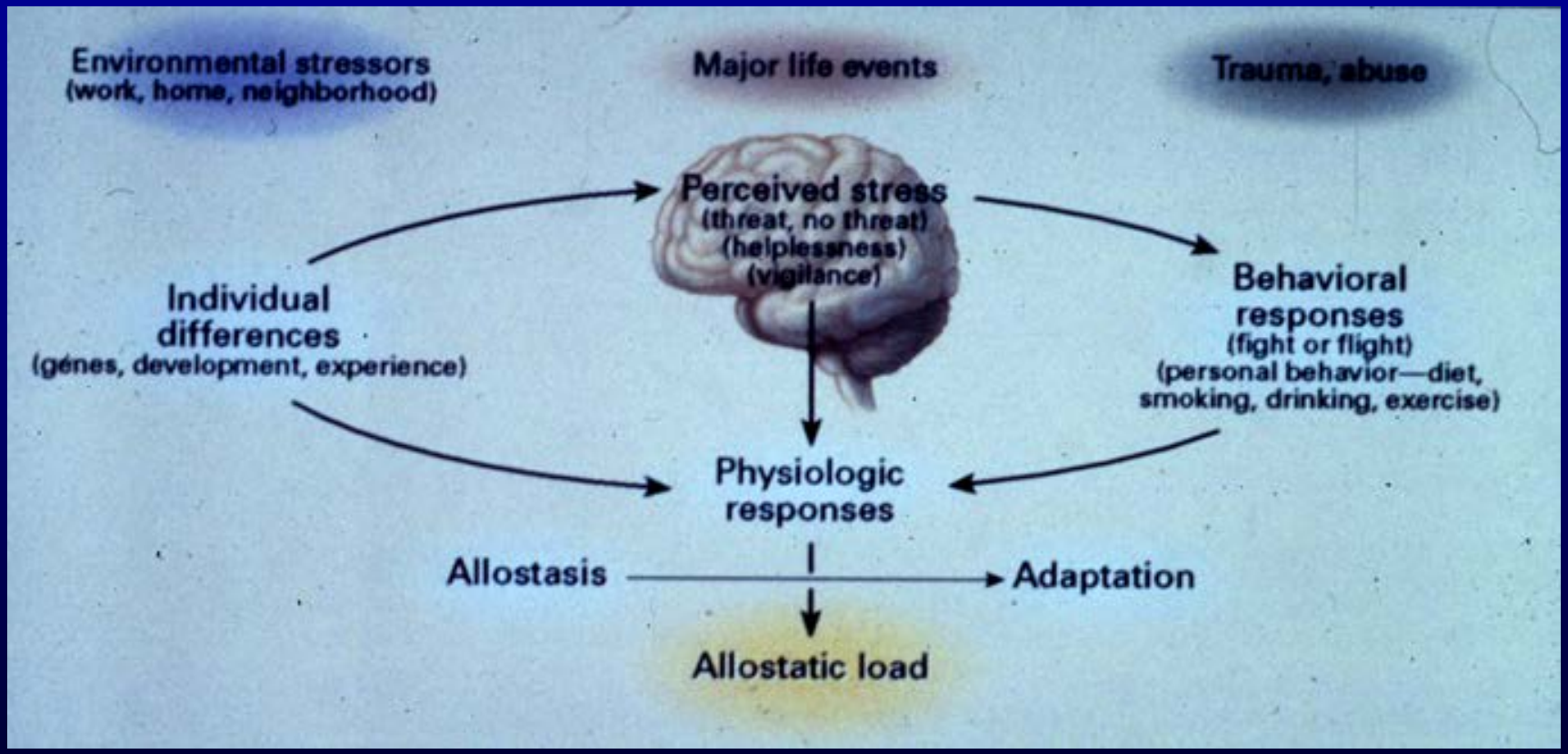


United States summary



Central role of the brain

Central Role of the Brain



McEwen BS, New England Journal of Medicine 1998

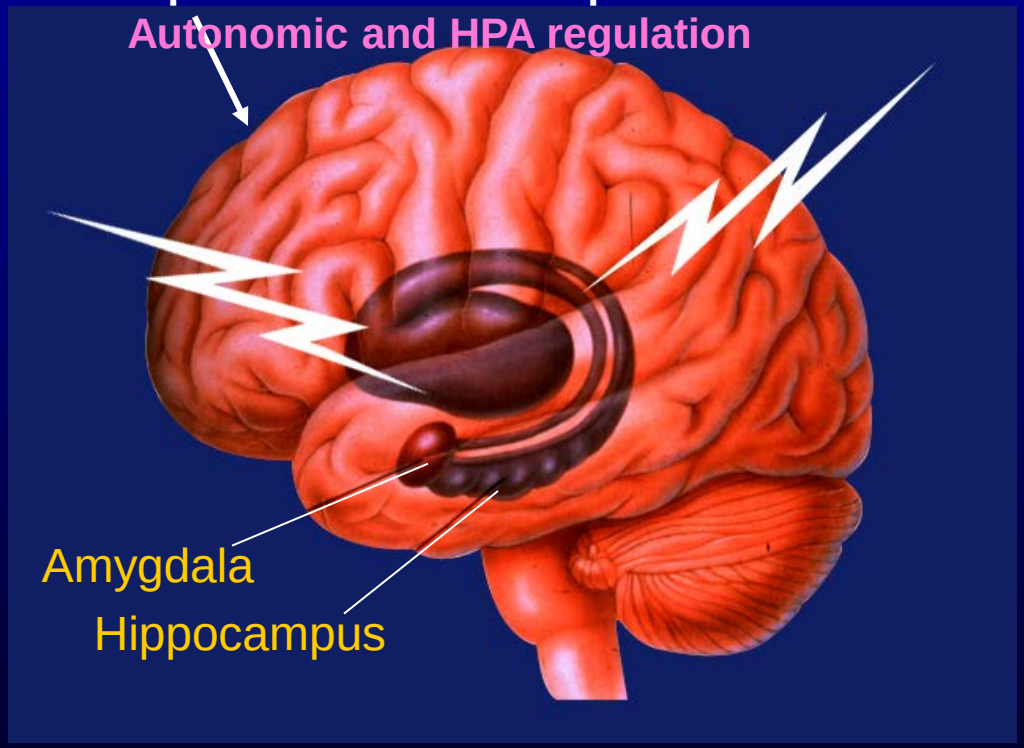
Brain Under Stress:

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

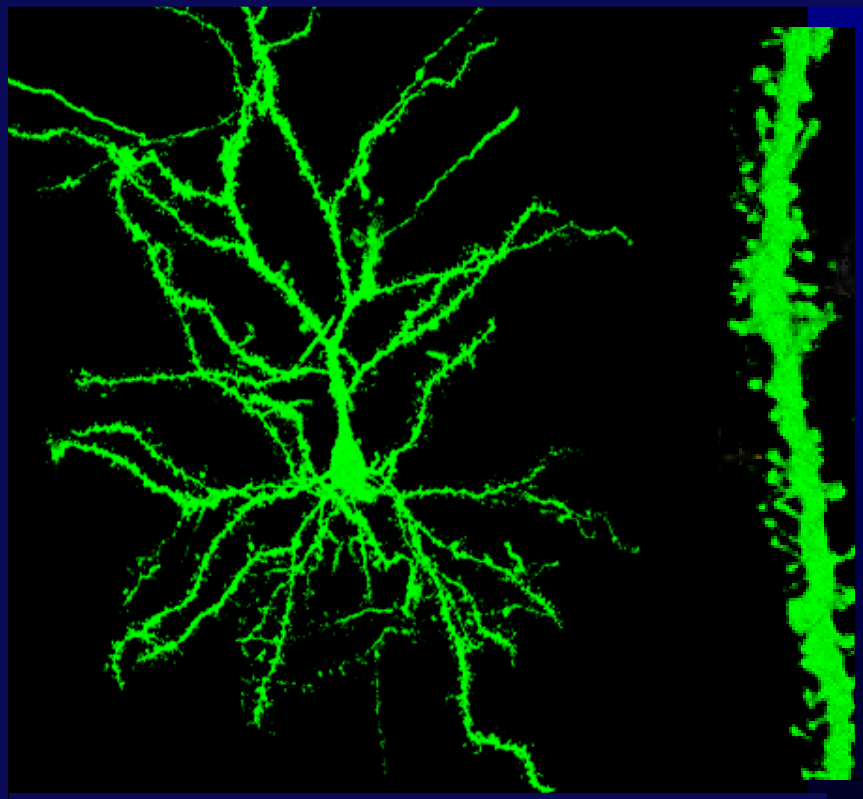
Emotion, fear, anxiety,

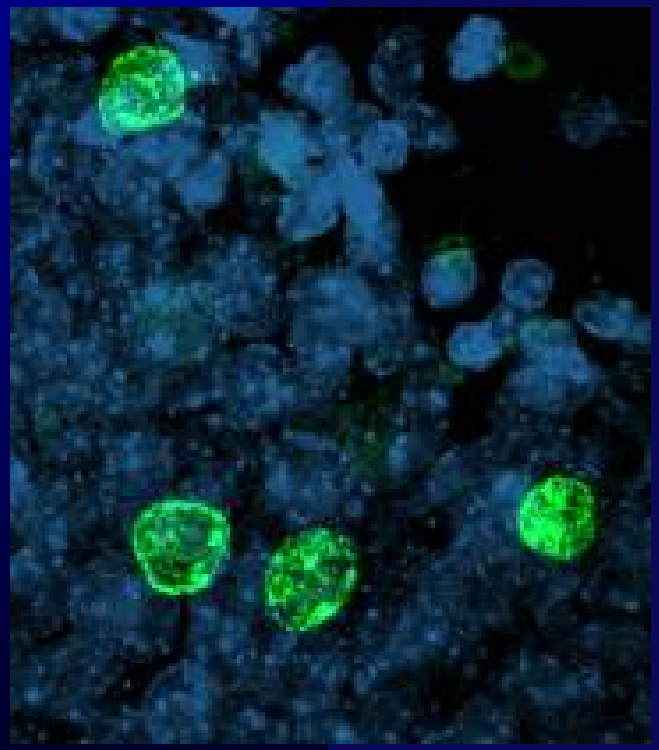
Aggression

Turns on HPA and

autonomic response

Structural plasticity in the adult brain is modulated by experience





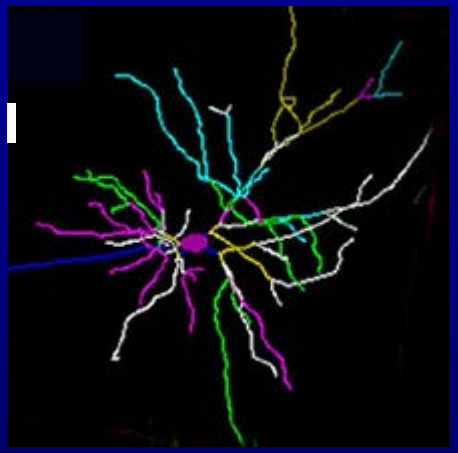
pses

Neurogenesis

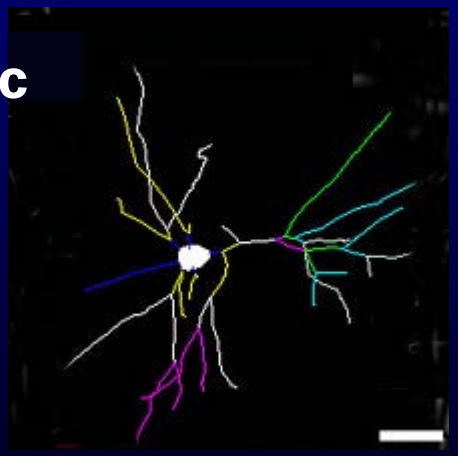
Stress causes neurons to shrink or grow

….but not necessarily to die

Control



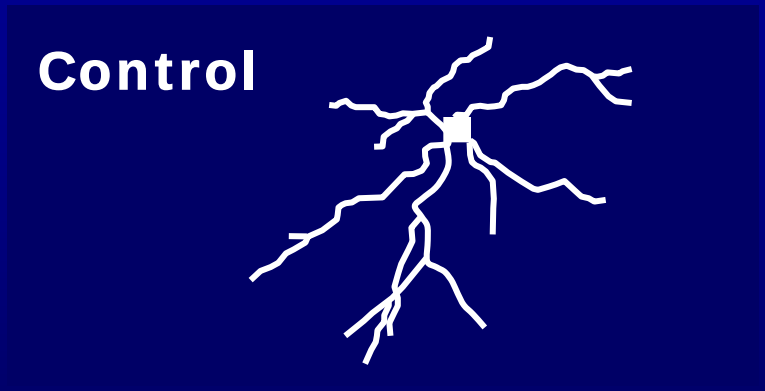
Chronic stress



Prefrontal Cortex

And Hippocampus

Control



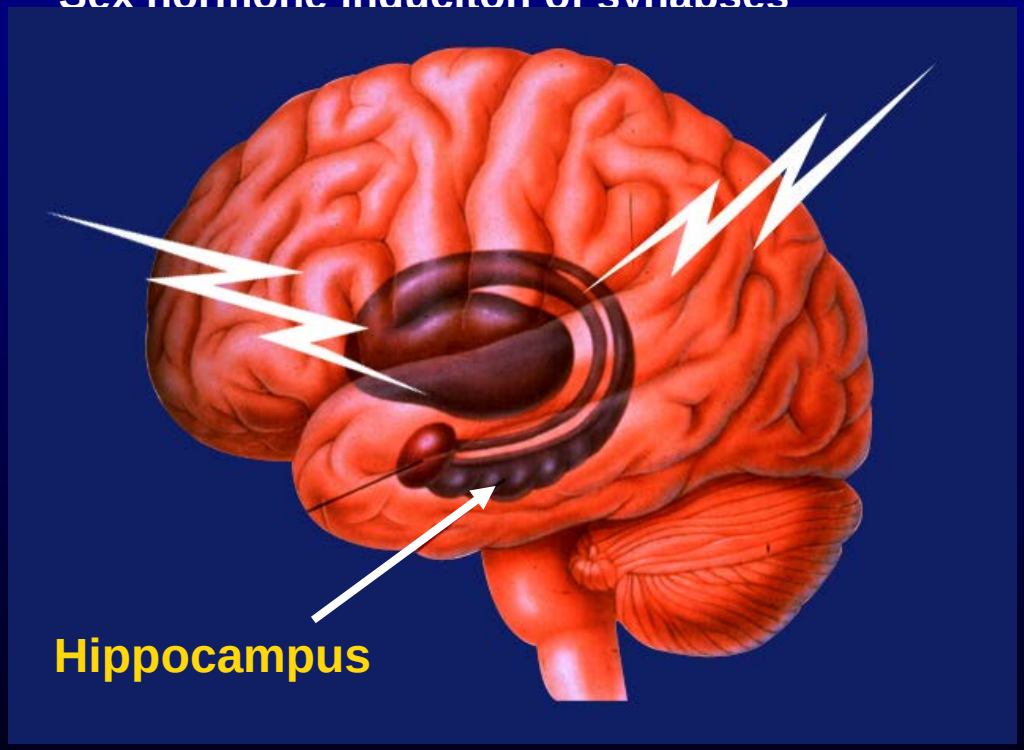
Chronic stress

Amygdala
OFC

The Human Hippocampus
Structural / functional changes

In Animal Models

- Dendrite shrinkage
- Loss of synapses
- Reduced neurogenesis
- Sex hormone induciton of synapses



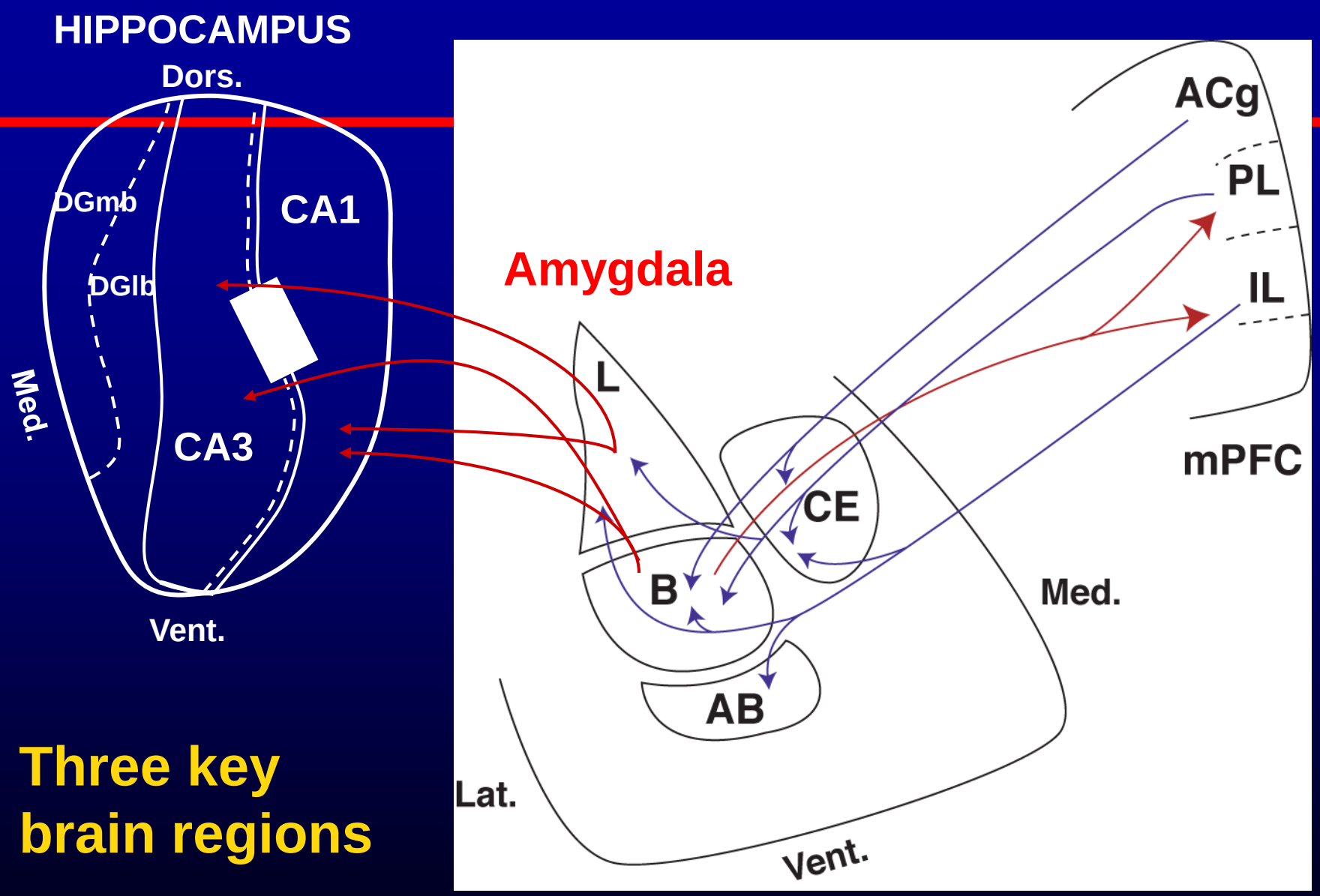
Contextual, episodic, spatial memory

Human Brain Imaging Results

Smaller volume in

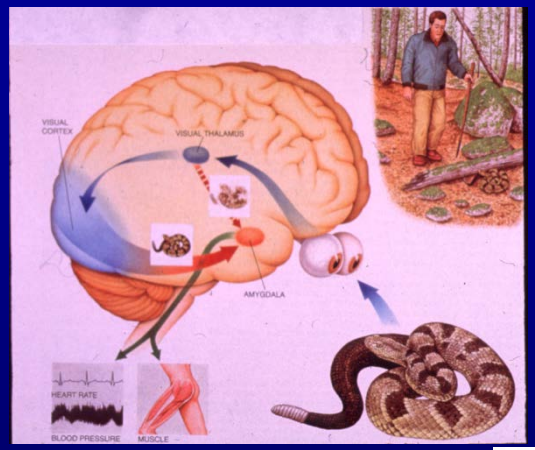
- Cushing's disease
- Diabetes
- Depression
- Post-traumatic stress disorder
- Chronic stress
- Chronic inflammation
- Jet lag
- Lack of exercise
- Low self esteem

-Learning –increased volume!



Three key brain regions

Amygdala



Joseph Ledoux and Elizabeth Phelps, New York University

Fear, anxiety, aggression

Autonomic activation

Fear conditioning

Chronic anxiety

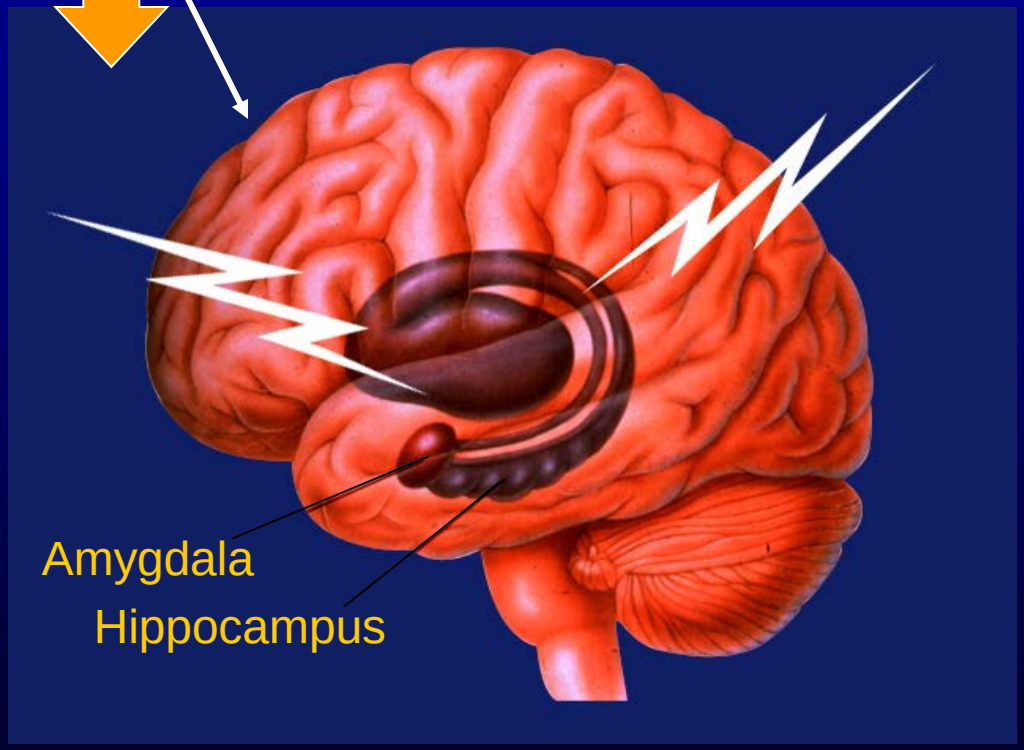
Facial expressions used to activate amygdala activity, autonomic activity, blood pressure and heart rate

The Human Brain Under Stress

Structural/functional changes

Prefrontal cortex

Neurons shrink with chronic stress



Executive function

Attention shifting - mental flexibility

Extinction of fear conditioning

Working memory

Ability to suppress negative thoughts

Learned helplessness

Autonomic regulation

HPA regulation

Lessons from the medial prefrontal cortex

1. Shrinkage of dendrites is reversible in young adult rodents.

2. Evidence in humans that there is also reversible plasticity after chronic stress.

3. In rodent models, circadian disruption causes dendrites to shrink and impairs cogntive flexibility.

4. In rodent models, there is loss of resilience with aging.

5. In rodent models, females show a different response to chronic stress.

Types of Stress

(our own species)

Positive Stress

- Exhilaration from a challenge that has a satisfying outcome
- Sense of mastery and control
- Good self-esteem
- Good emotional control and impulse control
- Good decision making capacity and mental flexibility

Tolerable Stress

- Adverse life events but good social and emotional support

Toxic Stress

- Chaos, abuse, neglect, “risky families”
- Absence of emotional support and stability
- Low self-esteem
- Poor emotional and impulse control; impaired judgment
- _____

<u>Biological embedding vs cumulative effects</u>:
Adverse childhood experiences (ACE) from toxic stress:
long-lasting - cognitive, behavioral, systemic

Developmental Issues for Children

Low socioeconomic status

Poor language skills and executive function
and other effects on learning ability

Chaos in home

- Greater helplessness and distress, poor self regulatory behavior
- Obesity, elevated blood pressure and cardiovascular reactivity

Lasting effects of early life adversity on body fat,
systemic inflammation and poor dental health

Abuse and neglect

Physical and mental health
Shorter lifespan

“Risky families” - cold and unsupportive

Many same consequences but not as extensively studied

ACE – health consequences

Table 1. Health and social problems and the ACE score

Problems from the baseline data	Outcomes associated with the ACE score
Prevalent diseases	Ischemic heart disease, cancer, chronic lung disease, skeletal fractures, sexually transmitted diseases, liver disease
Risk factors for common diseases/poor health	Smoking, alcohol abuse, promiscuity, obesity, illicit drug use, injection drug use, multiple somatic symptoms, poor self-rated health, high perceived risk of AIDS
Mental health	Depressive disorders, anxiety, hallucinations, panic reactions, sleep disturbances, memory disturbances, poor anger control
Sexual and reproductive health	Early age at first intercourse, sexual dissatisfaction, teen pregnancy, unintended pregnancy, teen paternity, fetal death
General health and social problems	High perceived stress, impaired job performance, relationship problems, marriage to an alcoholic, risk of perpetrating or being a victim of domestic violence, premature mortality in family members

Anda et al / Am J Prev Med 2010;39(1):93–98

What we know from research on animal models.

-Maternal care - quality and frequency but also consistency

-Benefits of novel experiences

-Neural basis of attachment in spite of abuse

-Deleterious effects of maternal anxiety

-Importance of intrauterine environment - metabolism, obesity

SPECIAL COMMUNICATION

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

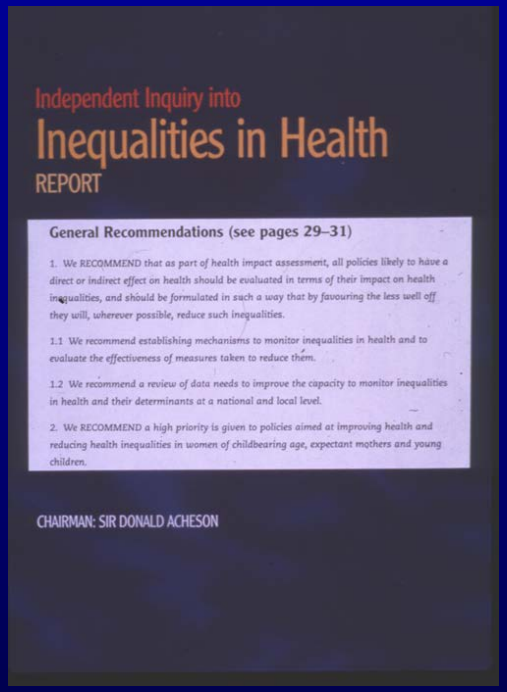
Building a New Framework for Health Promotion and Disease Prevention

Jack P. Shonkoff, MD
W. Thomas Boyce, MD
Bruce S. McEwen, PhD

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.

JAMA 2009;301(21):2252-2259 www.jama.com

All public policies are health policies



Independent Inquiry into

Inequalities in Health

REPORT

General Recommendations (see pages 29–31)

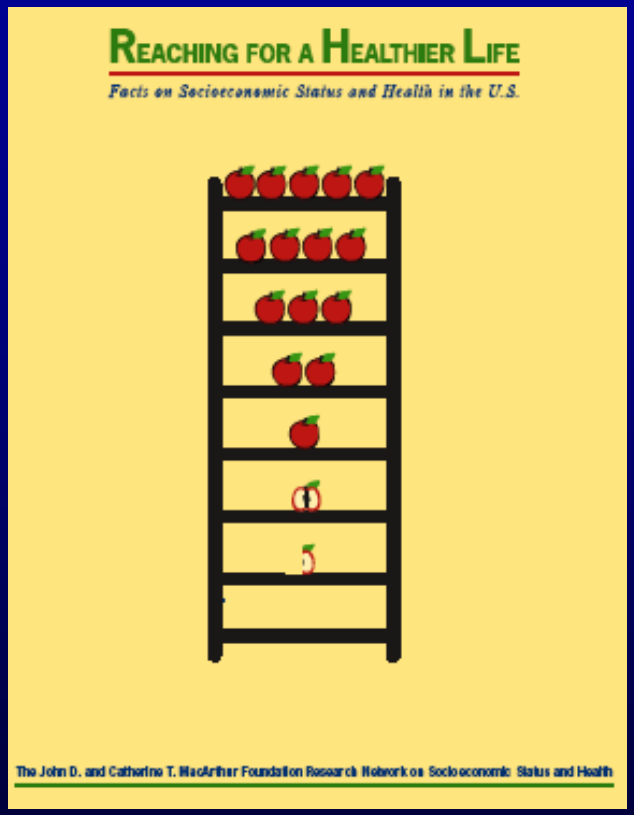
1. We RECOMMEND that as part of health impact assessment, all policies likely to have a direct or indirect effect on health should be evaluated in terms of their impact on health inequalities, and should be formulated in such a way that by favouring the less well off they will, wherever possible, reduce such inequalities.

1.1 We recommend establishing mechanisms to monitor inequalities in health and to evaluate the effectiveness of measures taken to reduce them.

1.2 We recommend a review of data needs to improve the capacity to monitor inequalities in health and their determinants at a national and local level.

2. We RECOMMEND a high priority is given to policies aimed at improving health and reducing health inequalities in women of childbearing age, expectant mothers and young children.

CHAIRMAN: SIR DONALD ACHESON



REACHING FOR A HEALTHIER LIFE

Facts on Socioeconomic Status and Health in the U.S.

The John D. and Catherine T. MacArthur Foundation Research Network on Socioeconomic Status and Health

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