Of Molecules and Mind:

Stress, the Individual and the Social Environment

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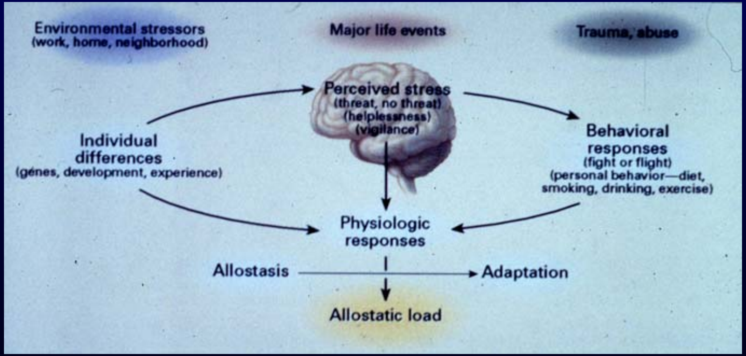
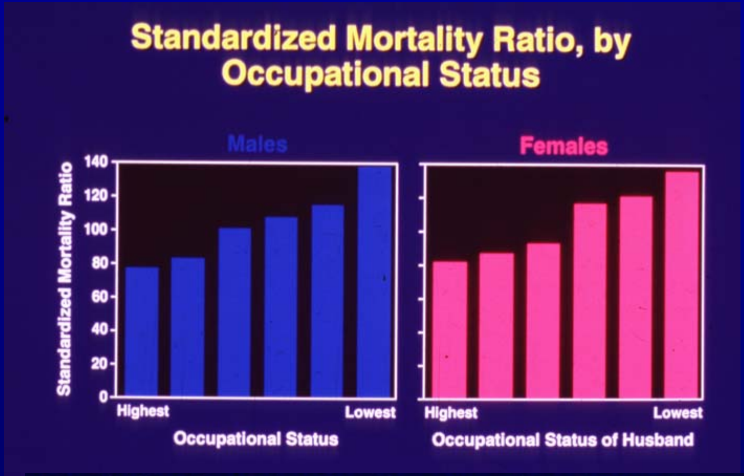
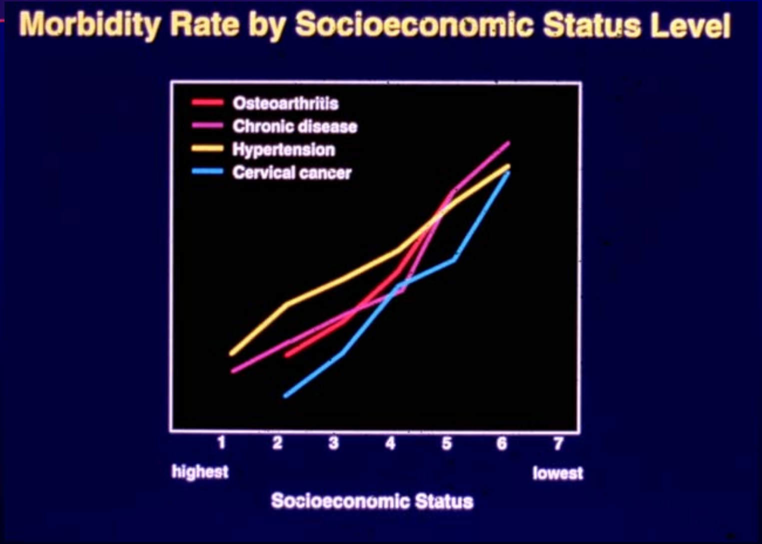


Income and Education: Effects on Longievity and Health



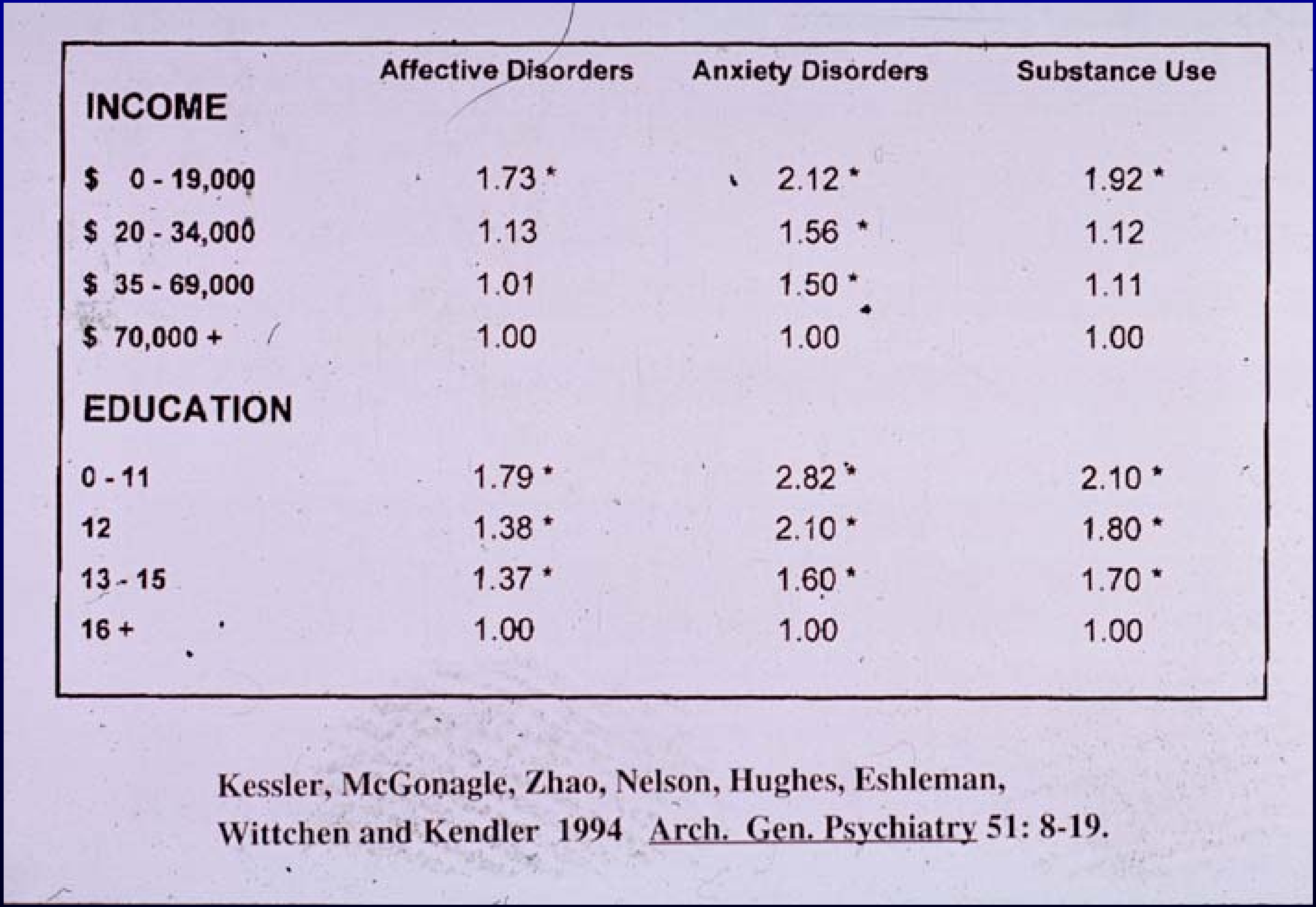
Standardized Mortality Ratio, by Occupational Status



Morbidity Rate by Socioeconomic Status Level

How does SES get "under the skin"?

Income and education: gradients of mental health



	Affective Disorders	Anxiety Disorders	Substance Use
INCOME			
$ 0 - 19,000	1.73 *	2.12 *	1.92 *
$ 20 - 34,000	1.13	1.56 *	1.12
$ 35 - 69,000	1.01	1.50 *	1.11
$ 70,000 +	1.00	1.00	1.00
EDUCATION			
0 - 11	1.79 *	2.82 *	2.10 *
12	1.38 *	2.10 *	1.80 *
13 - 15	1.37 *	1.60 *	1.70 *
16 +	1.00	1.00	1.00

Kessler, McGonagle, Zhao, Nelson, Hughes, Eshleman,
Wittchen and Kendler 1994 Arch. Gen. Psychiatry 51: 8-19.

How does SES get “under the skin”?

How do brain and body communicate?

Mind

"The seat of awareness, thought, volition and feeling" **Oxford English Dictionary**

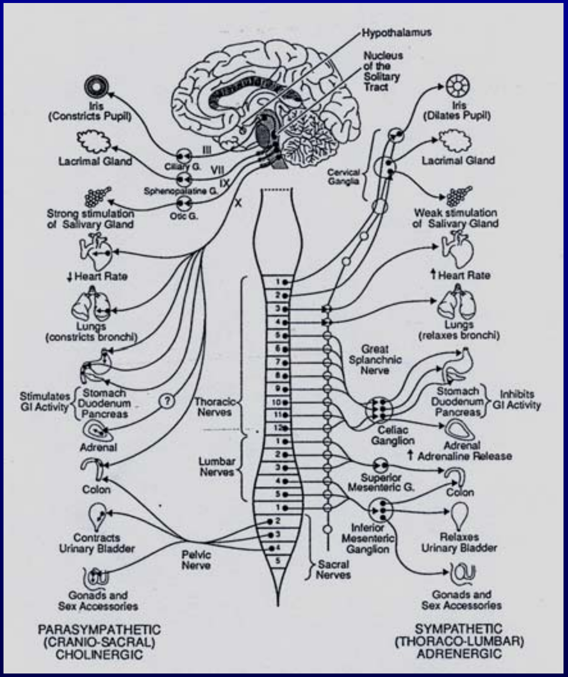
Feeling/emotion: perception of autonomic, visceral reactions to an event - Wm James Principles of Psychology

….reflects the physical and social environment.

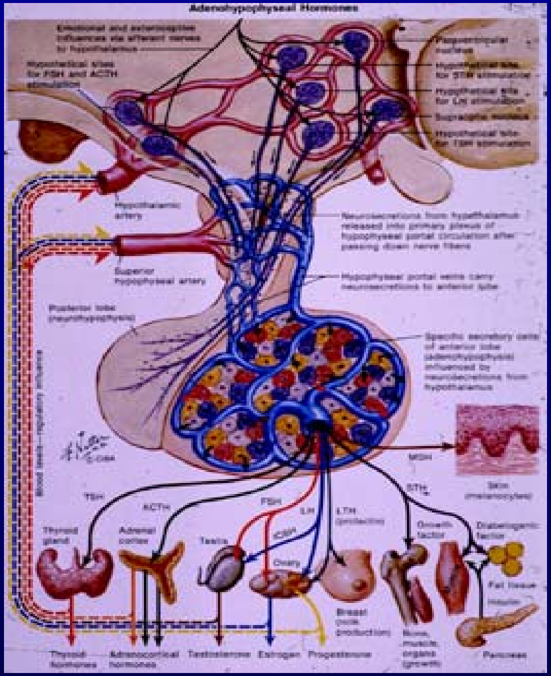
….involves the whole body (visceral sensations, pain, e.g., feeling sick or well).

….represents two-way communication via nerves, immune and neuroendocrine systems.

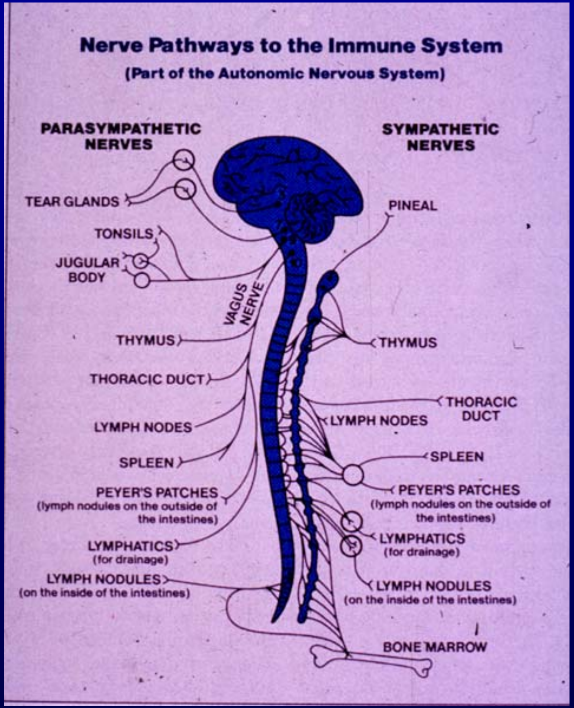
Three Major Systems for Brain - Body Communication



Autonomic nervous system

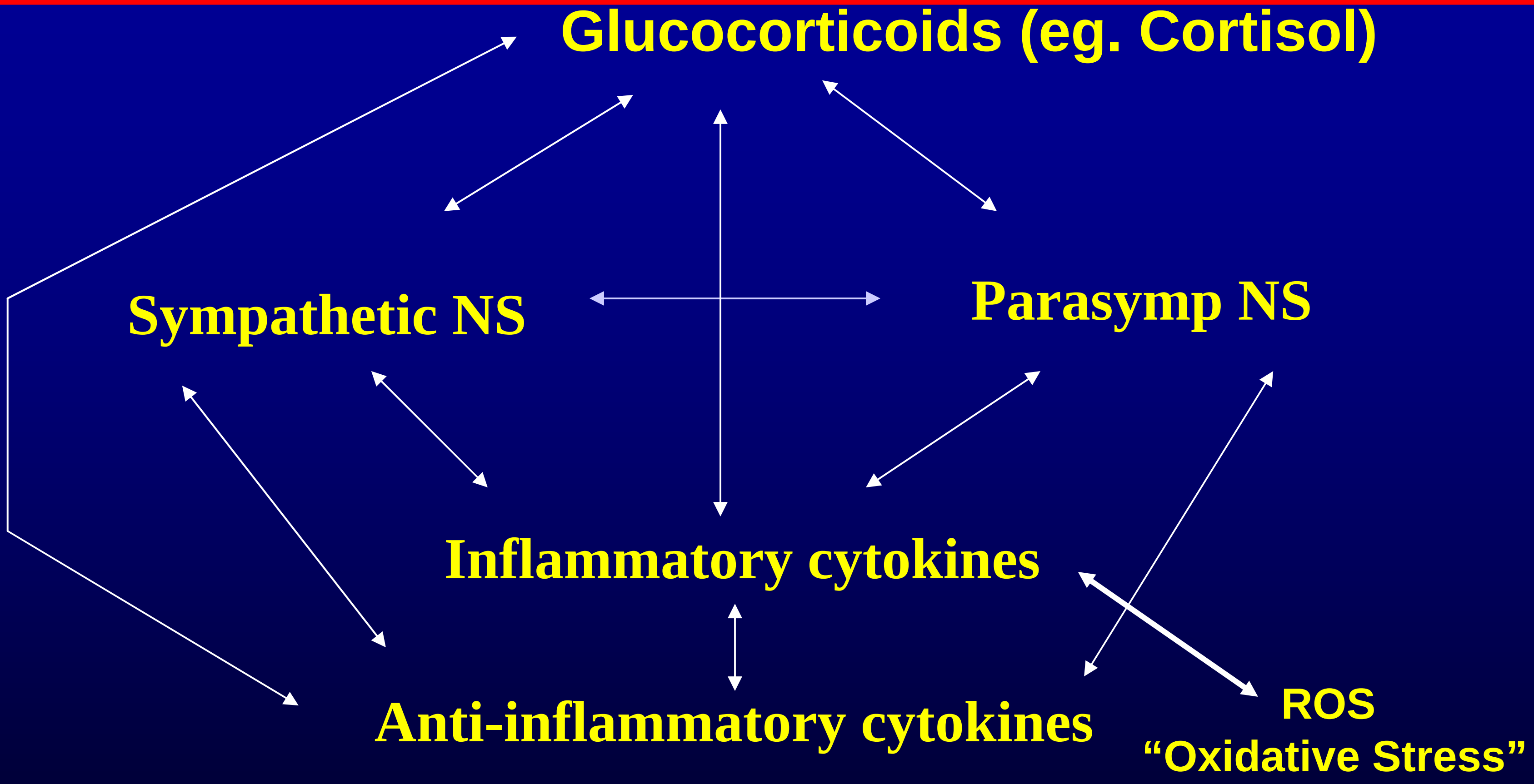


Neuroendocrine System



Immune System

Mediators of allostasis and allostatic load



Glucocorticoids (eg. Cortisol)

Sympathetic NS

Parasymp NS

Inflammatory cytokines

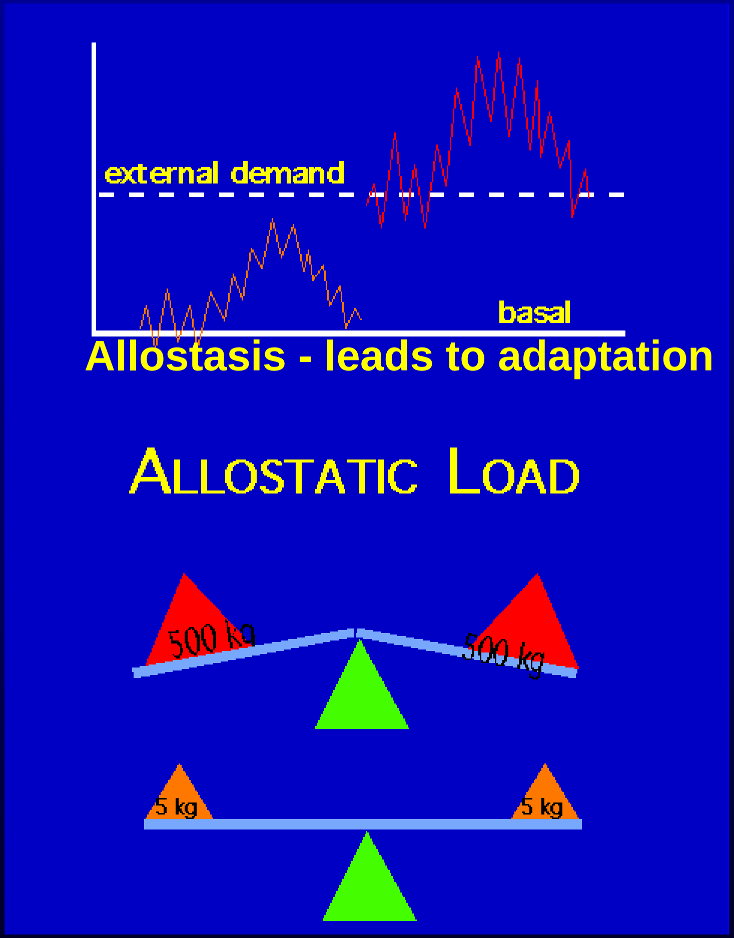
Anti-inflammatory cytokines

ROS
“Oxidative Stress”

Networks of systemic mediators of allostasis:

NON-LINEARITY!!

Stress - a challenge to the body
PROTECTION VS. DAMAGE

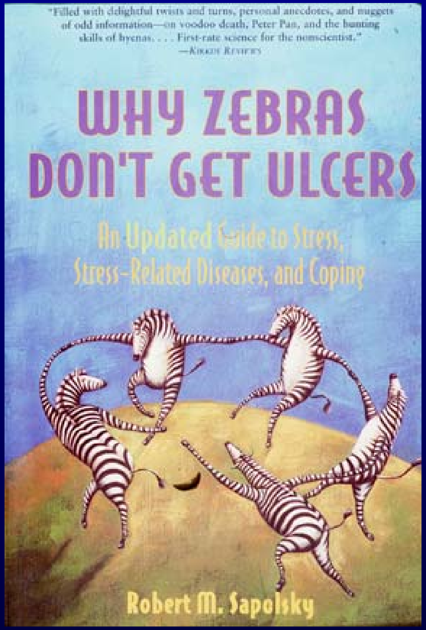


Allostasis - leads to adaptation

Sterling and Eyer 1988; McEwen and Stellar 1993

What is Stress?

Stressed vs. Stressed Out



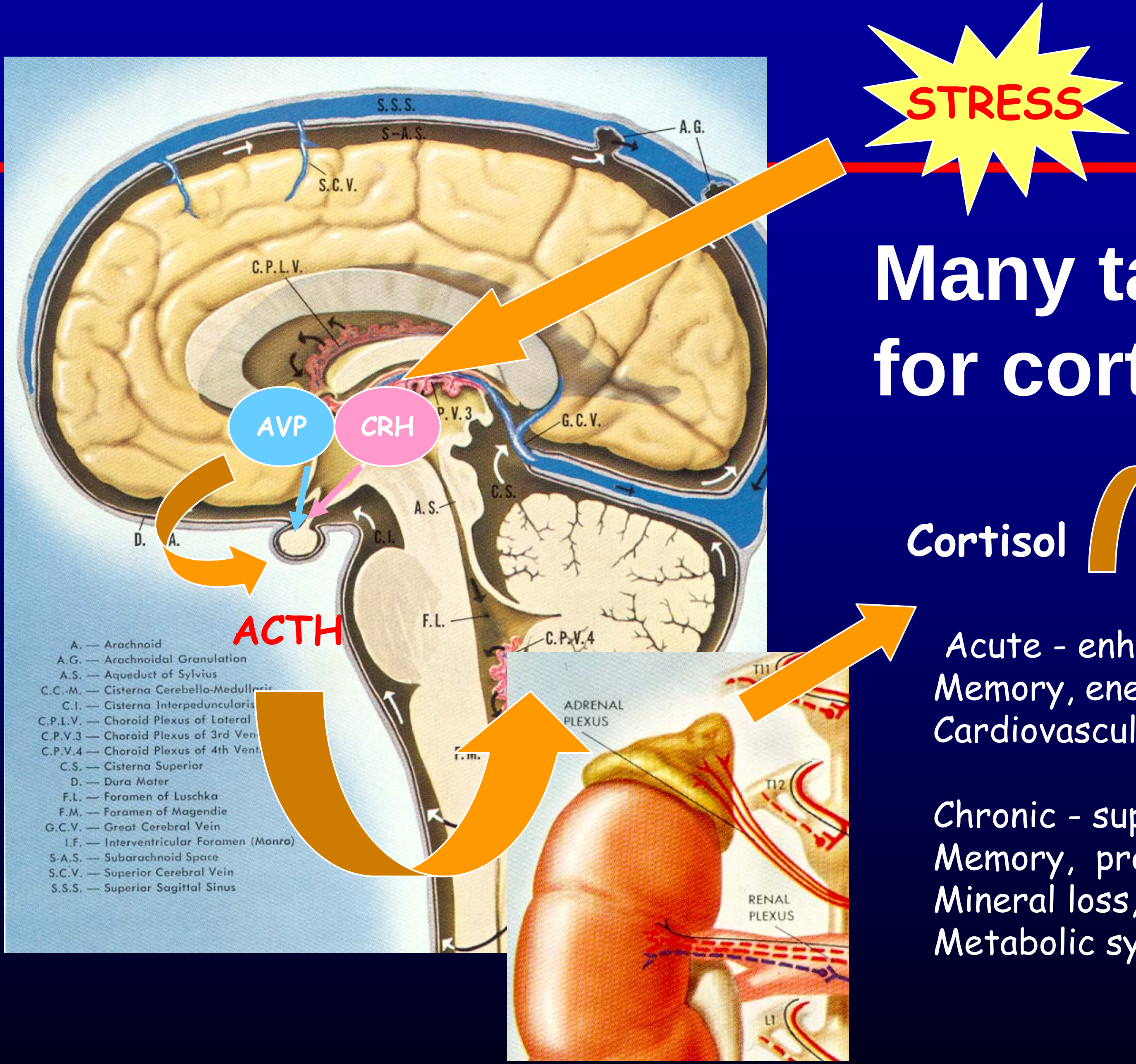
Fight or flight

Anxiety

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.

Health-risky behaviors

Many targets for cortisol

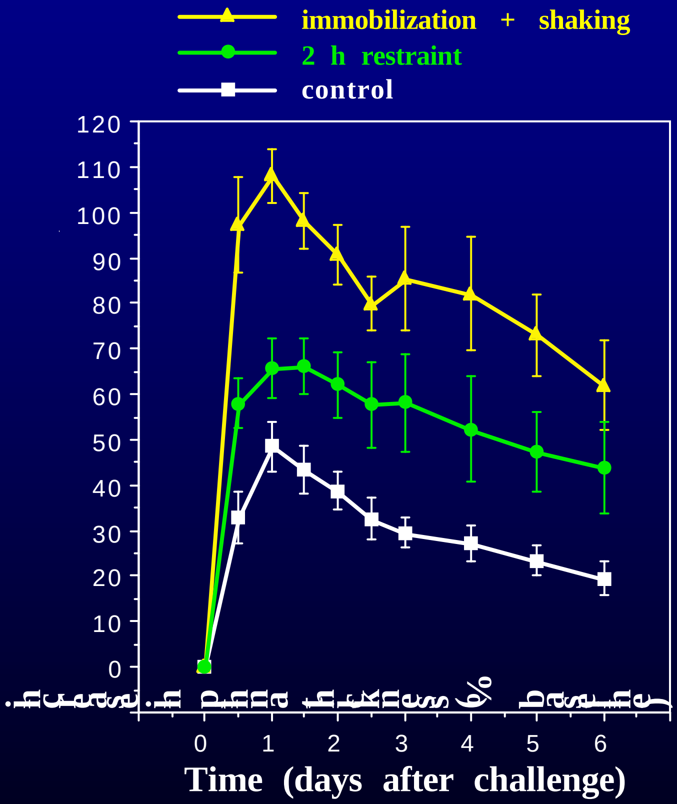


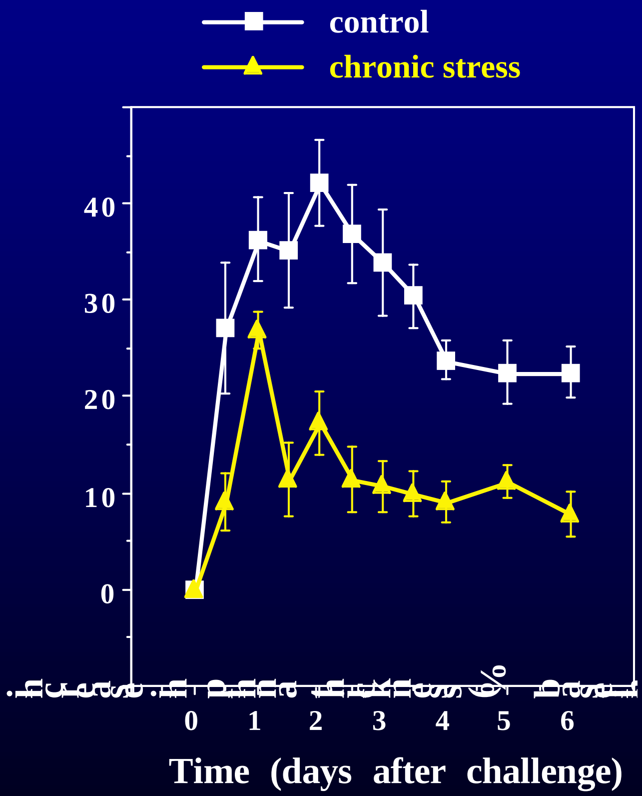
Cortisol

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

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

Acute versus Chronic Stress





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 atherosclerosis 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 load
Psychosocial stress is a major factor

Sleep deprivation as a chronic stressor:

Disturbed allostasis and resulting allostatic load

Increased blood pressure;
decreased parasympathetic tone.

Elevated evening cortisol, glucose, insulin.

Elevated inflammatory cytokines.

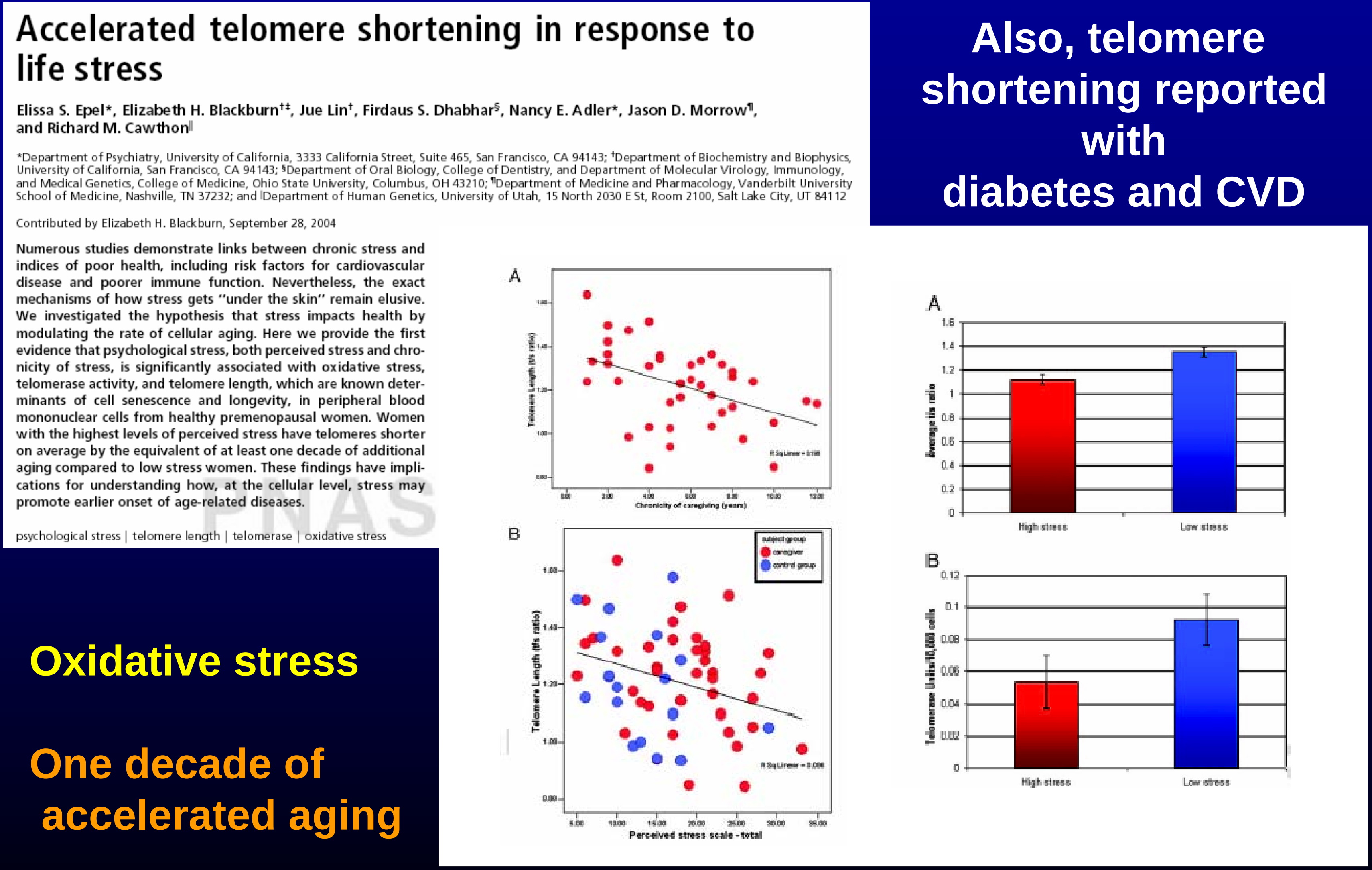
Increased appetite, which can increase 1-3
after over-eating.

Depressed mood.

Impaired cognitive function.

Caregiver Stress and Accelerated Aging: Telomere Length and Telomerase Activity

Also, telomere shortening reported with diabetes and CVD



Accelerated telomere shortening in response to life stress

Elissa S. Epel*, Elizabeth H. Blackburn[†‡], Jue Lin[†], Firdaus S. Dhabhar[§], Nancy E. Adler*, Jason D. Morrow[¶], and Richard M. Cawthon[‖]

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Contributed by Elizabeth H. Blackburn, September 28, 2004

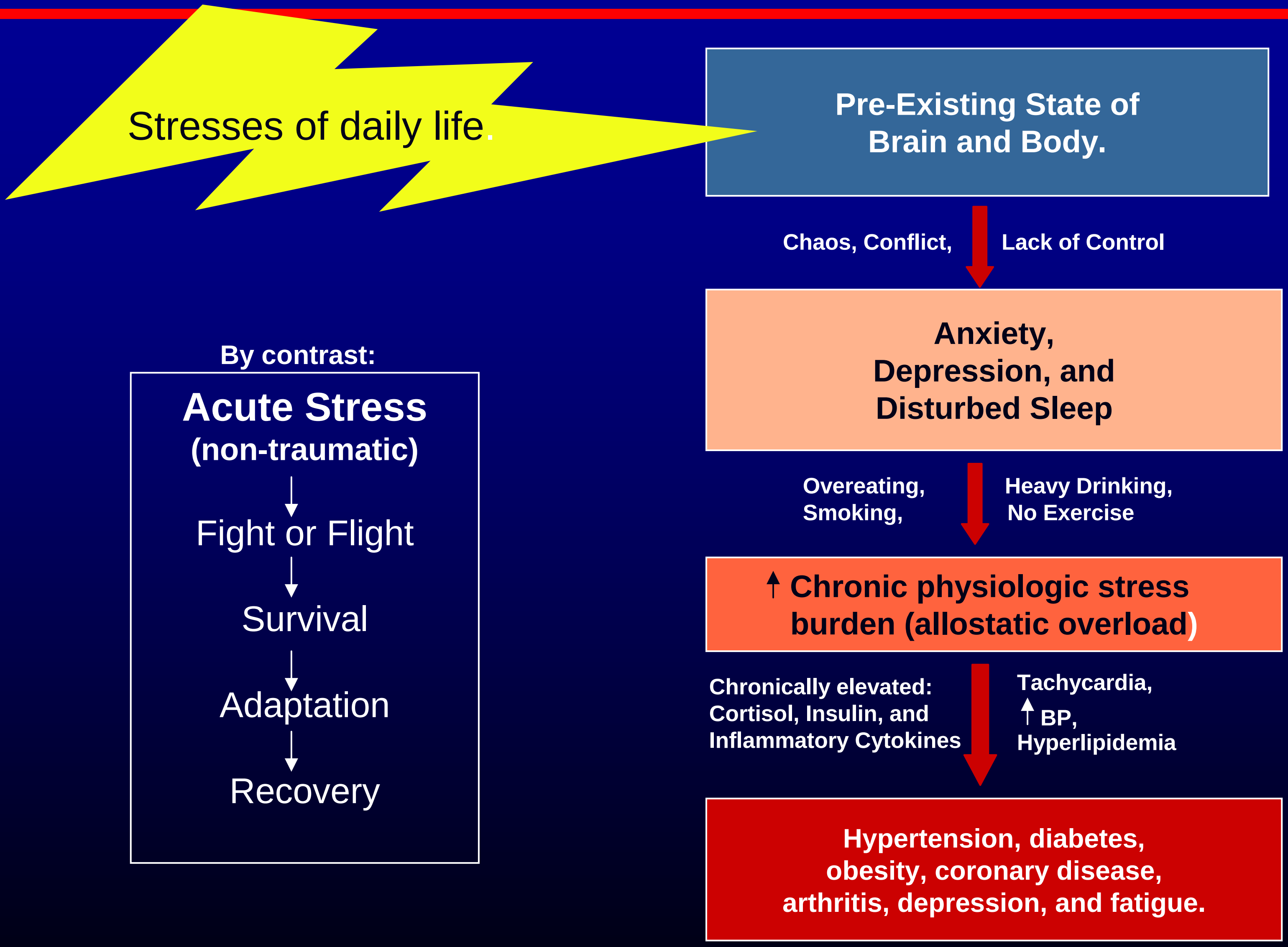
Numerous studies demonstrate links between chronic stress and indices of poor health, including risk factors for cardiovascular disease and poorer immune function. Nevertheless, the exact mechanisms of how stress gets "under the skin" remain elusive. We investigated the hypothesis that stress impacts health by modulating the rate of cellular aging. Here we provide the first evidence that psychological stress, both perceived stress and chronicity of stress, is significantly associated with oxidative stress, telomerase activity, and telomere length, which are known determinants of cell senescence and longevity, in peripheral blood mononuclear cells from healthy premenopausal women. Women with the highest levels of perceived stress have telomeres shorter on average by the equivalent of at least one decade of additional aging compared to low stress women. These findings have implications for understanding how, at the cellular level, stress may promote earlier onset of age-related diseases.

psychological stress | telomere length | telomerase | oxidative stress

Oxidative stress

One decade of accelerated aging

How Chronic Stress in Daily Life Affects Health and Behavior



Stresses of daily life.

Pre-Existing State of Brain and Body.

Chaos, Conflict, ↓ **Lack of Control**

**Anxiety,
Depression, and
Disturbed Sleep**

**Overeating,
Smoking,** ↓ **Heavy Drinking,
No Exercise**

↑ Chronic physiologic stress burden (allostatic overload)

**Chronically elevated:
Cortisol, Insulin, and
Inflammatory Cytokines** ↓ **Tachycardia,
↑ BP,
Hyperlipidemia**

**Hypertension, diabetes,
obesity, coronary disease,
arthritis, depression, and fatigue.**

By contrast:

**Acute Stress
(non-traumatic)**

↓

Fight or Flight

↓

Survival

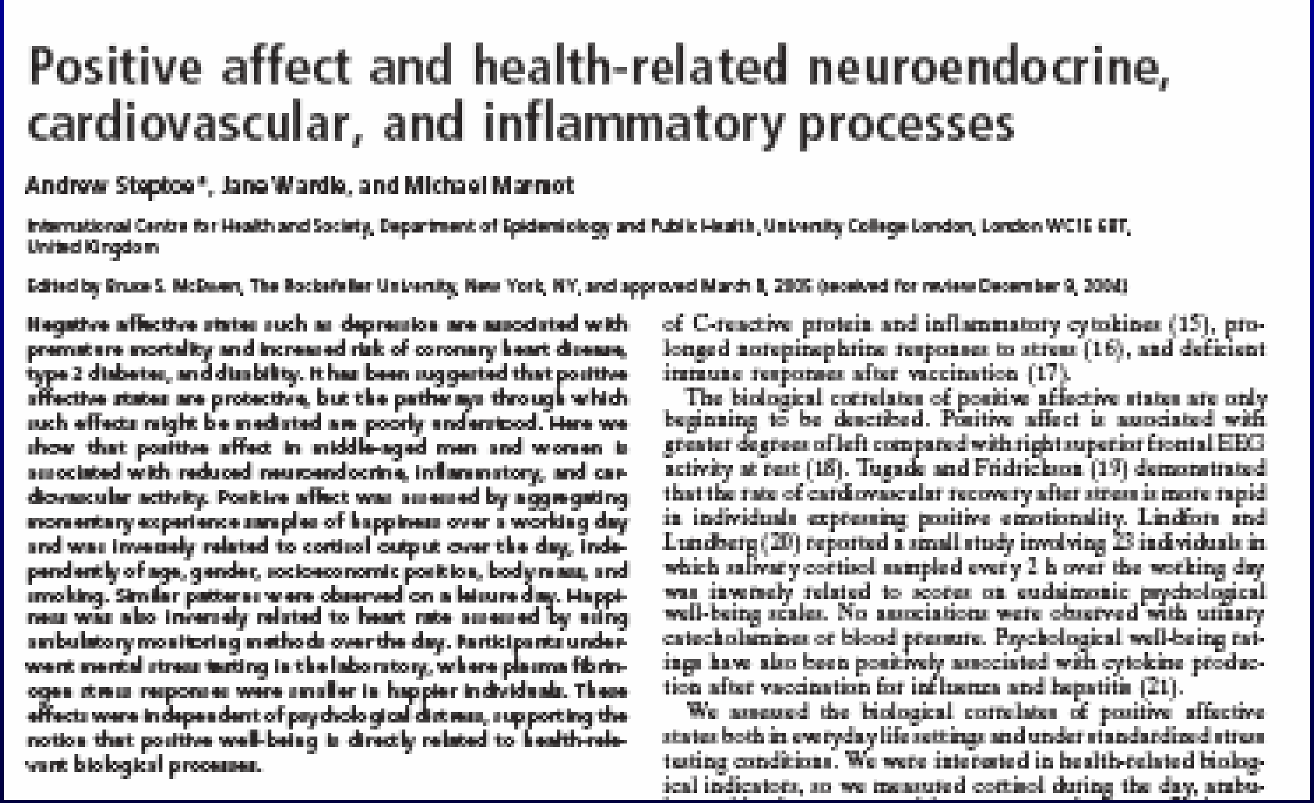
↓

Adaptation

↓

Recovery

What is the physiology of positive affect?



Positive affect and health-related neuroendocrine, cardiovascular, and inflammatory processes

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Edited by Bruce S. McEwen, The Rockefeller University, New York, NY, and approved March 8, 2005 (received for review December 9, 2004)

Negative affective states such as depression are associated with premature mortality and increased risk of coronary heart disease, type 2 diabetes, and disability. It has been suggested that positive affective states are protective, but the pathways through which such effects might be mediated are poorly understood. Here we show that positive affect in middle-aged men and women is associated with reduced neuroendocrine, inflammatory, and cardiovascular activity. Positive affect was assessed by aggregating momentary experience samples of happiness over a working day and was inversely related to cortisol output over the day, independently of age, gender, socioeconomic position, body mass, and smoking. Similar patterns were observed on a leisure day. Happiness was also inversely related to heart rate assessed by using ambulatory monitoring methods over the day. Participants underwent mental stress testing in the laboratory, where plasma fibrinogen stress responses were smaller in happier individuals. These effects were independent of psychological distress, supporting the notion that positive well-being is directly related to health-relevant biological processes.

of C-reactive protein and inflammatory cytokines (15), prolonged norepinephrine responses to stress (16), and deficient immune responses after vaccination (17).

The biological correlates of positive affective states are only beginning to be described. Positive affect is associated with greater degrees of left compared with right superior frontal EEG activity at rest (18). Tugade and Fredrickson (19) demonstrated that the rate of cardiovascular recovery after stress is more rapid in individuals expressing positive emotionality. Lindfors and Lundberg (20) reported a small study involving 23 individuals in which salivary cortisol sampled every 2 h over the working day was inversely related to scores on eudaimonic psychological well-being scales. No associations were observed with urinary catecholamines or blood pressure. Psychological well-being ratings have also been positively associated with cytokine production after vaccination for influenza and hepatitis (21).

We assessed the biological correlates of positive affective states both in everyday life settings and under standardized stress testing conditions. We were interested in health-related biological indicators, so we measured cortisol during the day, ambu-

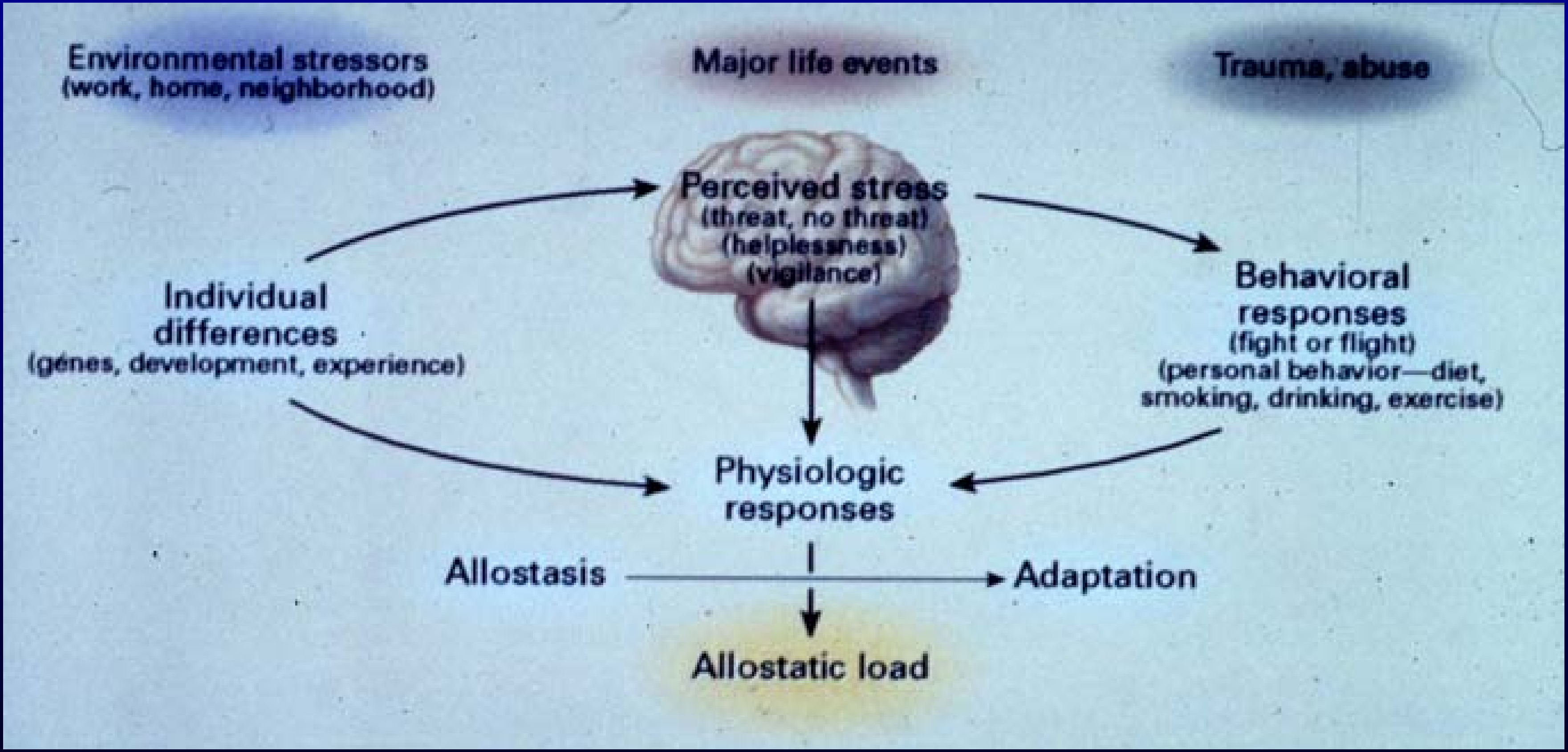
Lower cortisol, lower heart rate,
lesser fibrinogen change to stressor

“Positive health” - more than absence of allostatic load?

How does stress affect the brain?

STRESS

Central Importance of the Brain



Environmental stressors
(work, home, neighborhood)

Major life events

Trauma, abuse

Perceived stress
(threat, no threat)
(helplessness)
(vigilance)

Individual differences
(genes, development, experience)

Behavioral responses
(fight or flight)
(personal behavior—diet, smoking, drinking, exercise)

Physiologic responses

Allostasis

Adaptation

Allostatic load

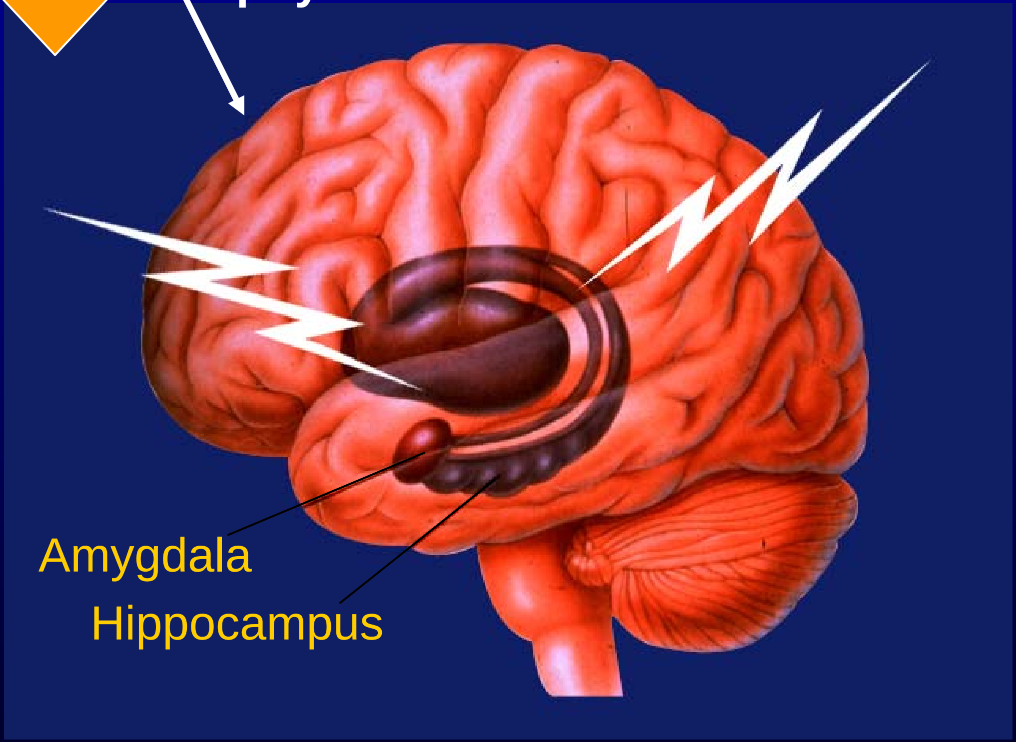
The Human Brain Under Stress:
key brain regions

↓

Prefrontal cortex

Executive function, working memory

Atrophy



↓

Hippocampus

Contextual, episodic, spatial memory

Atrophy

↑

Amygdala

Emotion. fear, anxiety

Hypertrophy.

later atrophy

Repeated stress:

effects on behavior and structural remodeling

Resident-intruder model:
ree shrew (E. Fuchs)

Behavioral changes:

Impaired spatial learning.

Increased aggression.

Increased fear

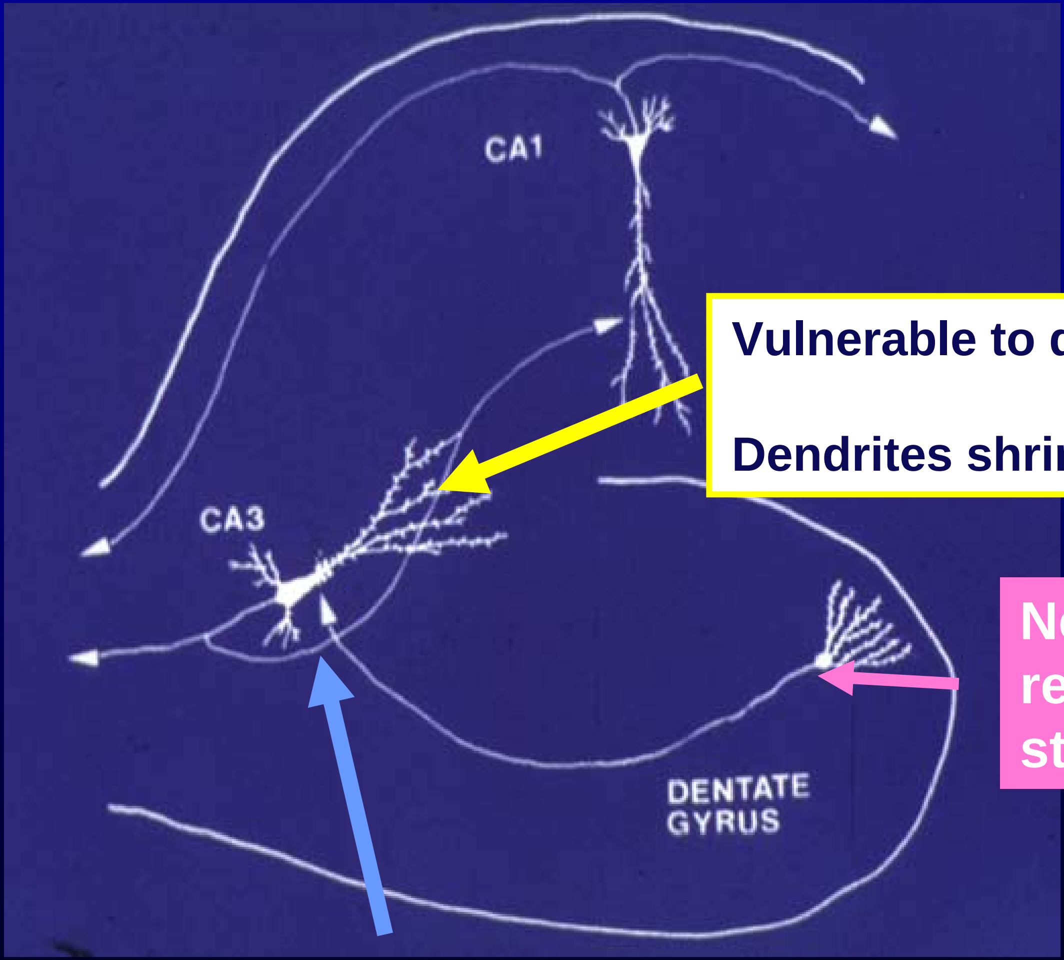
Behavioral depression
Learned helplessness

Attention set shifting impairment

Structural remodeling

Reduced DG neurogenesis and volume.
Shortened dendrites - CA3
Shortened dendrites - PFC
Expanded dendrites - OFC
Increased dendrites - BLA

Dentate gyrus - CA3:
plasticity and vulnerability



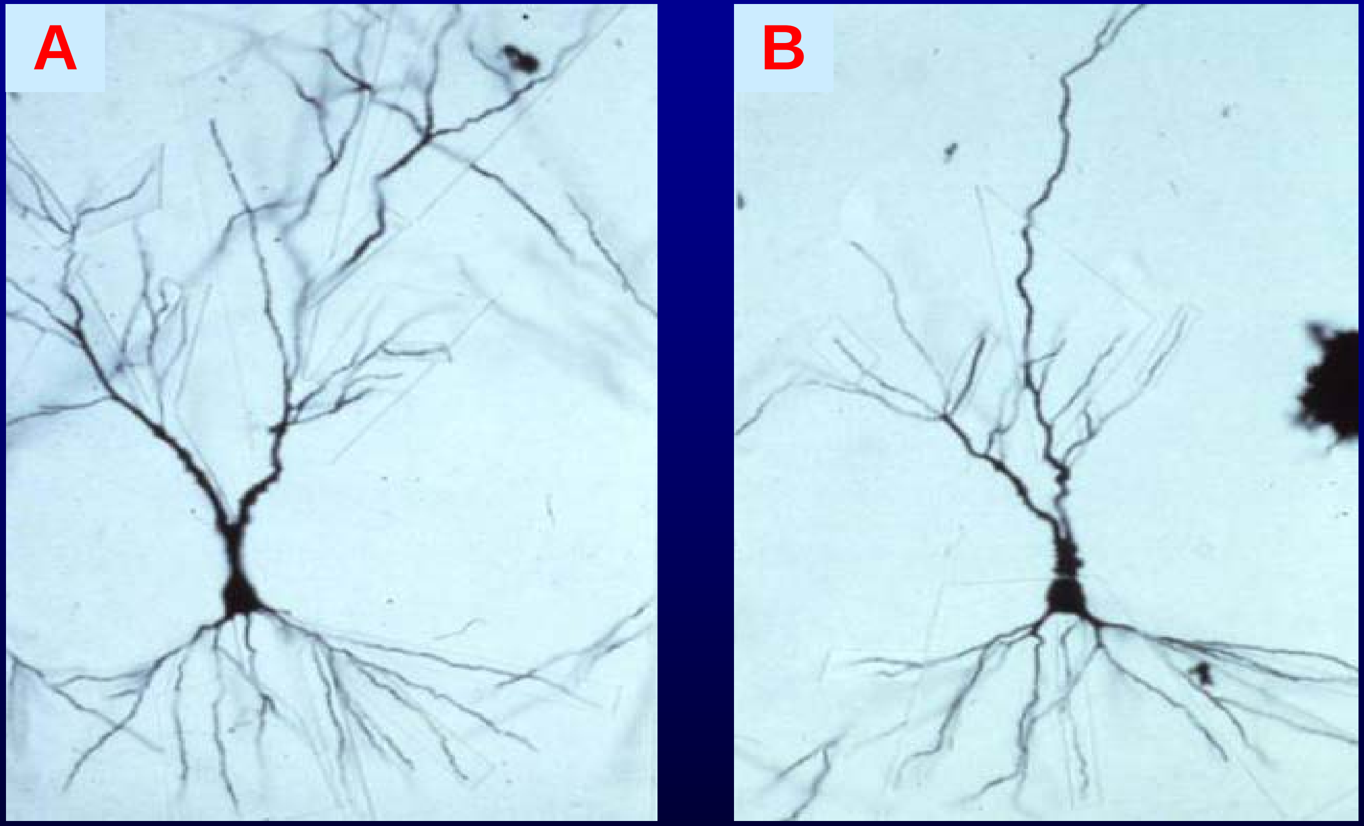
Vulnerable to damage.

Dendrites shrink with stress

Neurogenesis reduced by stress

Mossy fiber terminals:
glutamate release

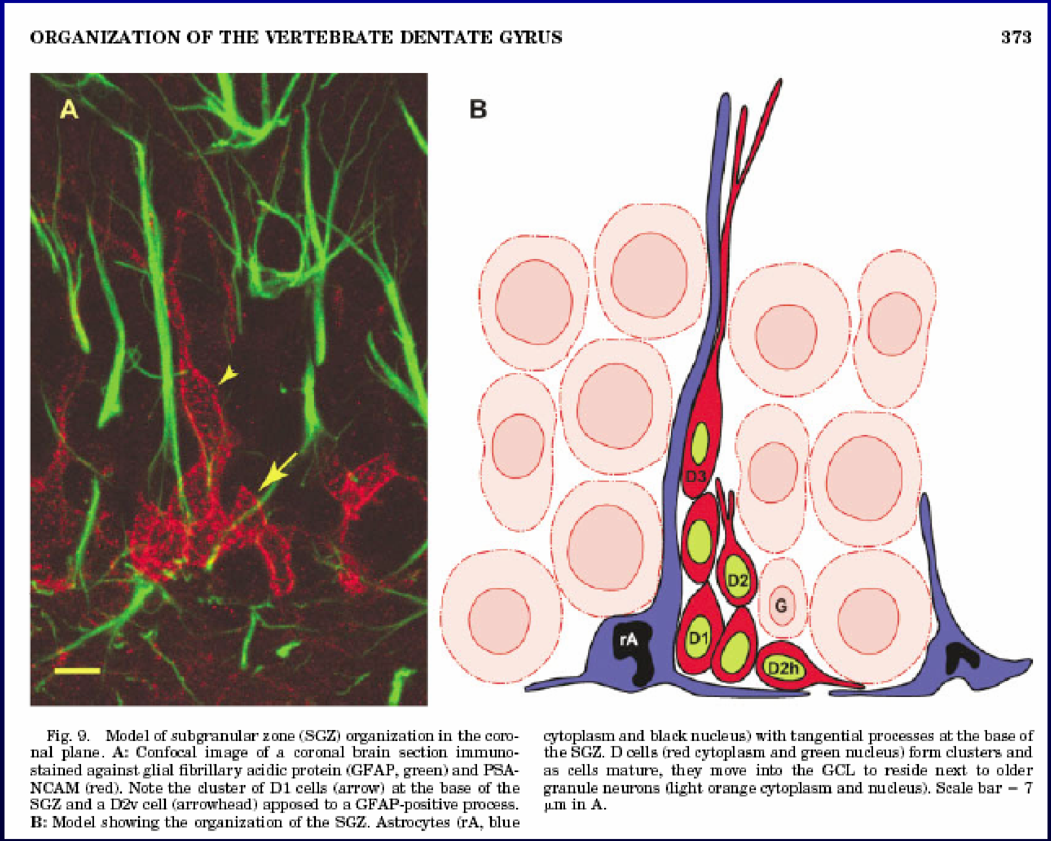
Hippocampus:
Dendritic atrophy after stress



Rat hippocampal neuron before (A)
and after (B) 3-week repeated stress

McEwen, 1999

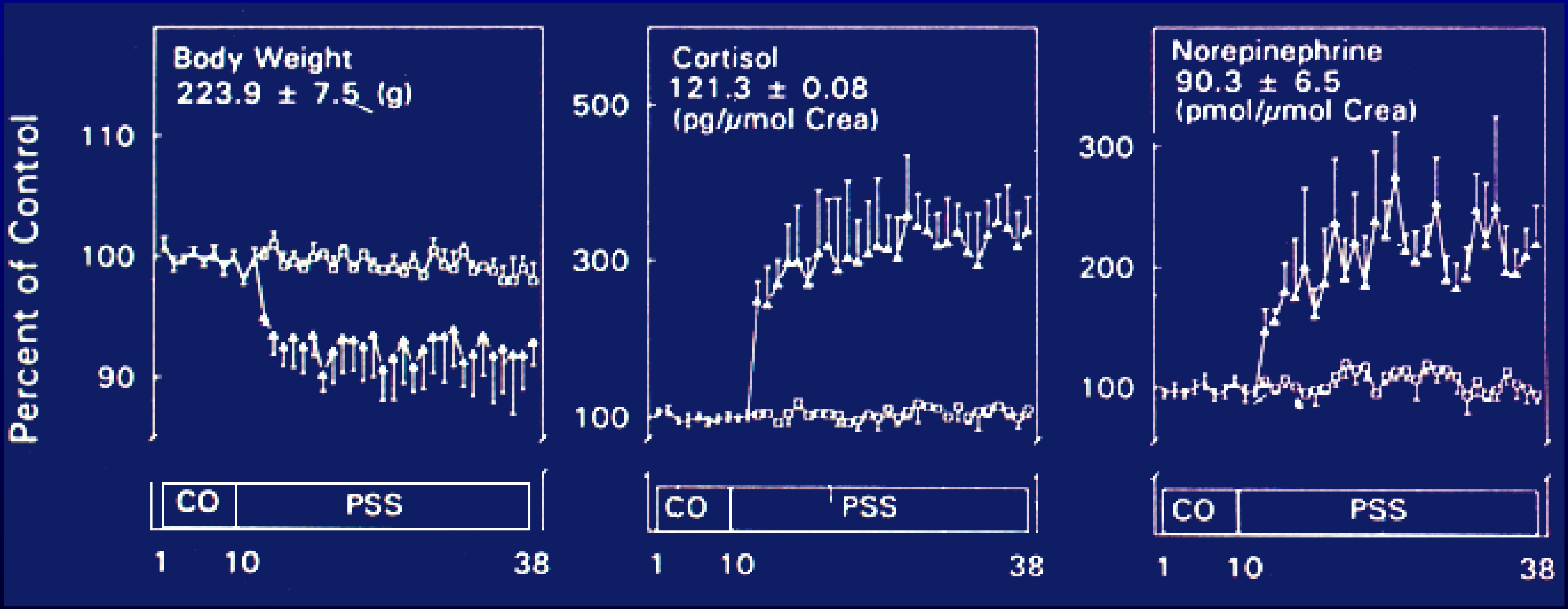
Neurogenesis in hippocampus



ORGANIZATION OF THE VERTEBRATE DENTATE GYRUS 373

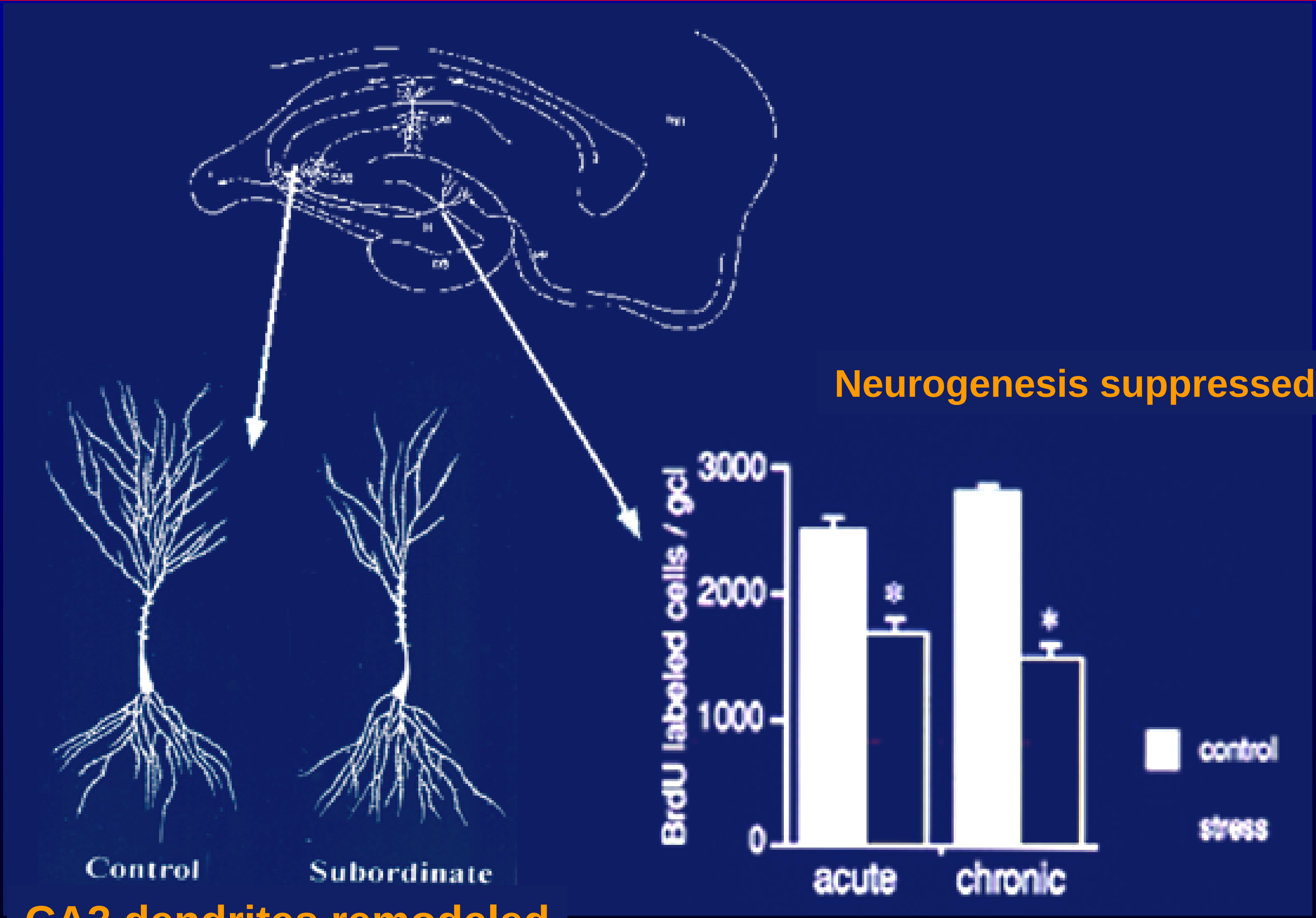
Fig. 9. Model of subgranular zone (SGZ) organization in the coronal plane. **A:** Confocal image of a coronal brain section immunostained against glial fibrillary acidic protein (GFAP, green) and PSA-NCAM (red). Note the cluster of D1 cells (arrow) at the base of the SGZ and a D2v cell (arrowhead) apposed to a GFAP-positive process. **B:** Model showing the organization of the SGZ. Astrocytes (rA, blue cytoplasm and black nucleus) with tangential processes at the base of the SGZ. D cells (red cytoplasm and green nucleus) form clusters and as cells mature, they move into the GCL to reside next to older granule neurons (light orange cytoplasm and nucleus). Scale bar = 7 μm in A.

Exercise increase neurogenesis; stress suppresses neurogenesis
Antidepressants increase neurogenesis



28 Days of Resident-Intruder Stress

Chronic Confrontation with Dominant Causes Remodeling of Hippocampus



Neurogenesis suppressed

CA3 dendrites remodeled

Prolonged depression: hippocampal atrophy

Sheline et al. • Hippocampal Volume Loss with Depression But Not Age

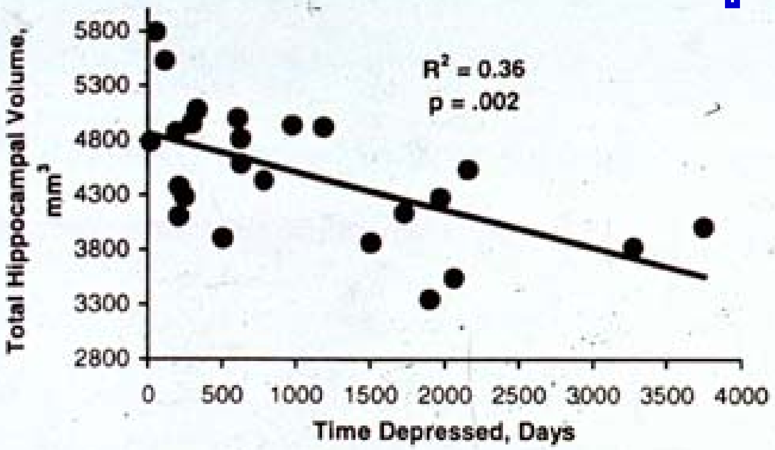


Figure 3. Correlation between duration of depression and hippocampal volume. The Pearson correlation between cumulative lifetime total days of major depression was derived from the Diagnostic Interview for Genetic Studies using the Post Life Charting Method (Post et al., 1988) and the total hippocampal gray matter volumes.

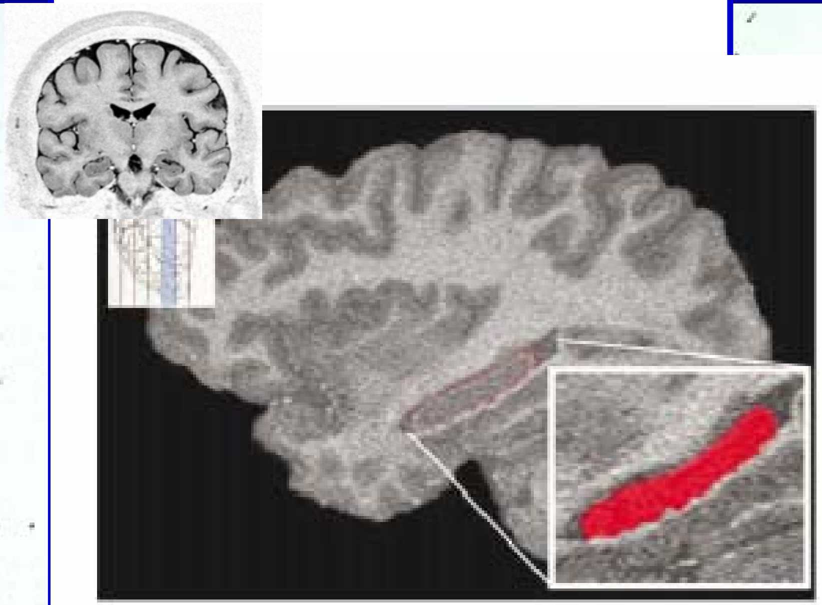
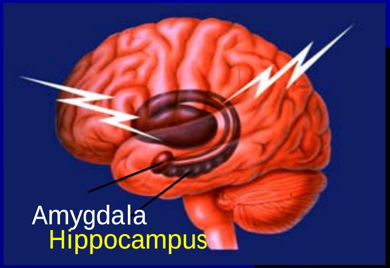
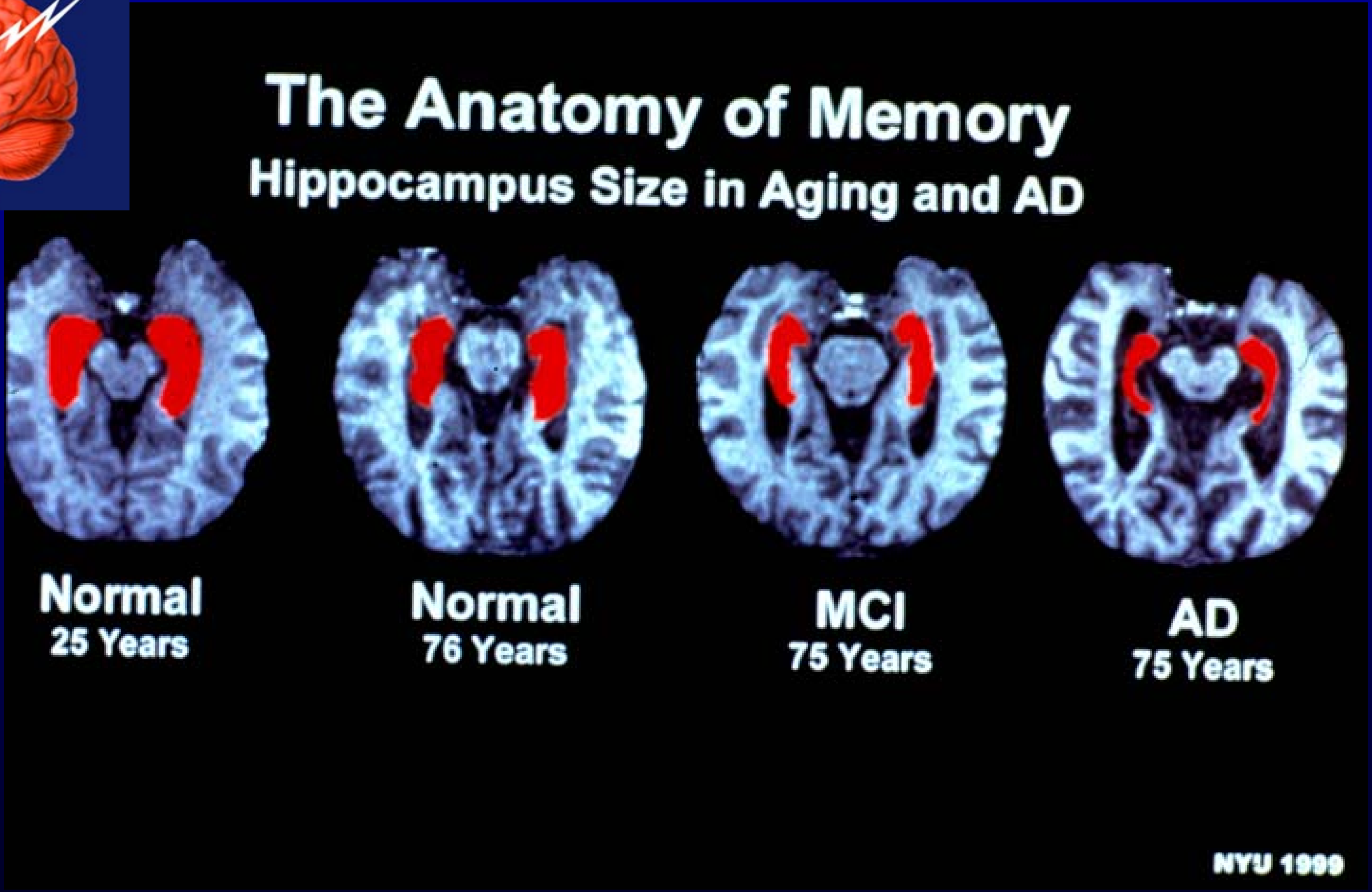


Fig. 1. Saggital MRI of the hippocampus. The HC gray matter (outlined in red) was selected to be measured. Included were the cornu ammonis, dentate gyrus, and subiculum. Excluded were the indusium griseum, amygdalar nuclei, alveus, fimbria, and surrounding white-matter structures.

Why happens during aging?

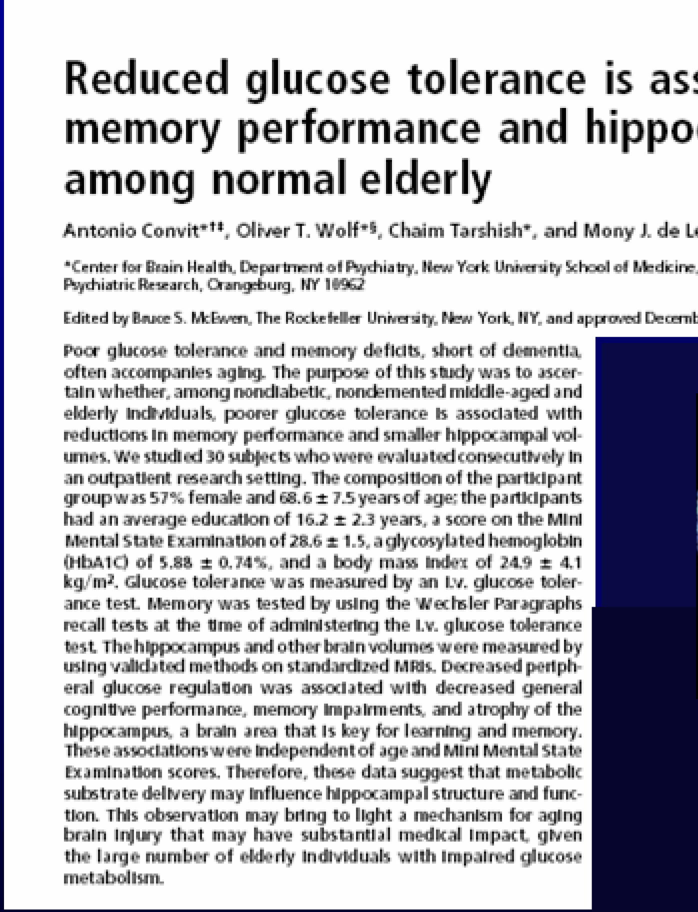



The Anatomy of Memory

Hippocampus Size in Aging and AD

A Shrinking Hippocampus

MILD COGNITIVE IMPAIRMENT (MCI) and GLUCOSE TOLERANCE



Reduced glucose tolerance is associated with poor memory performance and hippocampal atrophy among normal elderly

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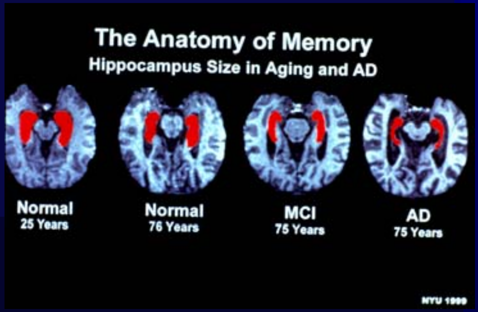
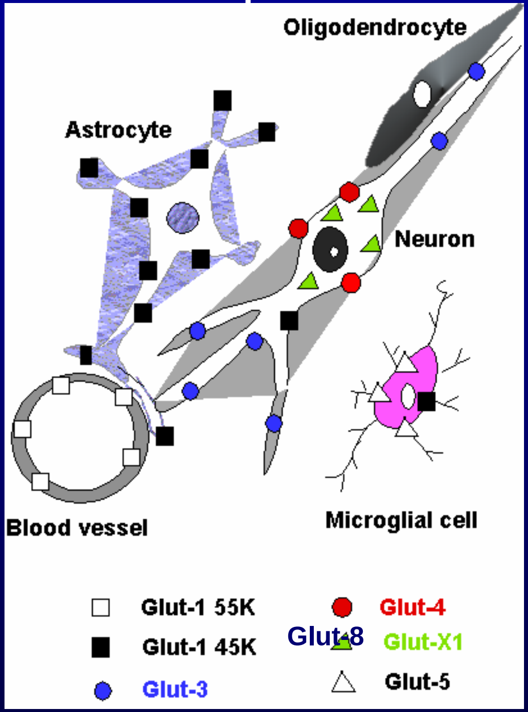
*Center for Brain Health, Department of Psychiatry, New York University School of Medicine, New York, NY 10016; and †Nathan Kline Institute for Psychiatric Research, Orangeburg, NY 10962

Edited by Bruce S. McEwen, The Rockefeller University, New York, NY, and approved December 17, 2002 (received for review October 8, 2002)

Poor glucose tolerance and memory deficits, short of dementia, often accompanies aging. The purpose of this study was to ascertain whether, among nondiabetic, nondemented middle-aged and elderly individuals, poorer glucose tolerance is associated with reductions in memory performance and smaller hippocampal volumes. We studied 30 subjects who were evaluated consecutively in an outpatient research setting. The composition of the participant group was 57% female and 68.6 ± 7.5 years of age; the participants had an average education of 16.2 ± 2.3 years, a score on the Mini Mental State Examination of 28.6 ± 1.5, a glycosylated hemoglobin (HbA1C) of 5.88 ± 0.74%, and a body mass index of 24.9 ± 4.1 kg/m². Glucose tolerance was measured by an i.v. glucose tolerance test. Memory was tested by using the Wechsler Paragraphs recall tests at the time of administering the i.v. glucose tolerance test. The hippocampus and other brain volumes were measured by using validated methods on standardized MRIs. Decreased peripheral glucose regulation was associated with decreased general cognitive performance, memory impairments, and atrophy of the hippocampus, a brain area that is key for learning and memory. These associations were independent of age and Mini Mental State Examination scores. Therefore, these data suggest that metabolic substrate delivery may influence hippocampal structure and function. This observation may bring to light a mechanism for aging brain injury that may have substantial medical impact, given the large number of elderly individuals with impaired glucose metabolism.



Glucose transporters in brain



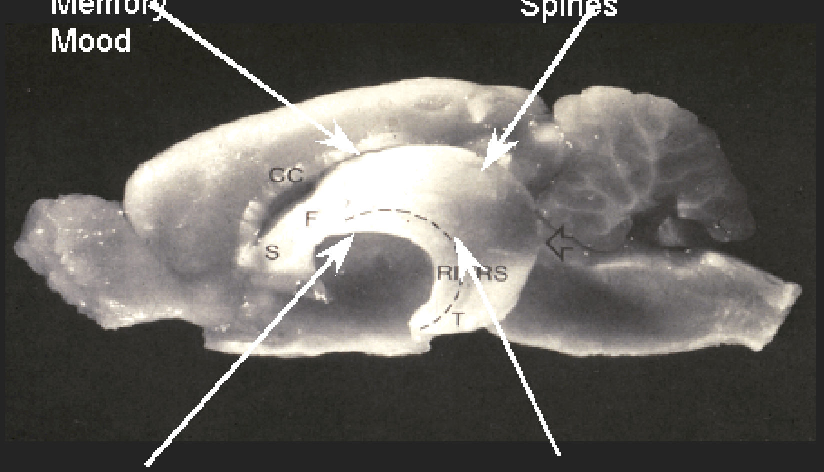
MCI **associated with rising cortisol**

MCI **associated with glucose intolerance**

MCI **- increased risk for Alzheimer’s**

Diabetes (type 2) **- increased risk for Alzheimer’s**

Protein/peptide hormones enter and affect the brain



Leptin
16kD
Excitability
Memory
Mood

Ghrelin
3.5 **kD**
Memory
Spines

IGF-1
7.6kD
Neurogenesis
Neuroprotection

Insulin
5.8kD
Glucose transporter
Neuroprotection

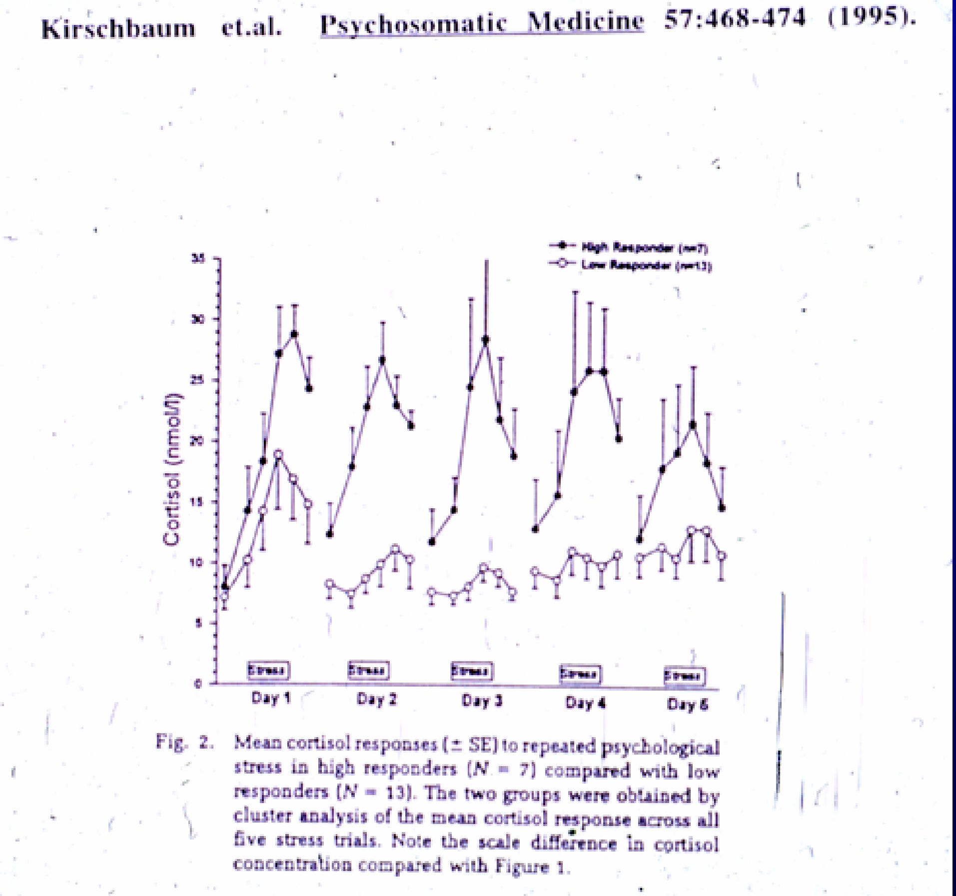
Is there a neurobiology of self esteem?

Poor HPA shut-off after stress

and

a smaller

hippocampus



Kirschbaum et.al. Psychosomatic Medicine 57:468-474 (1995).

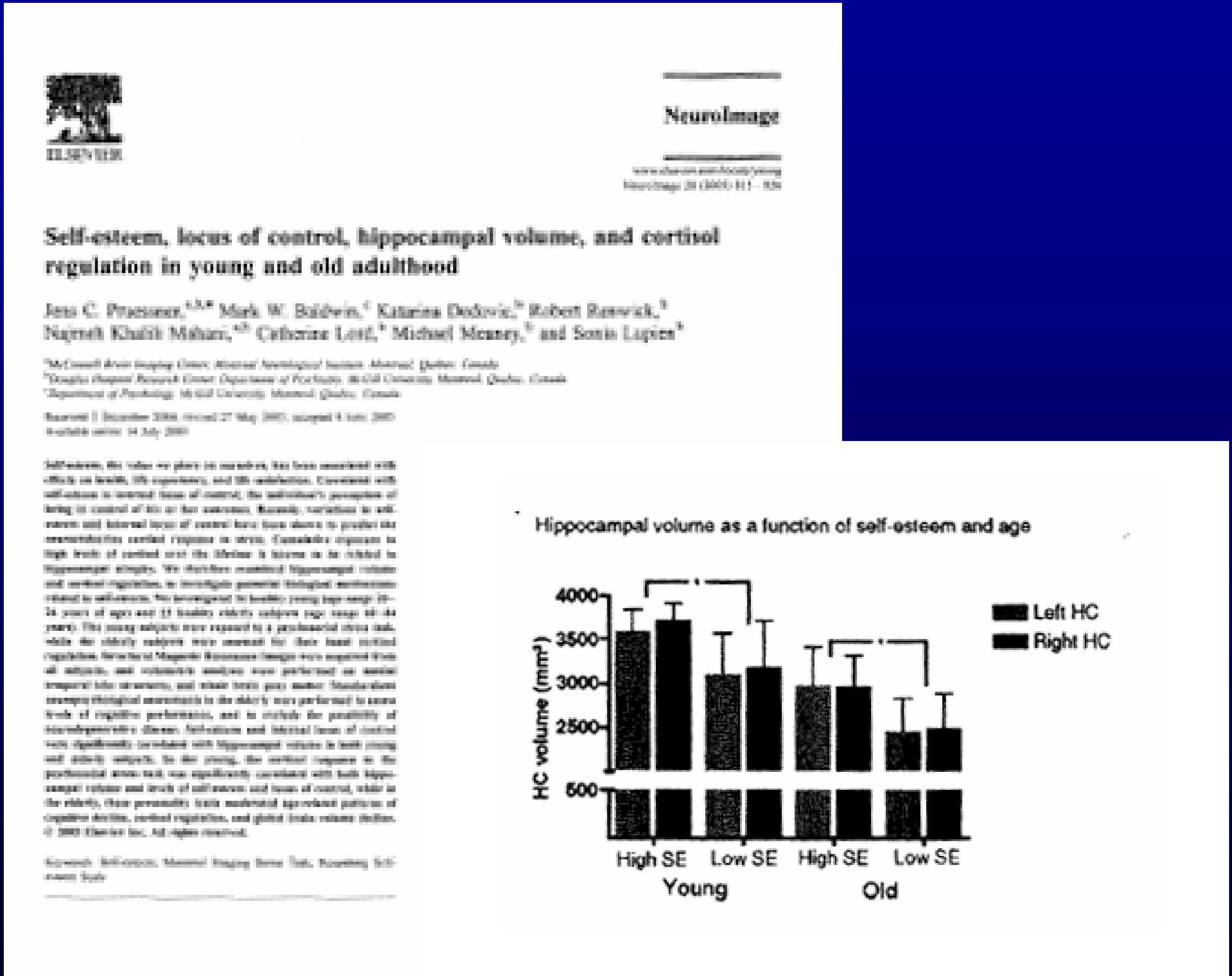
Fig. 2. Mean cortisol responses (± SE) to repeated psychological stress in high responders ($N = 7$) compared with low responders ($N = 13$). The two groups were obtained by cluster analysis of the mean cortisol response across all five stress trials. Note the scale difference in cortisol concentration compared with Figure 1.

<u>Glucocorticoid Cascade Hypothesis</u>

Vicious cycle and hippocampal shrinkage

Failure to habituate HPA response to public speaking

Is there a neurobiology of self esteem?



NeuroImage

Self-esteem, locus of control, hippocampal volume, and cortisol regulation in young and old adulthood

Jens C. Pruessner,[a,b,*] Mark W. Baldwin,[c] Katarina Dedovic,[b] Robert Renwick,[b] Najmeh Khalili Mahani,[a,b] Catherine Lord,[b] Michael Meaney,[b] and Sonia Lupien[b]

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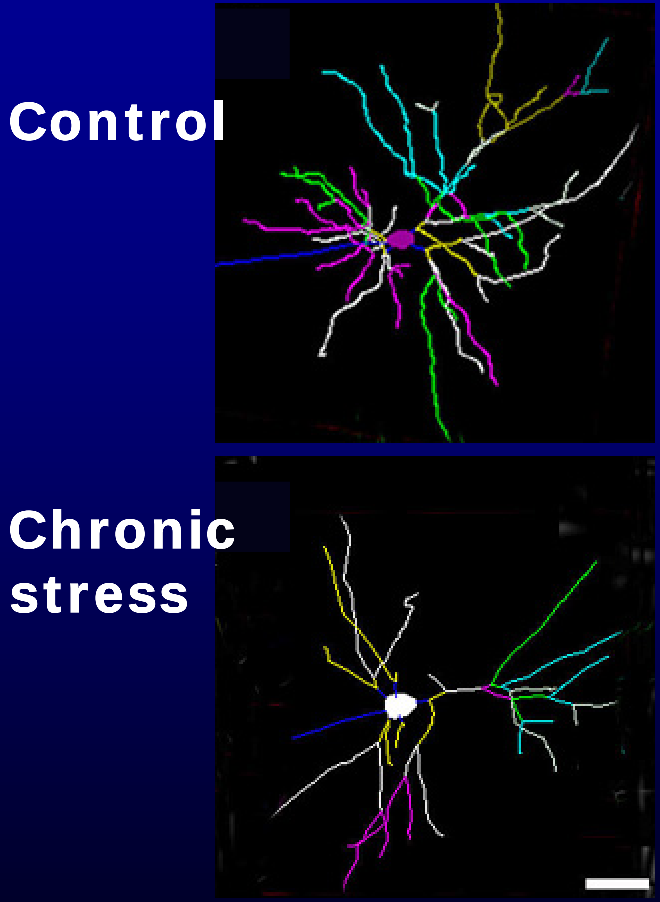
[c] Department of Psychology, McGill University, Montreal, Quebec, Canada

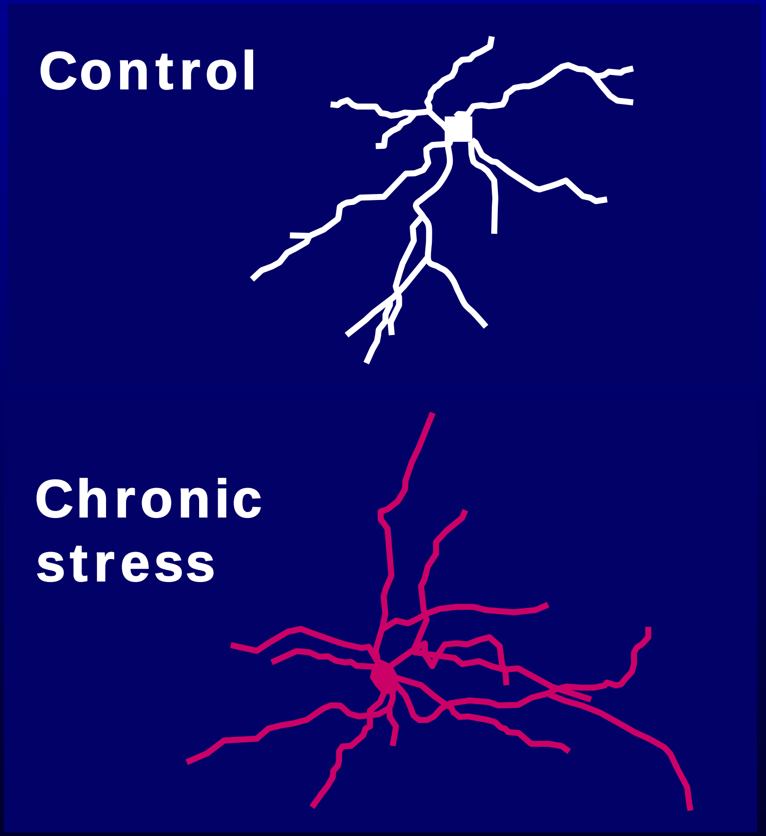
Hippocampal volume as a function of self-esteem and age

Stress causes neurons to shrink or grow

….but not necessarily to die

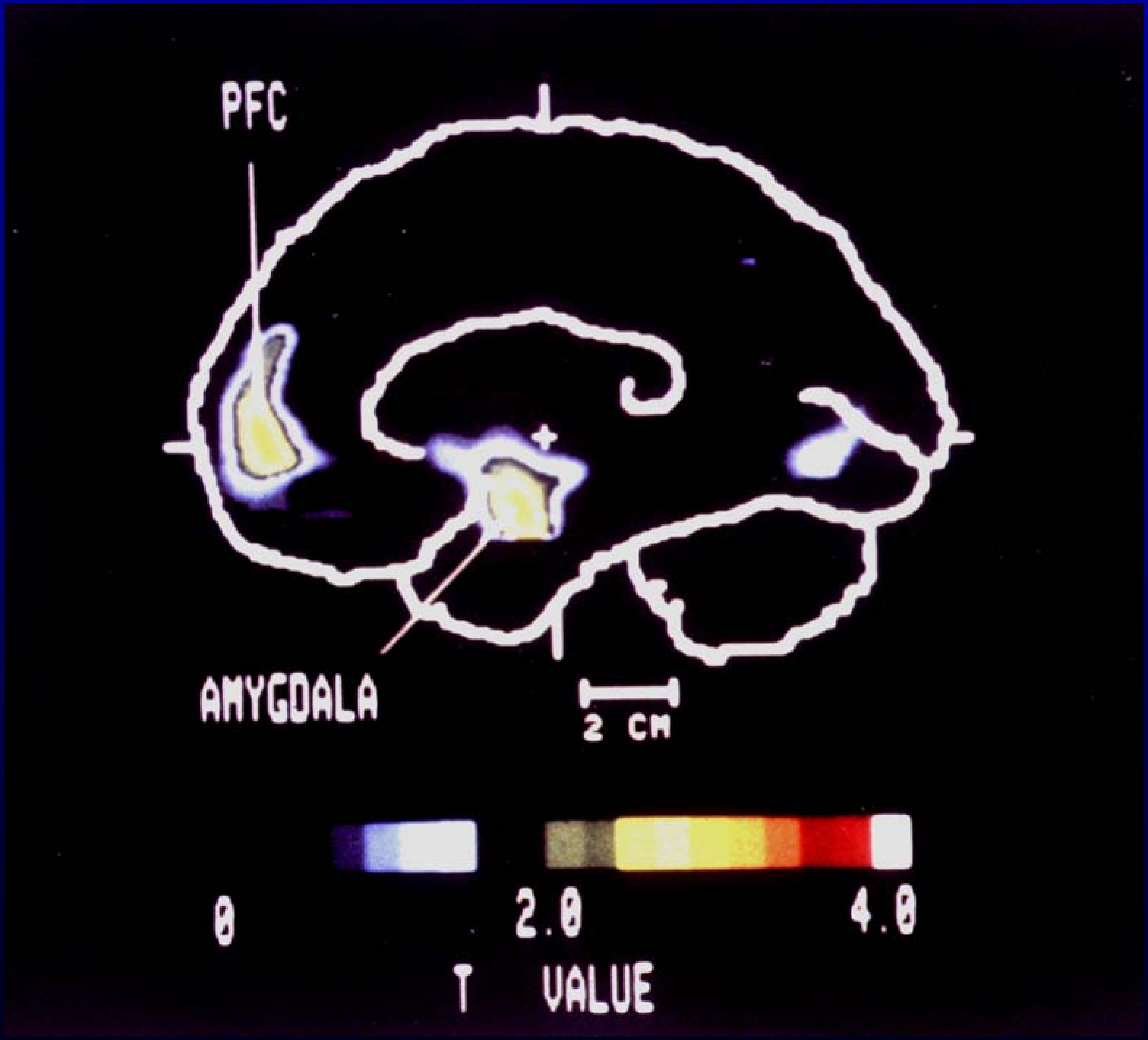


Prefrontal Cortex

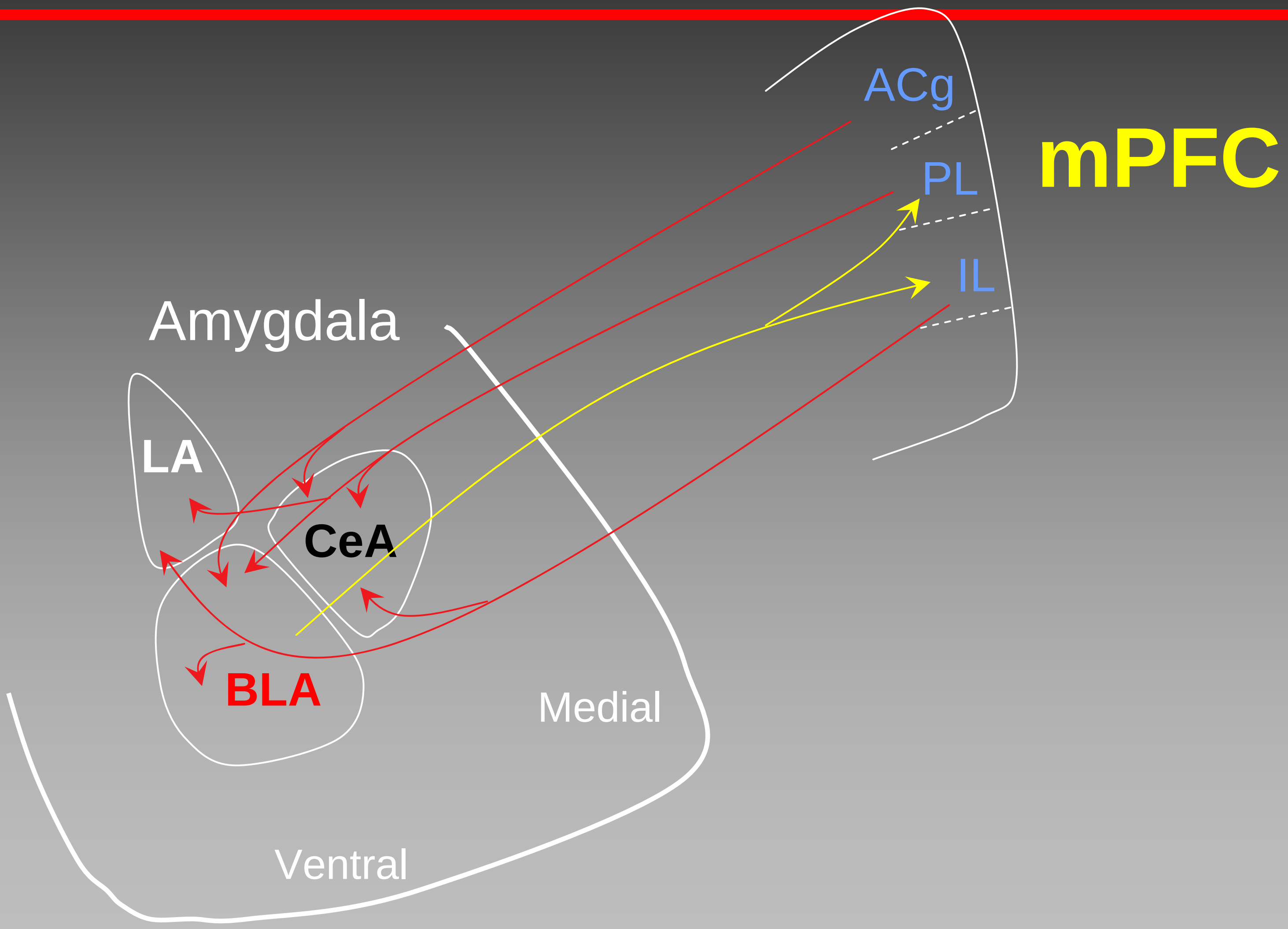


Amygdala

Amydala and PFC are Hyperactive in Depression and Anxiety Disorders

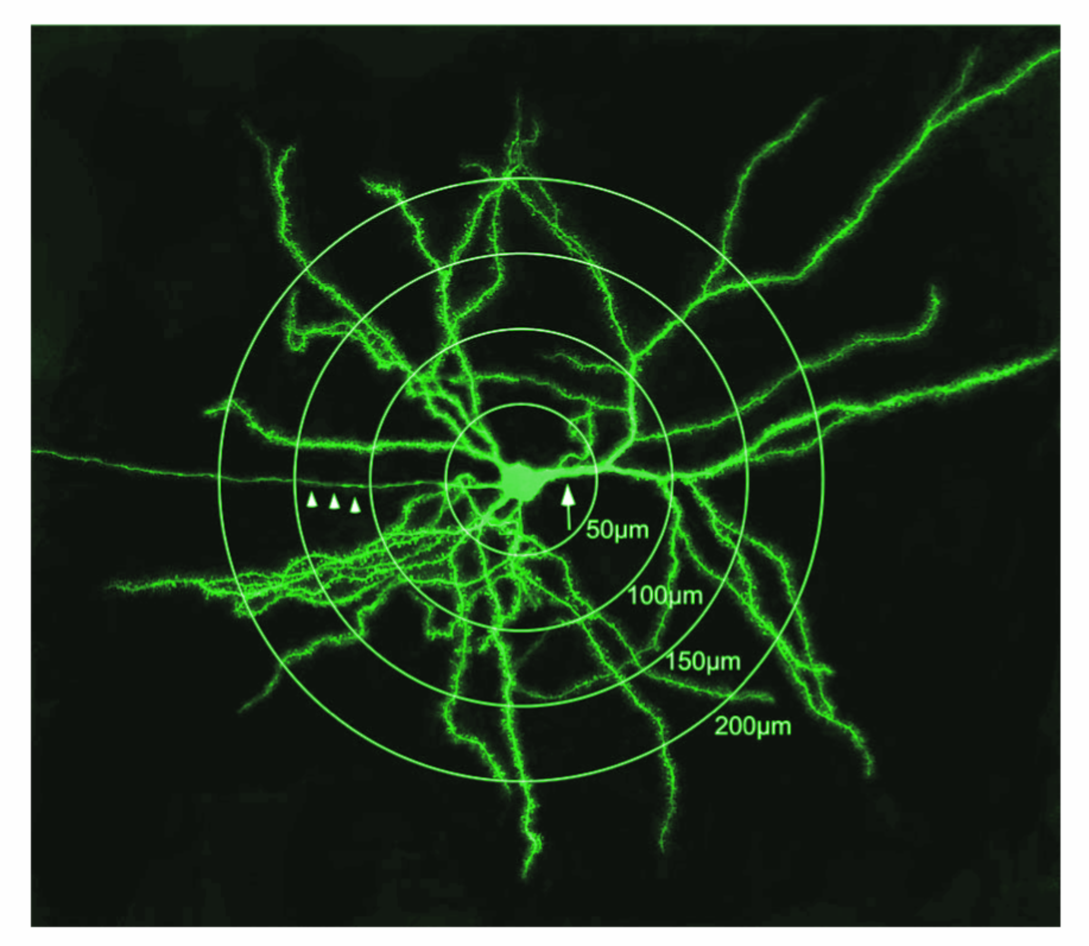


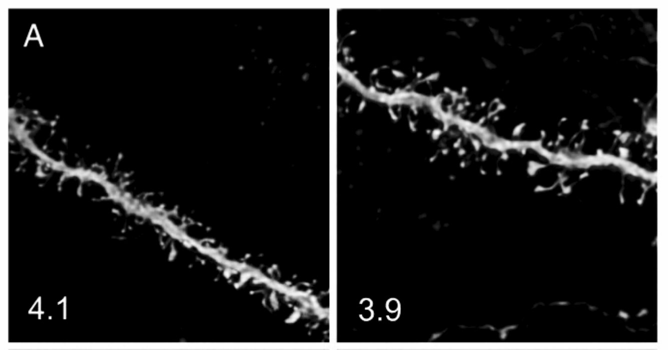
mPFC: external influences and responses



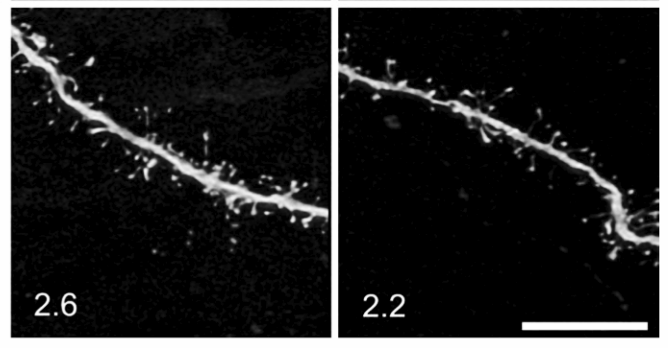
Effects of Stress on Prefrontal Cortical Morphology

1. 21 days of repeated restraint stress, 6 hours daily
2. Layer II/III pyramidal cells loaded with iontophoretic injections of Lucifer yellow for imaging after perfusion on day 22
1. Cells reconstructed in 3D (40x) and dendrites imaged on confocal at 100x





Spine density: controls



Spine density: stressed

(Radley et al, 2005)

Translation to medical students under stress

Perceived Stress Scale- 10 Item

Instructions: The questions in this scale ask you about your feelings and thoughts during the last month.
In each case, please indicate with a check how often you felt or thought a certain way.

1. In the last month, how often have you been upset because of something that happened unexpectedly?

2. In the last month, how often have you felt that you were unable to control the important things in your life?

3. In the last month, how often have you felt nervous and "stressed"?

4. In the last month, how often have you felt confident about your ability to handle your personal problems?

5. In the last month, how often have you felt that things were going your way?

6. In the last month, how often have you found that you could not cope with all the things that you had to do?

7. In the last month, how often have you been able to control irritations in your life?

8. In the last month, how often have you felt that you were on top of things?

9. In the last month, how often have you been angered because of things that were outside of your control?

10. In the last month, how often have you felt difficulties wer piling up so high that you could not overcome them?

___0=never ___1=almost never ___2=sometimes ___3=fairly often ___4=very often

Prefrontal cortex:

processes that might be affected by stress

Executive function

Attention shifting - mental flexibility

Extinction of fear conditioning

Working memory

Ability to suppress negative thoughts

Learned helplessness

Parasympathetic regulation

HPA regulation

Early Life Experiences

Importance of maternal care

Prenatal stress
Prolonged separation of pups
from mother

Increased rate of
brain aging

Birth

Increased stress hormone secretion
throughout postnatal life

Postnatal handling
Maternal behavior - licking
of pups

Decreased rate of
brain aging

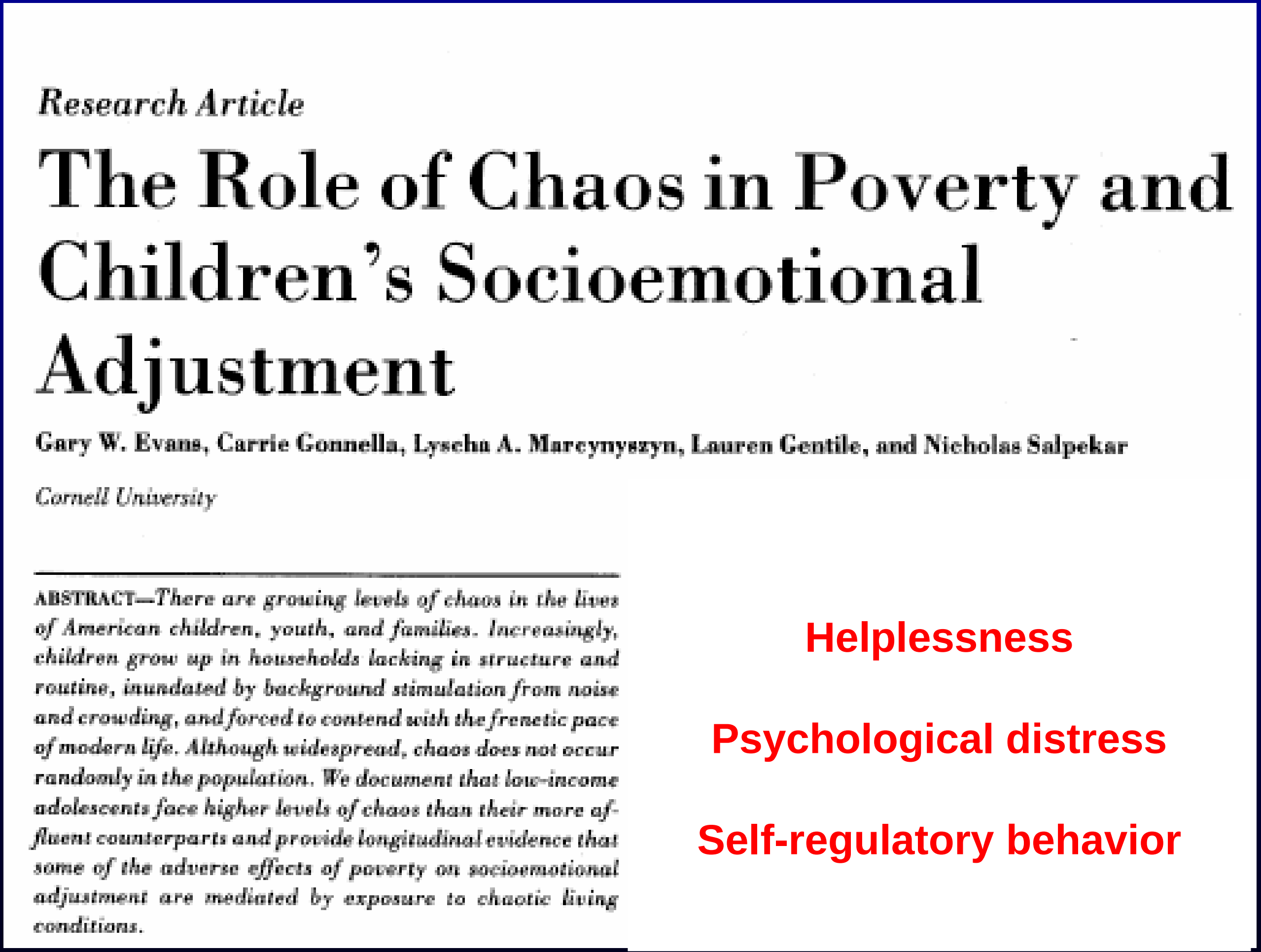
Birth

Decreased stress hormone secretion
throughout postnatal life

Gestation — Neonatal life — Puberty to adulthood — Senescence

Work of Levine, Denenberg, Ader, Meaney and others

The Role of Chaos in Poverty and Children's Socioemotional Adjustment



Research Article

The Role of Chaos in Poverty and Children's Socioemotional Adjustment

Gary W. Evans, Carrie Gonnella, Lyscha A. Marcynyszyn, Lauren Gentile, and Nicholas Salpekar

Cornell University

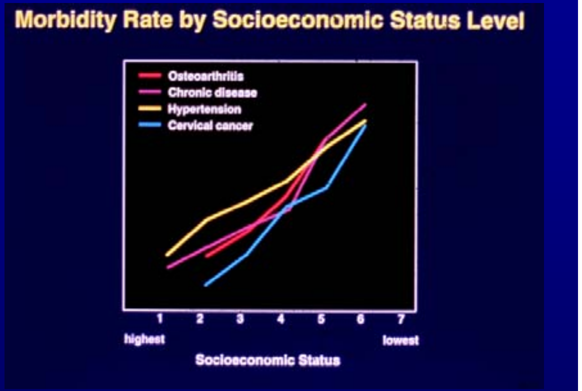
ABSTRACT—*There are growing levels of chaos in the lives of American children, youth, and families. Increasingly, children grow up in households lacking in structure and routine, inundated by background stimulation from noise and crowding, and forced to contend with the frenetic pace of modern life. Although widespread, chaos does not occur randomly in the population. We document that low-income adolescents face higher levels of chaos than their more affluent counterparts and provide longitudinal evidence that some of the adverse effects of poverty on socioemotional adjustment are mediated by exposure to chaotic living conditions.*

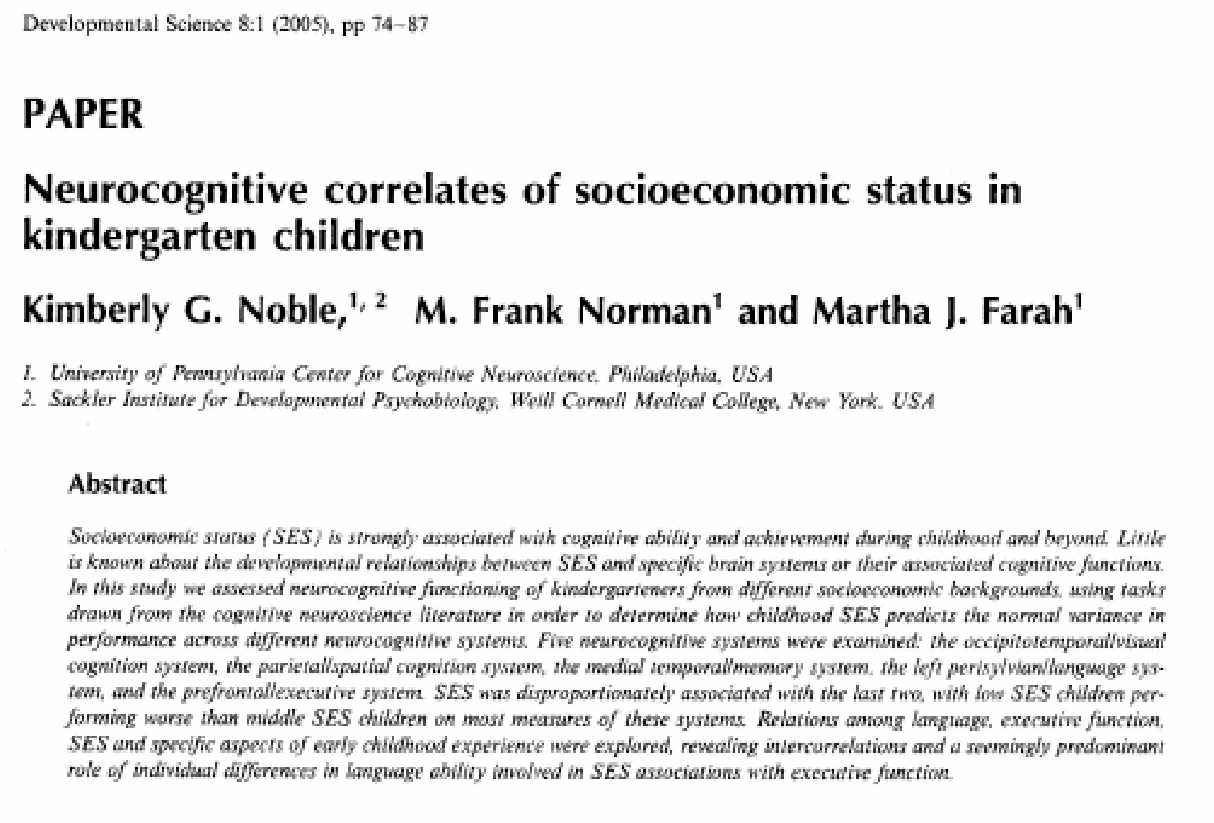
Helplessness

Psychological distress

Self-regulatory behavior

Socioeconomic status:
impaired language and executive function in children




Developmental Science 8:1 (2005), pp 74–87

PAPER

Neurocognitive correlates of socioeconomic status in kindergarten children

Kimberly G. Noble,[1, 2] **M. Frank Norman**[1] **and Martha J. Farah**[1]

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2. *Sackler Institute for Developmental Psychobiology, Weill Cornell Medical College, New York, USA*

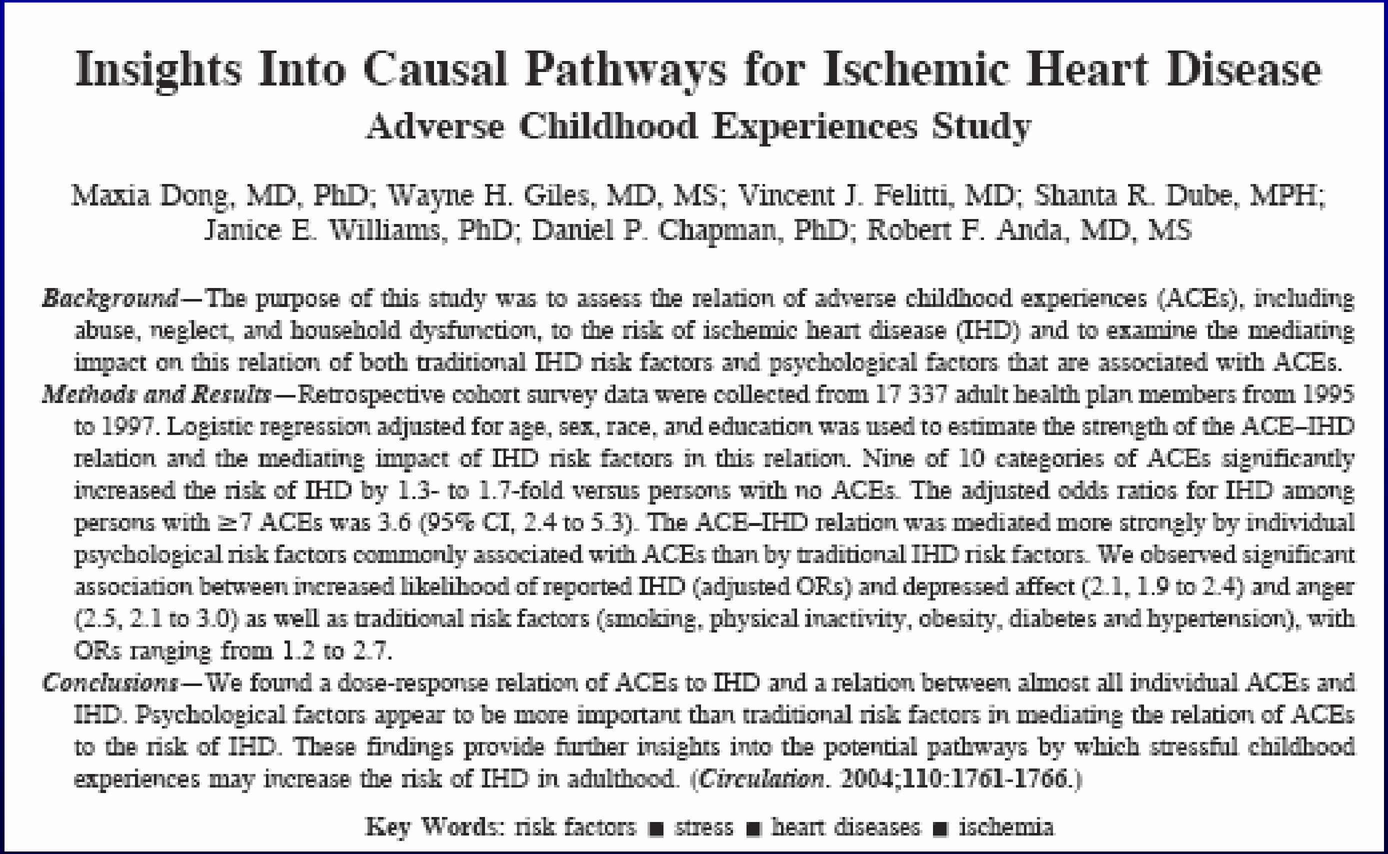
Abstract

Socioeconomic status (SES) is strongly associated with cognitive ability and achievement during childhood and beyond. Little is known about the developmental relationships between SES and specific brain systems or their associated cognitive functions. In this study we assessed neurocognitive functioning of kindergarteners from different socioeconomic backgrounds, using tasks drawn from the cognitive neuroscience literature in order to determine how childhood SES predicts the normal variance in performance across different neurocognitive systems. Five neurocognitive systems were examined: the occipitotemporal/visual cognition system, the parietal/spatial cognition system, the medial temporal/memory system, the left perisylvian/language system, and the prefrontal/executive system. SES was disproportionately associated with the last two, with low SES children performing worse than middle SES children on most measures of these systems. Relations among language, executive function, SES and specific aspects of early childhood experience were explored, revealing intercorrelations and a seemingly predominant role of individual differences in language ability involved in SES associations with executive function.

Effects of adversity at 9 years old on blood pressure and body mass
Gary Evans

Impaired language, executive function

Adverse Childhood Experiences



Insights Into Causal Pathways for Ischemic Heart Disease

Adverse Childhood Experiences Study

Maxia Dong, MD, PhD; Wayne H. Giles, MD, MS; Vincent J. Felitti, MD; Shanta R. Dube, MPH;
Janice E. Williams, PhD; Daniel P. Chapman, PhD; Robert F. Anda, MD, MS

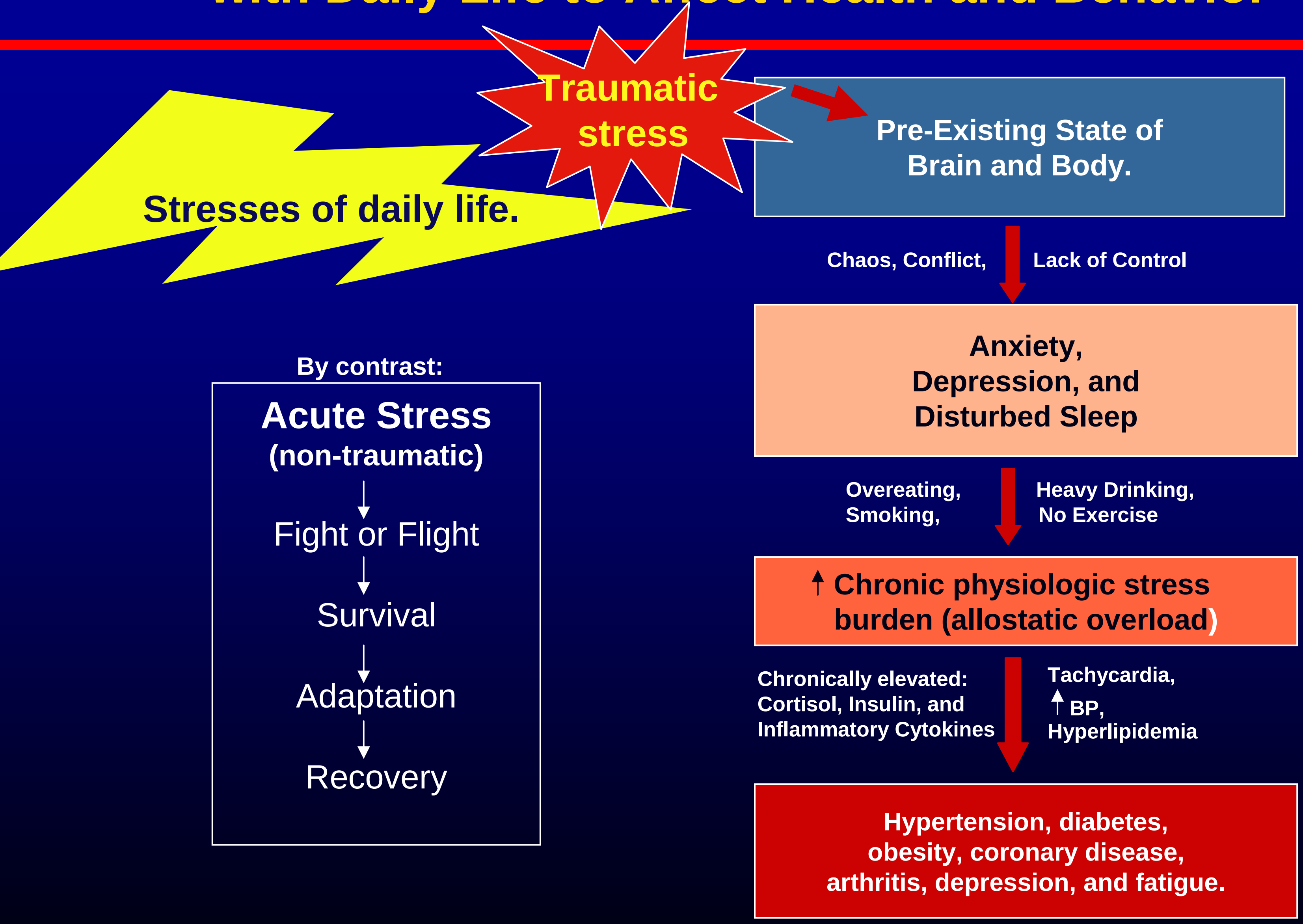
Background**—**The purpose of this study was to assess the relation of adverse childhood experiences (ACEs), including abuse, neglect, and household dysfunction, to the risk of ischemic heart disease (IHD) and to examine the mediating impact on this relation of both traditional IHD risk factors and psychological factors that are associated with ACEs.

Methods and Results**—**Retrospective cohort survey data were collected from 17 337 adult health plan members from 1995 to 1997. Logistic regression adjusted for age, sex, race, and education was used to estimate the strength of the ACE–IHD relation and the mediating impact of IHD risk factors in this relation. Nine of 10 categories of ACEs significantly increased the risk of IHD by 1.3- to 1.7-fold versus persons with no ACEs. The adjusted odds ratios for IHD among persons with ≥7 ACEs was 3.6 (95% CI, 2.4 to 5.3). The ACE–IHD relation was mediated more strongly by individual psychological risk factors commonly associated with ACEs than by traditional IHD risk factors. We observed significant association between increased likelihood of reported IHD (adjusted ORs) and depressed affect (2.1, 1.9 to 2.4) and anger (2.5, 2.1 to 3.0) as well as traditional risk factors (smoking, physical inactivity, obesity, diabetes and hypertension), with ORs ranging from 1.2 to 2.7.

Conclusions**—**We found a dose-response relation of ACEs to IHD and a relation between almost all individual ACEs and IHD. Psychological factors appear to be more important than traditional risk factors in mediating the relation of ACEs to the risk of IHD. These findings provide further insights into the potential pathways by which stressful childhood experiences may increase the risk of IHD in adulthood. (*Circulation*. 2004;110:1761-1766.)

Key Words: risk factors ■ stress ■ heart diseases ■ ischemia

How Traumatic Stress and Chronic Stress Interact with Daily Life to Affect Health and Behavior



Traumatic stress

Stresses of daily life.

Pre-Existing State of Brain and Body.

Chaos, Conflict, Lack of Control

Anxiety, Depression, and Disturbed Sleep

Overeating, Smoking, Heavy Drinking, No Exercise

↑ Chronic physiologic stress burden (allostatic overload)

Chronically elevated: Cortisol, Insulin, and Inflammatory Cytokines

Tachycardia, ↑ BP, Hyperlipidemia

Hypertension, diabetes, obesity, coronary disease, arthritis, depression, and fatigue.

By contrast:

Acute Stress (non-traumatic)

↓

Fight or Flight

↓

Survival

↓

Adaptation

↓

Recovery

Let’s not forget about genes

Nature-Nurture Interactions: Study in New Zealand

Monoamine oxidase genes influence whether childhood abuse will be transmitted from abuser to child

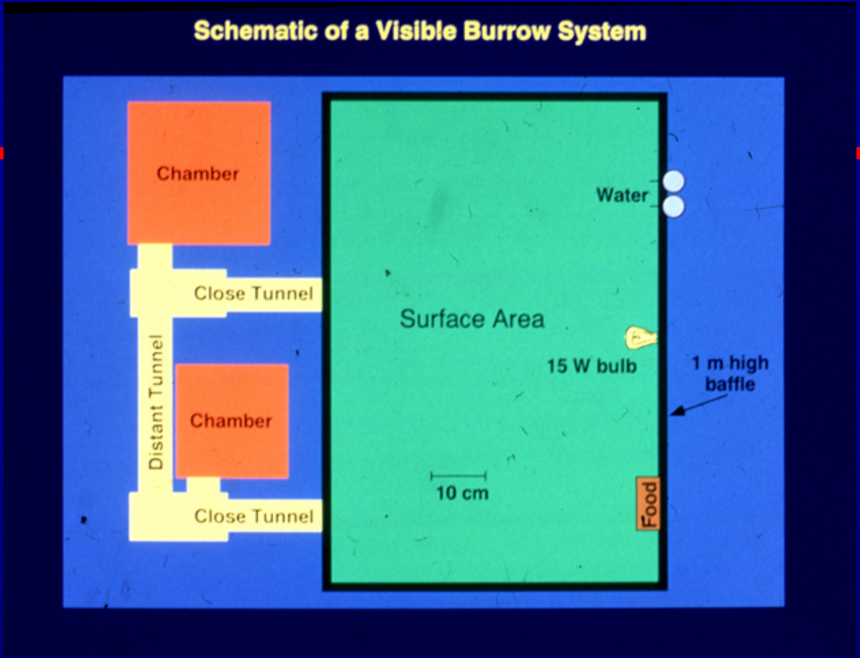
Caspi, A.; McClay, J.; Moffitt, T. E.; Mill, J.; Martin, J.; Craig, I. W.; Taylor, A., and Poulton, R.
Role of genotype in the cycle of violence in maltreated children.
Science. 2002; 297:851-854.

Serotonin transporter genes influence vulnerability to life-stress in causing depression

Caspi, A.; Sugden, K.; Moffitt, T. E.; Taylor, A.; Craig, I. W.; Harrington, H.; McClay, J.; Mill, J.;
Martin, J.; Braithwaite, A., and Poulton, R.
Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene.
Science. 2003; 301:386-389.

Influence of social hierarchies

Chronic Stress: VBS

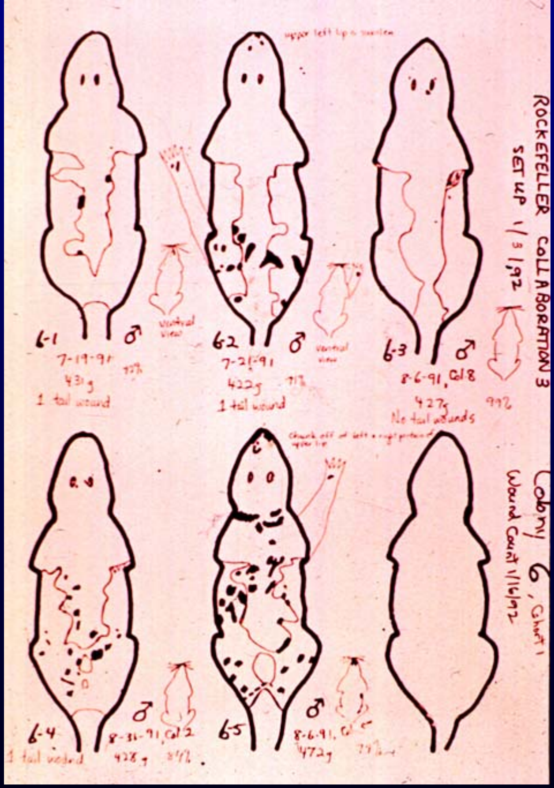


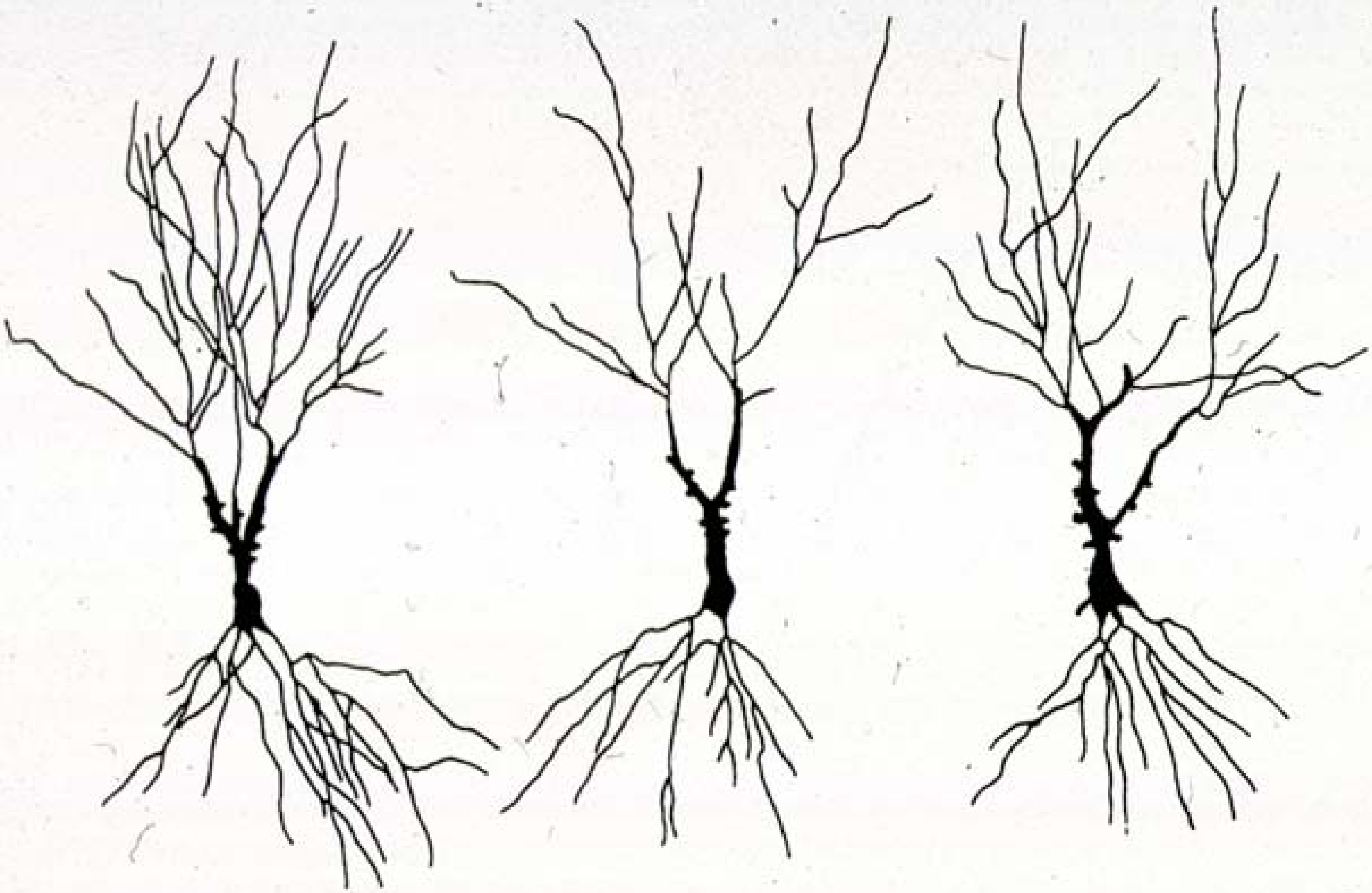
5 males, 2 females

Dominant has fewest scars

Subordinates - low testosterone and high stress hormones;   numerous changes in brain chemistry.

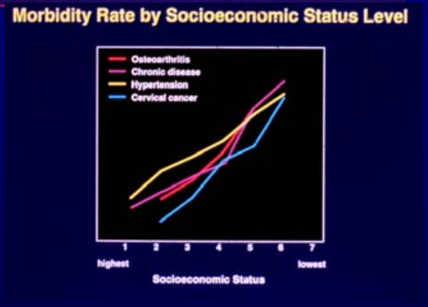
Some subordinates are more stressed than others.

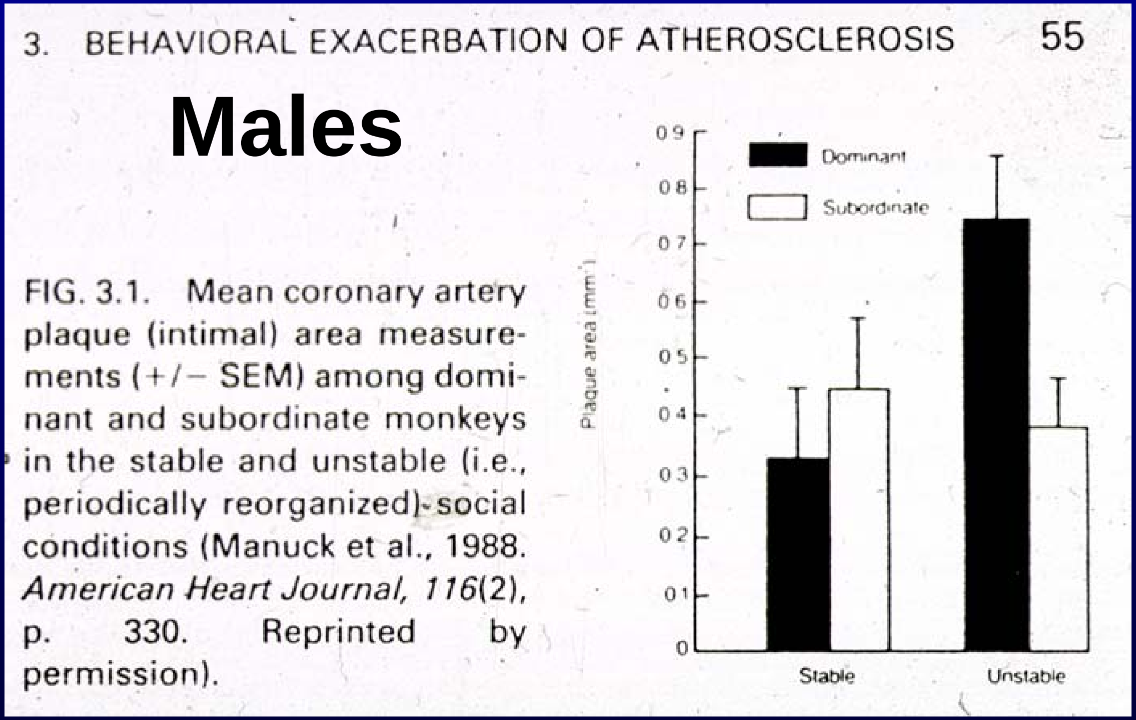




CONTROL DOMINANT SUBORDINATE

Unstable Social Hierarchies and CVD





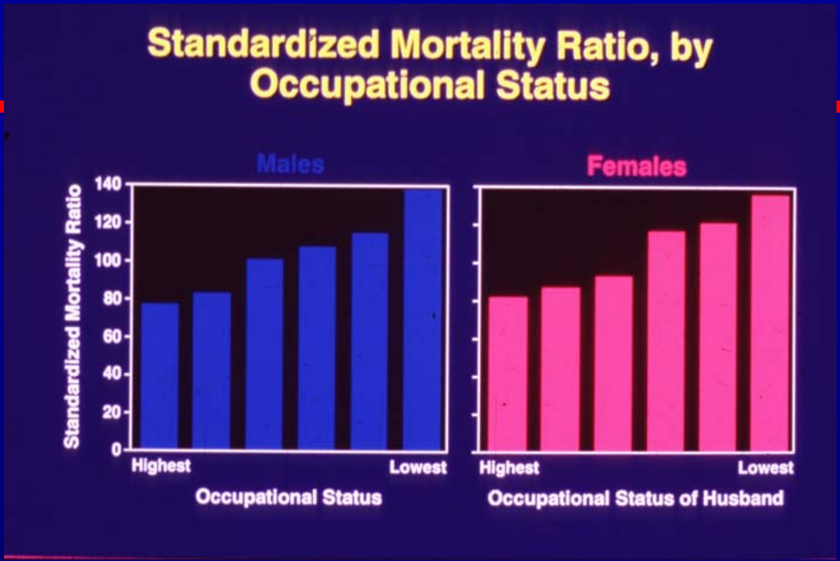
3. BEHAVIORAL EXACERBATION OF ATHEROSCLEROSIS 55

Males

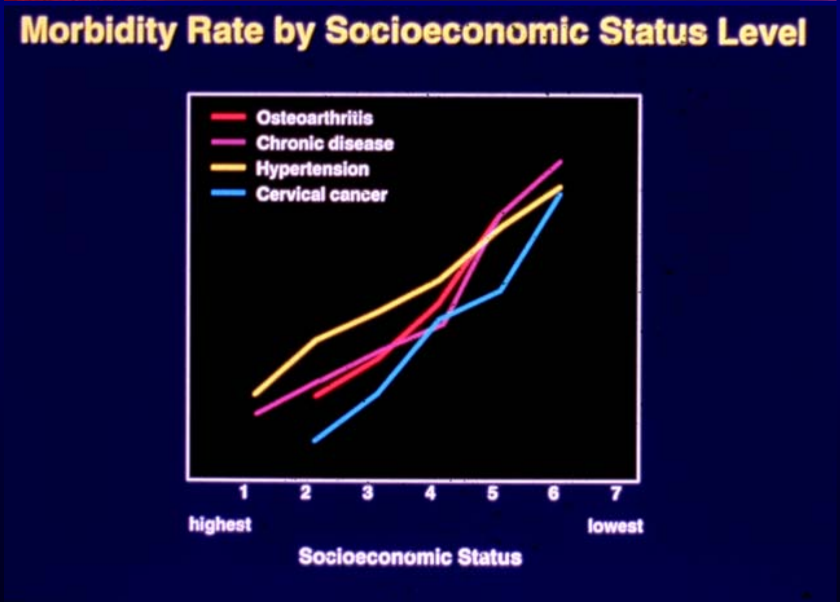
FIG. 3.1. Mean coronary artery plaque (intimal) area measurements (+/− SEM) among dominant and subordinate monkeys in the stable and unstable (i.e., periodically reorganized) social conditions (Manuck et al., 1988. *American Heart Journal, 116*(2), p. 330. Reprinted by permission).

For females, subordinate social status Increase atherosclerosis

Psychosocial Factors in Causation of Disease



Standardized Mortality Ratio, by Occupational Status



Morbidity Rate by Socioeconomic Status Level

Social position
  -perceived
  -actual

Discrimination
  - perceived
  - actual

Education/resources
  -money, intellect
  -life skills

Access/use of healthcare

Lifestyle
  -diet
  -alcohol
  -smoking
  -exercise

Stressors from
  - work
  - family
  - neighborhood
  - life events

How does SES get “under the skin”?

Interventions

Pharmaceutical agents that help treat stress and consequences of allostatic load

Beta blockers.

Prazosin for PTSD

Anxiolytics.

Antidepressants.

Glucocorticoid receptor antagonists.

CRF antagonists.

Anti-diabetic medications - eg, metformin

Anti-craving - eg endocannabinoid antagonists.

Anti-inflammatory medications.

Top down interventions

Social support

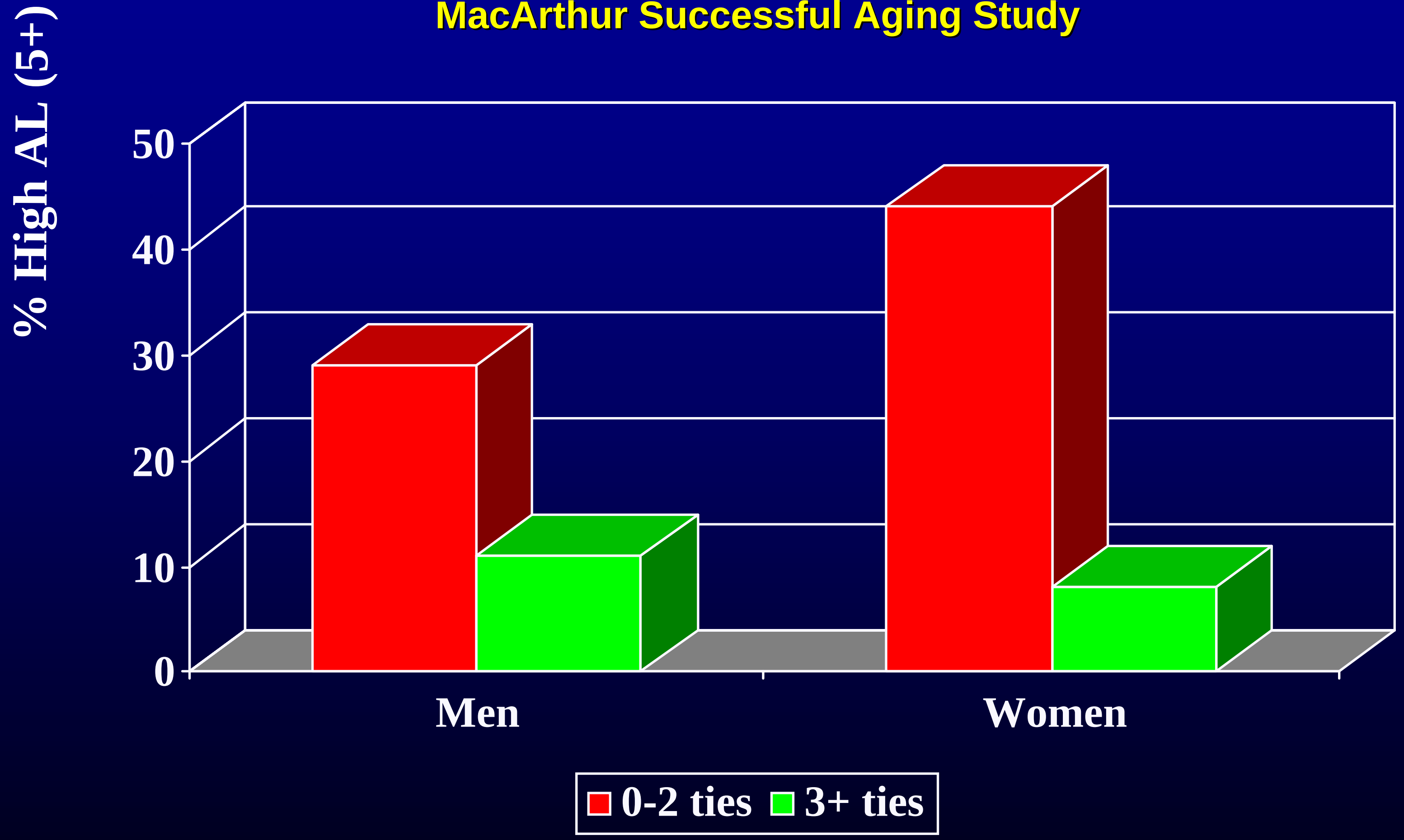
Physical activity

Programs that combine both

Top-down interventions: social integration

Social Integration REDUCES Allostatic Load:

MacArthur Successful Aging Study



Teresa Seeman, UCLA, and colleagues

Physical activity reduces allostatic load

Diabetes Prevention Program: Exercise

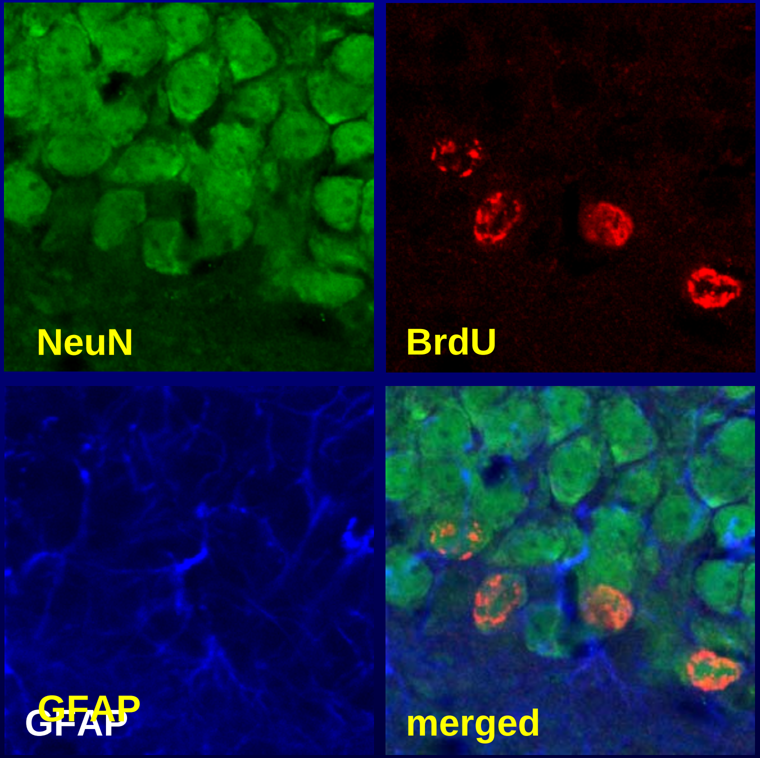
http://www.preventdiabetes.com/)

"Participants randomly assigned to <u>intensive lifestyle intervention</u> Reduced their risk of getting type 2 diabetes by 58 percent. On average, this group maintained their physical activity at 30 minutes per day, usually with walking or other moderate intensity exercise, and lost 5-7 percent of their body weight. Participants randomized to treatment with metformin reduced their risk of getting type 2 diabetes by 31 percent"

**Exercise improves aspects of cognitive function,
esp, PFC and hippocampus**

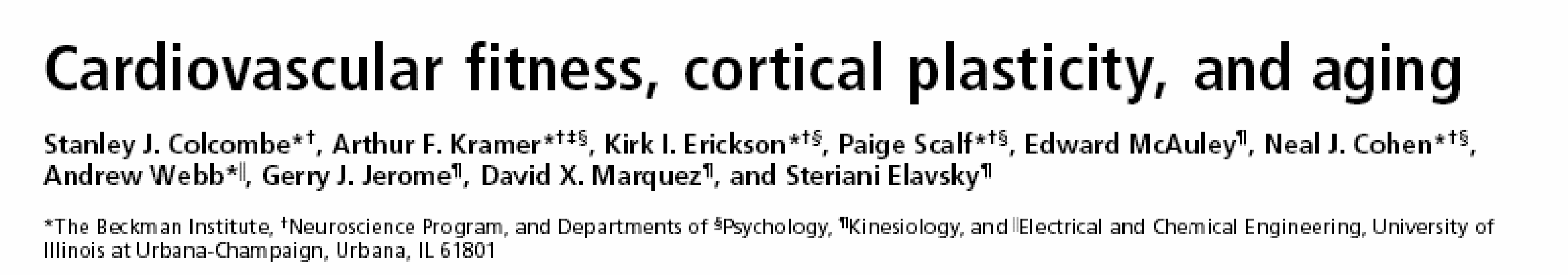
**Exercise is also an effective treatment for depression
and increases neurogenesis.**

Exercise stimulates neurogenesis



Neurotrophins increase in brain
IGF-1 enters brain and mediates increased neurogenesis
(Anti-depressants also increase neuronal proliferation)

Top-down interventions: exercise



Cardiovascular fitness, cortical plasticity, and aging

Stanley J. Colcombe[*,†], Arthur F. Kramer[*,†,‡,§], Kirk I. Erickson[*,†,§], Paige Scalf[*,†,§], Edward McAuley[¶], Neal J. Cohen[*,†,§], Andrew Webb[*,‖], Gerry J. Jerome[¶], David X. Marquez[¶], and Steriani Elavsky[¶]

[*]The Beckman Institute, [†]Neuroscience Program, and Departments of [§]Psychology, [¶]Kinesiology, and [‖]Electrical and Chemical Engineering, University of Illinois at Urbana-Champaign, Urbana, IL 61801

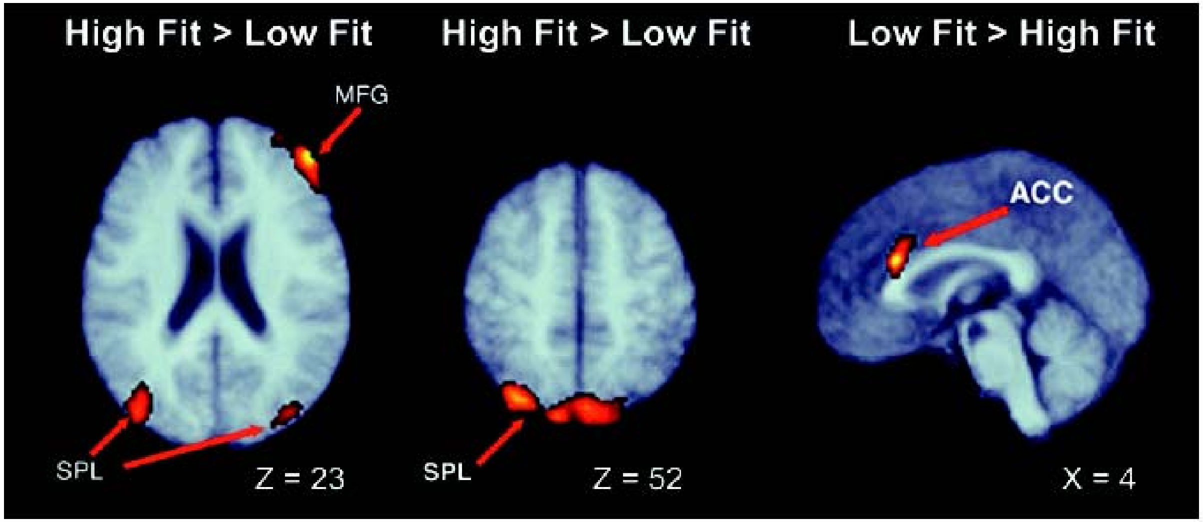
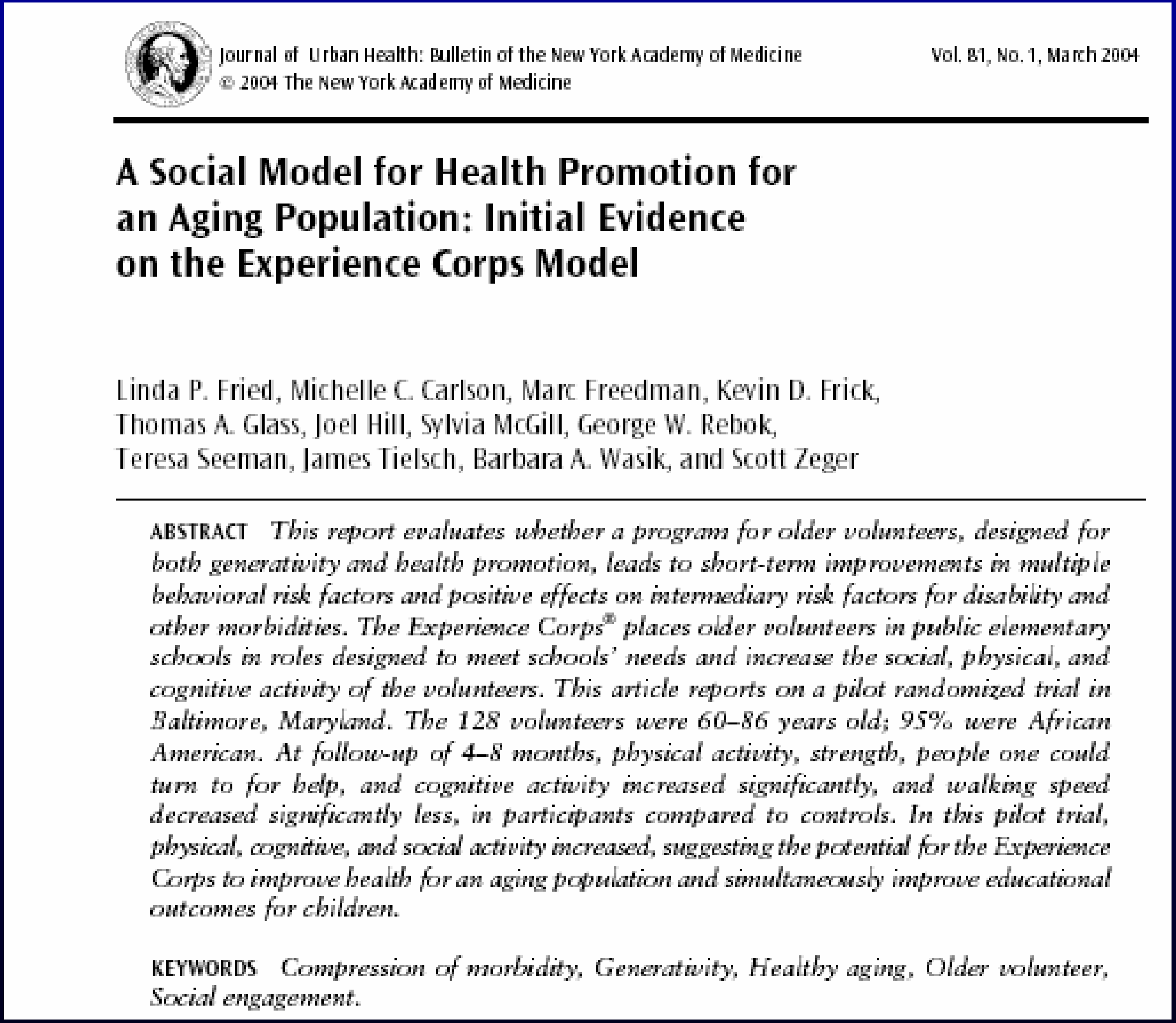


Fig. 2. Regional differences in cortical recruitment as a function of cardiovascular fitness. See Table 1 for cluster descriptions.

Attentional network: prefrontal and parietal cortex

Benefits of activity, social interactions and finding meaning and purpose in life



Journal of Urban Health: Bulletin of the New York Academy of Medicine
Vol. 81, No. 1, March 2004

A Social Model for Health Promotion for an Aging Population: Initial Evidence on the Experience Corps Model

Linda P. Fried, Michelle C. Carlson, Marc Freedman, Kevin D. Frick,
Thomas A. Glass, Joel Hill, Sylvia McGill, George W. Rebok,
Teresa Seeman, James Tielsch, Barbara A. Wasik, and Scott Zeger

ABSTRACT *This report evaluates whether a program for older volunteers, designed for both generativity and health promotion, leads to short-term improvements in multiple behavioral risk factors and positive effects on intermediary risk factors for disability and other morbidities. The Experience Corps® places older volunteers in public elementary schools in roles designed to meet schools' needs and increase the social, physical, and cognitive activity of the volunteers. This article reports on a pilot randomized trial in Baltimore, Maryland. The 128 volunteers were 60–86 years old; 95% were African American. At follow-up of 4–8 months, physical activity, strength, people one could turn to for help, and cognitive activity increased significantly, and walking speed decreased significantly less, in participants compared to controls. In this pilot trial, physical, cognitive, and social activity increased, suggesting the potential for the Experience Corps to improve health for an aging population and simultaneously improve educational outcomes for children.*

KEYWORDS *Compression of morbidity, Generativity, Healthy aging, Older volunteer, Social engagement.*

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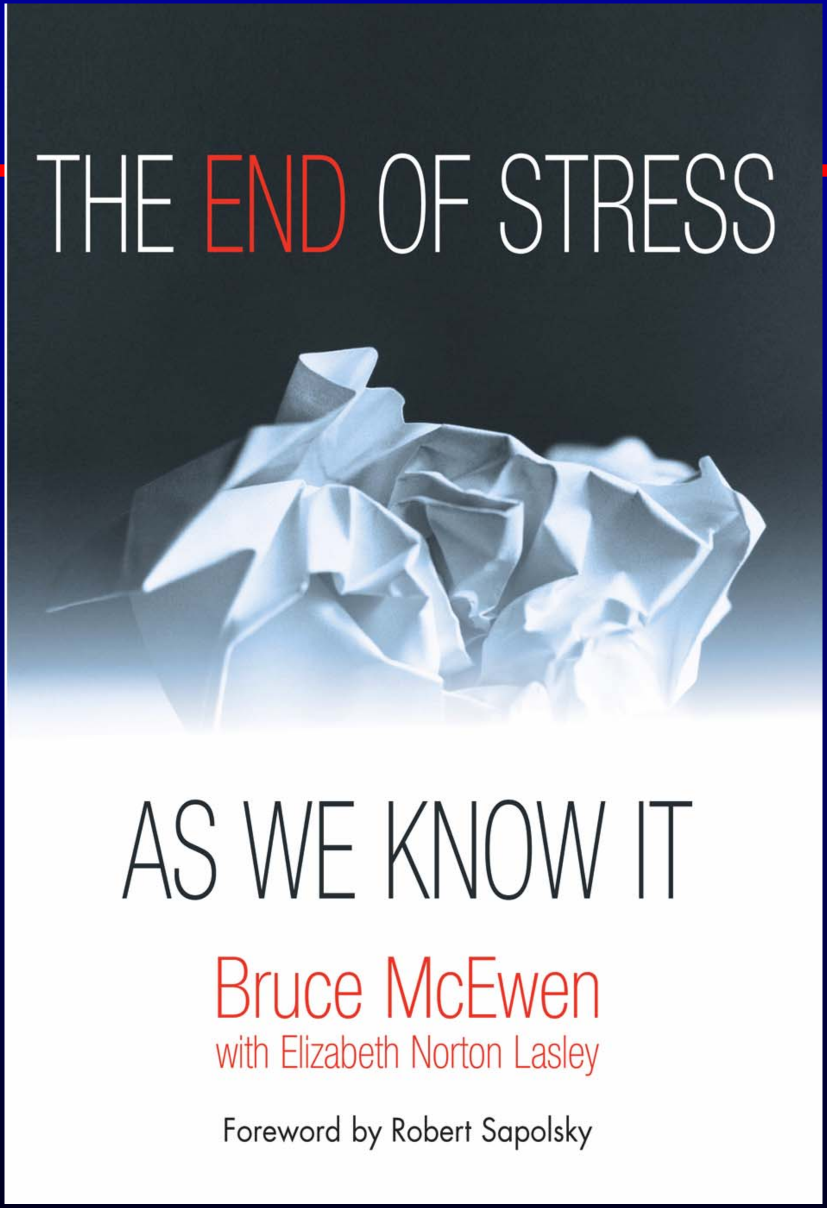
Center for the Neuroscience of Fear and Anxiety
(Joseph Ledoux, Center Director)
NIH Grant MH 41256 to BMc

MacArthur Foundation Research Network
on Socioeconomic Status and Health



THE END OF STRESS

AS WE KNOW IT

Bruce McEwen
with Elizabeth Norton Lasley

Foreword by Robert Sapolsky

How Does One Measure Allostatic Load?

From MacArthur Successful Aging Study

- Cardiovascular
- HPA Axis
- Symp. Nerv. System
- Metabolism

- Resting Systolic, Diastolic BP
- Ur. cortisol (12 hr), DHEA-S
- Ur. NE, EPI (12hr)
- Gly. Hemoglobin, HDL/total Cholesterol, WHR

Teresa Seeman, Burt Singer, Ralph Horwitz, Jack Rowe

Predictions from Increased Allostatic Load: MacArthur Successful Aging Study

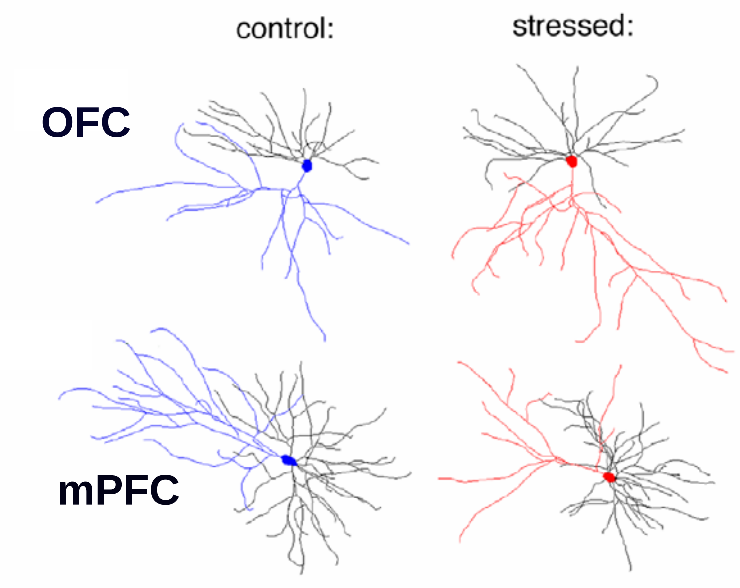
- 7-year All Cause Mortality
- Incident CVD
- Change in Physical performance
- Change in Cognitive performance

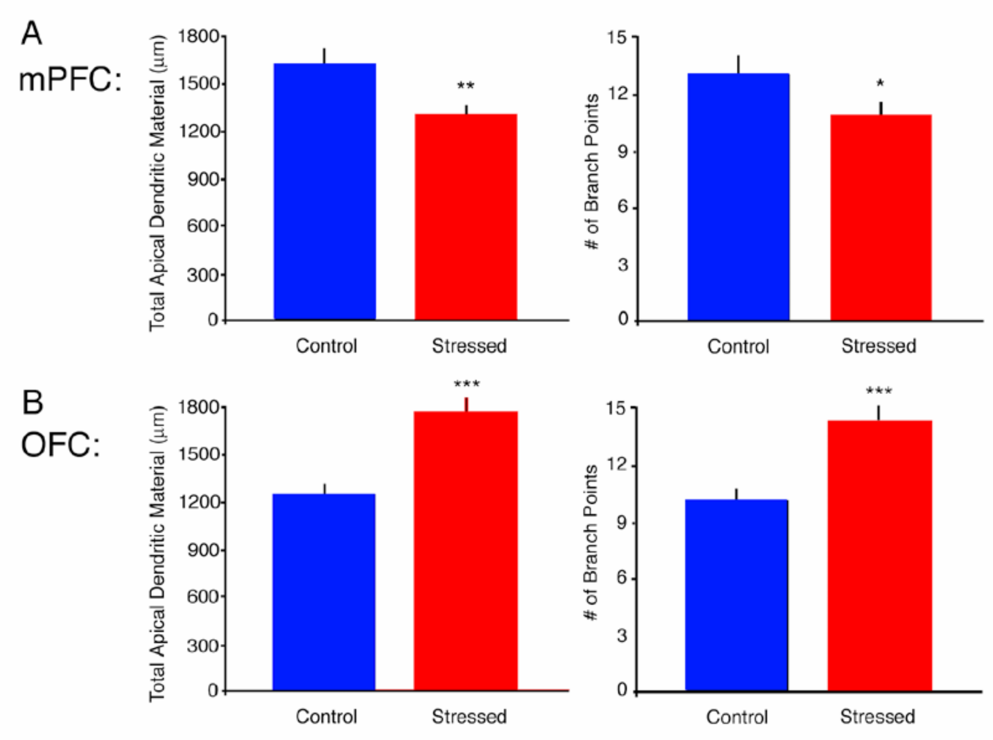
Additions to Operationalization of Allostatic Load

• Inflammation	• IL-6, CRP, fibrinogen
• Lung Fx	• Peak Flow rate
• Renal Fx	• Creatinine clearance
• Cardiovascular	• Heart rate variability

Effects of Stress on Frontal Cortical Morphology

21d Stress induces contrasting effects in mPFC and OFC





Liston et al, 2006.