Experience Shapes the Brain Across the Lifecourse

Epigenetics, Biological Embedding and Cumulative Change

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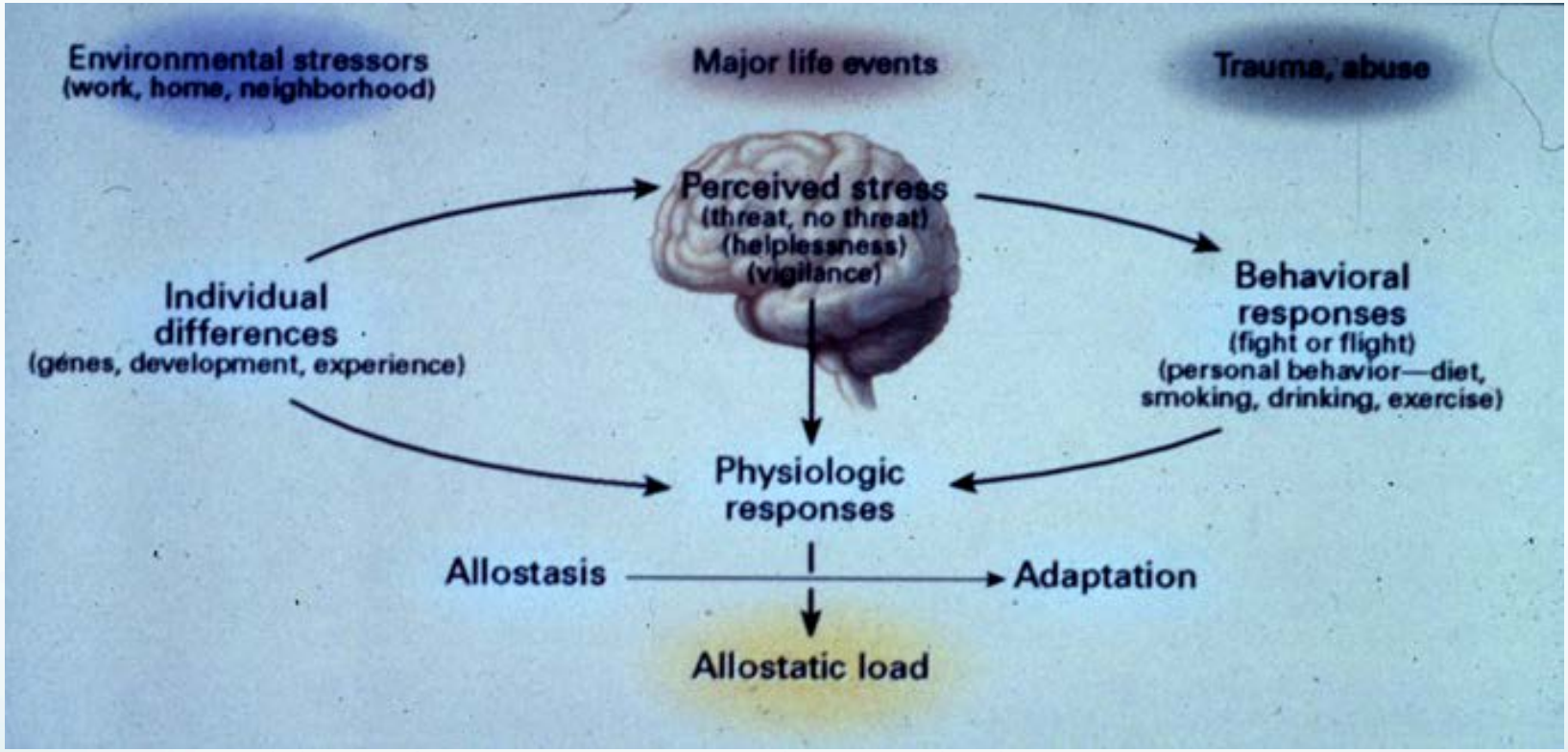
MEMBER, NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD

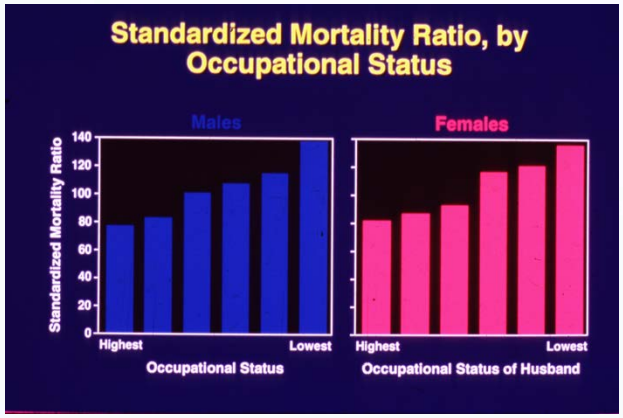
Social environment and health
Central Role of the Brain

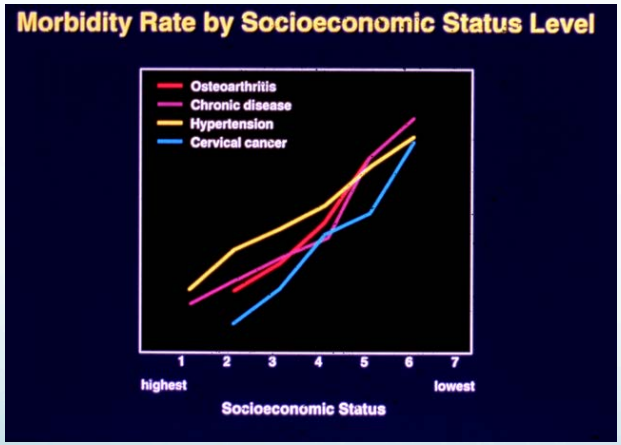


Protective and Damaging Effects of Stress Mediators

McEwen B. New England J. Med. 1998

Psychosocial Factors in Causation of Disease
Linear Gradient Across SES





How does SES get "under the skin"?

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

Lifecourse Health Development: Past, Present and Future

Neal Halfon · Kandyce Larson · Michael Lu ·
Ericka Tullis · Shirley Russ

1.0 Germs, Genes and the biomedical model (antibiotics – ie "magic bullets")

2.0 Multiple risks and the biopsychsocial model (stress, health behaviors, social environment).
George Engel 1977

3.0 Lifecourse Health Development (epigenetics, context sensitive genes complex systems biology.)

Epigenetics

BIOLOGICAL EMBEDDING AND CUMULATIVE CHANGE

Emergence of individual/species characteristics during development (Waddington 1942) .

Now means " above the genome" – not changing DNA sequence

Refers to the gene-environment interactions that bring about the phenotype of an individual.

- **Modifications of histones - unfolding/folding of chromatin to expose or hide genes**

- **Binding of transcription regulators to DNA response elements on genes**

- **Methylation of cytosine bases in DNA without changing genetic code**

- **MicroRNA's – regulate mRNA survival and translation to protein**

--Transposons and retrotransposons – DNA rearrangements and insertions

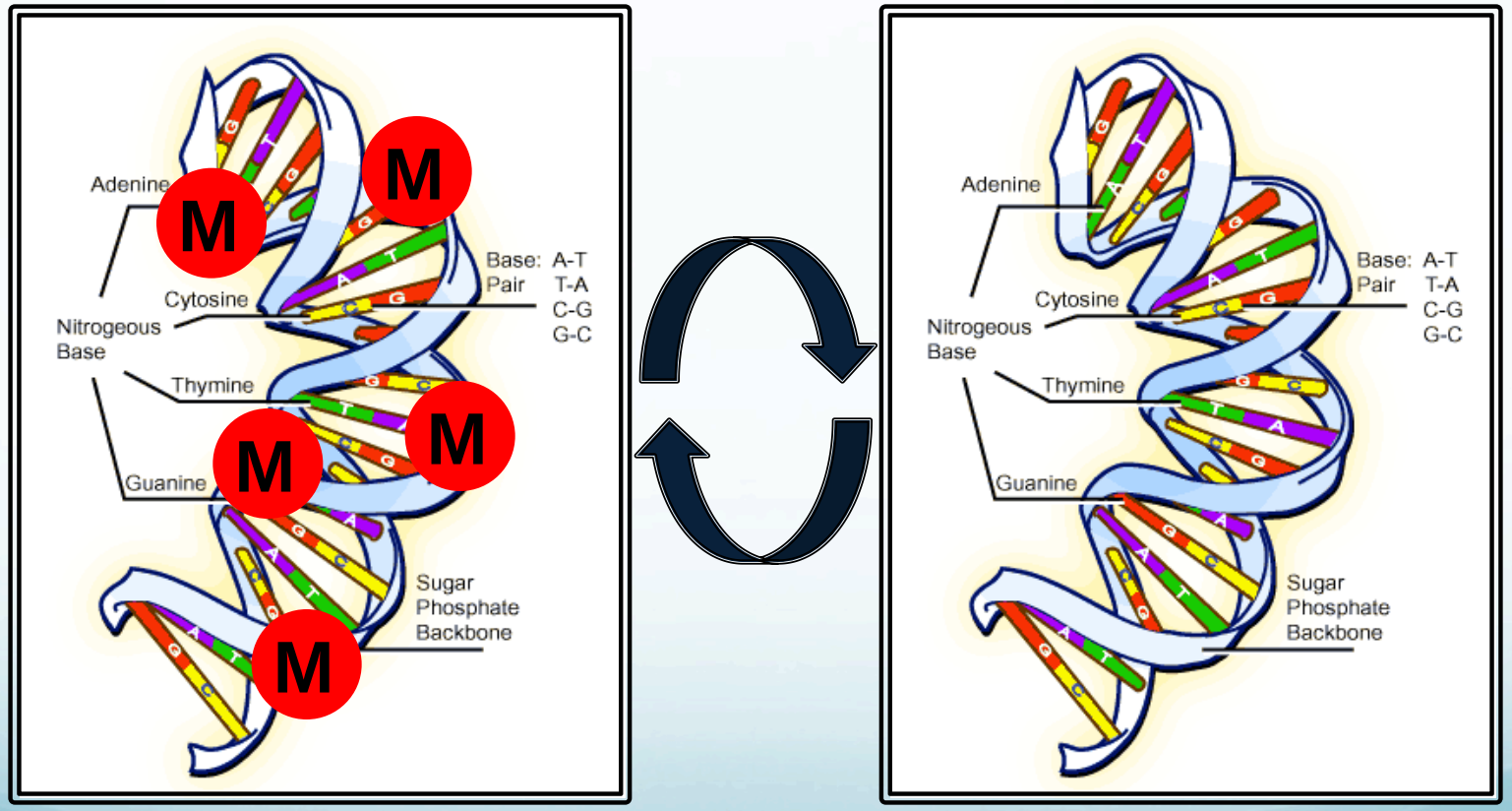
Effects can extend to next generation

Examples: obesity; parental behavior

http://www.pbs.org/wgbh/nova/sciencenow/3411/02.html

Methylation of CpG residues in DNA

An epigenetic mechanism



Epigenetic differences arise during the lifetime of monozygotic twins

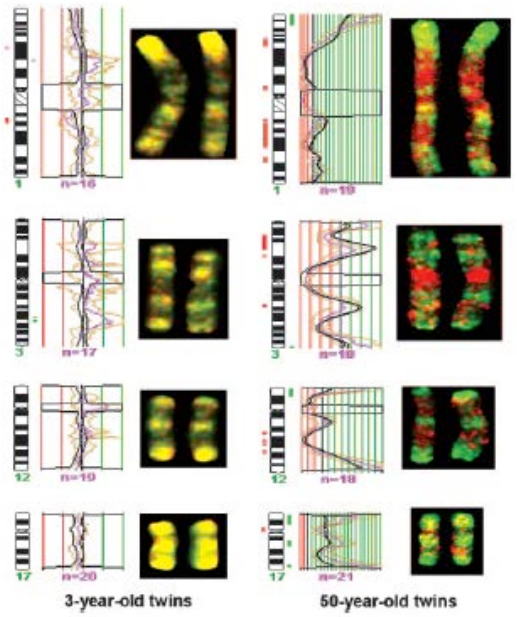
Mario F. Fraga*, Esteban Ballestar*, Maria F. Paz*, Santiago Ropero*, Fernando Setien*, Maria L. Ballestar†, Damia Heine-Suñer‡, Juan C. Cigudosa§, Miguel Urioste¶, Javier Benitez¶, Manuel Boix-Chornet†, Abel Sanchez-Aguilera†, Charlotte Ling‖, Emma Carlsson‖, Pernille Poulsen**, Allan Vaag**, Zarko Stephan††, Tim D. Spector††, Yue-Zhong Wu‡‡, Christoph Plass‡‡, and Manel Esteller*§§

*Epigenetics, §Cytogenetics, and ¶Genetic Laboratories, Spanish National Cancer Centre (CNIO), Melchor Fernandez Almagro 3, 28029 Madrid, Spain; †Department of Behavioral Science, University of Valencia, 46010 Valencia, Spain; ‡Molecular Genetics Laboratory, Genetics Department, Son Dureta Hospital, 07014 Palma de Mallorca, Spain; ‖Department of Clinical Sciences, University Hospital Malmö, Lund University, S-205 02 Malmö, Sweden; **Steno Diabetes Center, 2820 Gentofte, Denmark; ††Twin Research and Genetic Epidemiology Unit, St. Thomas' Hospital, London SE1 7EH, United Kingdom; and ‡‡Human Cancer Genetics Program, Department of Molecular Virology, Immunology, and Medical Genetics, Ohio State University, Columbus, OH 43210

Edited by Stanley M. Gartler, University of Washington, Seattle, WA, and approved May 23, 2005 (received for review January 17, 2005)

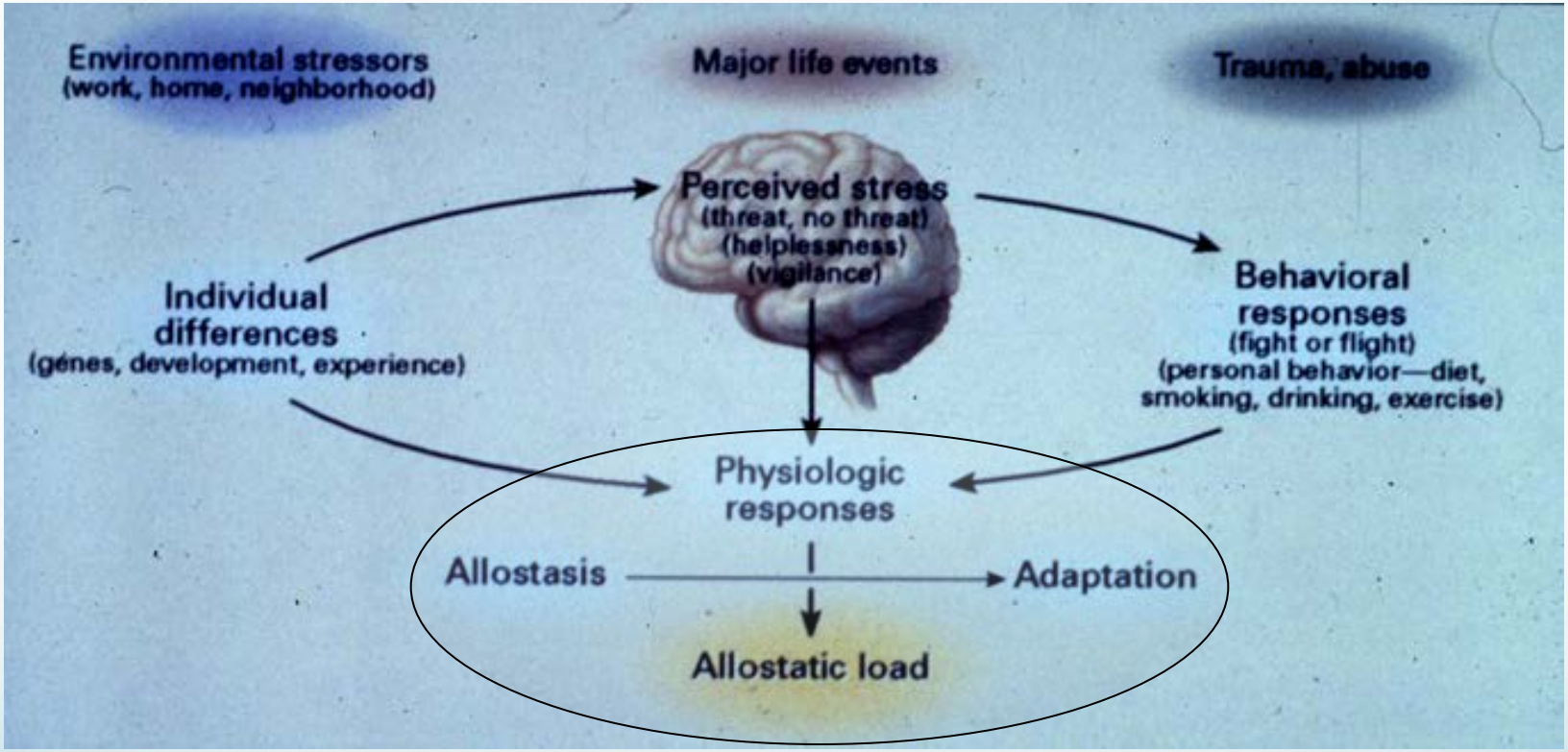
Monozygous twins share a common genotype. However, most monozygotic twin pairs are not identical; several types of phenotypic discordance may be observed, such as differences in susceptibilities to disease and a wide range of anthropomorphic features. There are several possible explanations for these observations, but one is the existence of epigenetic differences. To address this issue, we examined the global and locus-specific differences in DNA methylation and histone acetylation of a large cohort of monozygotic twins. We found that, although twins are epigenetically indistinguishable during the early years of life, older monozygous twins exhibited remarkable differences in their overall content and genomic distribution of 5-methylcytosine DNA and histone acetylation, affecting their gene-expression portrait. These findings indicate how an appreciation of epigenetics is missing from our understanding of how different phenotypes can be originated from the same genotype.

DNA methylation | epigenetics | histones

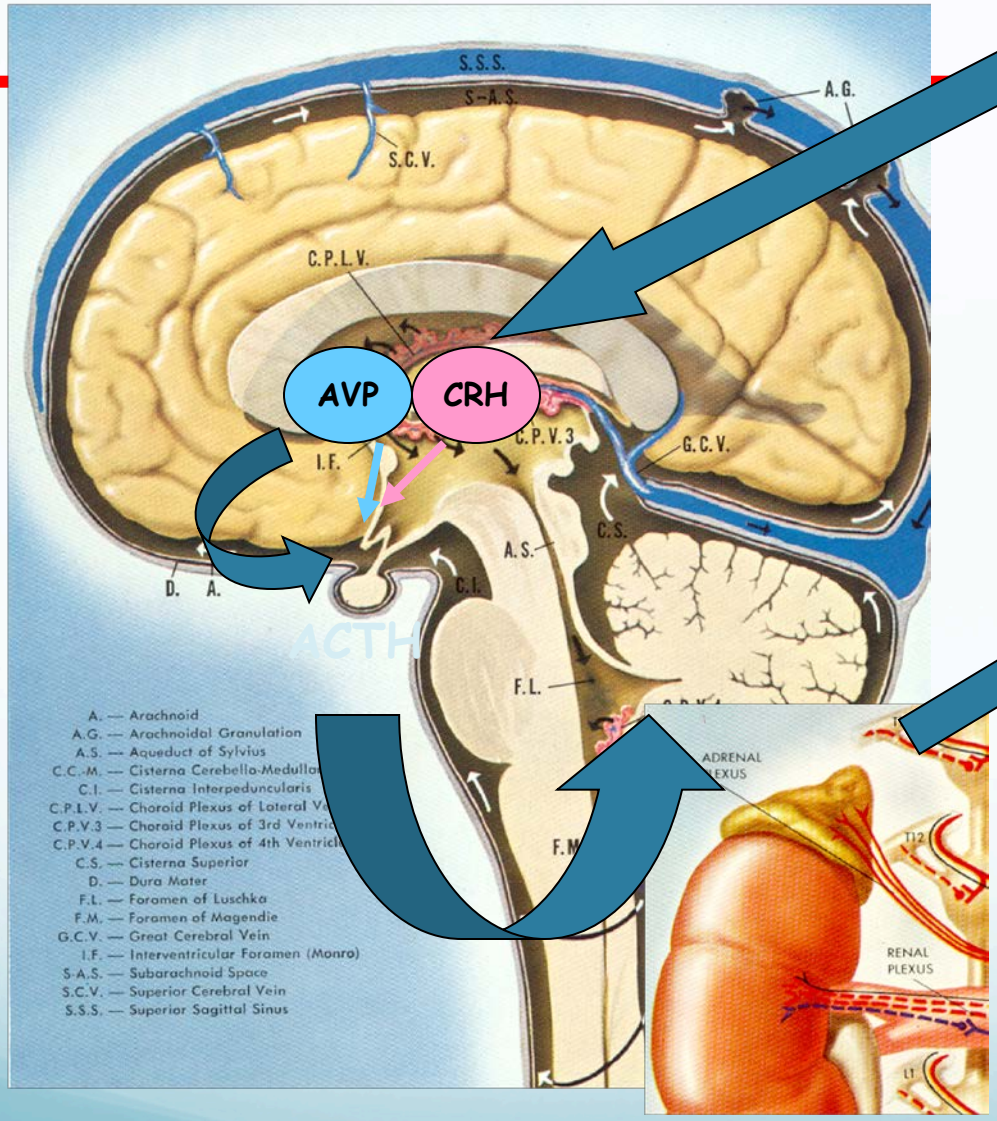


Social environment and health

Allostasis and allostatic load



What about STRESS?



STRESS

Many targets for cortisol

Cortisol

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

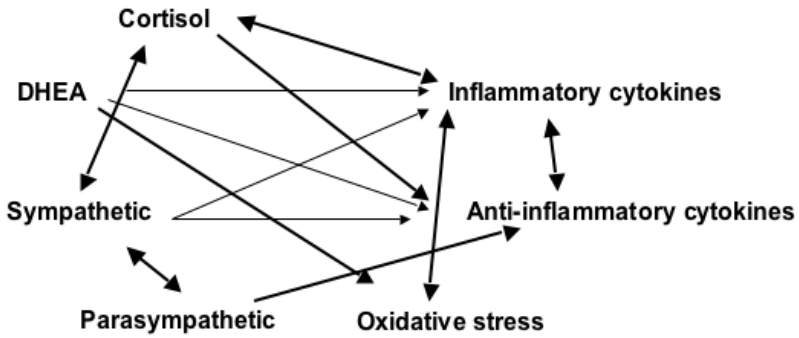
Chronic - suppresses immune, Memory, promotes bone Mineral loss, muscle wasting; Metabolic syndrome

Mediators of stress and adaptation

NETWORK OF ALLOSTASIS

CNS function

Metabolism



Cardiovascular function

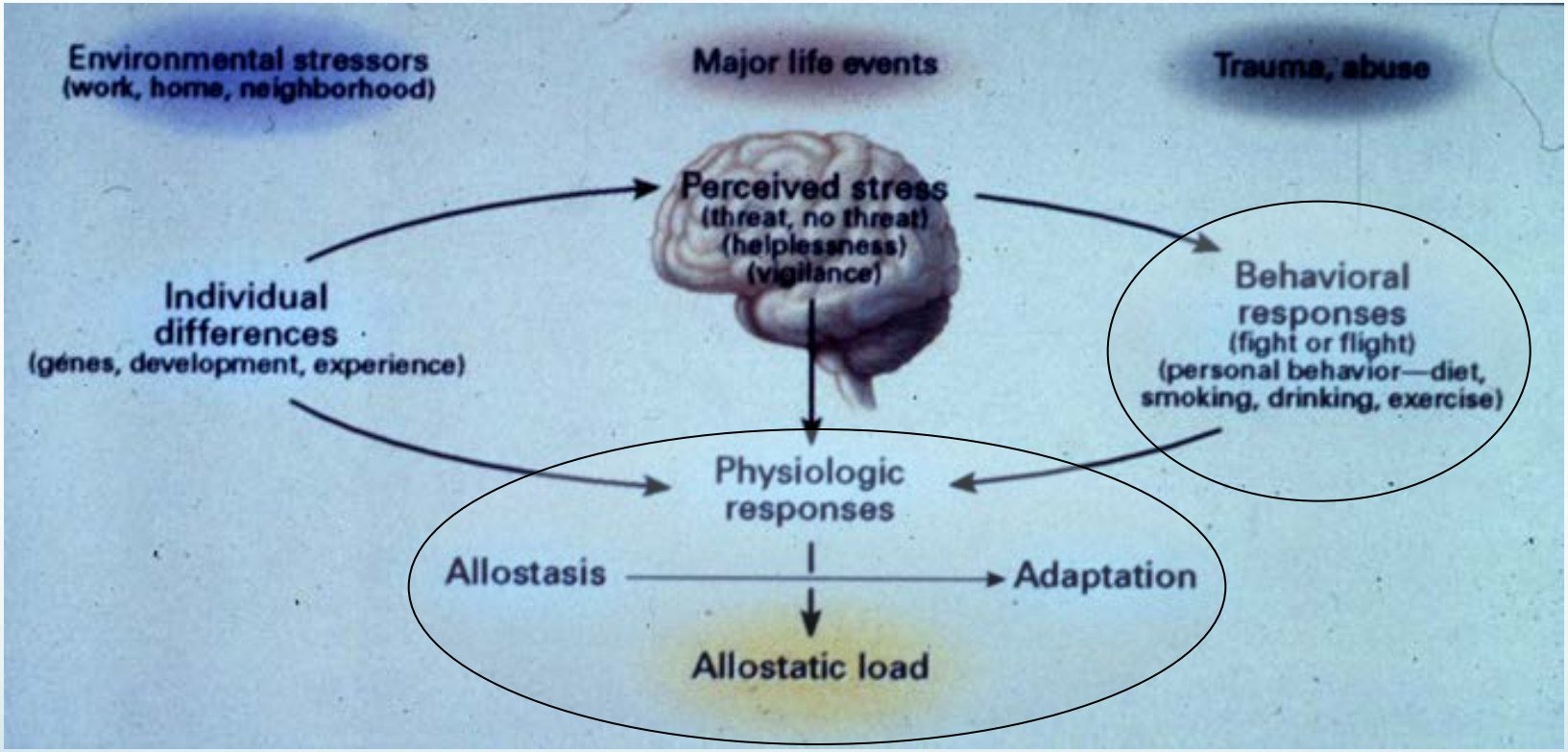
Immune function

Biphasic and non-linear

Dysregulation by
-unhealthy lifestyle, poor sleep, toxic chemicals -feed into network of allostasis (eg elevated inflammation, cortisol)

Social environment and health

Health-related behaviors



Choice of life style is part of being "stressed out"
Sometimes we have no choice!

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

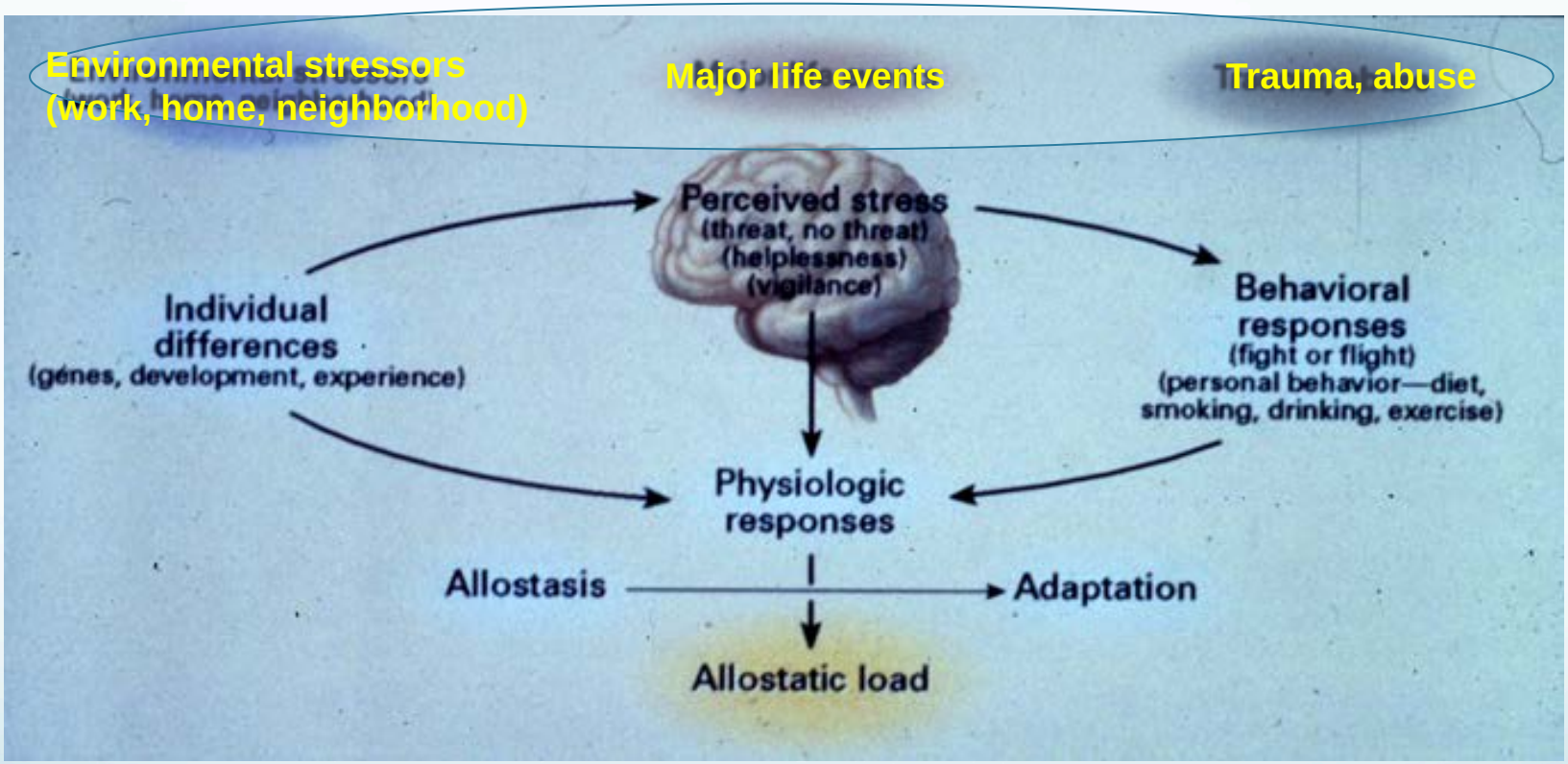
Neglecting regular, moderate exercise

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

Social environment and health

Stressors



Protective and Damaging Effects of Stress Mediators

McEwen B. New England J. Med. 1998

Types of Stress

Positive Stress

- Exhilaration from a challenge that has a satisfying outcome
- Sense of mastery and control
- Good self esteem

Tolerable Stress

- Adverse life events but good social and emotional support
- Sense of mastery and control
- Good self esteem

Toxic Stress – *lack of sense of control*

- Poor social and emotional support
- *Compromised brain architecture due to early life adversity*
- *Context sensitive genotype makes it worse*

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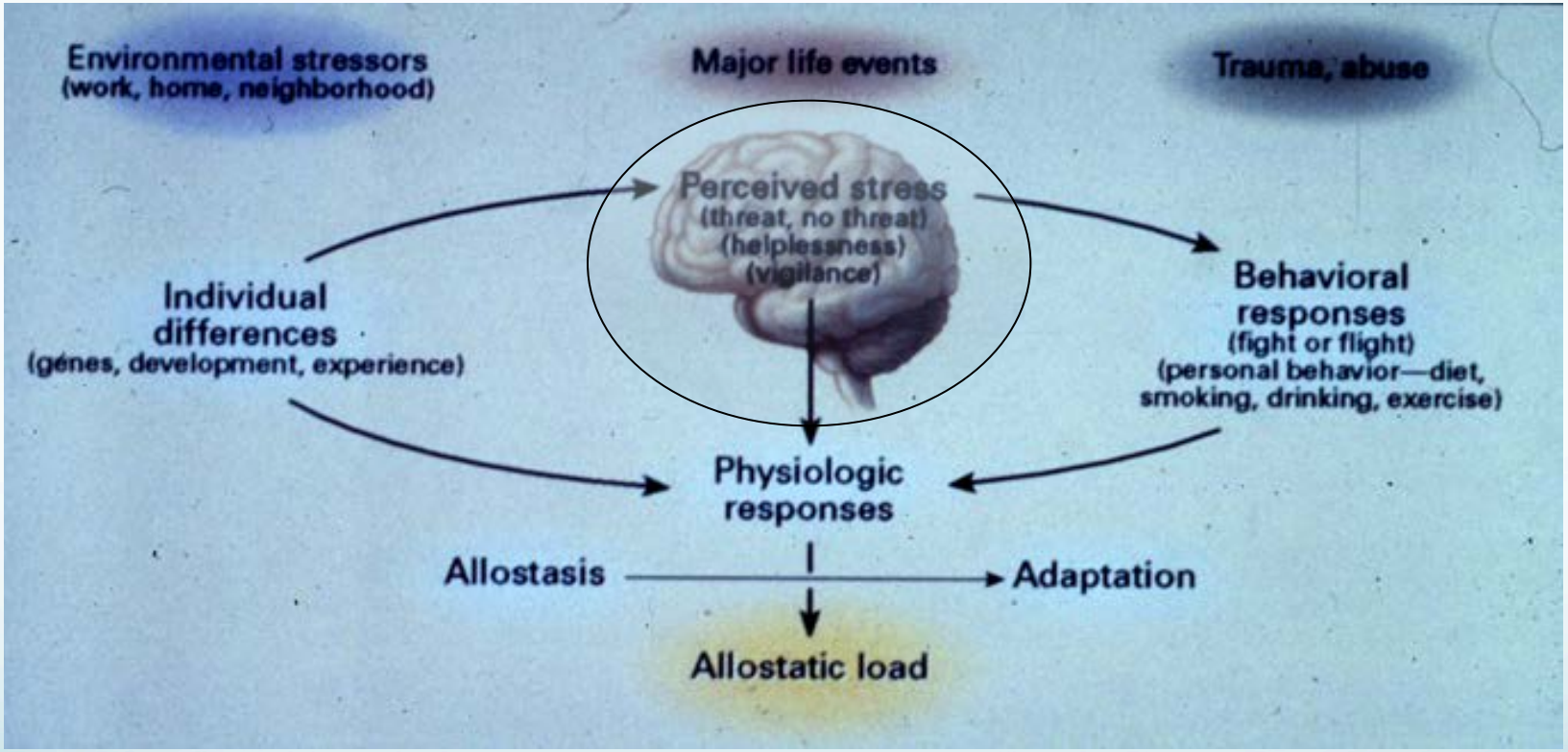
The Brain as a Primary Target of Stress

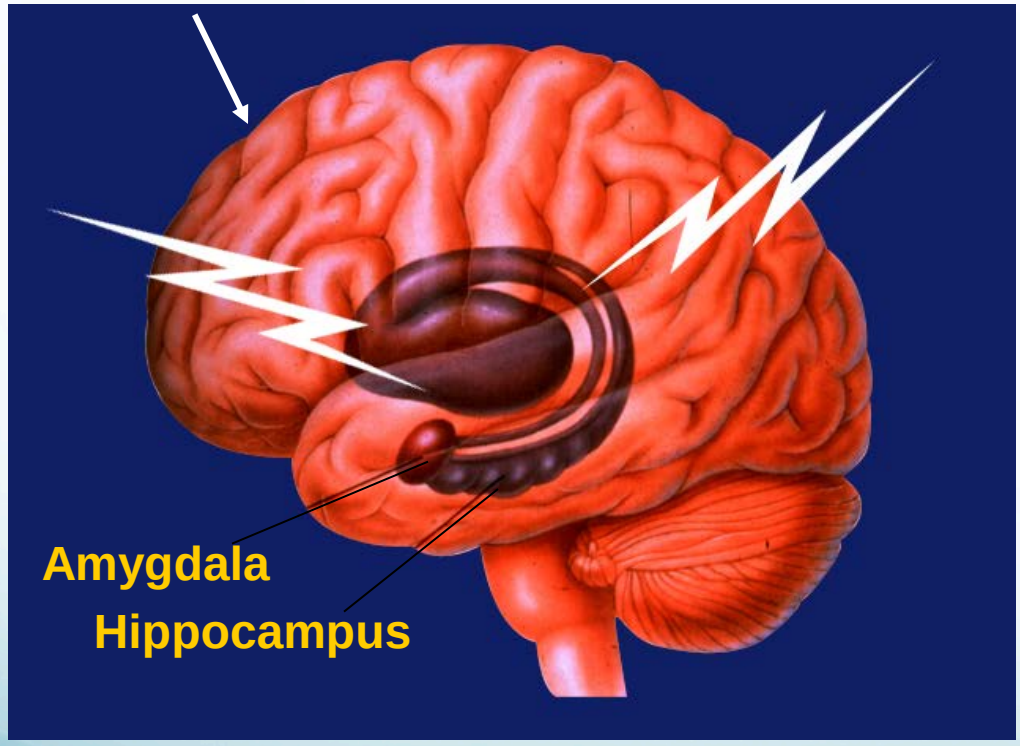


The Human Brain Under Stress

Other key brain regions

Prefrontal cortex

Decision making, working memory,
Self regulatory behaviors: mood, impulses
Helps shut off stress response



Hippocampus

Contextual, episodic, spatial memory

Helps shut off stress response

Amygdala

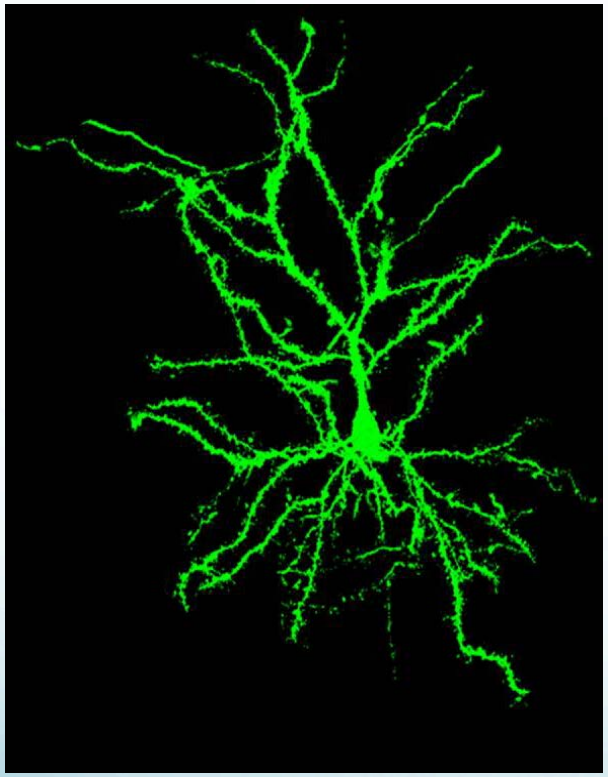
Emotion, fear, anxiety,

Aggression

Turns on stress hormones and increases heart rate

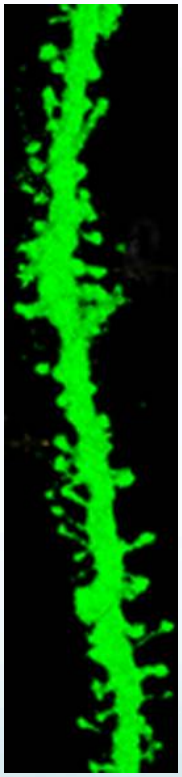
Remodeling of neural architecture

In adult as well as developing brain



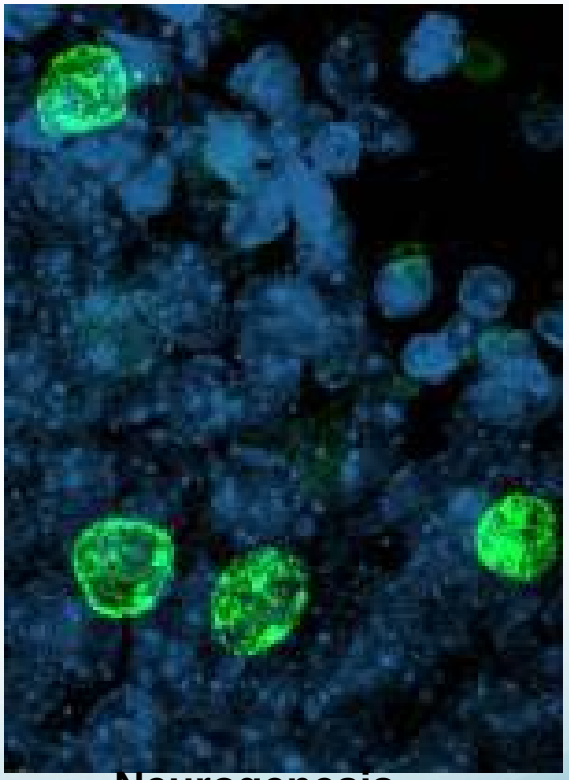
Dendrites

Shrink and expand



Synapses

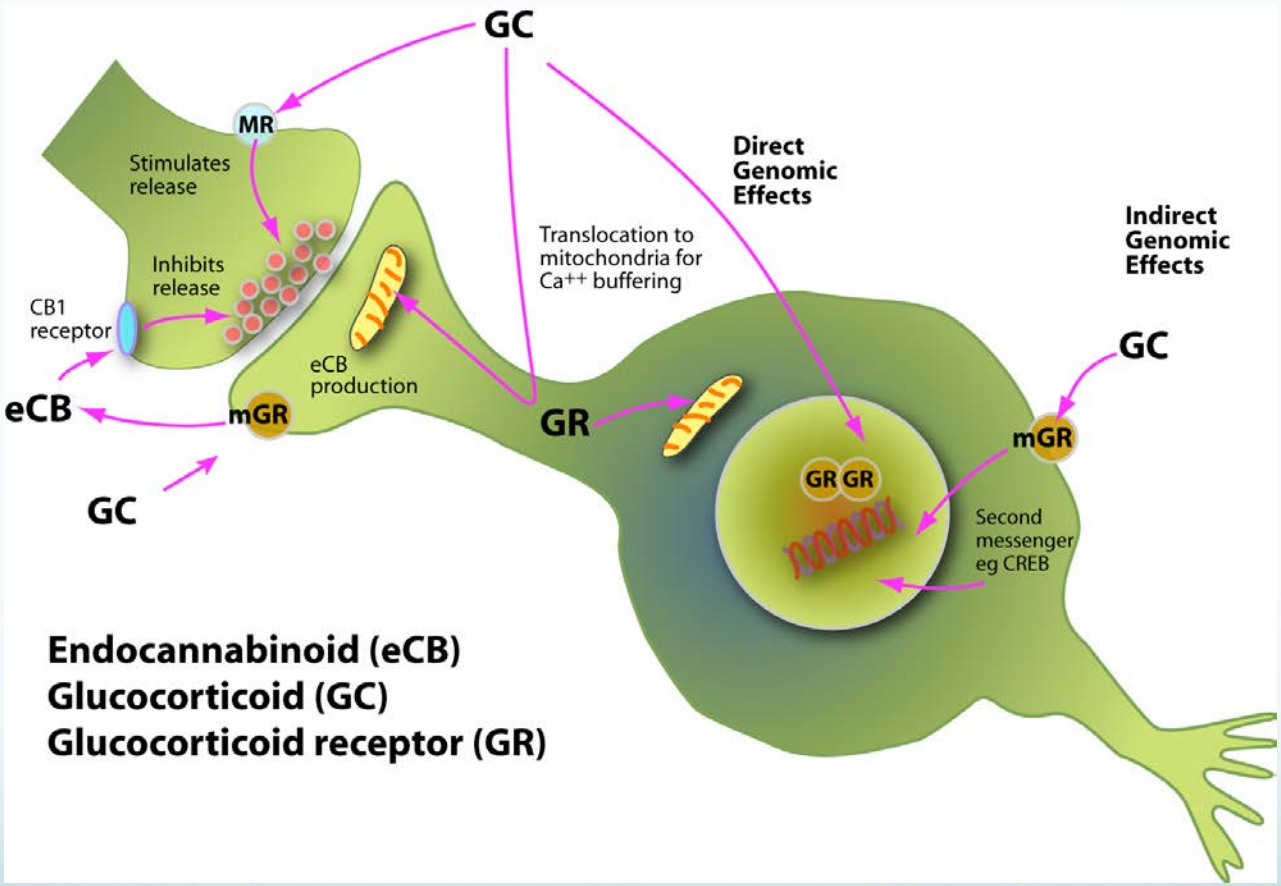
Disappear and are replaced



Neurogenesis

Continues in some brain areas

Diverse Mechanisms of Adrenal Steroid Action

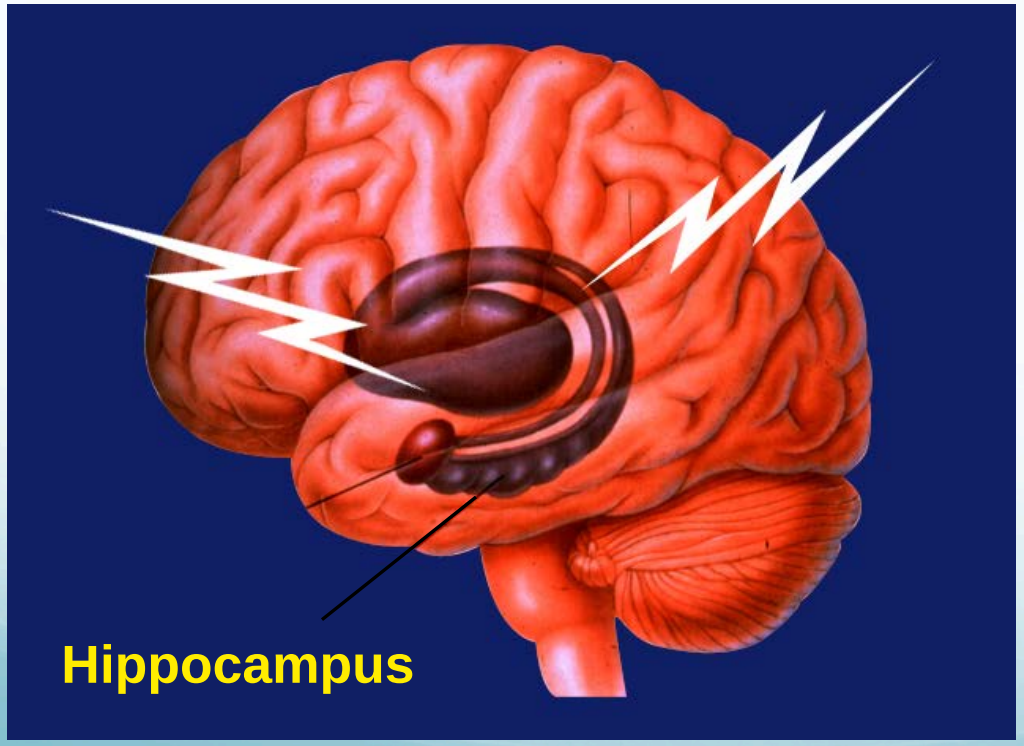


The Brain Under Stress

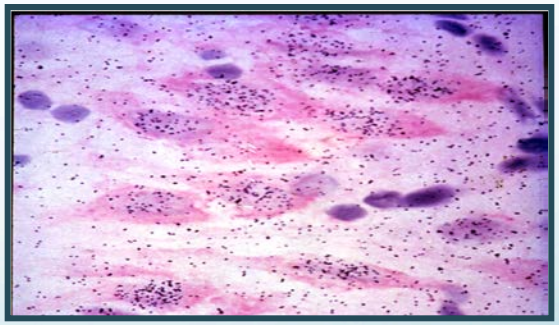
Receptors for Adrenal Steroids in Hippocampus

Memory of daily events, spatial memory

Mood regulation – target of depression



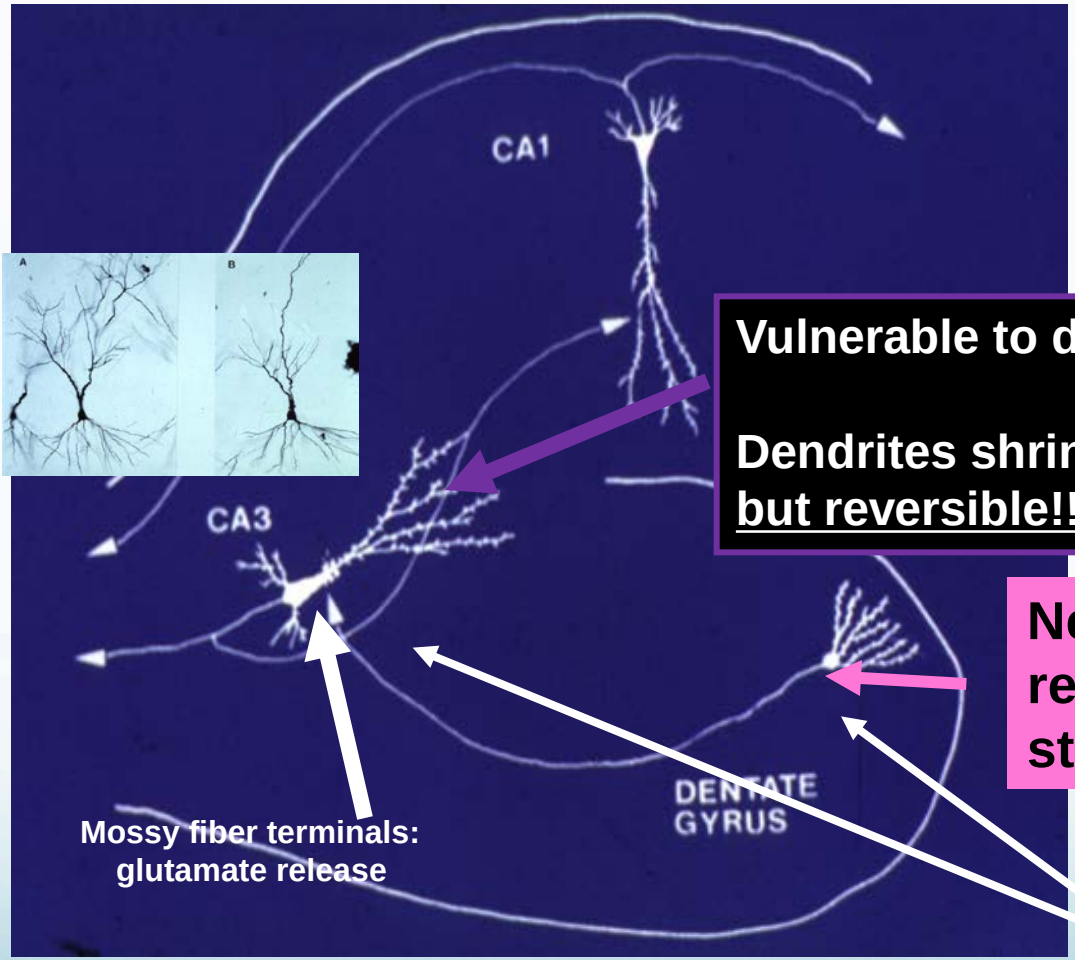
Adrenal steroid receptors in hippocampus



Receptors in cell nuclei regulate gene expression

Stress, Glucocorticoids and other modulators

Dentate gyrus - CA3: plasticity and vulnerability



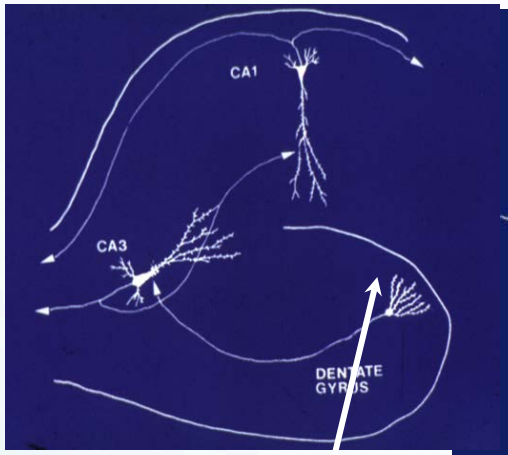
Brain Under Stress

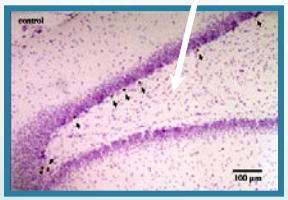
Effects of chronic stress on dentate gyrus neurogenesis

Hippocampus

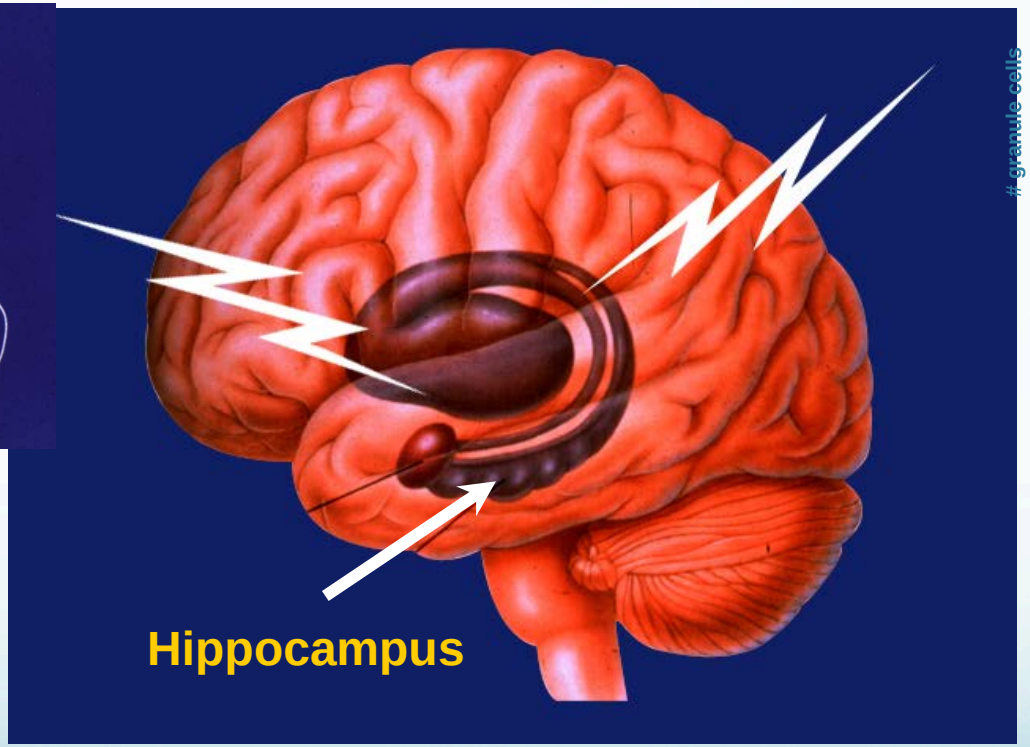
Contextual, episodic, spatial memory

Mood regulation – target of depression

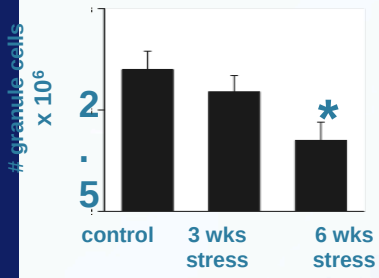


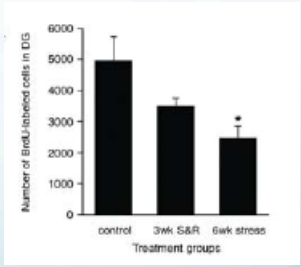


Neurogenesis



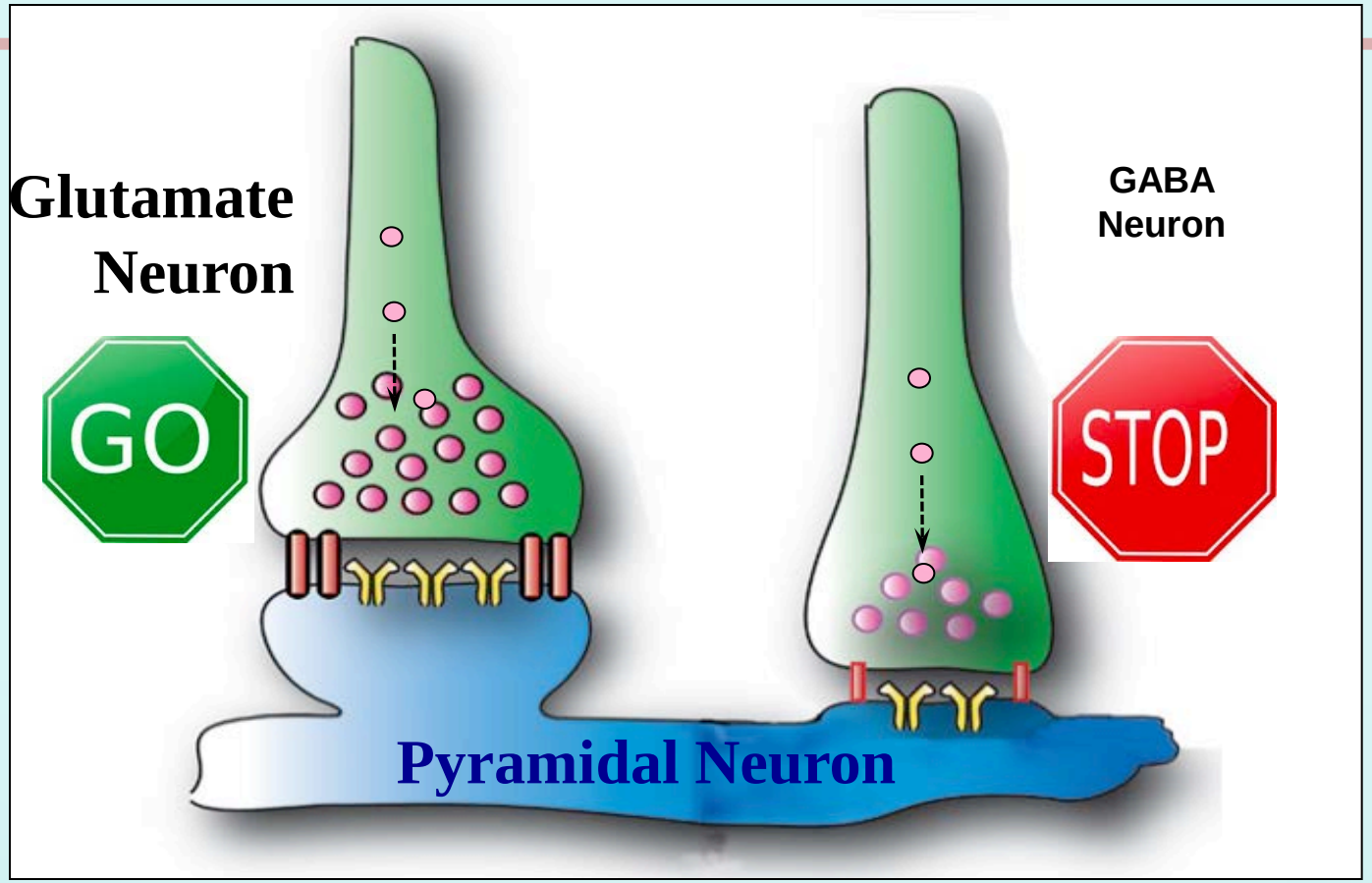
Stress decreases granule cell #





Stress inhibits neurogenesis

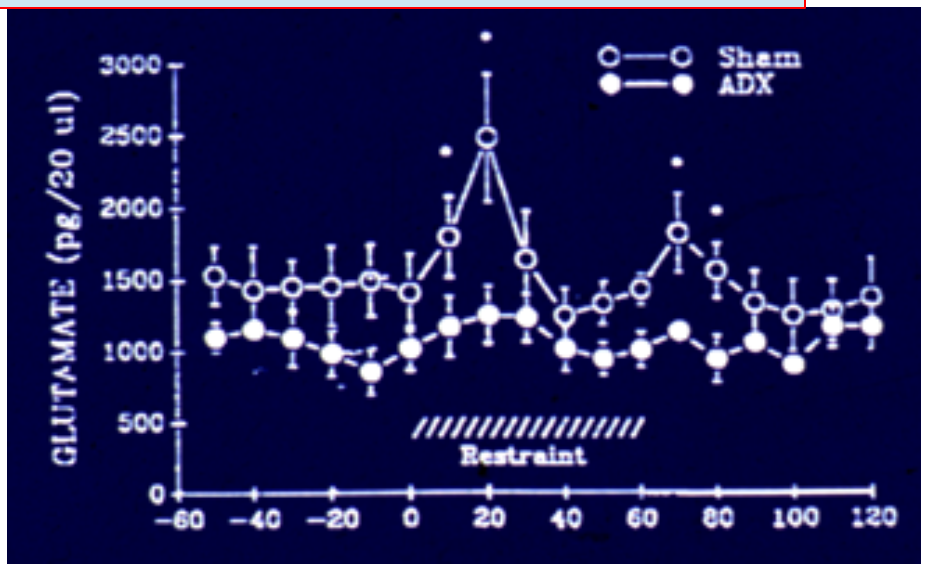
Excitatory *Inhibitory*



Key role of glutamate in brain plasticity and normal brain function

The Stressed Glutamatergic Synapse and Link to Cortisol

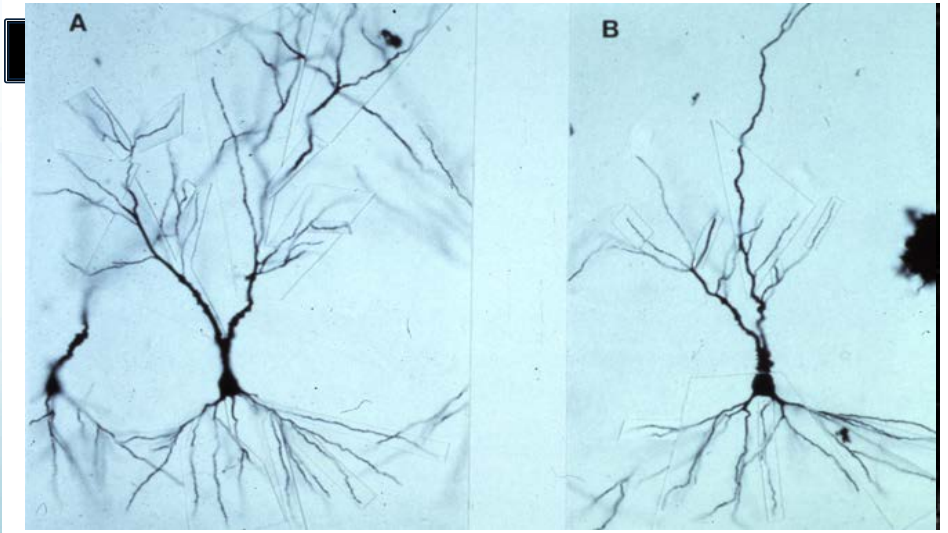
Stress induces strong elevation of extracellular glutamate levels that is dependent on adrenal glands



Lowy M,Gault L,Yamamoto BK,'93

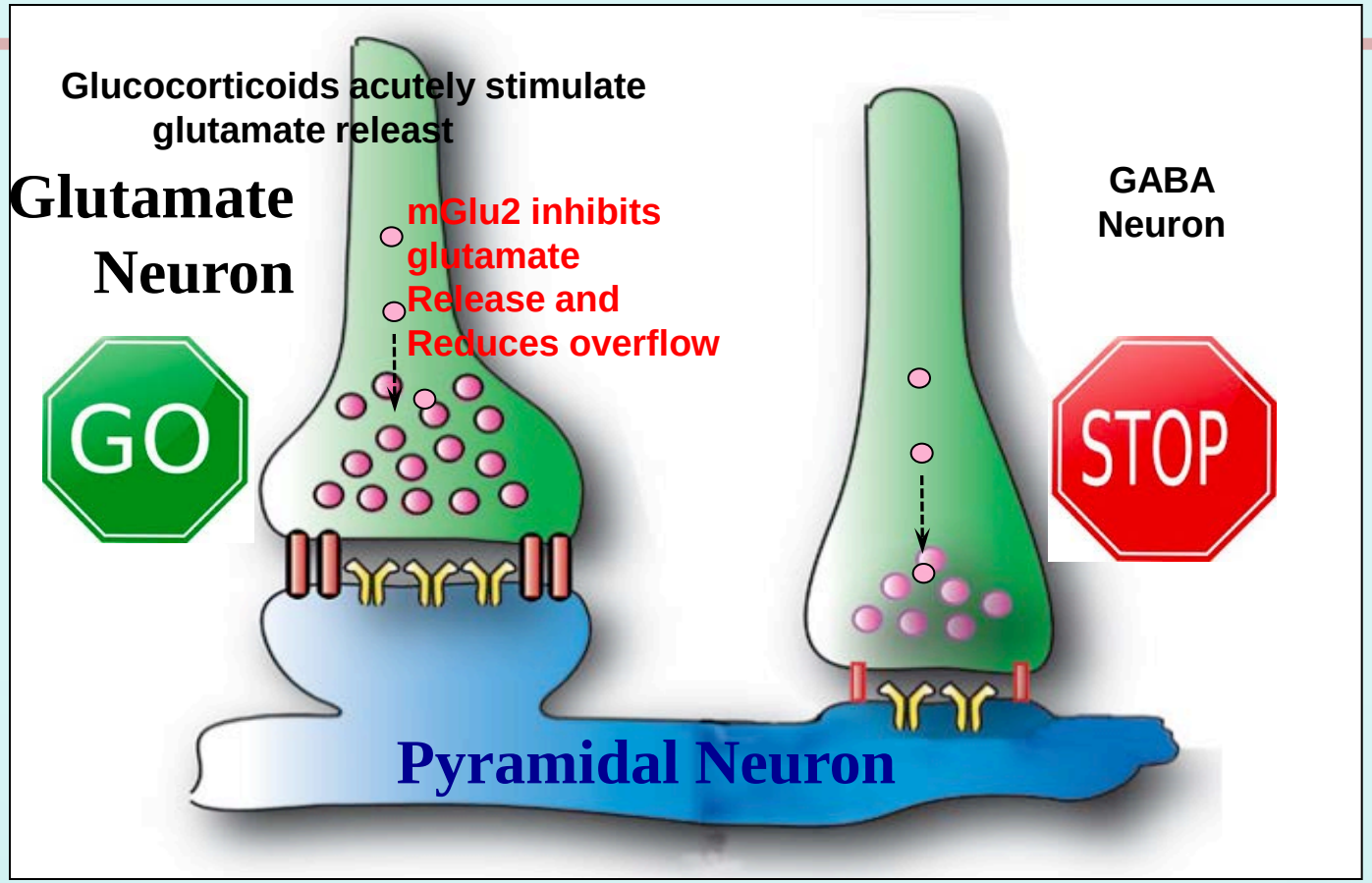
Chronic stress effects on dendritic remodeling are blocked by blocking NMDA receptors, as well as blocking adrenal steroid synthesis

Control **Chronic stress**



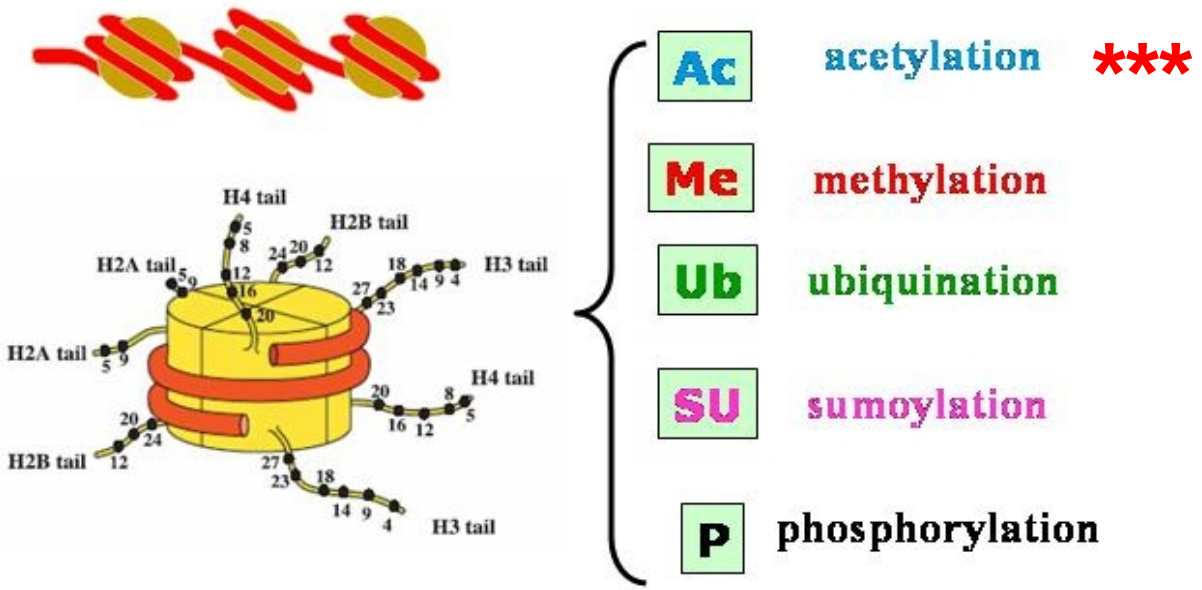
Magarinos AM, McEwen BS, '95

Excitatory *Inhibitory*



Key role of glutamate brain plasticity but glutamate overflow contributes to depression and many neurodegenerative diseases

What about epigenetic regulation by histone modifications?



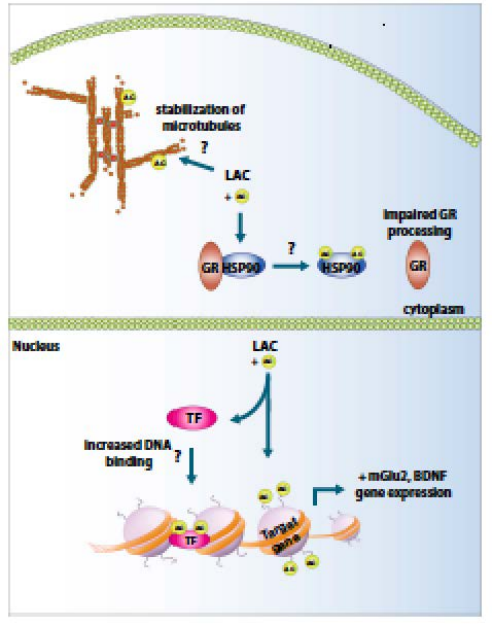
The figure illustrates nucleosome models and major posttranslational modifications which play essential roles in gene expression regulation and disease processes

L-acetylcarnitine causes rapid antidepressant effects through the epigenetic induction of mGlu2 receptors

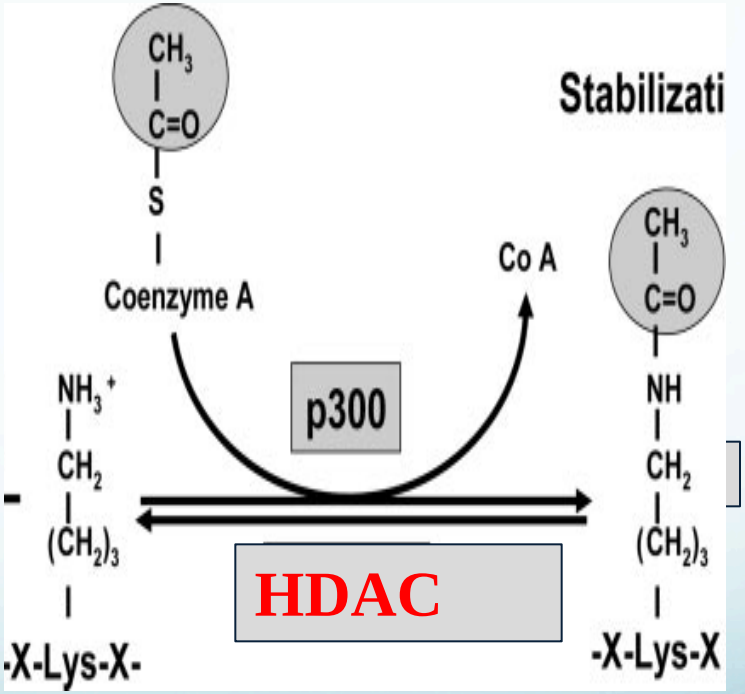
Carla Nasca[a,1], Dionysios Xenos[a], Ylenia Barone[b], Alessandra Caruso[a], Sergio Scaccianoce[a], Francesco Matrisciano[a], Giuseppe Battaglia[c], Aleksander A. Mathé[d], Anna Pittaluga[e], Luana Lionetto[f], Maurizio Simmaco[f], and Ferdinando Nicoletti[a,c]

[a]Department of Physiology and Pharmacology, University of Rome "Sapienza," 00185 Rome, Italy; [b]Psychiatric Clinic, Department of Systems Medicine, University of Rome "Tor Vergata," 00133 Rome, Italy; [c]Istituto di Ricovero e Cura a Carattere Scientifico Neuromed, 86077 Pozzilli, Italy; [d]Clinical Neuroscience, Psychiatry, Karolinska Institutet, Karolinska University Hospital Huddinge, 14186 Stockholm, Sweden; [e]Center of Excellence for Biomedical Research, University of Genoa, 16132 Genoa, Italy; and [f]Department of Neuroscience and Mental Health, St. Andrea Hospital, 00189 Rome, Italy

Edited* by Bruce S. McEwen, The Rockefeller University, New York, NY, and approved December 27, 2012 (received for review September 15, 2012)

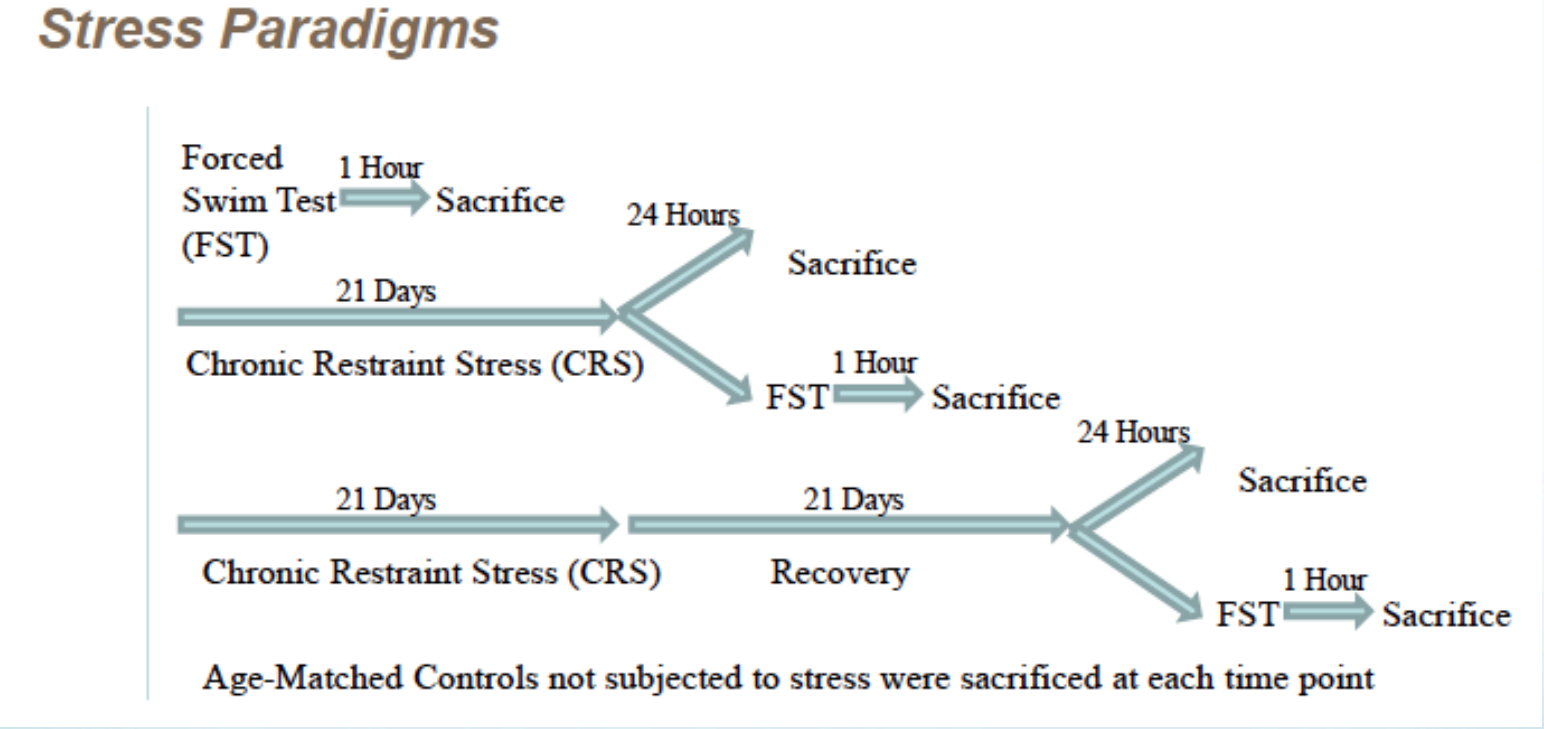


Acetylcarnitine promotes acetylation;
HDAC inhibitors prevent de-acetylation



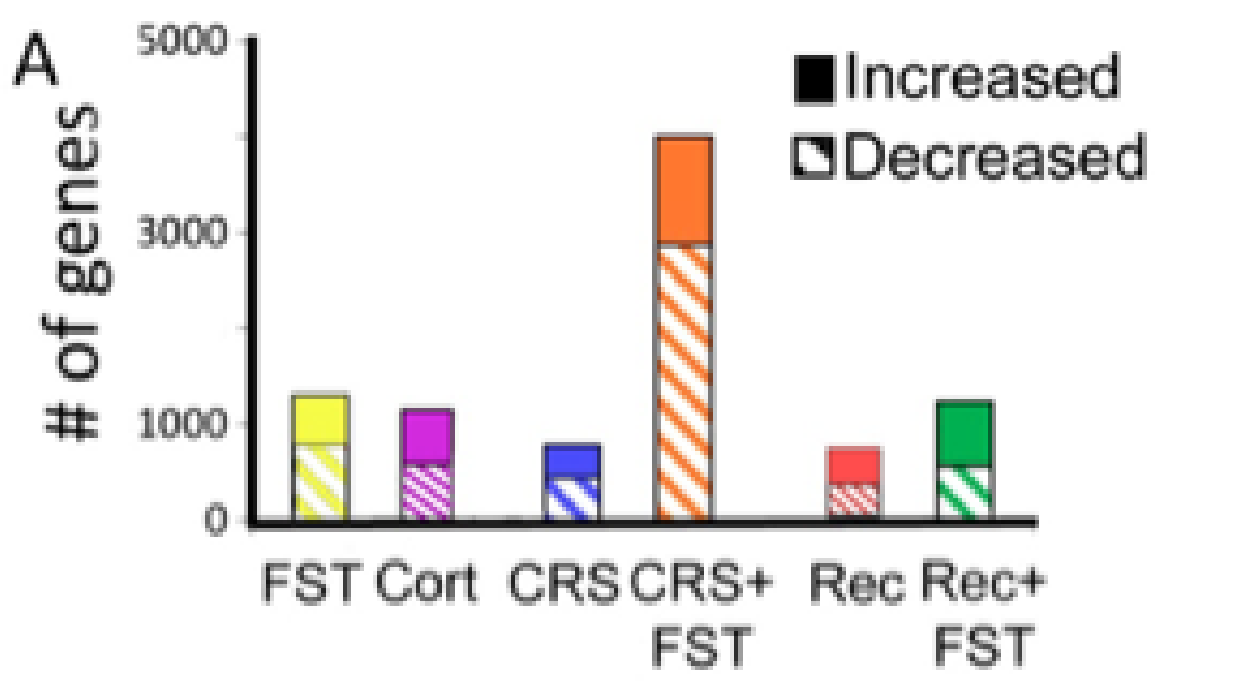
Dr. Carla Nasca

Gene expression profiles change with chronic stress and recovery



Ongoing studies in mice by Drs. Jason Gray and Carla Nasca

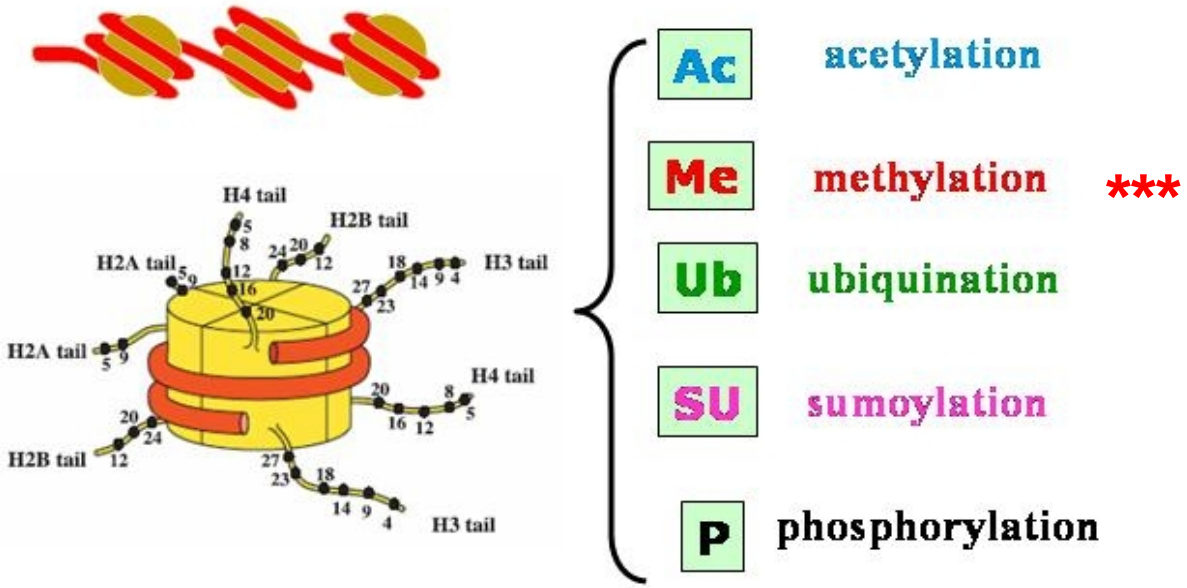
Number of genes turned on or off in hippocampus by acute novel stress or glucocorticoid injection



Chronic restraint stress (CRS) sensitizes hippocampus to acute novel stress

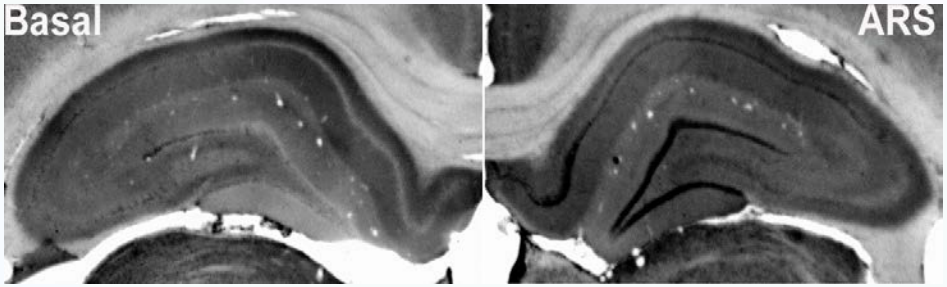
Dr. Jason Gray (Mol Psychiatry 2013)

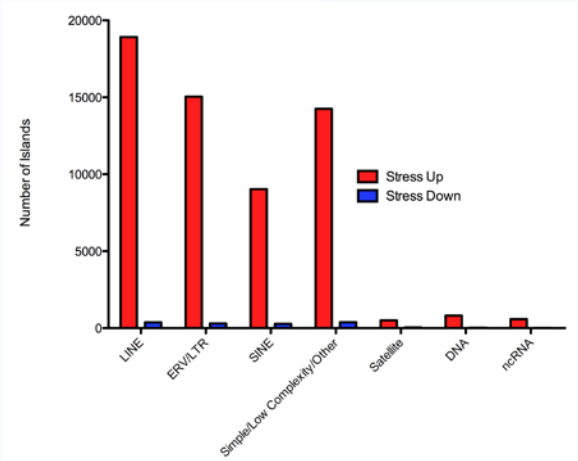
What about epigenetic regulation?



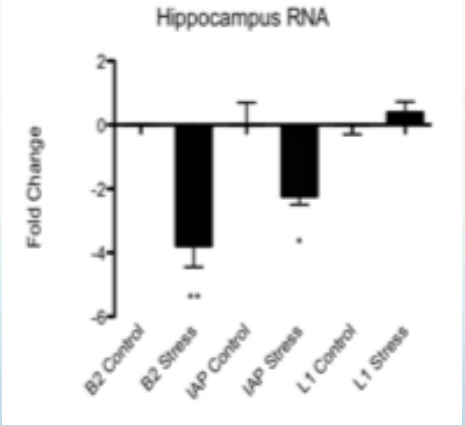
The figure illustrates nucleosome models and major posttranslational modifications which play essential roles in gene expression regulation and disease processes

Acute Stress (ARS) Increases H3K9me3 …
…..and Represses DNA of Retrotransposon Loci
that are trapped by Chromosome Immuno Precipitation……



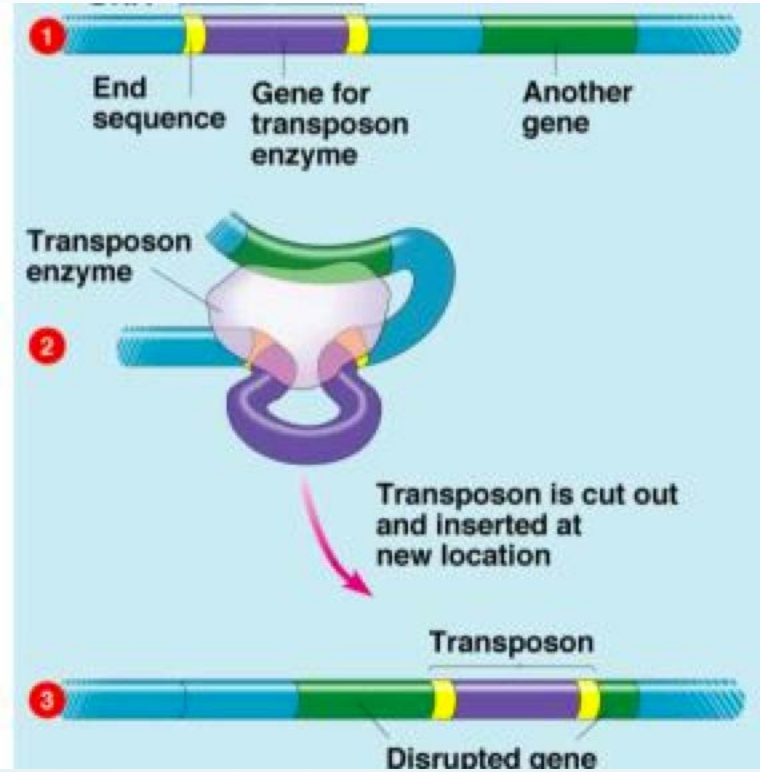


…and that repression reduces RNA that is transcribed from those loci



Dr. Richard Hunter

Jumping Genes: Transponsons and Retrotransposons



Barbara McClintock

Summary: Stress – Good and Bad

Role in Synaptic Function, Adaptive Plasticity and Damage

Synaptic functions: enhancement

- Synaptic transmission.
- Long-term potentiation.
- Learning - re: self-preservati

Synaptic functions: suppression

- Synaptic transmission.
- Long-term potentiation.
- Learning - less-important things

Adaptive plasticity

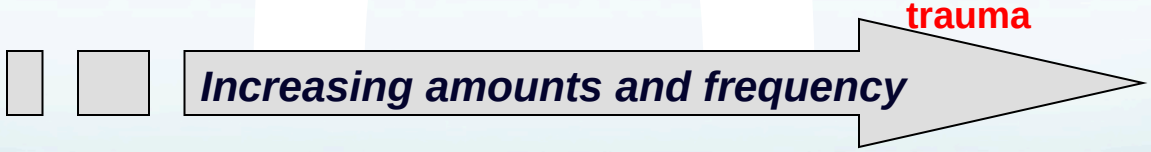
- Suppression of neurogenesis.
- Mediates dendritic remodeling.

Loss of resilience

> Neurochemical distortion
> Impaired remodeling
and lack of recovery from stress

Damage potentiation:

- Mediates excitotoxicity in seizures, stroke, & head trauma



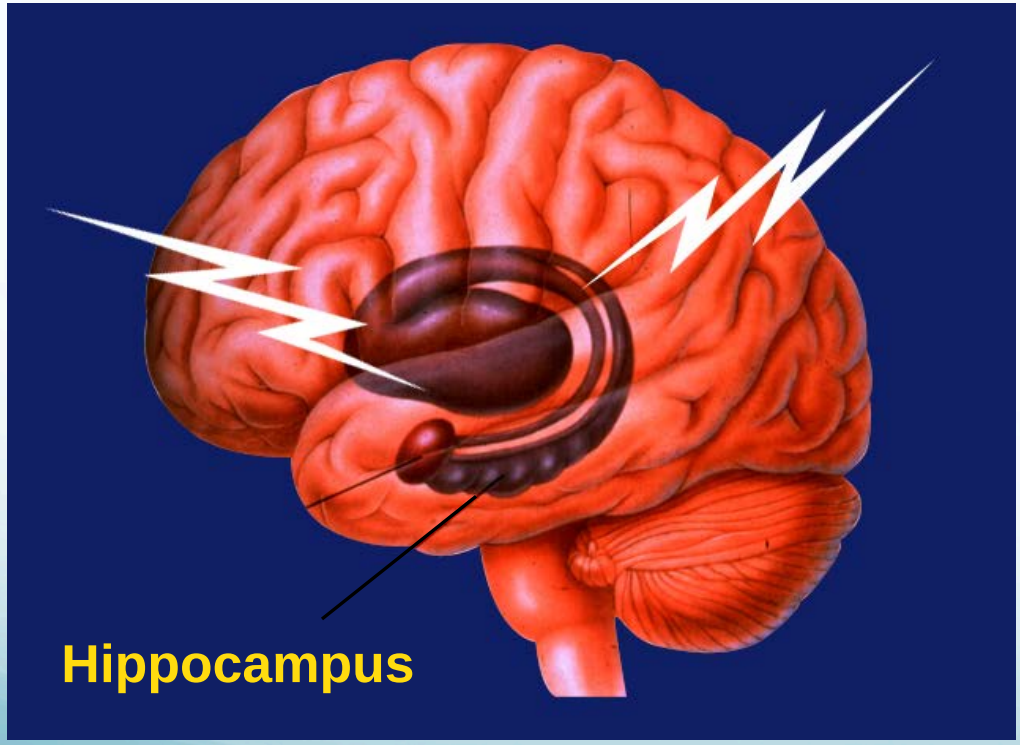
Adrenal steroids and excitatory amino acids modulate both limbs of inverted U

*****Chronic stress: how much protection vs. destabiization?**

The Human Hippocampus Under Stress

Contextual, episodic, spatial memory

Mood regulation – target of depression



Hippocampus *ATROPHIES* in:

- **Major depression**
- **Type 2 diabetes**
- **Post-traumatic stress disorder**
- **Cushing's disease**

***ALSO* as a result of:**

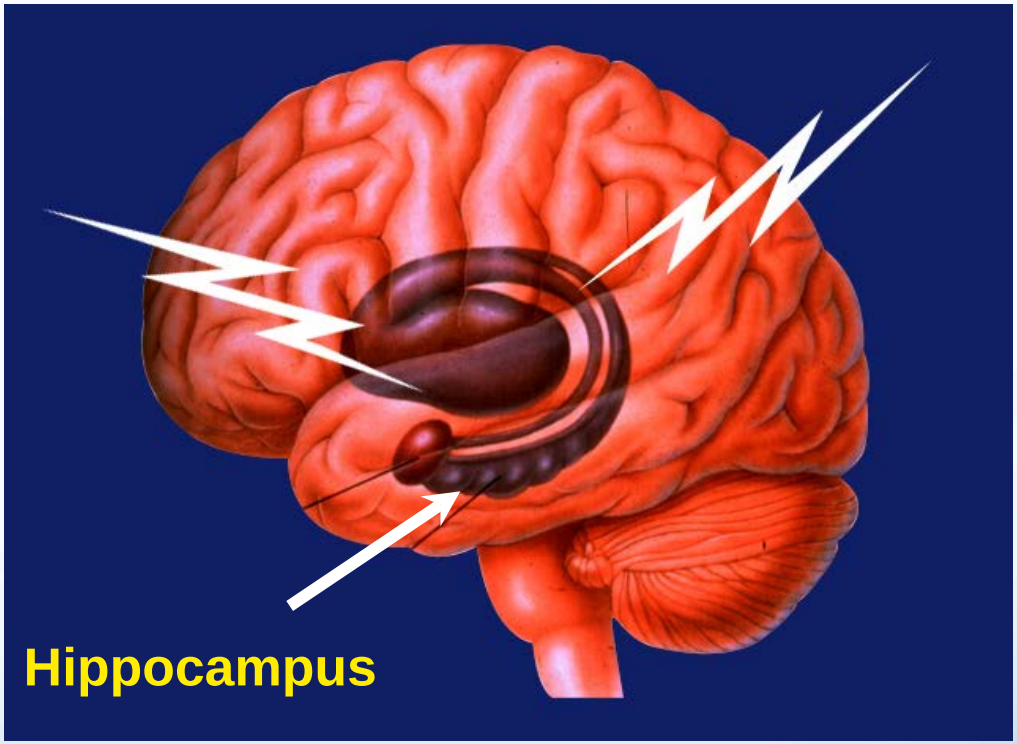
- **Chronic stress**
- **Chronic jet lag**
- **Lack of exercise**
- **Chronic inflammation**

The Human Hippocampus Under Stress

The Positive Side of the Story

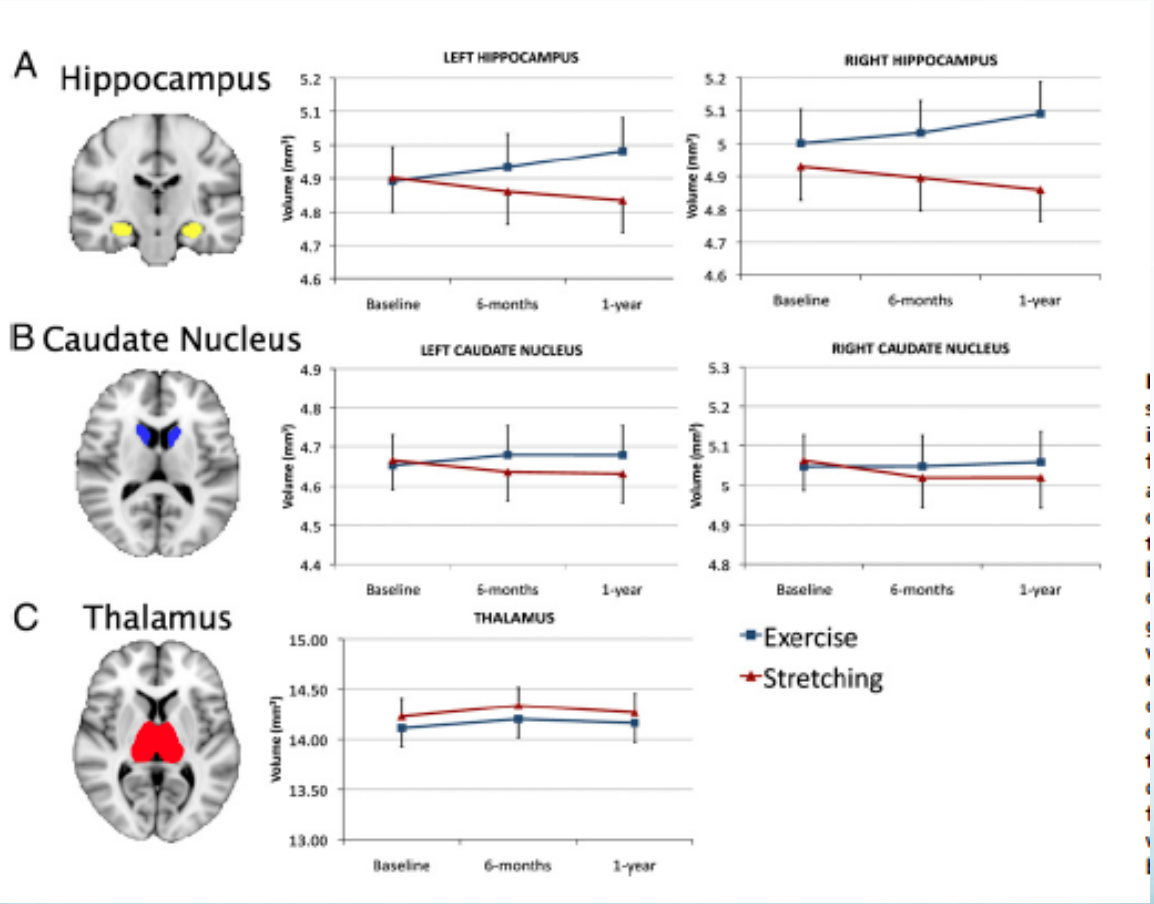
Hippocampus INCREASES in size with:

- **Regular exercise**
- **Intense learning**
- **Anti-depressant treatment**

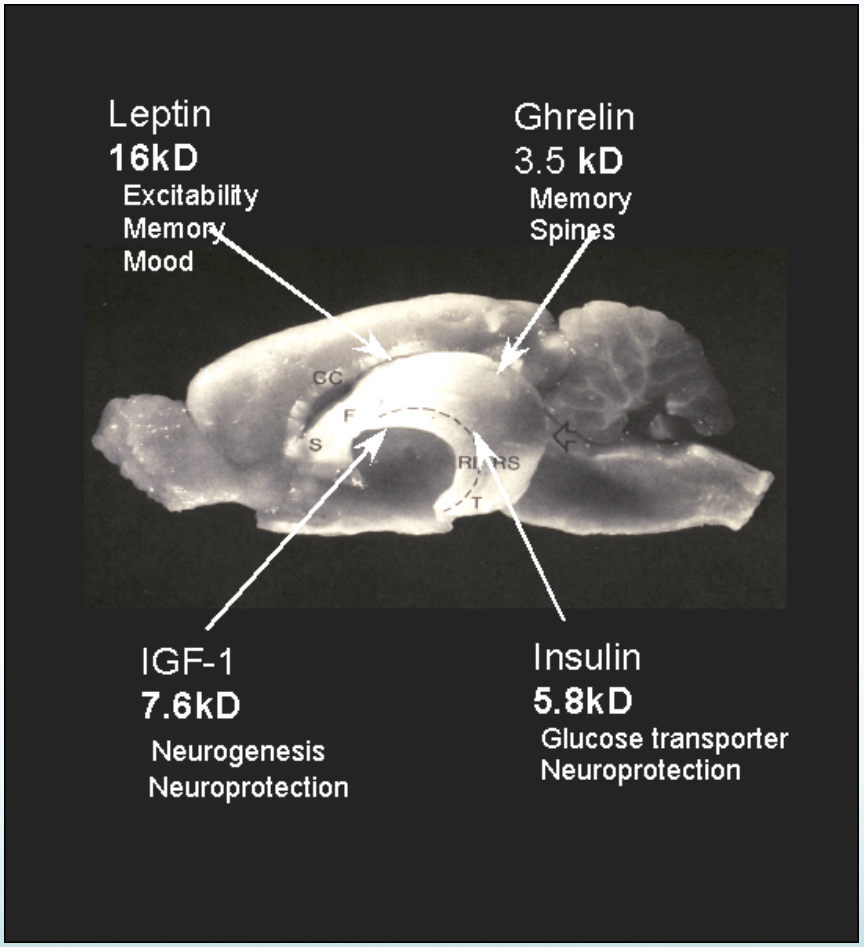


Exercise training increases size of hippocampus and improves memory

Kirk I. Erickson[a], Michelle W. Voss[b,c], Ruchika Shaurya Prakash[d], Chandramallika Basak[e], Amanda Szabo[f], Laura Chaddock[b,c], Jennifer S. Kim[b], Susie Heo[b,c], Heloisa Alves[b,c], Siobhan M. White[f], Thomas R. Wojcicki[f], Emily Mailey[f], Victoria J. Vieira[f], Stephen A. Martin[f], Brandt D. Pence[f], Jeffrey A. Woods[f], Edward McAuley[b,f], and Arthur F. Kramer[b,c,1]



Protein/peptide hormones enter and affect the brain



Metabolic syndrome and diabetes have impact on brain white matter, hippocampal volume And cognitive function. They are a risk factor for dementia later in life.

Lifecourse Health Development: Past, Present and Future

Neal Halfon · Kandyce Larson · Michael Lu ·
Ericka Tullis · Shirley Russ

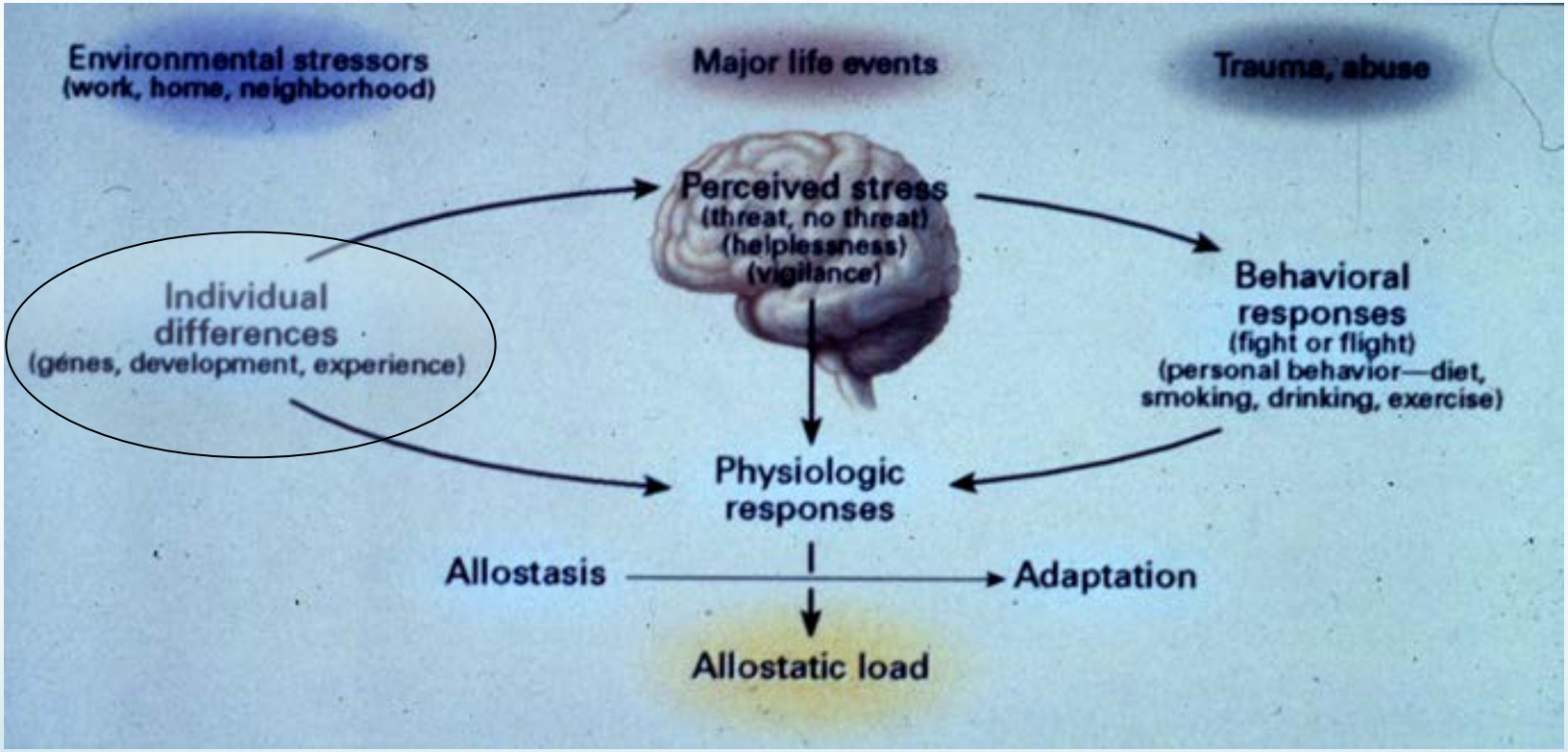
1.0 Germs, Genes and the biomedical model
(antibiotics – ie "magic bullets")

2.0 Multiple risks and the biopsychsocial model
(stress, health behaviors, social environment).
George Engel 1977

3.0 Lifecourse Health Development
(epigenetics, context sensitive genes complex systems biology.)

Toxic stress effects and brain development

Social environment and health
Central Role of the Brain



BIOLOGICAL EMBEDDING
Reactive or "context sensitive" alleles
Epigenetic modifications – transgenerational via DNA and behavior

Gene x Environment Interactions

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

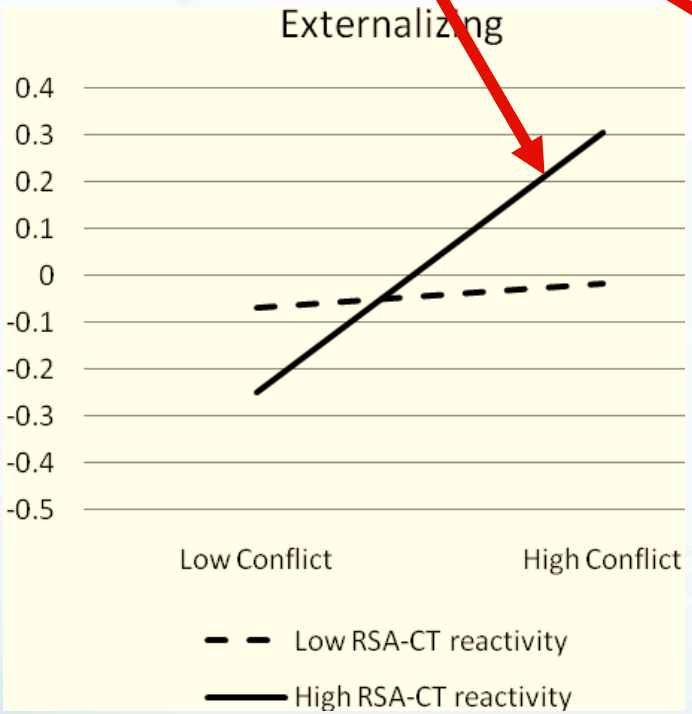
Caspi, A.; McClay, J.; Moffitt, T. E.; Mill, J.; Martin, J.; Craig, I. W.; Taylor, A., and Poulton, R.
Role of genotype in the cycle of violence in maltreated children.
Science. 2002; 297:851-854.

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

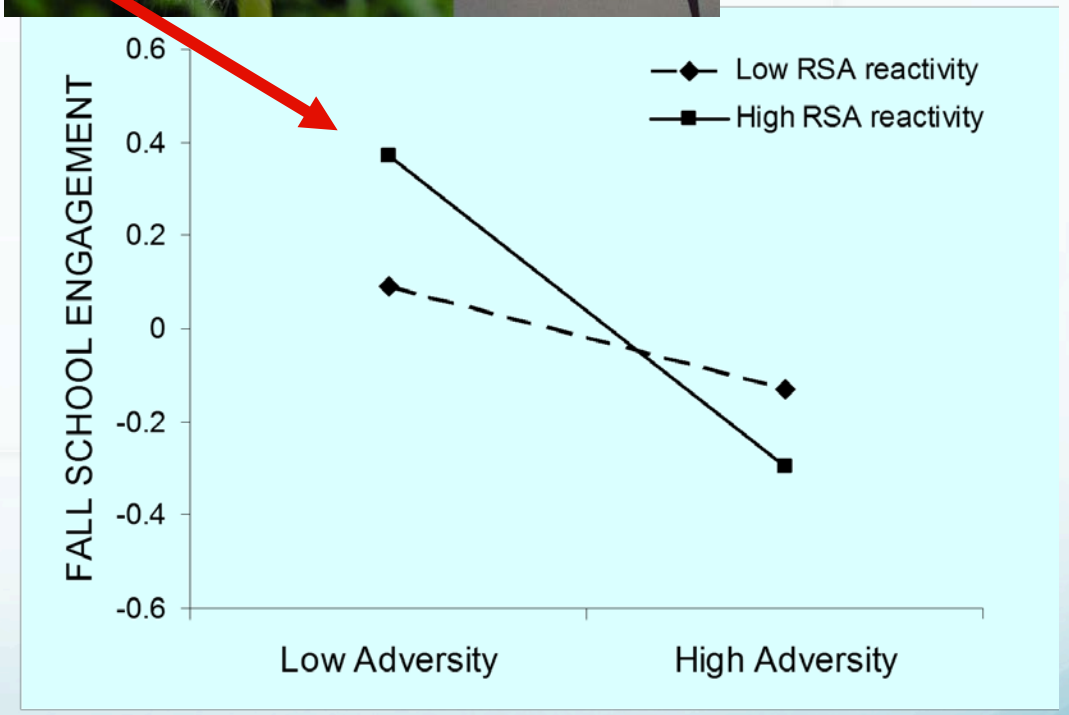
Caspi, A.; Sugden, K.; Moffitt, T. E.; Taylor, A.; Craig, I. W.; Harrington, H.; McClay, J.; Mill, J.; Martin, J.; Braithwaite, A., and Poulton, R.
Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene.
Science. 2003; 301:386-389.

Study in New Zealand

The Dandelion and the Orchid



Effects of marital conflict on child externalizing behavior at age 5 (Obradovic et al., 2011, *Development and Psychopathology)*



Effects of family adversity on children's school engagement at age 5 (Obradovic et al., 2010, *Child Development)*

Developmental Issues for Children

Low socioeconomic status

Poor language skills and executive function
and other effects on learning ability
Hart and Risley "Meaningful Differences"

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 accumulation, systemic inflammation and poor dental health
Gary Evans, Andrea Danese, Greg Miller, Edith Chen

"Risky families" – cold, unsupportive, neglect

Many same consequences but not as extensively studied
This may be an increasing problem with both parents working and ongoing financial and other concerns
Shelley Taylor, Rena Repetti, Teresa Seeman

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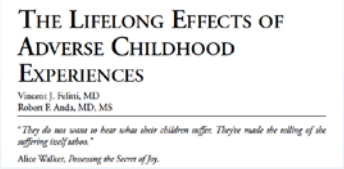
Shelley Taylor, Rena Repetti, Teresa Seeman

Adverse Childhood Experiences (ACE)

Table 10-1. Categories of Adverse Childhood Experiences

Abuse, by Category	Prevalence (%)
Psychological (by parents)	11%
Physical (by parents)	28%
Sexual (anyone)	22%
Neglect, by Category	
Emotional	15%
Physical	10%
Household Dysfunction, by Category	
Alcoholism or drug use in home	27%
Divorce or loss of biological parent <18	23%
Depression or mental illness in home	17%
Mother treated violently	13%
Imprisoned household member	5%


THE LIFELONG EFFECTS OF ADVERSE CHILDHOOD EXPERIENCES

Vincent J. Felitti, MD
Robert F. Anda, MD, MS

"They do not want to hear what their children suffer. They've made the telling of the suffering itself taboo."

Alice Walker, Possessing the Secret of Joy.

ACE FOUND AT ALL SES LEVELS

LASTING EPIGENETIC EFFECTS ON BRAIN ARCHITECTURE AND SYSTEMIC PHYSIOLOGY

Adverse Childhood Experience – Health Consequences

carried out in Kaiser-Permanente Health System in California

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

Heart disease, smoking, obesity

Drug abuse, high risk for AIDS

Depression, anxiety, anger control

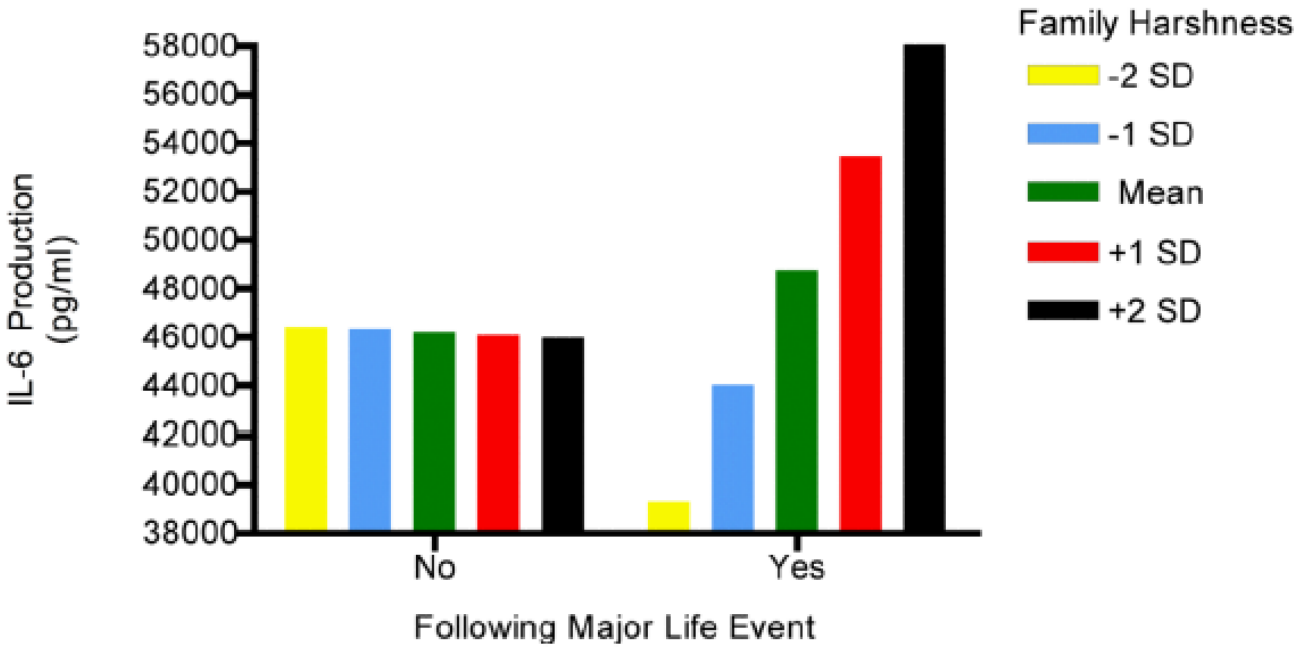
Anti-social behavior

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

Psychol Sci. 2010 June ; 21(6): 848–856. doi:10.1177/0956797610370161.

HARSH FAMILY CLIMATE IN EARLY LIFE PRESAGES THE EMERGENCE OF PRO-INFLAMMATORY PHENOTYPE IN ADOLESCENCE

Gregory E. Miller, Ph.D. and **Edith Chen, Ph.D.**
Department of Psychology, University of British Columbia

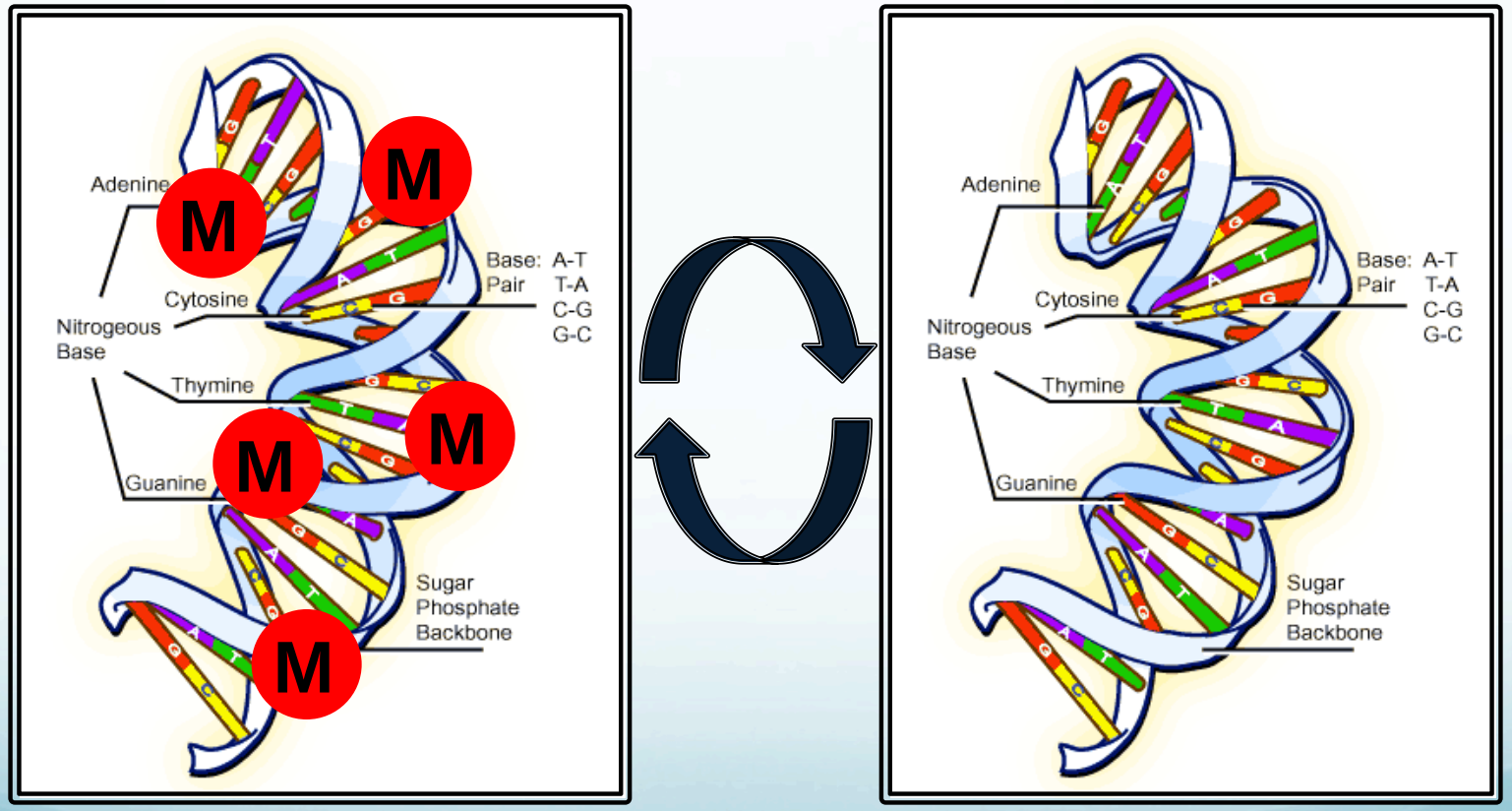


A mechanism converting psychosocial stress into mononuclear cell activation

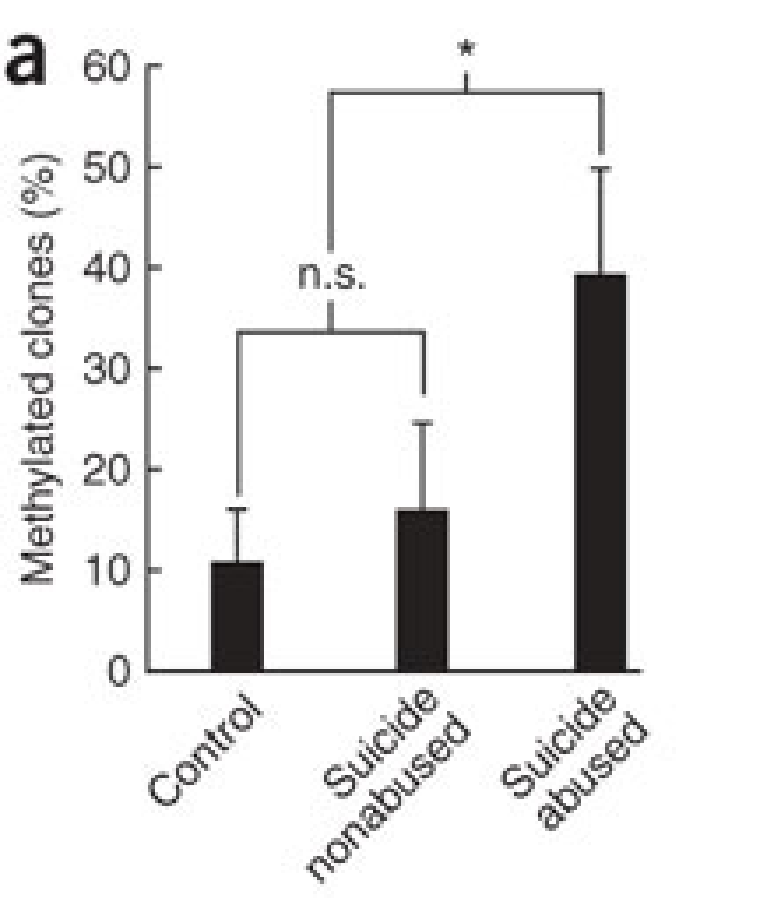
Angelika Bierhaus*[,1], Jutta Wolf[†,§], Martin Andrassy*, Nicolas Rohleder[§], Per M. Humpert*, Dimitri Petrov*, Roman Ferstl[¶], Maximilian von Eynatten*, Thoralf Wendt*, Gottfried Rudofsky*, Martina Joswig*, Michael Morcos*, Markus Schwaninger[‖], Bruce McEwen[**], Clemens Kirschbaum[§], and Peter P. Nawroth*

Methylation of CpG residues in DNA

An epigenetic mechanism



Childhood Abuse Associated with Increased DNA Methylation in the Human Brain

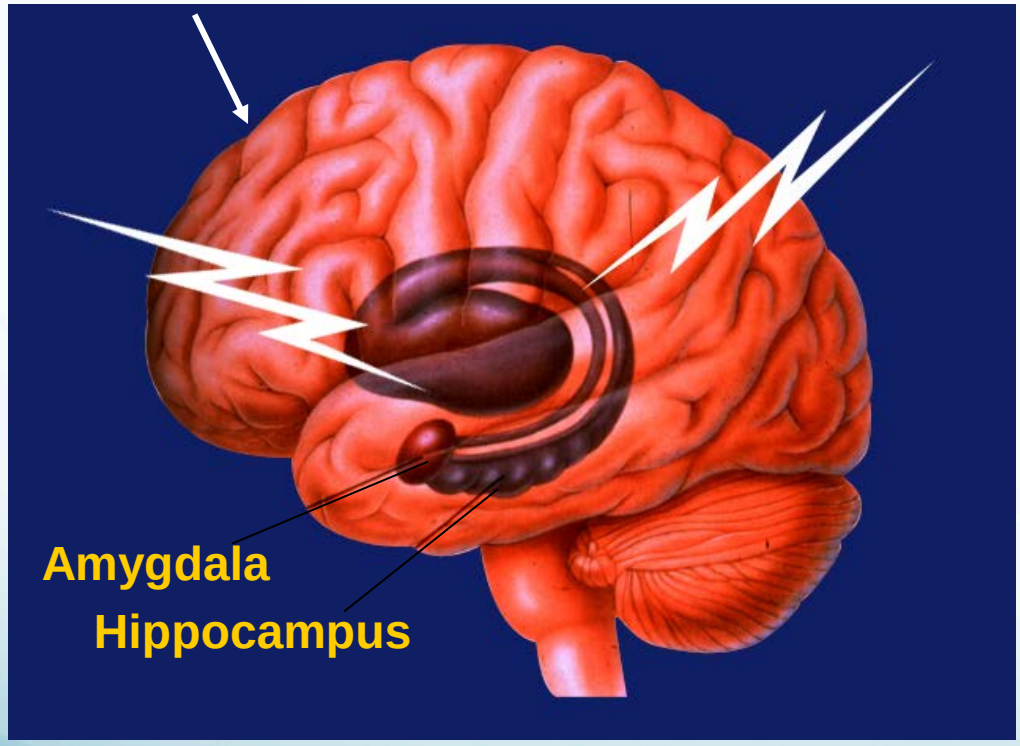


Focus on methylation of glucocorticoid receptor promotor and reduced GR expression.

McGowan et al. *Nature Neuroscience* (2009)

The Human Brain Under Stress

Developmental effects on hippocampus



Hippocampus

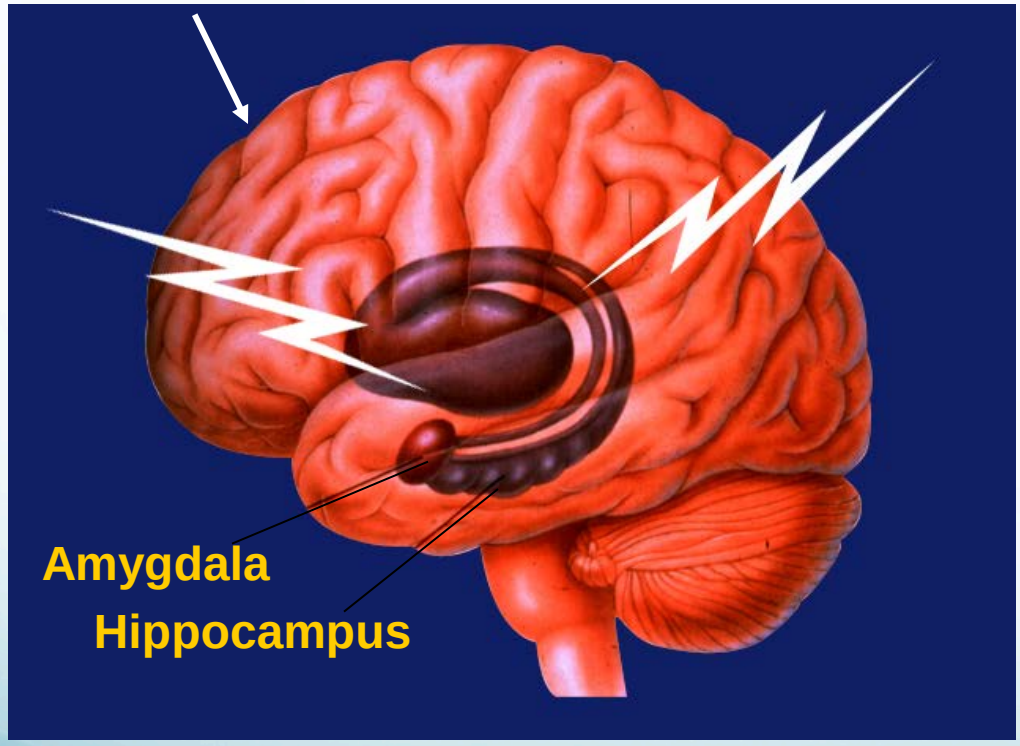
Contextual, episodic, spatial memory

Is smaller in

- **Early life abuse**
- **Low self esteem**
- **Risk for PTSD**

The Human Brain Under Stress

Developmental effects on amygdala



Amygdala

Emotion, fear, anxiety,

Aggression

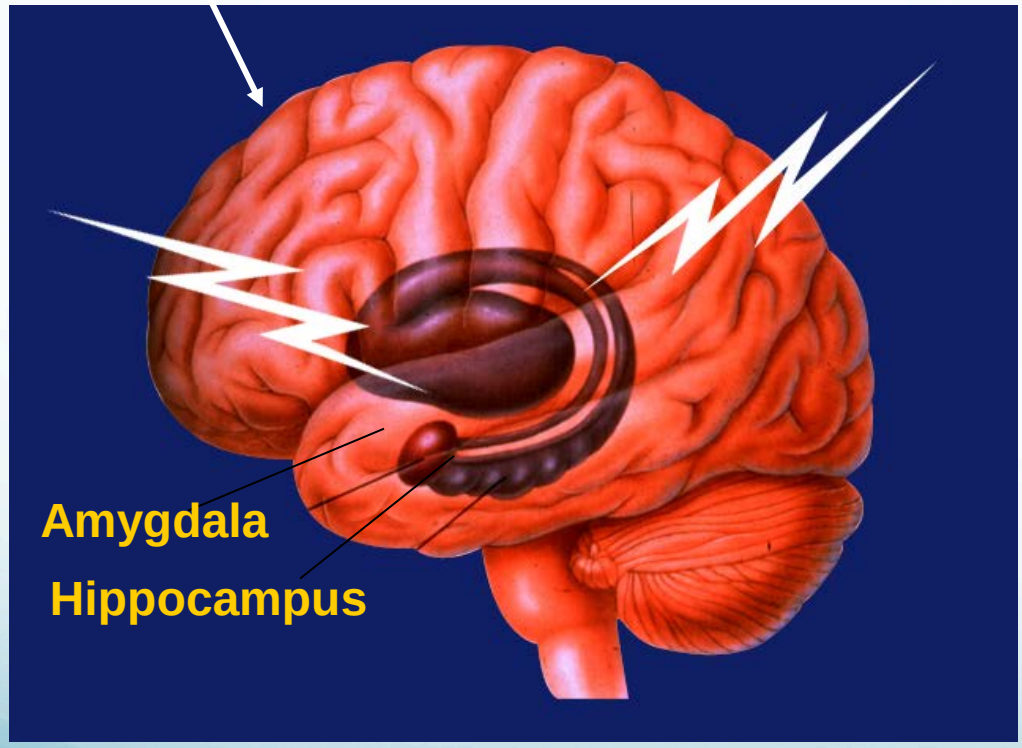
Larger and more active in depression, anxiety disorders

The Human Brain Under Stress

Developmental effects on prefrontal cortex

Prefrontal cortex

Decision making, working memory,
Self regulatory behaviors: mood, impulses
Underdeveloped with chaos, early life abuse



Life course health development

Prenatal - maternal stress, obesity, germ line

Early postnatal - biological embedding – adverse and positive

Adolescence - reduced fear learning and also reduced extinction

Young adults - life style, health behaviors, behavioral interventions

Aging - same as young adults + generativity, meaning and purpose

Interaction Shapes Brain Circuitry

An "Air Traffic Control System" in the Brain

Executive functioning is group of skills that help us to focus on multiple streams of information at the same time, set goals and make plans, make decisions in light of available information, revise plans, and resist hasty actions.

Prefrontal cortex

- **Executive function is a key biological foundation of school readiness as well as outcomes in health and employability**

What are Executive Function Skills?

Inhibitory Control — filter thoughts and impulses to resist temptation and distractions

Working Memory — hold and manipulate information in our heads over short periods of time

Cognitive flexibility — adjust to changed demands, priorities, or perspectives

Higher Childhood Self-Control Predicts…

…Better Adult Health

…Greater Adult Wealth

…Less Adult Crime

Keys to Healthy Development

What can be done?

A balanced approach to emotional, social, cognitive, and language development, starting in the earliest years of life.

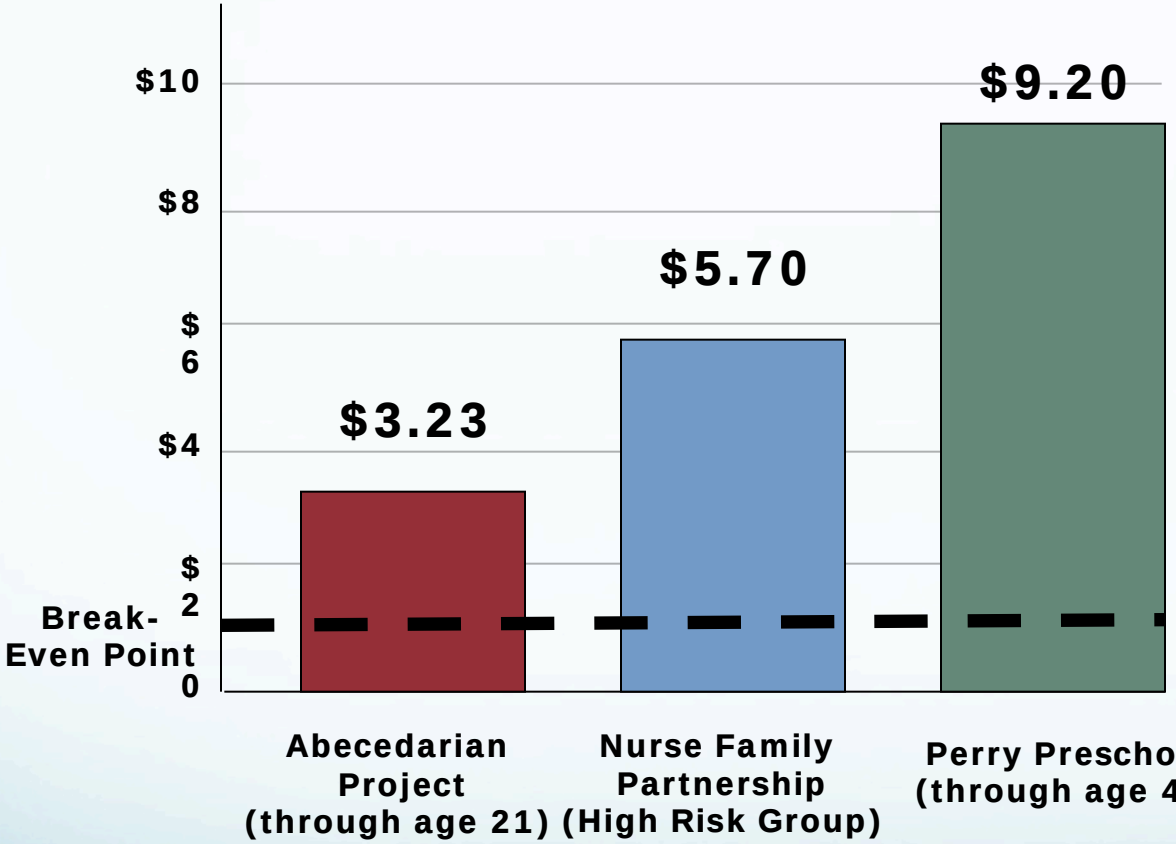
Supportive relationships and positive learning experiences that begin with parents but are strengthened by others outside the home.

Highly specialized interventions as early as possible for children and families experiencing significant adversity.

http://www.nursefamilypartnership.org/

Cost / Benefit Analyses Show Positive Returns

Early Childhood Programs Demonstrate Range of Benefits to Society



Total Return per $1 Invested

Sources: Karoly et al. (2005) Heckman et al. (2009)

Life course health development

Prenatal - maternal stress, obesity, germ line

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WHAT INTERVENTIONS CAN HELP INDIVIDUALS OVERCOME EFFECTS OF EARLY LIFE ADVERSITY?

THE CHALLENGE – FIND INTERVENTIONS

that "OPEN WINDOWS OF PLASTICITY"
and change brain structure and function

Regular physical activity

Increased hippocampal volume and PFC blood flow
and improved executive function and memory
Erickson, Kramer and colleagues Proc Natl Acad Sci U S A. 2011 108:3017-22

Mindfulness-Based Stress Reduction

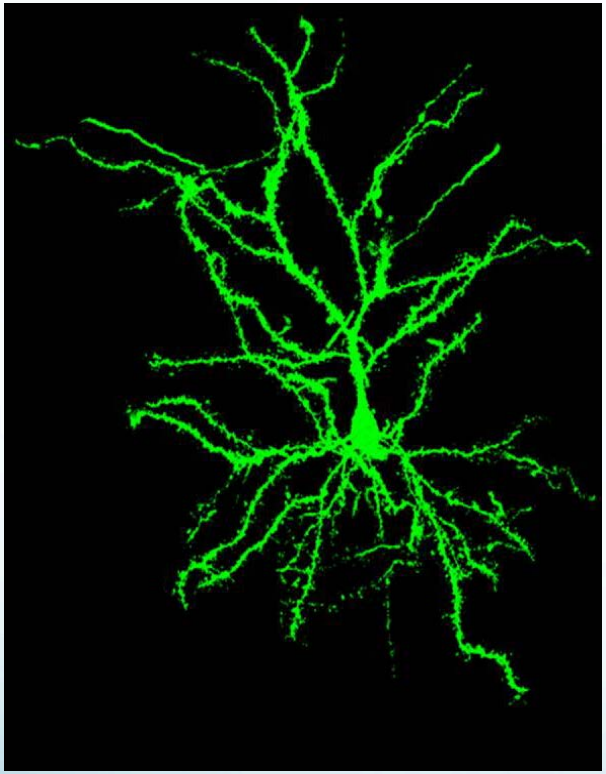
Reducing anxiety decreases amygdala volume
Holzel …Lazar. Soc Cogn Affect Neurosci. 2010 5:11-17 .

Social support and integration

Experience Corps for elderly volunteers
Improved executive function, PFC blood flow and overall health
Carlson, Erickson, Kramer, Seeman, Fried, J Gerontol A Biol Sci Med Sci. 2009 64:1275-82.
Meaning and purpose (eudaimonia)

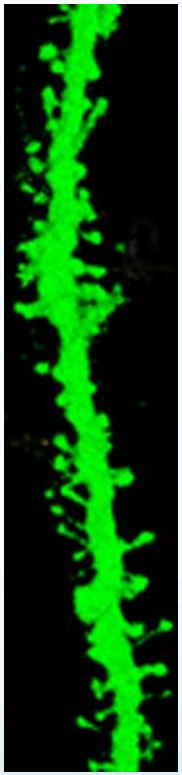
Looking to the Future

The adult brain shows plasticity and we are only beginning to recognize its potential!
THE WISDOM OF THE BODY (WALTER CANNON)



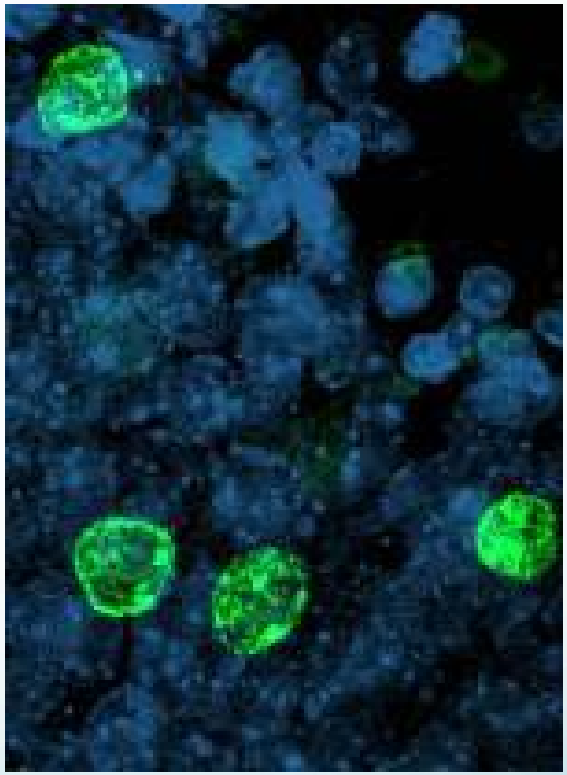
Dendrites

Shrink and expand



Synapses

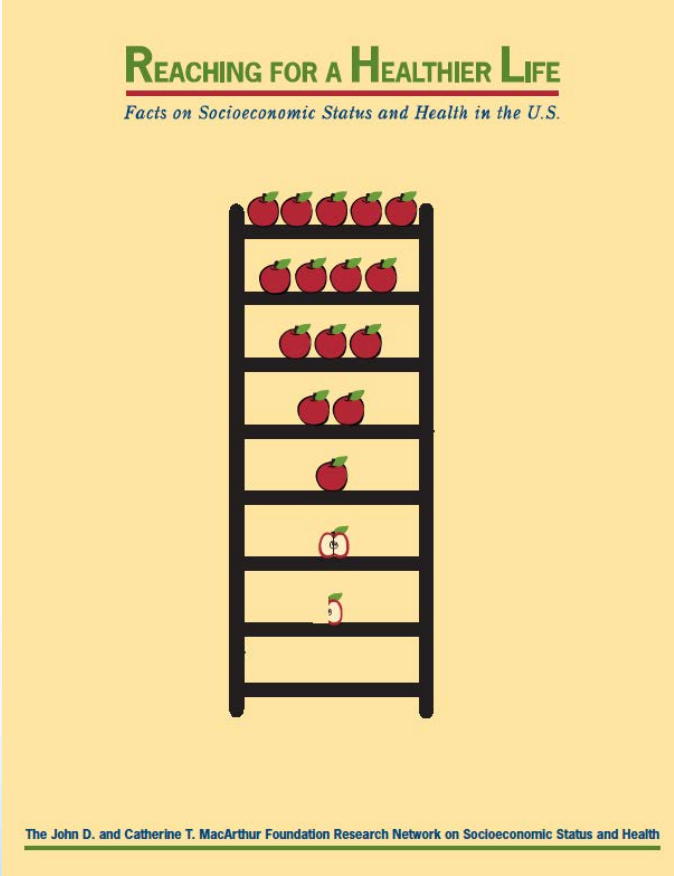
Disappear and are replaced



Neurogenesis

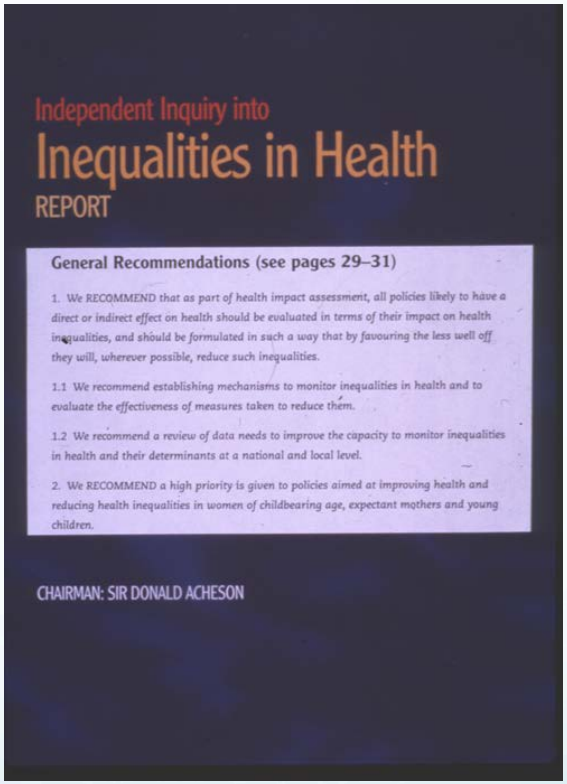
Continues in some brain areas

Improving health through informing the public…
…leading to policies of government and the private sector



The Biology of Disadvantage NY Annals 2010

UNNATURAL CAUSES video



All public policies are health policies!

Colleagues and Collaborators

Leiden University

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Ron de Kloet

Medical College of Wisconsin

Cecilia Hillard

Miriam Baker
Sarah Filipski
Josh Kogan
Mariel Rios
Todd Rubin
Chris Wilson
Dani Zeli

Adelaide Acquaviva
Maryse Aubourg
Halina Korsun

The "plasticity" group

Keith Akama

Nicole Bowles

Lisa Eiland

Jason Gray

Matt Hill

Richard Hunter

Ilia Karatsoreos

Yoav Litvin

Jordan Marocco

Melinda Miller

Carla Nasca

Constantine Pavlides

Beth Waters

Weill/Cornell

Kevin Bath

B.J. Casey

Francis Lee

Teri Milner

NYU

Joe Ledoux

Mt. Sinai Schl Med

Erik Bloss

Deena Goldwater

Patrick Hof

John Morrison

Jason Radley

Rebecca Shansky

National Centre for Biological Sciences (Bangalore)

Sumantra Chattarji

MacArthur Research Network on SES and Health

National Scientific Council for the Developing Child

Neuroimmune and inflammation Program
Karen Bulloch

National Council on the Developing Child

http://developingchild.harvard.edu/index.php/activities/council/

PREVENTION REDUCES HUMAN MISERY AND HAS A HUGE RETURN ON INVESTMENT FOR SOCIETY

- Adult disease prevention begins with reducing early toxic stress

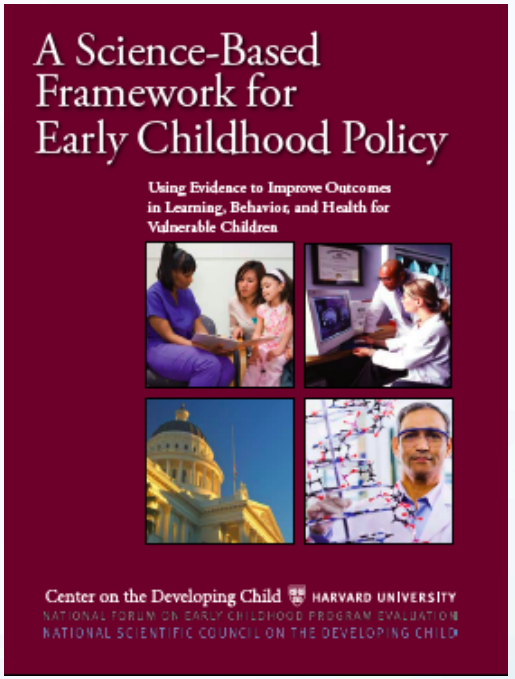
- Early childhood programs benefit lifelong health, not just education

- Promoting physical health benefits the brain

-Parent-child assistance: Opportunity for health promotion

For example:

•Nurse Family Partnership - David Olds



•NOW LOOKING AT WAYS TO REACTIVATE PLASTICITY AND HELP INDIVIDUALS WITH ACE TO OVERCOME BEHAVIOR AND PHYSICAL HEALTH PROBLEMS