Behavioral Medicine: Biobehavioral Pathways Linking Stress & Health

P134H - Announcements

- Experimetrix Extra Credit
- In class demonstration for Xcredit
- Lecture slides on website

Bmed: Symbiosis between Clinic & Laboratory

- Application of Psychological Principles to medically-relevant problems.
  - – Noncompliance: 35-80% prevalence

  Principle of Gradient of Reinforcement - immediate rewards/ punishments are more effective than delayed ones

  Principle of Avoidance – fear reduction serves as a reinforcment

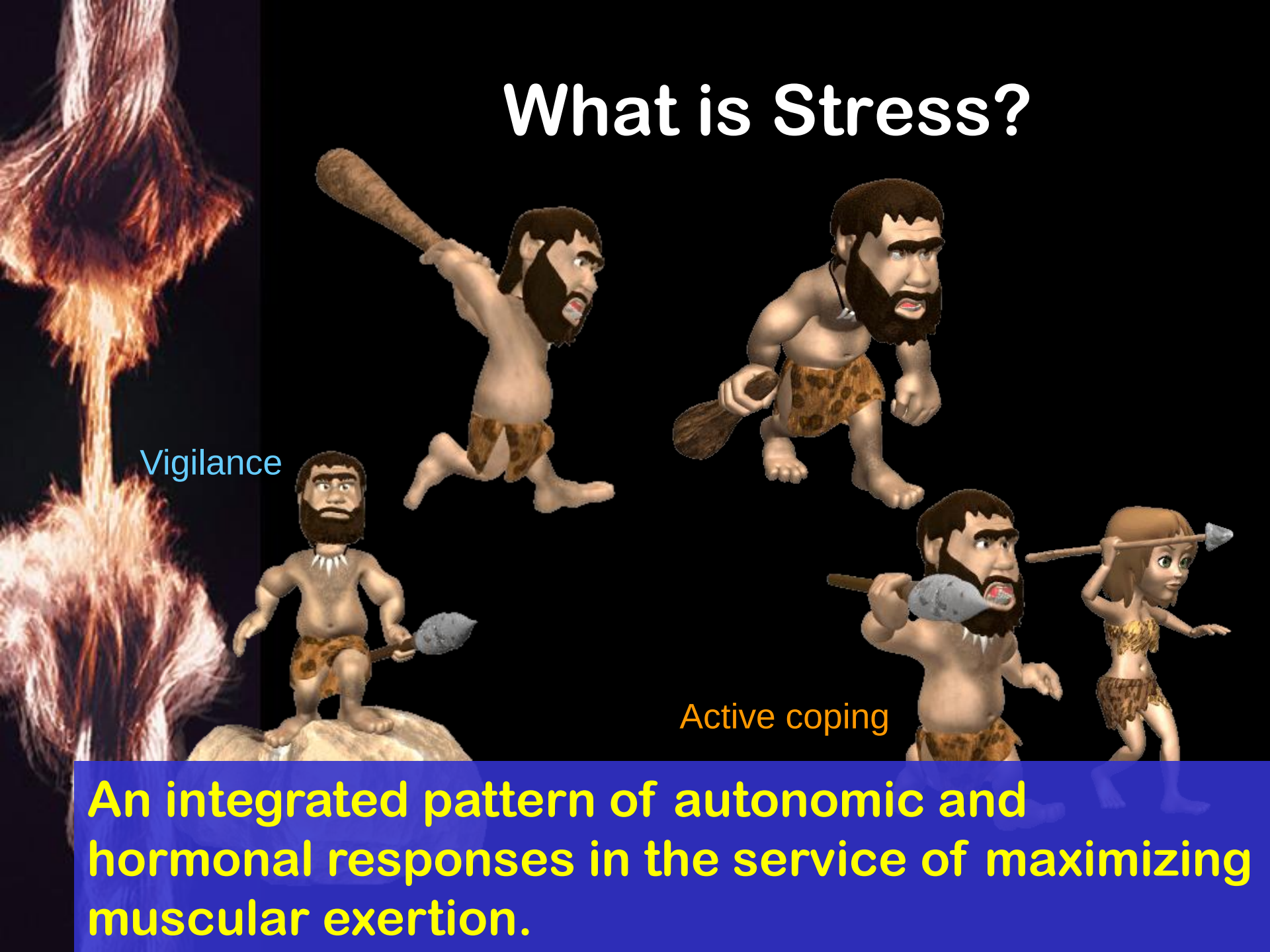
Unhealthy Target Behaviors for Behavior Therapy

- Tobacco-Use

- Alcohol Abuse

- Drug Addictions
- Hypertension

What is Stress?



Vigilance

Active coping

An integrated pattern of autonomic and hormonal responses in the service of maximizing muscular exertion.

GO
Action Activating
NO GO
Action Inhibiting
EFFORT
SAM axis
catechol amines
cortisol
DISTRESS
HPAC axis
DEMAND
High
ACTIVE
STRAIN
CONTROL
Low
[A]
[B]
HIGH
LOW
ACTIVE COPING
ß-adrenergic
β-adrenergic
α-adrenergic
PASSIVE COPING
α-adrenergic
APPROACH
Anger/Hostility
HR, SBP
DBP
AVOIDANCE
Defensiveness
[C]
[D]

James Henry's Stress Model

Species-Preservation

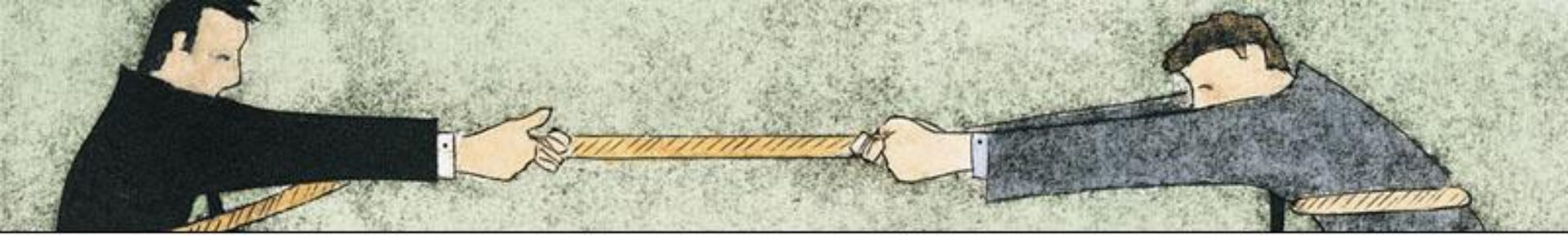
Oxytocinergic
Gonadotrophinergic

Self-Preservation

Adrenergic
Corticosteroidic

Left Hemispheric

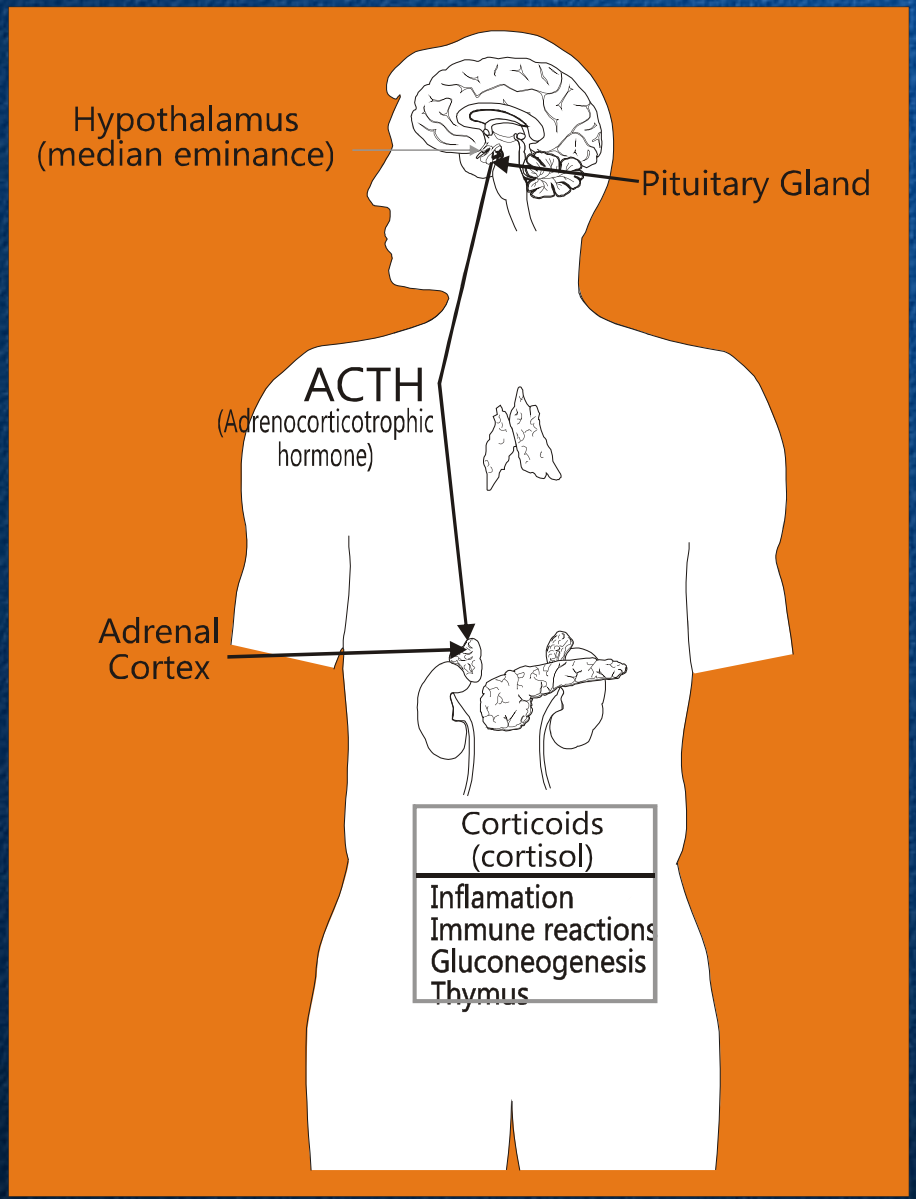
↓ Cortisol Responsiveness → ↓ Attachment Behavior, Social Competance



Model #1:
Selye General Adaptation Syndrome

- Alarm / Resistance / Exhaustion
- Body attempts to reestablish homeostasis (Resistance)
- If in the face of a persistent stressor there is a chronic drain of adaptive energy (physiological resources). The final depletion of adaptive physiological resources gives rise to the stage of target-organ exhaustion.

Selye's Major Mechanism of Stress



- According to the GAS model, stress was conceptualized as a non-specific response.
- Little emphasis on the characteristics of stress-eliciting stimuli (e.g. physical, emotional).
- Failed to account for individual response stereotypy & range of stress-related symptoms.

Model #2 Lachman's Model of Autonomic learning theory

Frequent, prolonged or intense emotional, physiological reactions can promote a learned pattern of those responses.

Which target-organ is decided by

- 1 - Genetic factors which biologically predispose the organ to harm [e.g. FH+ and BP reactivity]
- 2 - Environmental factors that predispose the organ to harm from psychophysiological arousal
- 3 - The specific structures involved in the physiological reactivity
- 4 - The magnitude of involvement during the physiological response

Model # 3 Sternbach's Model

1 - Individual Response stereotypy: characteristic response pattern shown by an individual

2 - Frequent activation of that response pattern

3 - Failure of homeostatic mechanisms. Slower recovery from activation

Model #4
Schwartz's Disregulation Model

Homeostatic disregulation --the breakdown of communication between specific parts of the system.

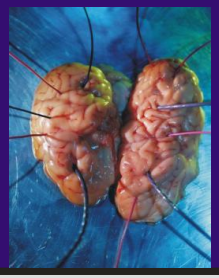
The process of negative feedback loops. [Rationale for biofeedback] Example of BP regulation

The Brain as a Health Care System

(G.E. Schwartz, 1977, 1979)

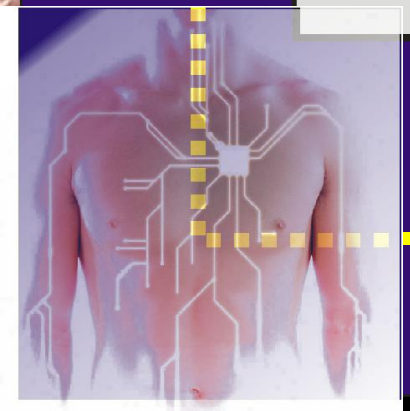
E
(1)

CNS
Information
Processing
(2)



Peripheral
Organs
(3)

Negative
Feedback
(4)



Biofeedback
(5)

Disregulation Model

CNS Information Processing

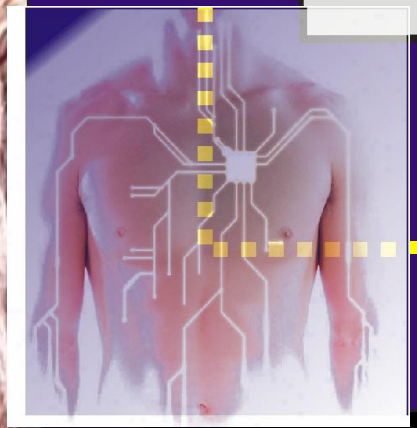
Thought Processes

Behavioral Output

Peripheral Organs

Negative Feedback

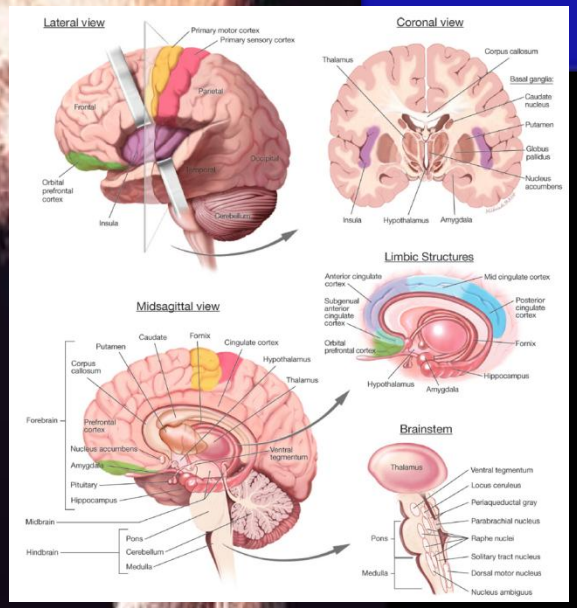
E



Error Detection/ Correction

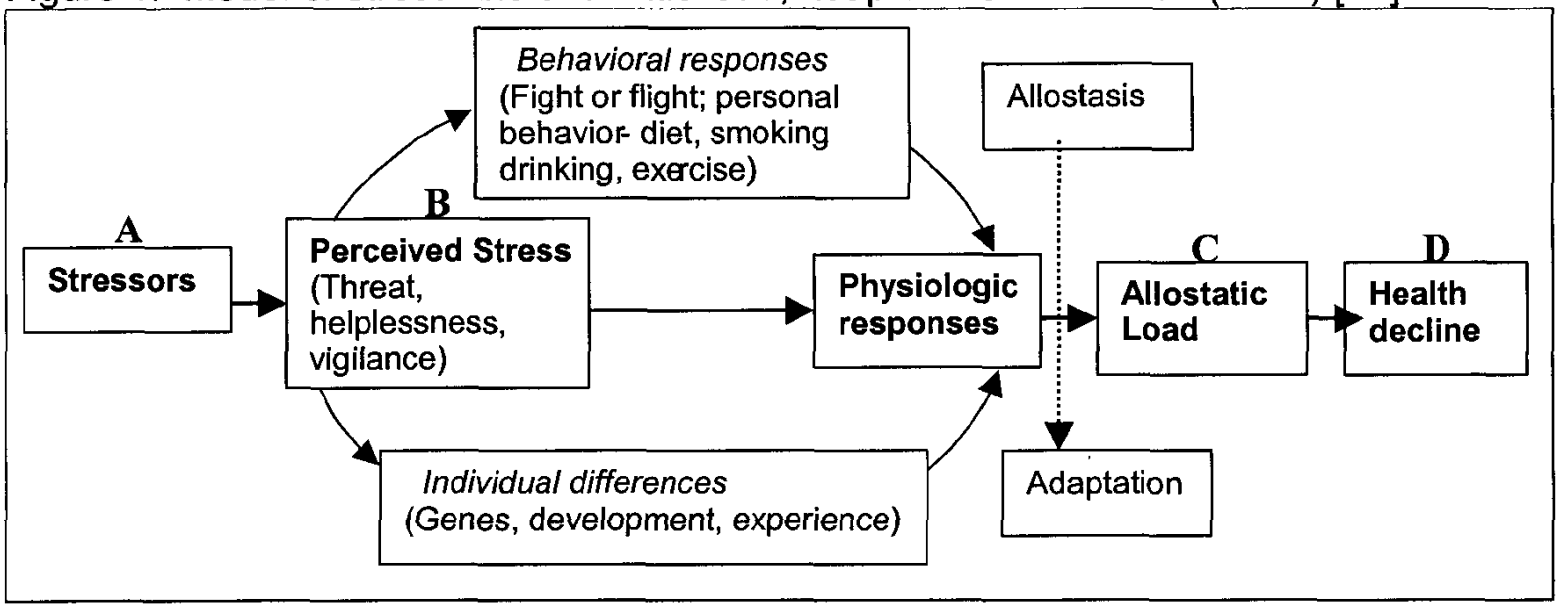
Model #5: Everly & Benson's Disorders of Arousal Model

- **Limbic System Hypersensitivity resulting from repeated extraordinary limbic excitation.**



Chronic Stress & Allostatic Load

Figure 1: Model of stress and allostatic load, adapted from McEwen (1998) [64]



Chronic stress increases allostatic load by four possible mechanisms:

1) repeated elevations of the body's response system caused by chronic stress;

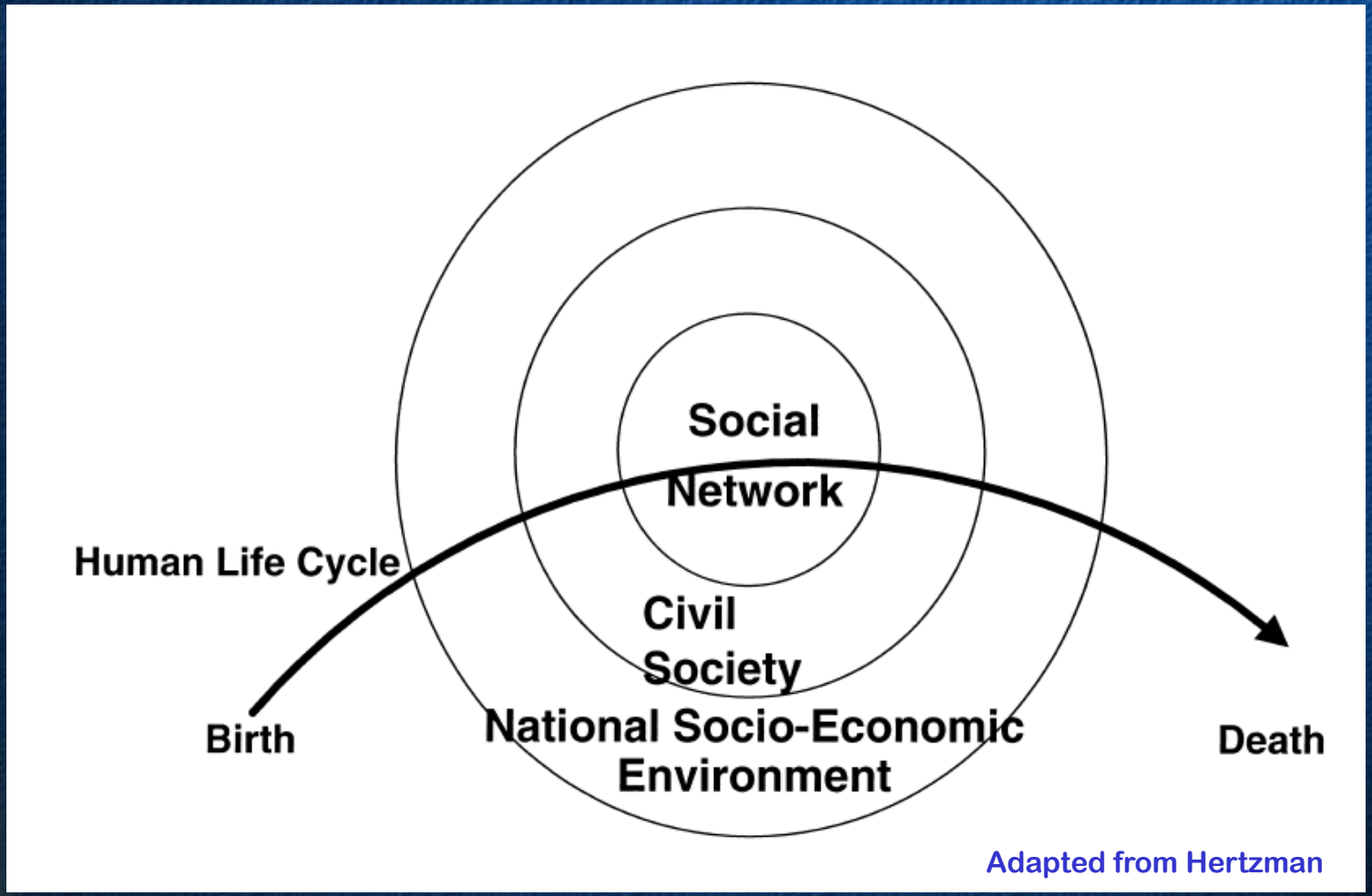
2) failure to habituate or adapt to the same stressor;

3) failure to shut off the body's response to a stressor; and

4) inadequate response to a stressor, causing other body systems to become overactive.

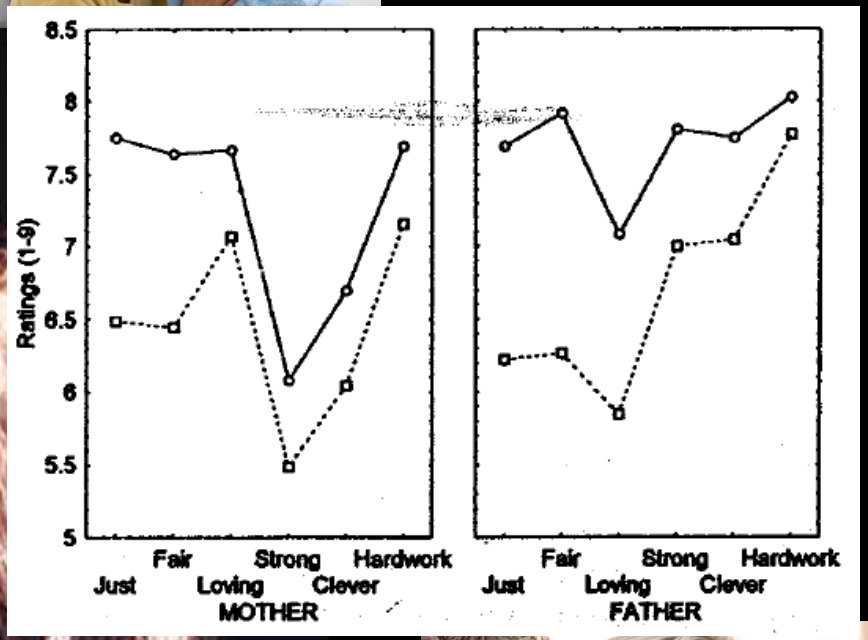
The result is an imbalance in multiple regulatory systems: cardiovascular and sympathetic nervous systems, hypothalamic-pituitary-adrenal (HPA) axis, and metabolic processes.

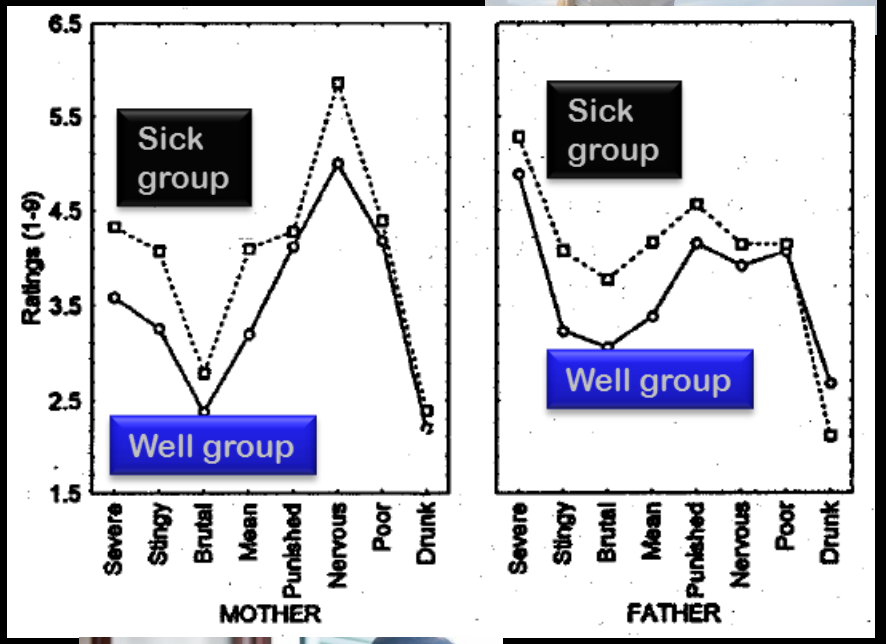
Framework for human development and the determinants of health

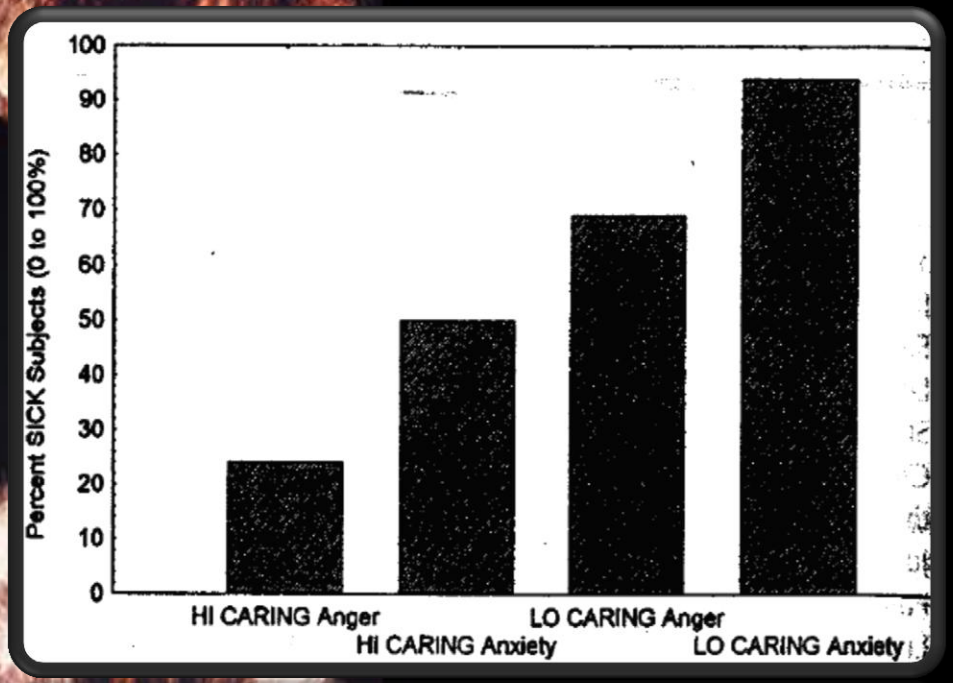


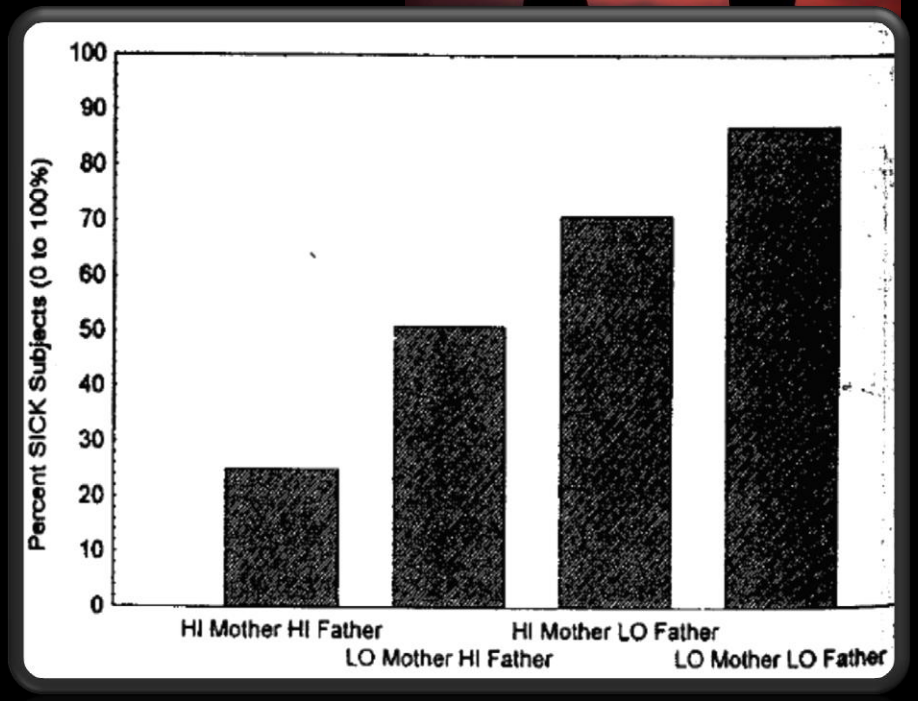
Perceptions of Parental Caring Predict Health Status in Midlife: A 35-Year

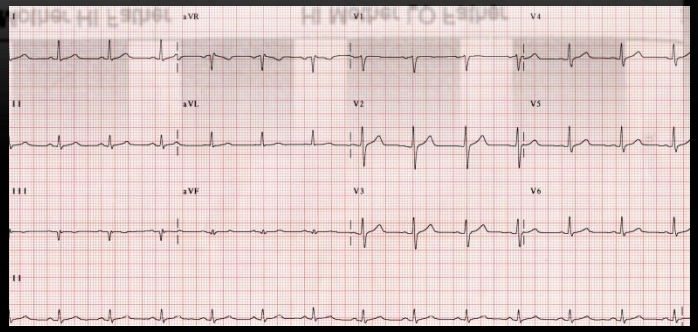
Follow-up of the Harvard Mastery of Stress Study



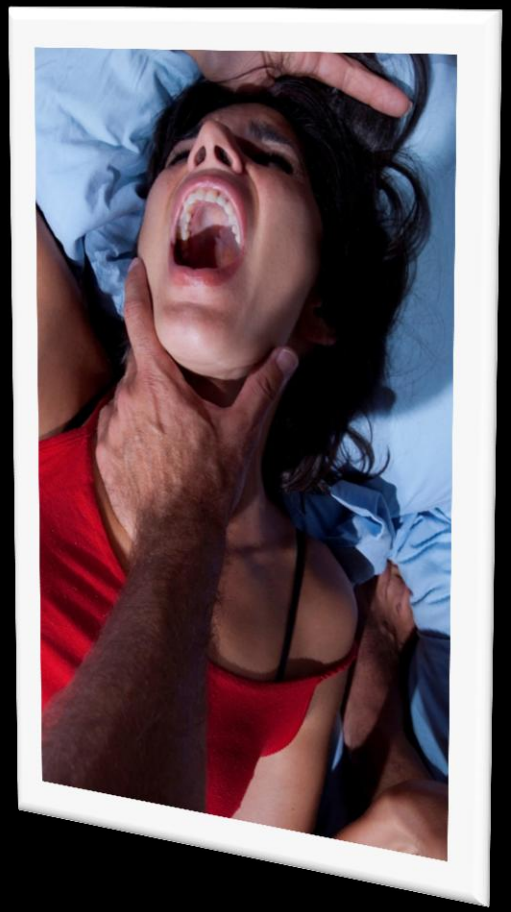



Percent SICK Subjects (0 to 100%)
100
90
80
70
60
50
40
30
20
10
0
HI CARING Anger
LO CARING Anger
HI CARING Anxiety
LO CARING Anxiety

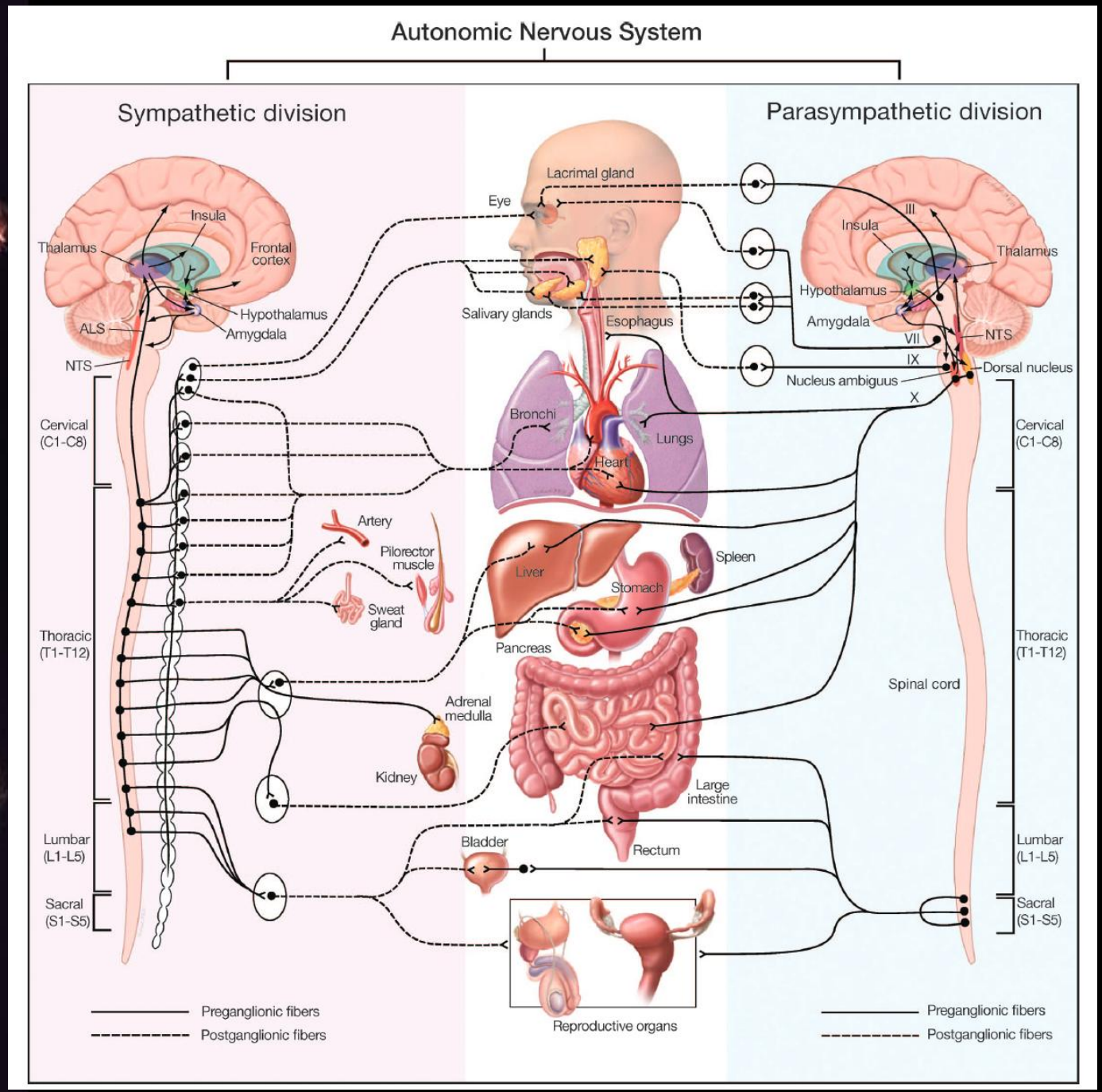

Percent SICK Subjects (0 to 100%)
100
90
80
70
60
50
40
30
20
10
0
HI Mother HI Father
HI Mother LO Father
LO Mother HI Father
LO Mother LO Father



Trauma



Trauma


Autonomic Nervous System
Sympathetic division
Parasympathetic division
Insula
Thalamus
Frontal cortex
Hypothalamus
Amygdala
ALS
NTS
Cervical (C1-C8)
Thoracic (T1-T12)
Lumbar (L1-L5)
Sacral (S1-S5)
Lacrimal gland
Eye
Salivary glands
Esophagus
Bronchi
Lungs
Heart
Artery
Pilorector muscle
Sweat gland
Liver
Spleen
Stomach
Pancreas
Adrenal medulla
Kidney
Large intestine
Bladder
Rectum
Reproductive organs
Spinal cord
III
VII
IX
X
Nucleus ambiguus
Dorsal nucleus
Preganglionic fibers
Postganglionic fibers

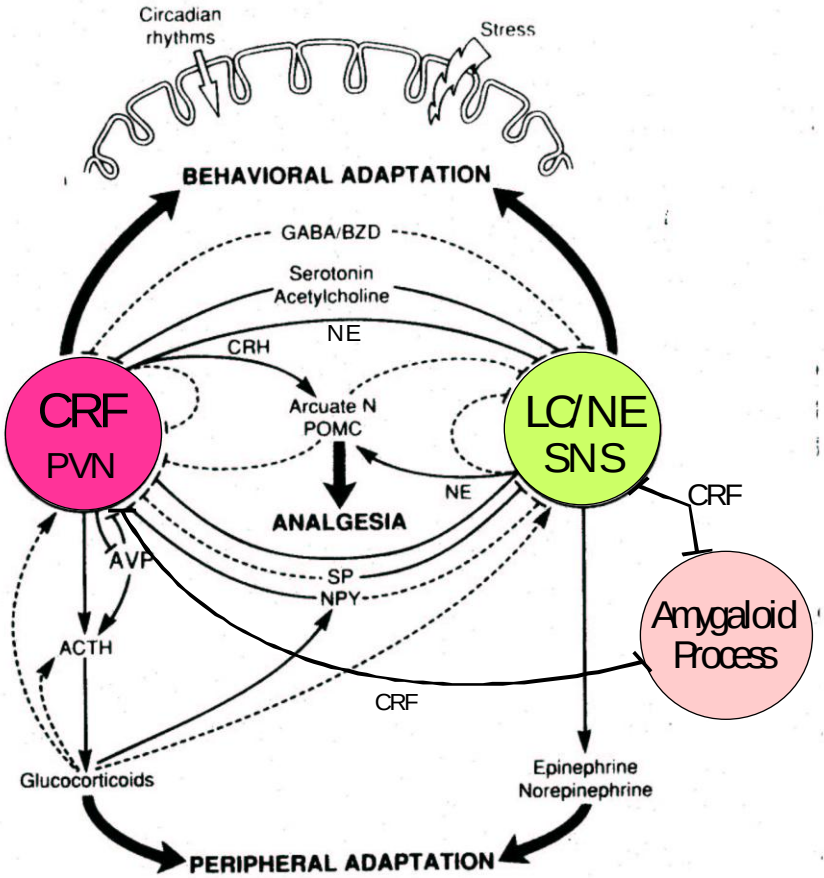
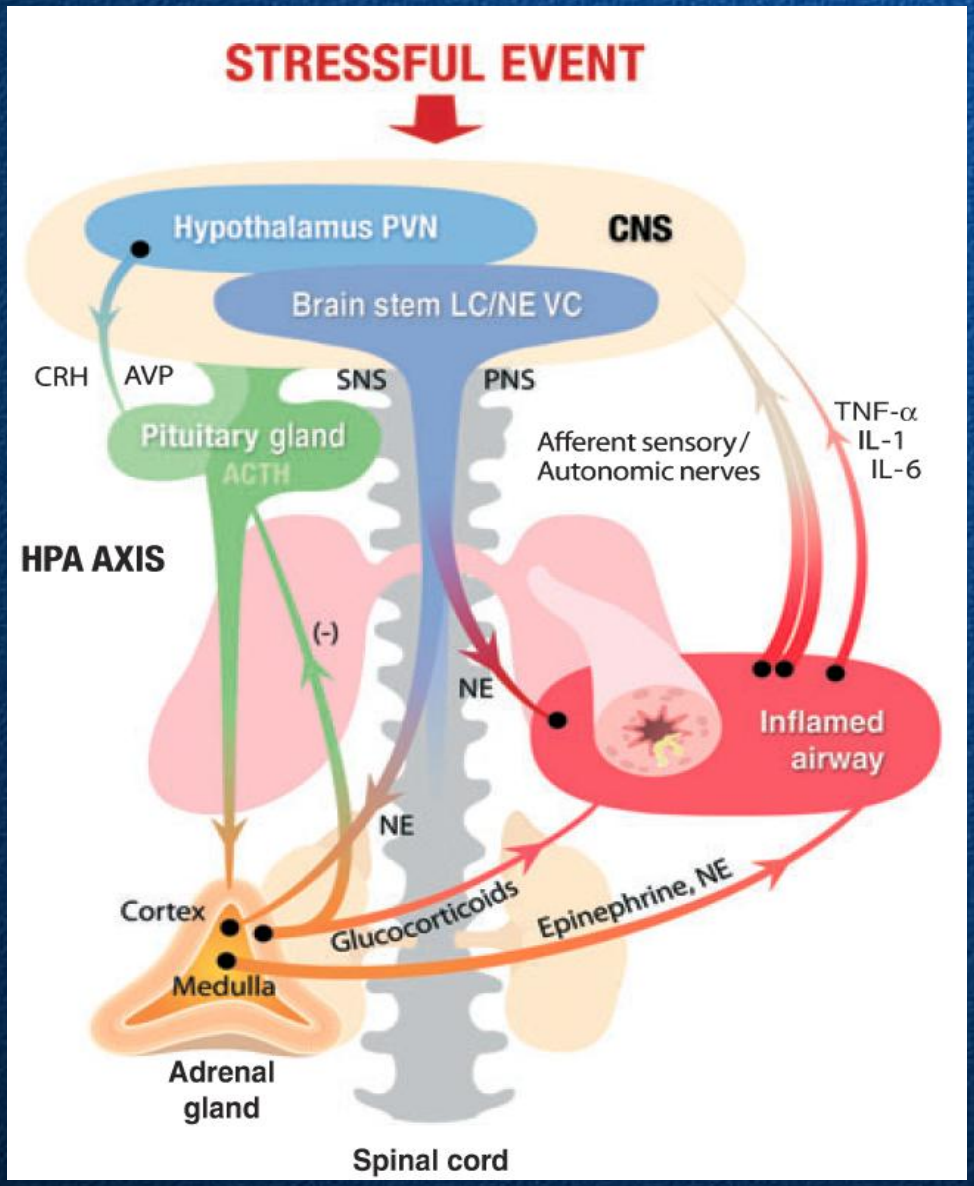
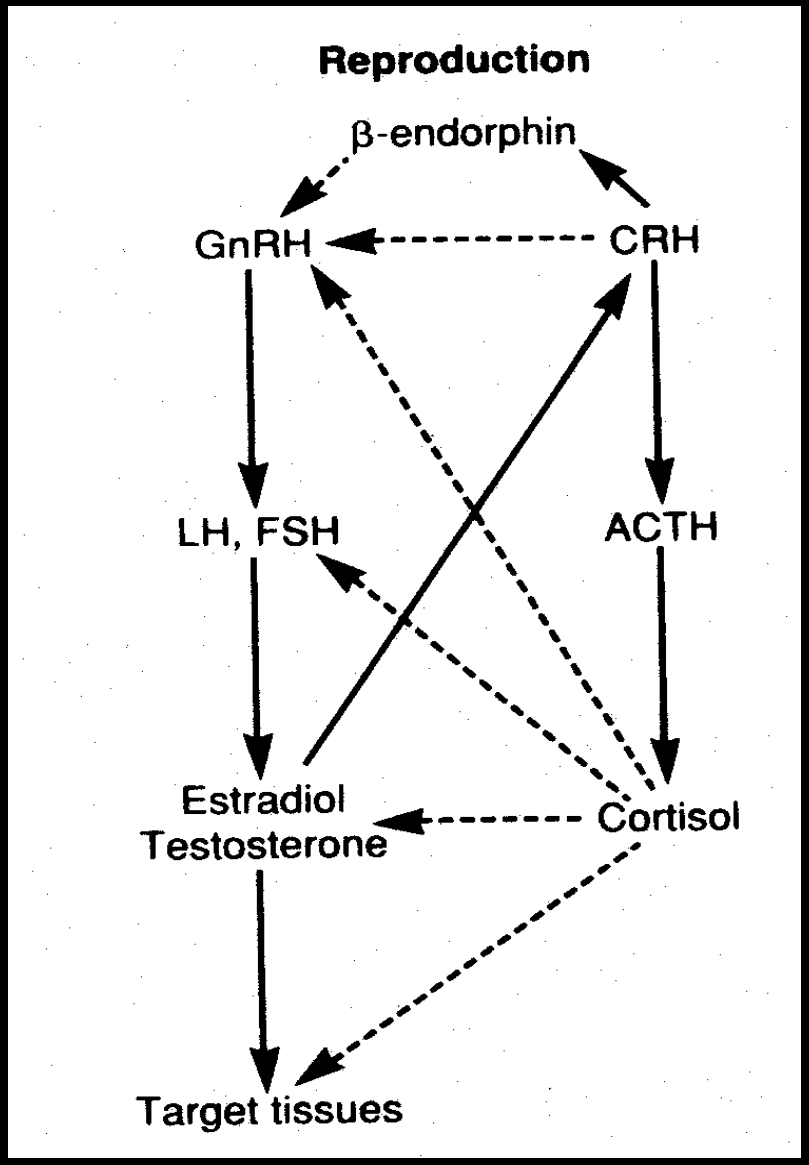


Figure 1 A simplified representation of the central and peripheral components of the stress system, their functional interrelations, and their relationships to other central nervous systems involved in the stress response. CRH, corticotropin releasing hormone; LC/NE Symp. Syst., locus ceruleus/norepinephrine-sympathetic system; POMC, proopiomelanocortin; AVP, arginine vasopressin; GABA, γ-aminobutyric acid; BZD, benzodiazepine; ACTH, corticotropin; NPY, neuropeptide Y; SP, substance P. Activation is represented by solid lines and inhibition by dashed lines. (Adapted from Chrousos, G. P. and Gold, P. W., *JAMA*, 267, 1244, 1992.)

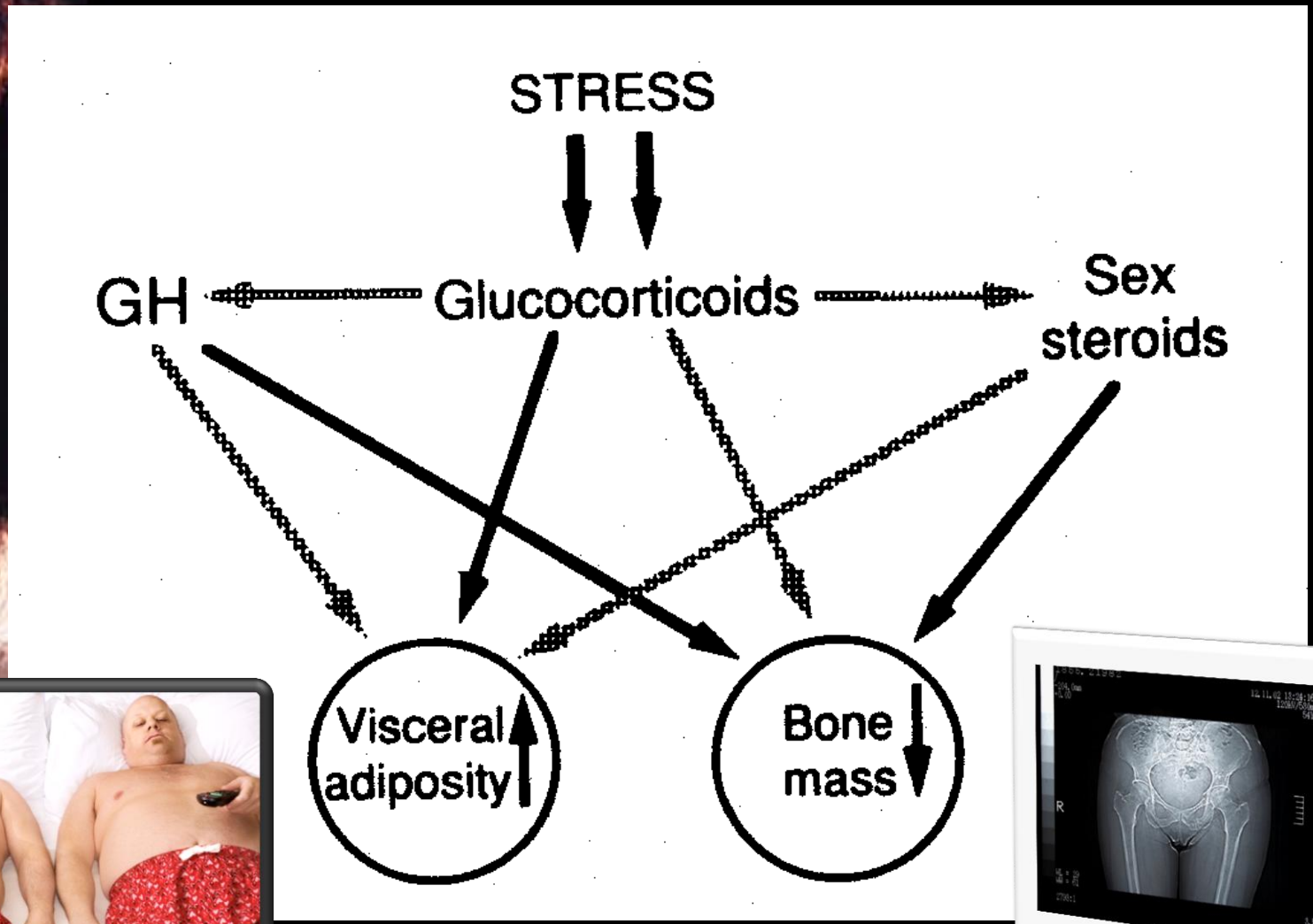
Interactions between stress systems

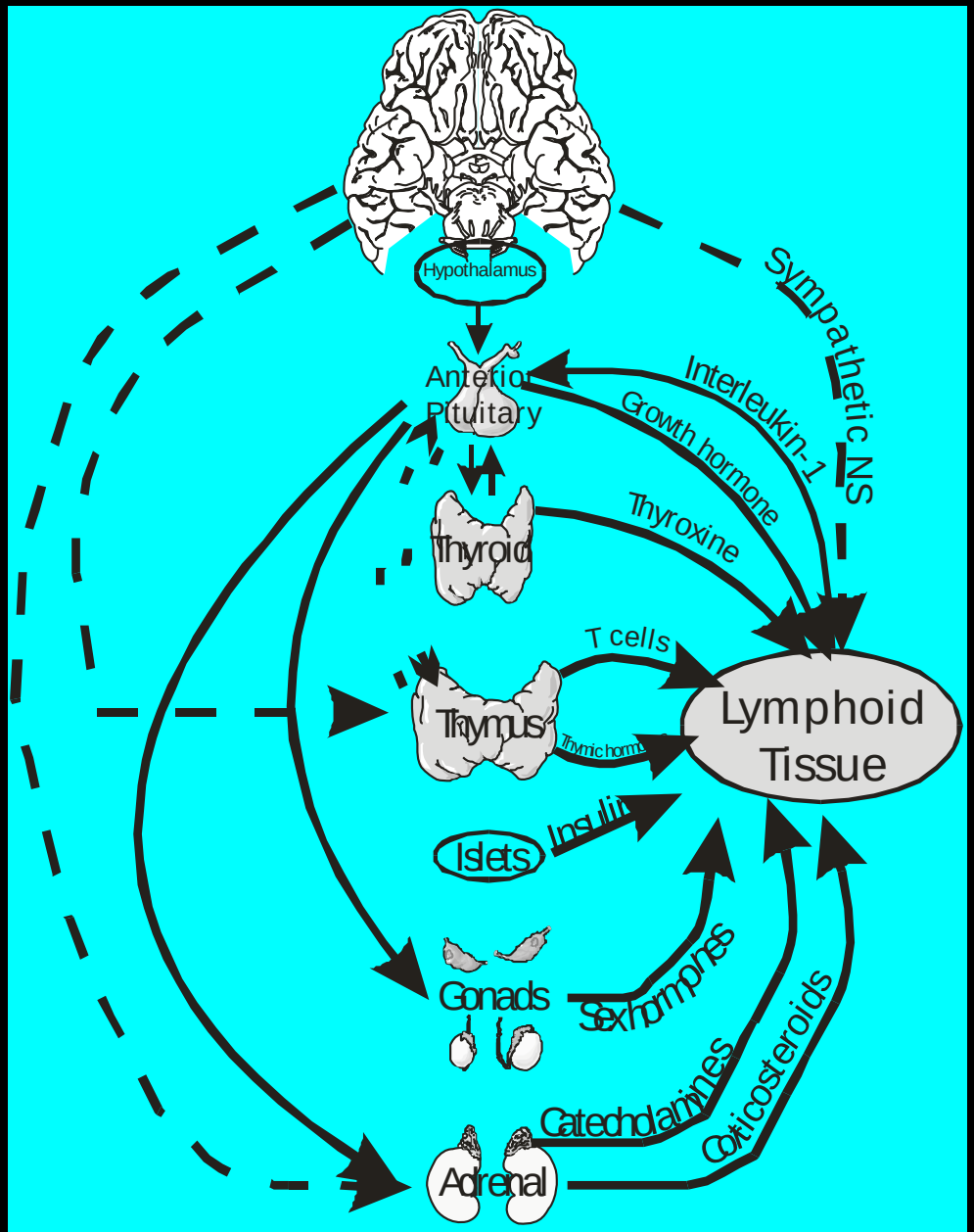


Cortisol-Sex Hormone Inter-relationships



Stress Neuro-endocrine Pathways





Neuroendocrine / Immune Interactions

Psychological/Trait Characteristics & Cardiovascular Disease Risk:

Mediating Roles of Serotonergic & Endorphinergic Pathways

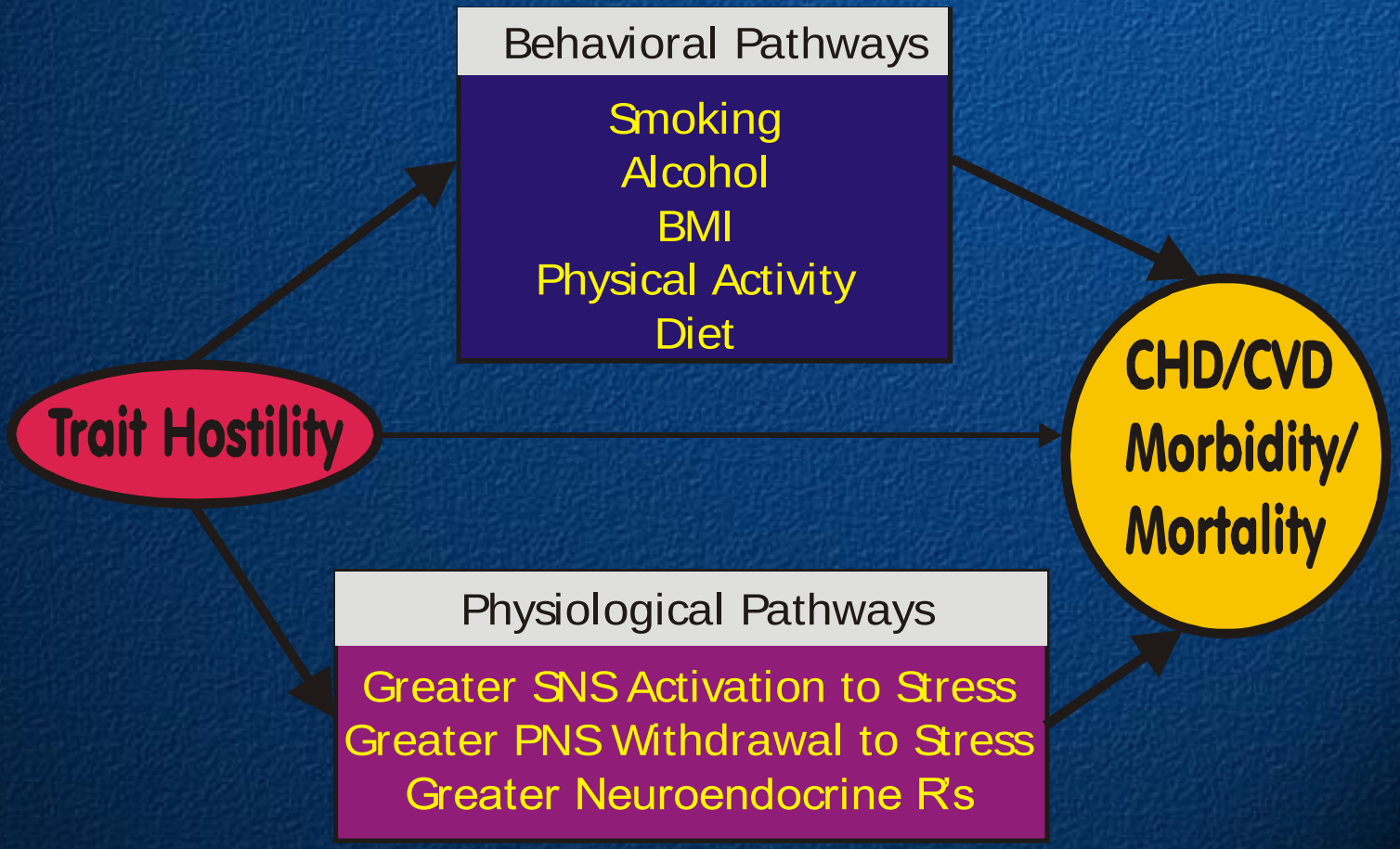
Psychological CVD Risk Factors

- Hostility/Anger
- Low Social Support

- Depression

- Defensive coping/denial

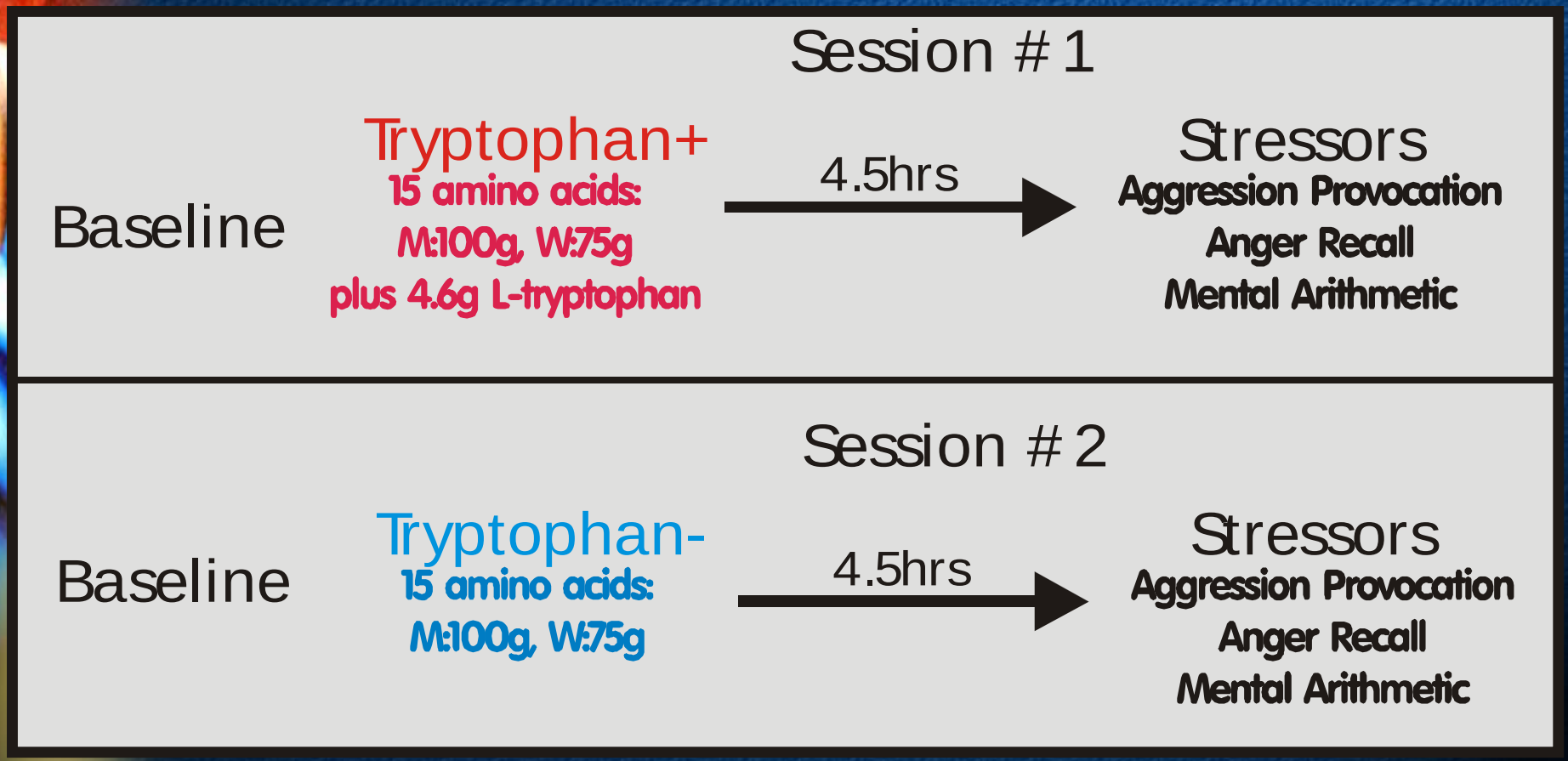
Hostility-CVD/CHD Linkages



Central Serotonin Deficiency Hypothesis

- Increased SNS Activity
- Myocardial vulnerability
- Aggressive/hostile behaviors
- Impulsivity/risk taking
- Depression

Design

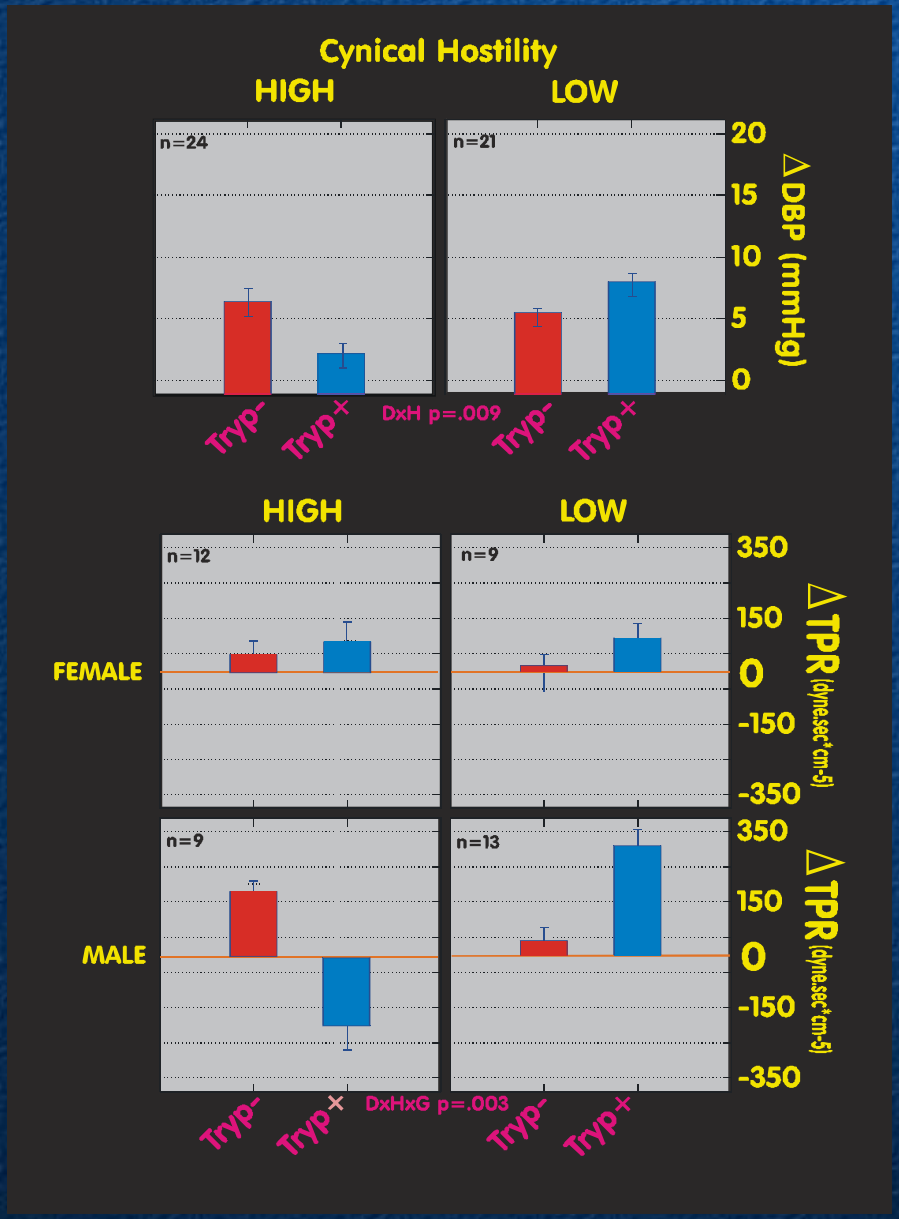

Session #1
Baseline
Tryptophan+
15 amino acids:
M:100g, W:75g
plus 4.6g L-tryptophan
4.5hrs
Stressors
Aggression Provocation
Anger Recall
Mental Arithmetic
Session #2
Baseline
Tryptophan-
15 amino acids:
M:100g, W:75g
4.5hrs
Stressors
Aggression Provocation
Anger Recall
Mental Arithmetic

Methods

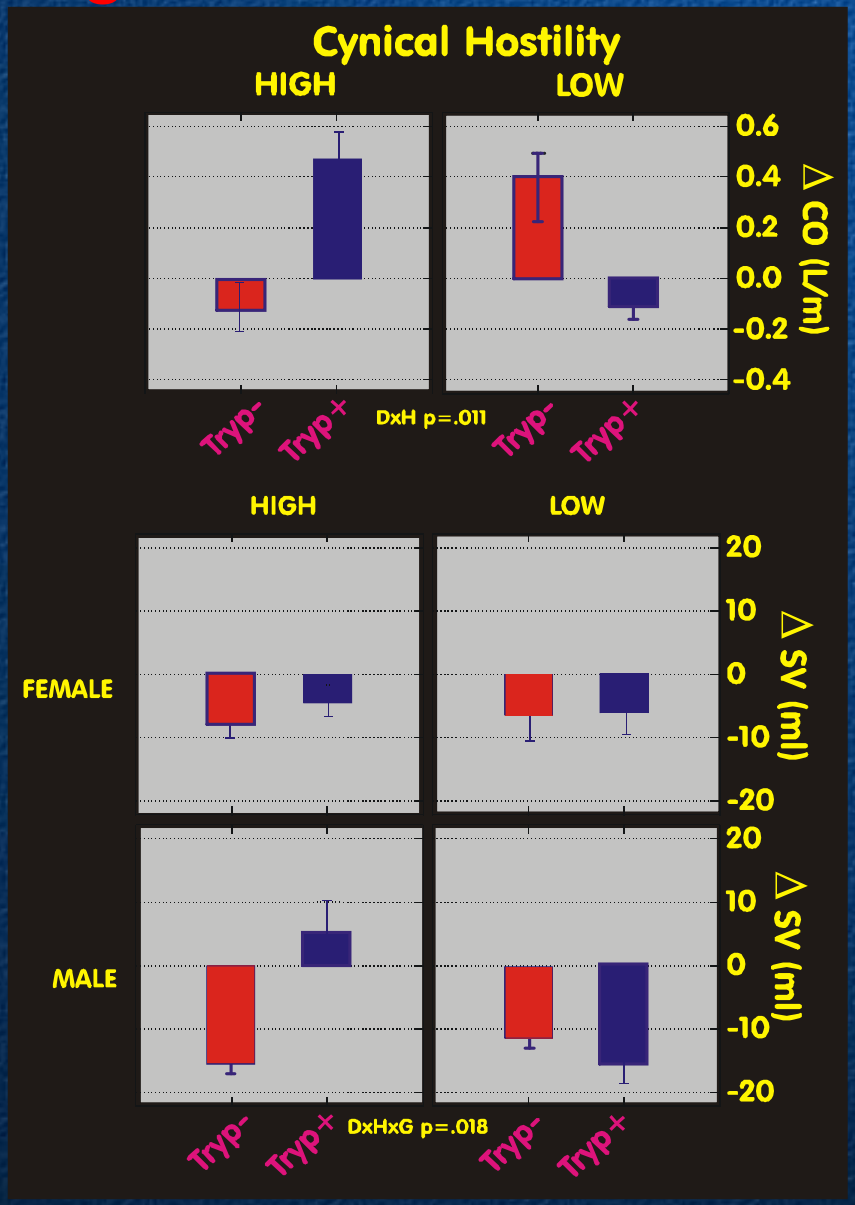
- 25 Men, 21 Women
- Healthy, 27 years old
- Cook Medley Hostility Scale

  Hi Ho >=18
- Auscultatory BP
- Non-invasive Impedance Cardiography: HR, SV, CO, TPR

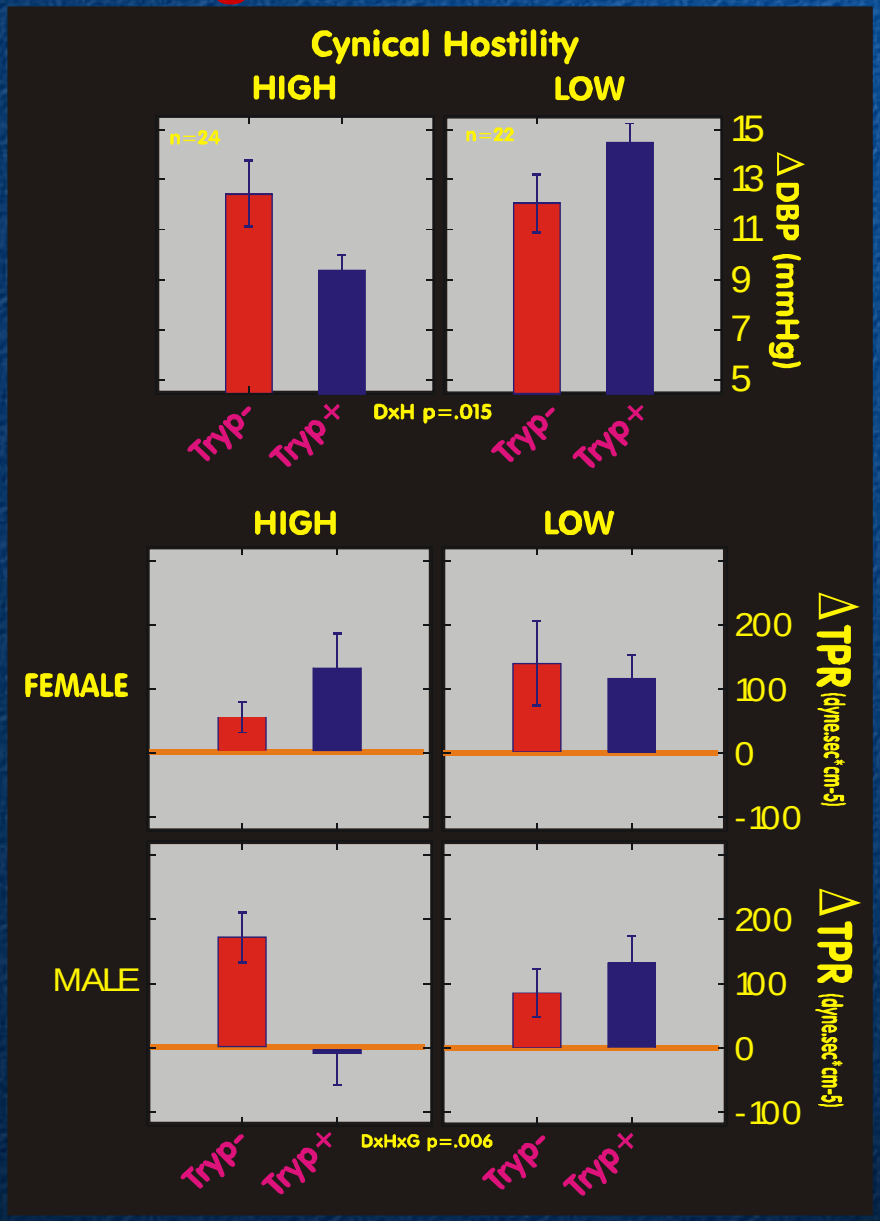
Anger Provocation Task



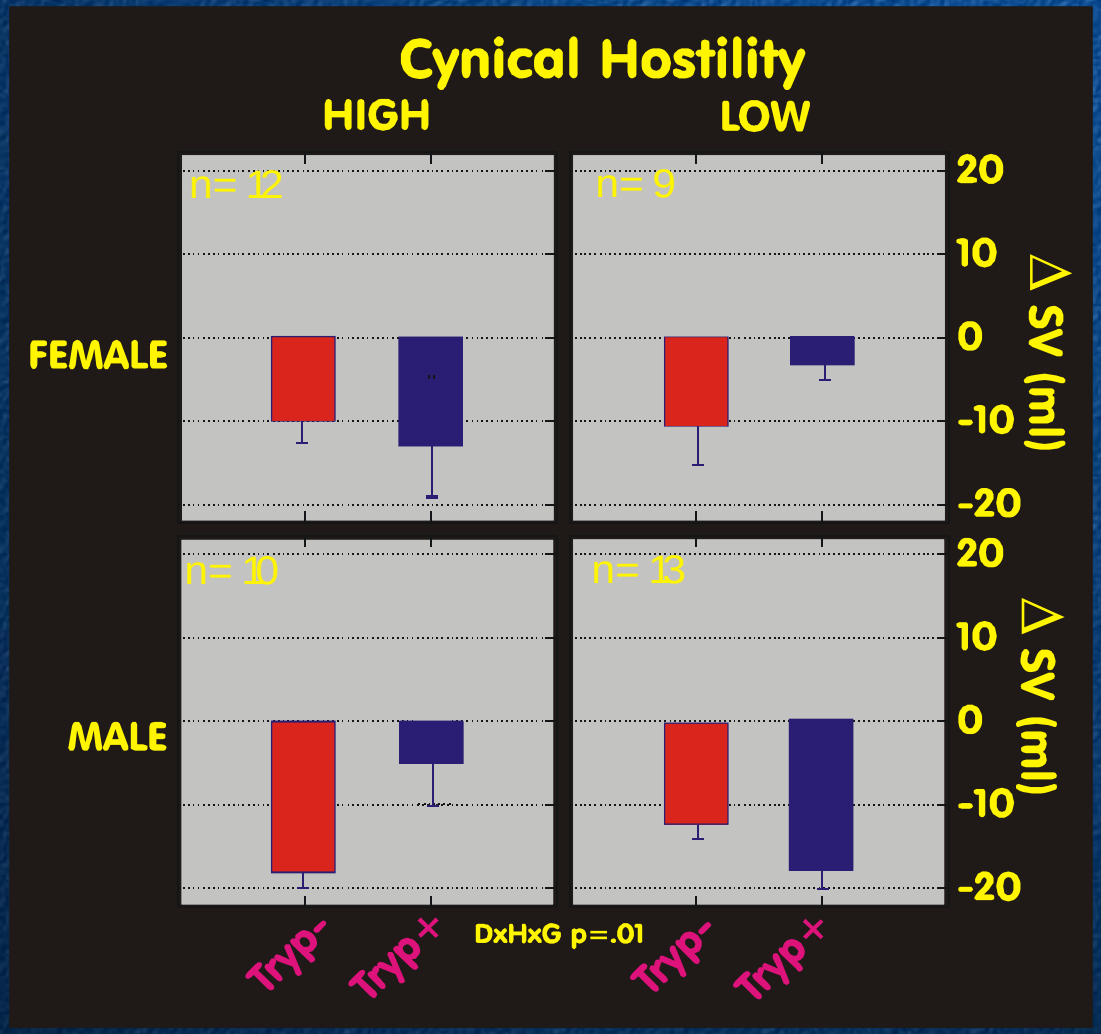
Anger Provocation Task



Anger Recall Task



Anger Recall Task



Conclusions

- Differential sensitivity to L-tryptophan as a function of Ho
- Mechanism of BP effects may Differ for men vs. women
- Consistent with CNS Serotonergic Deficiency Hypothesis
- Diet x phenotype interaction

Endogenous Opioids & CV Function

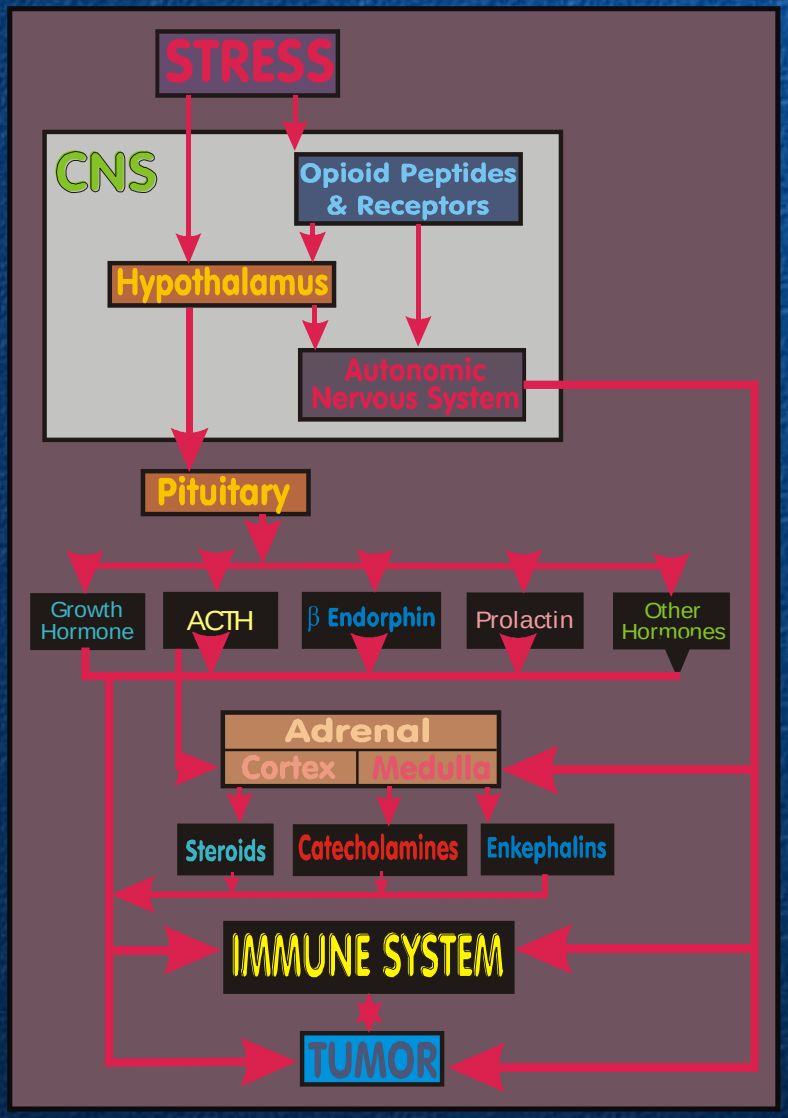
What is Repressive Coping?

See No Evil

Hear No Evil

Say No Evil

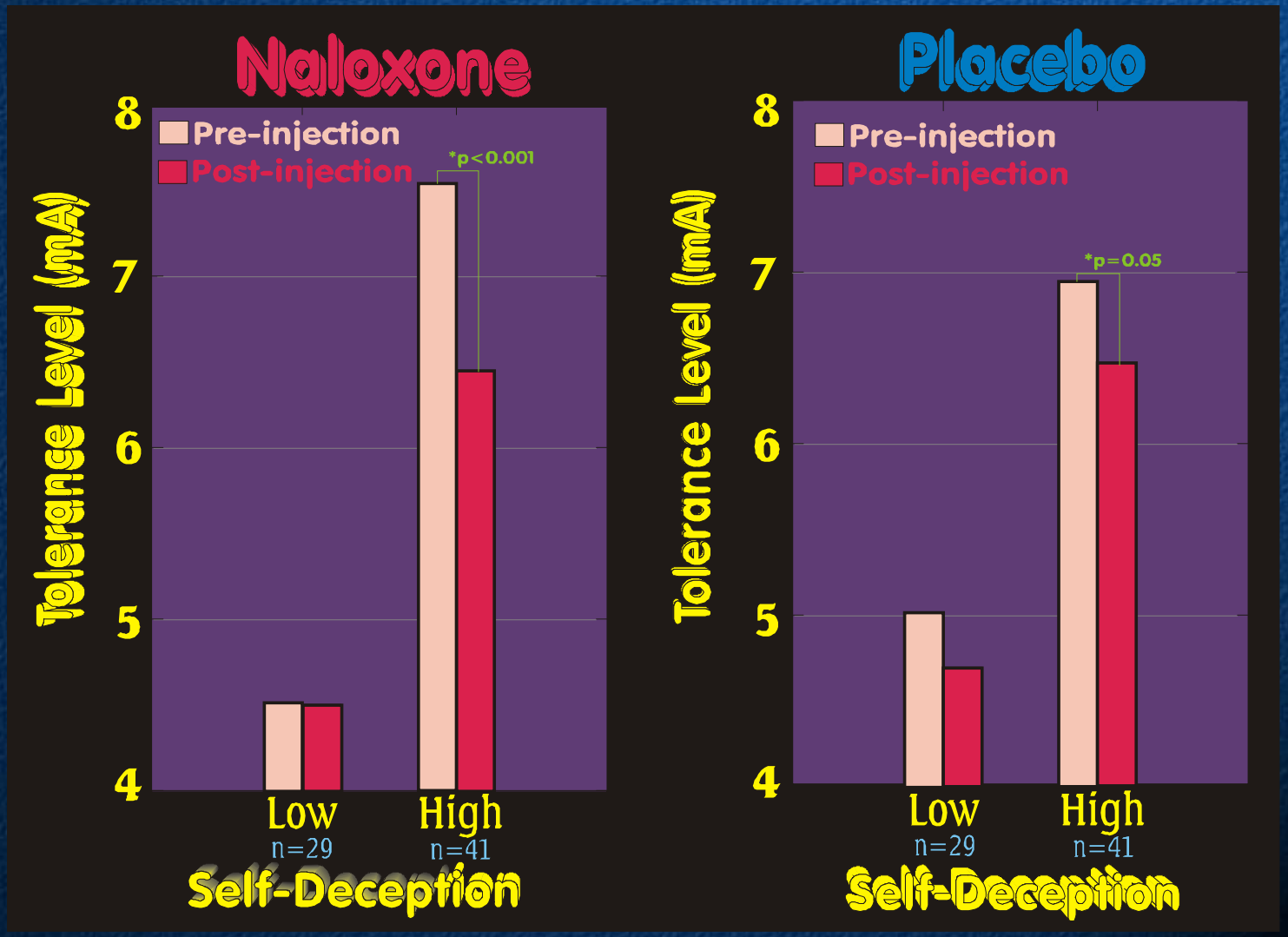
EOP's & Stress Axes Reactivity



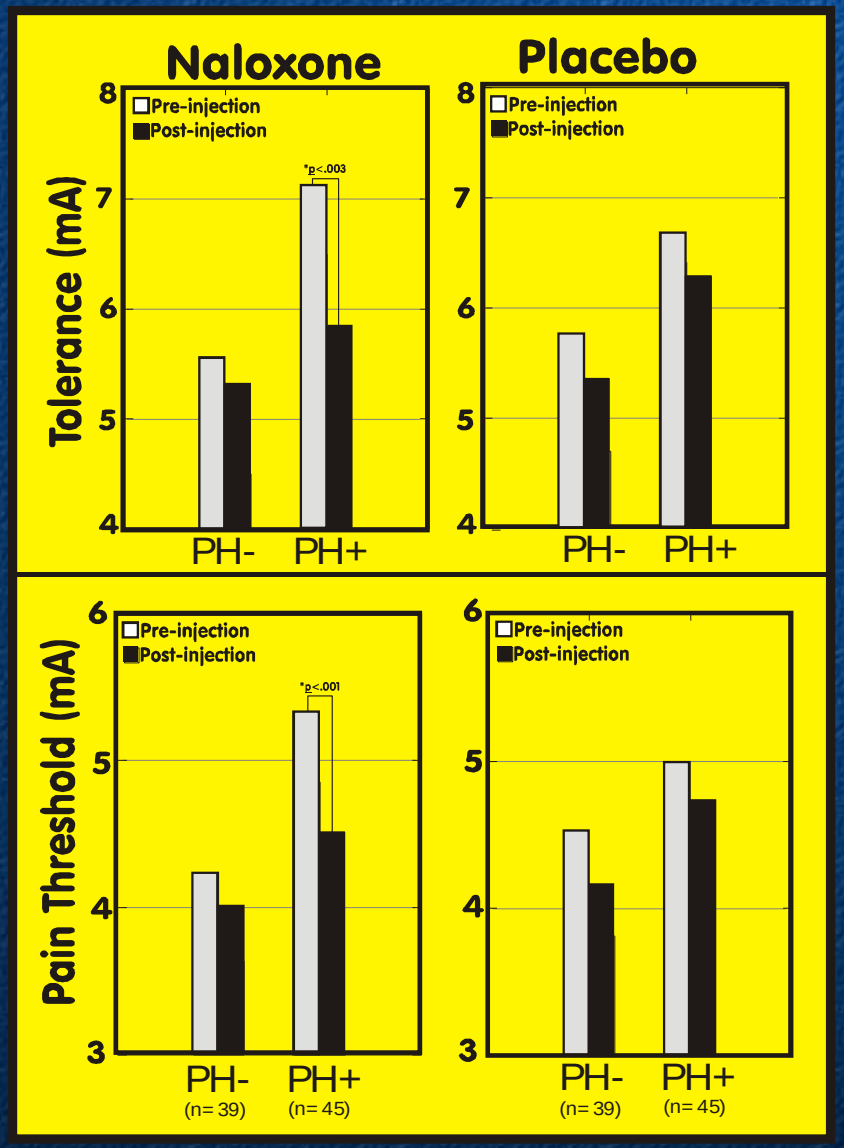
Adapted from Shavitz et al. (1985)

Study Protocol

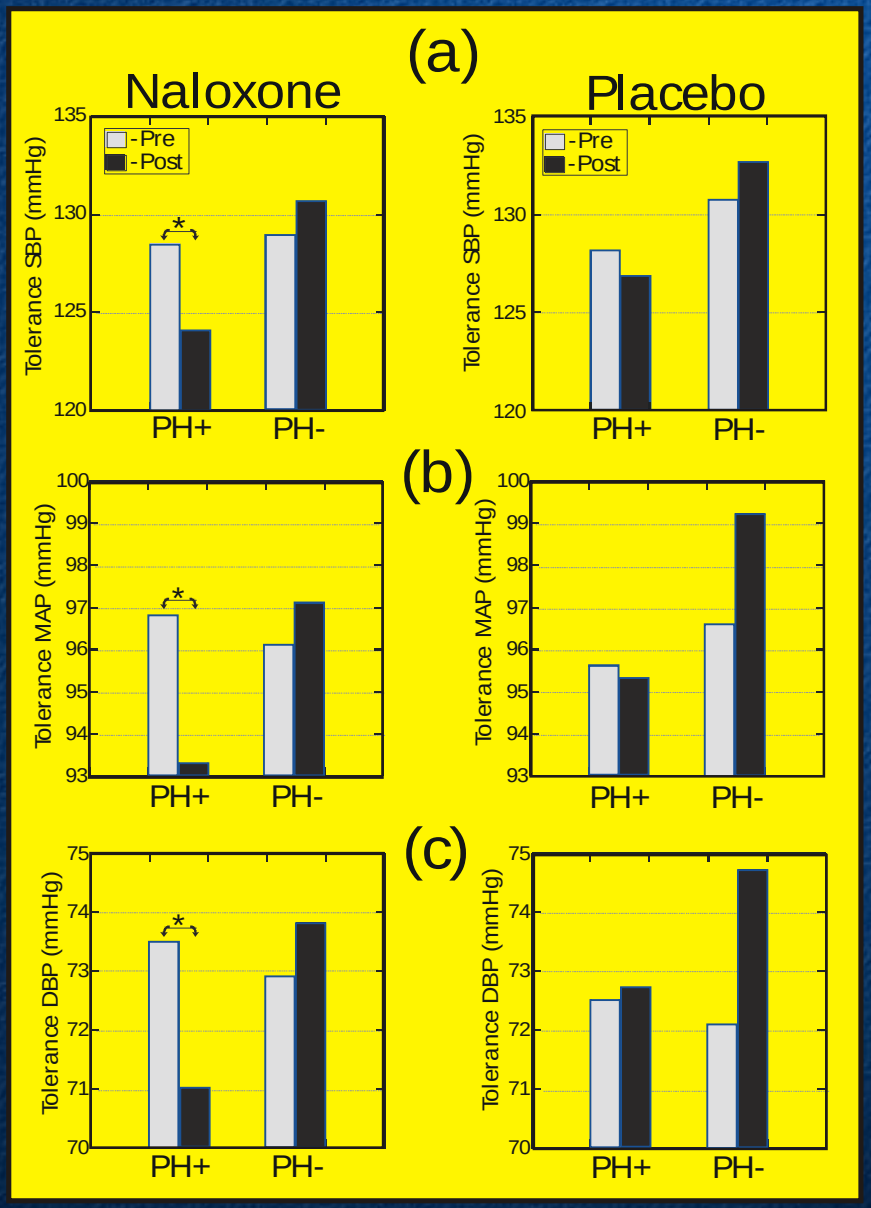
Defensiveness, Opioid Blockade & Pain



Pain, Opioid Blockade, & Family Hx of HTN



PH, Opioid Blockade, & Blood Pressure



Endogenous Opioids & Ambulatory BP: Effects of Gender & PH+: Study Protocol

Day 1: Ambulatory monitoring
3/hr: BP/HR; Mood; Activities; Social Interactions

Day 2: Return to Laboratory
Autobiographical memories/Significant exp.
Salivary Cortisol

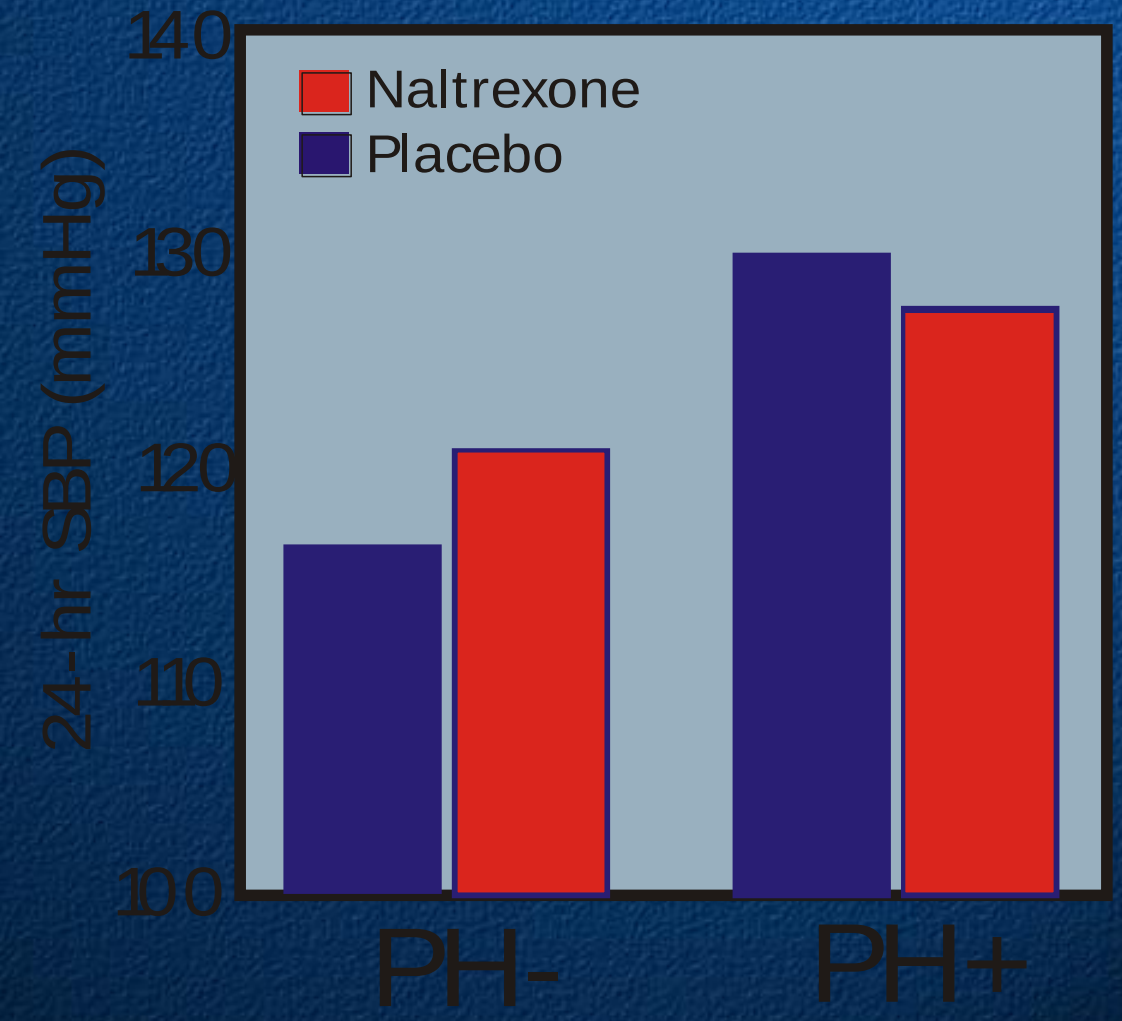
Day 3: Return to Laboratory
Drop off Diary & Watch

Day 8: Ambulatory monitoring
3/hr: BP/HR; Mood; Activities; Social Interactions
Session 1 emotion recall

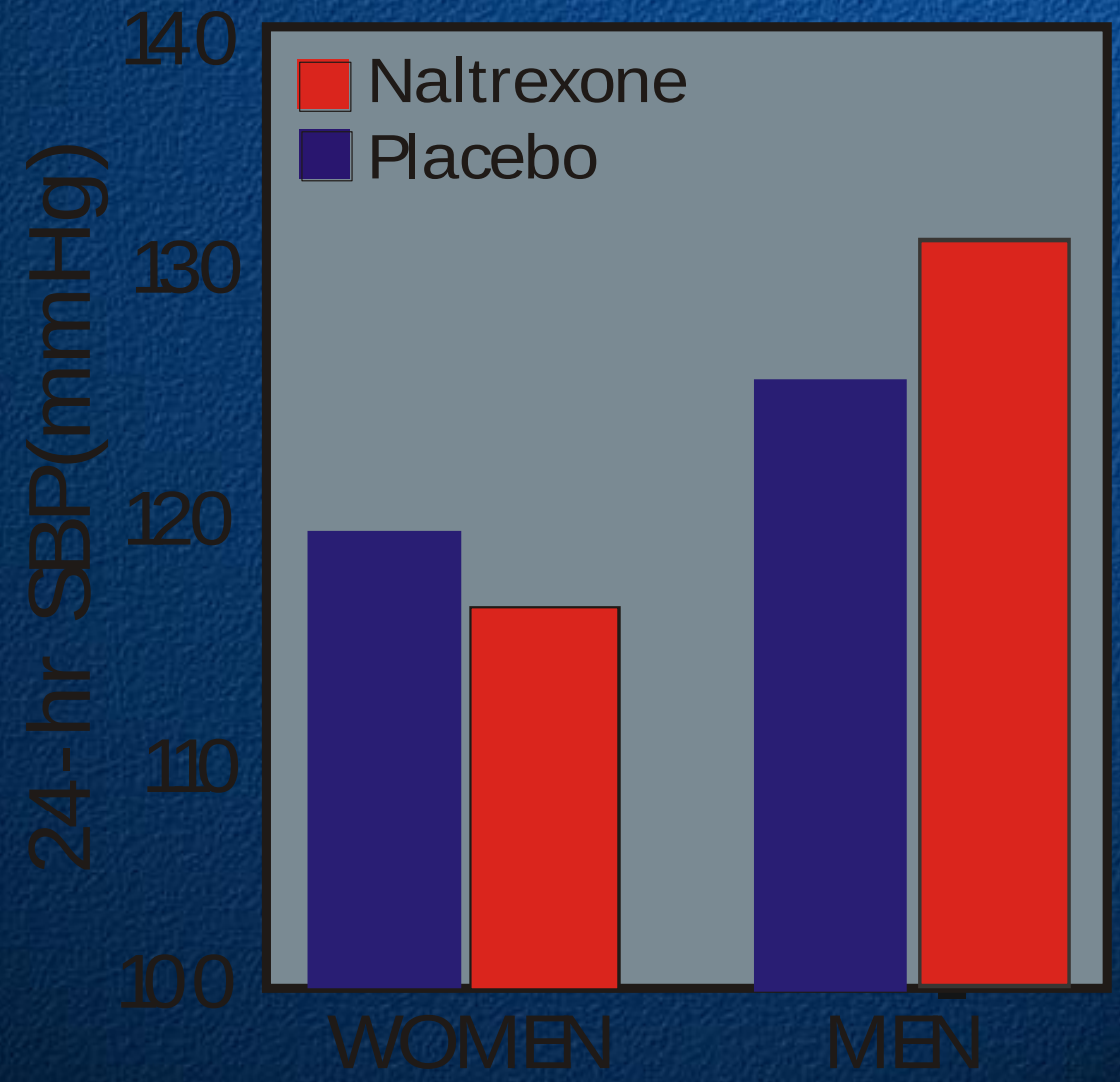
Day 9: Return to Laboratory
Autobiographical memories /Significant exp.
Salivary Cortisol

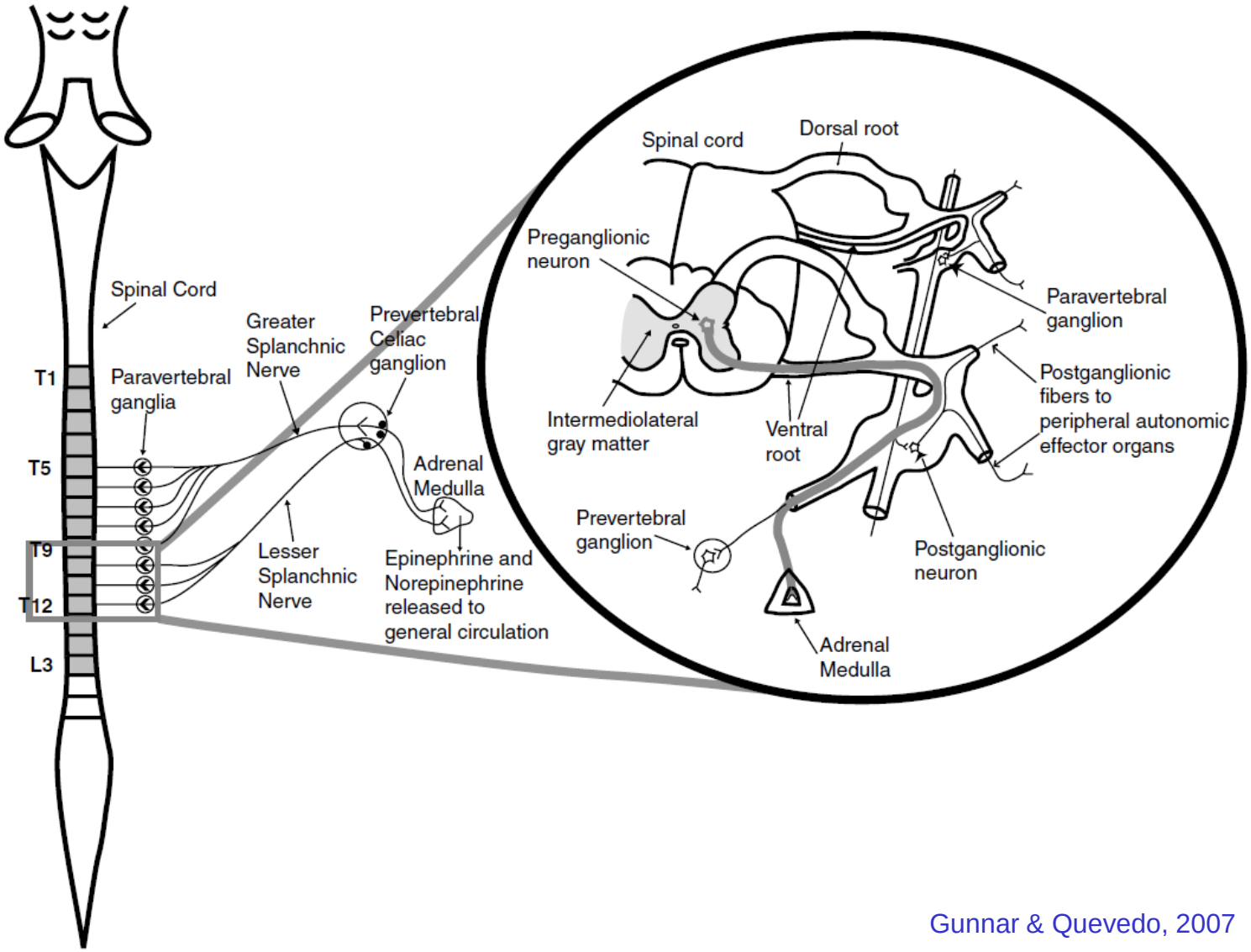
Day 10: Return to Laboratory
Drop off Diary & Watch

Effects of Opioid Blockade on 24-hr SBP: Interactions with PH HTN



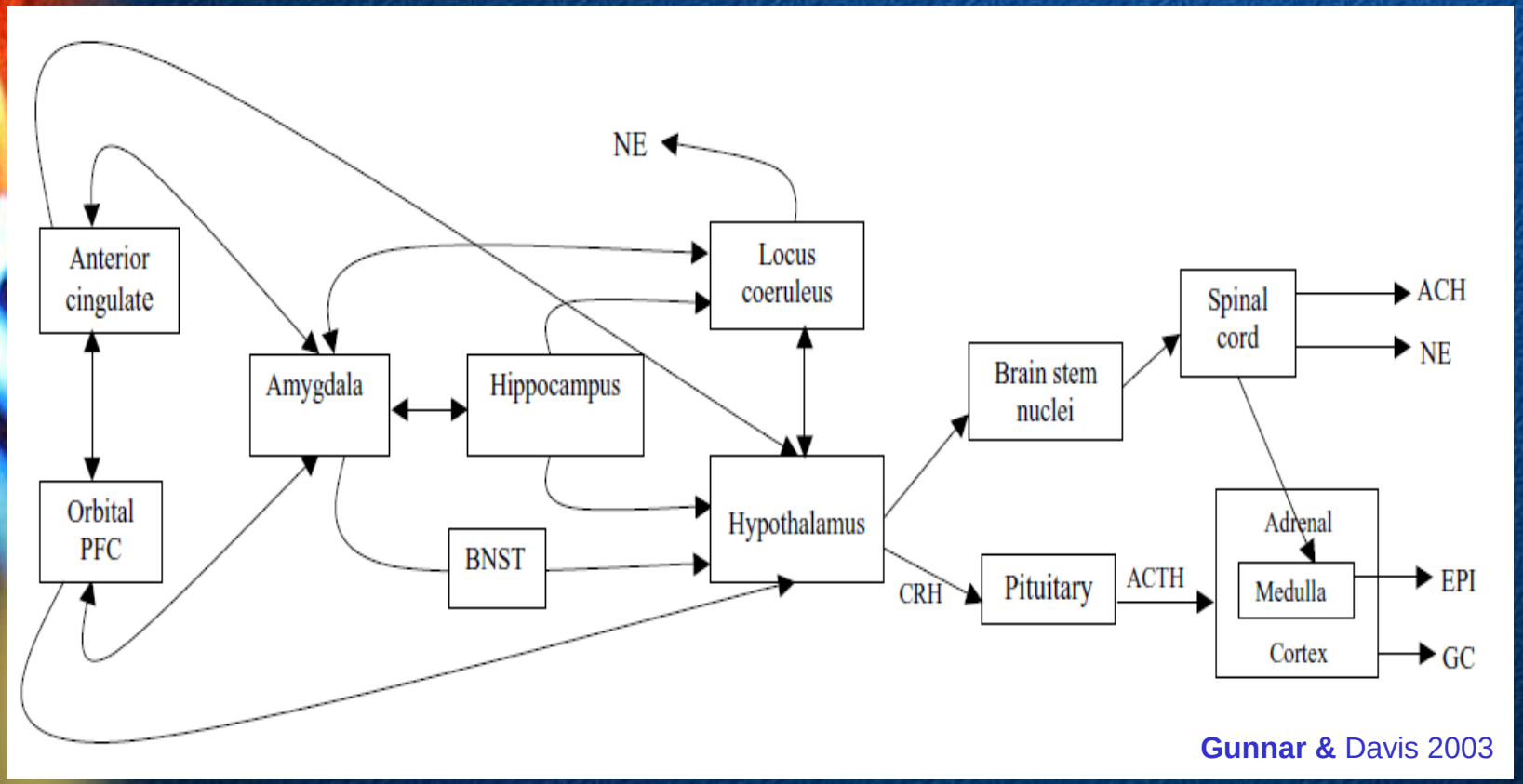
Effects of Opioid Blockade on 24-hr SBP: Interactions with Gender



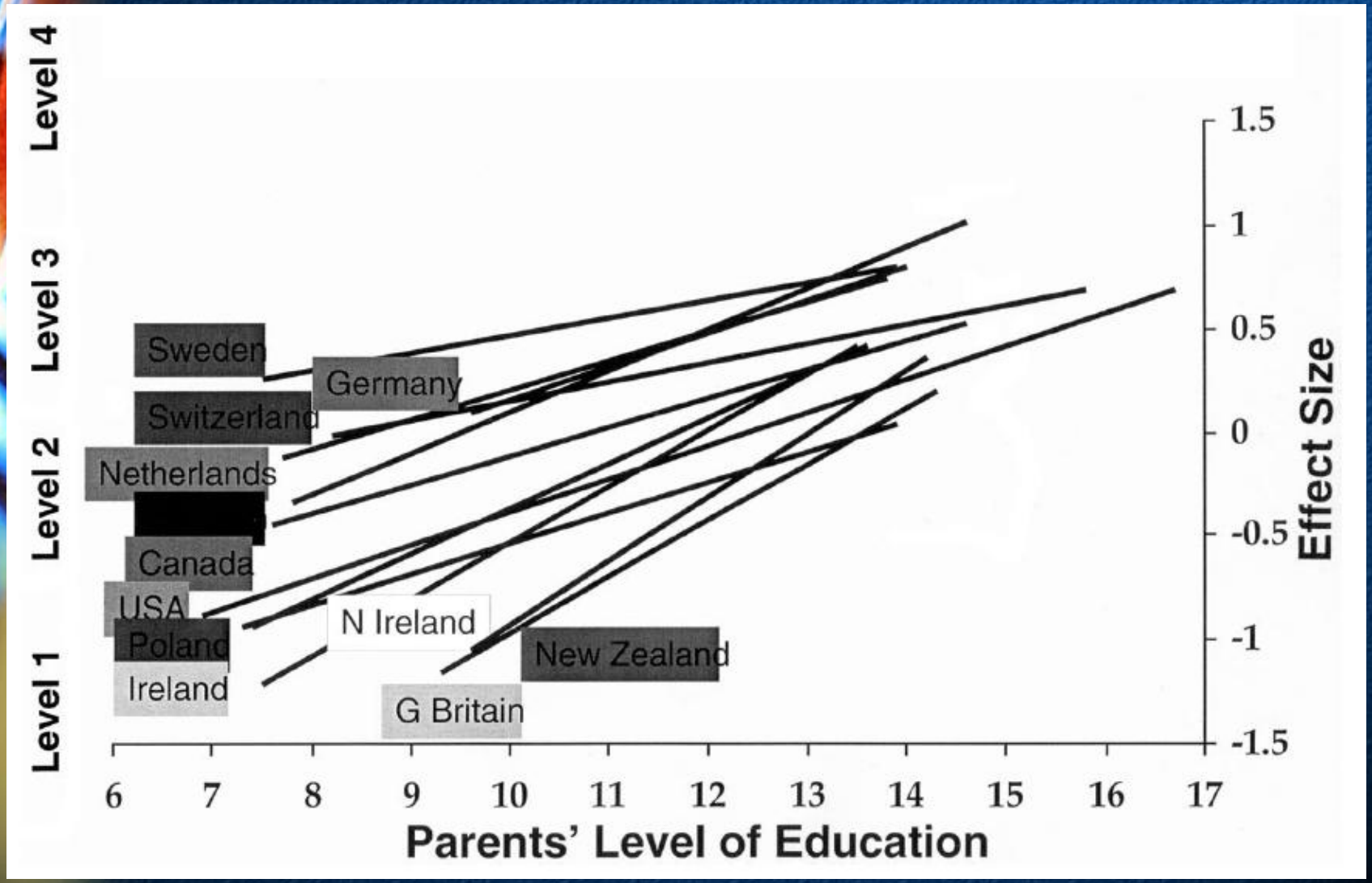


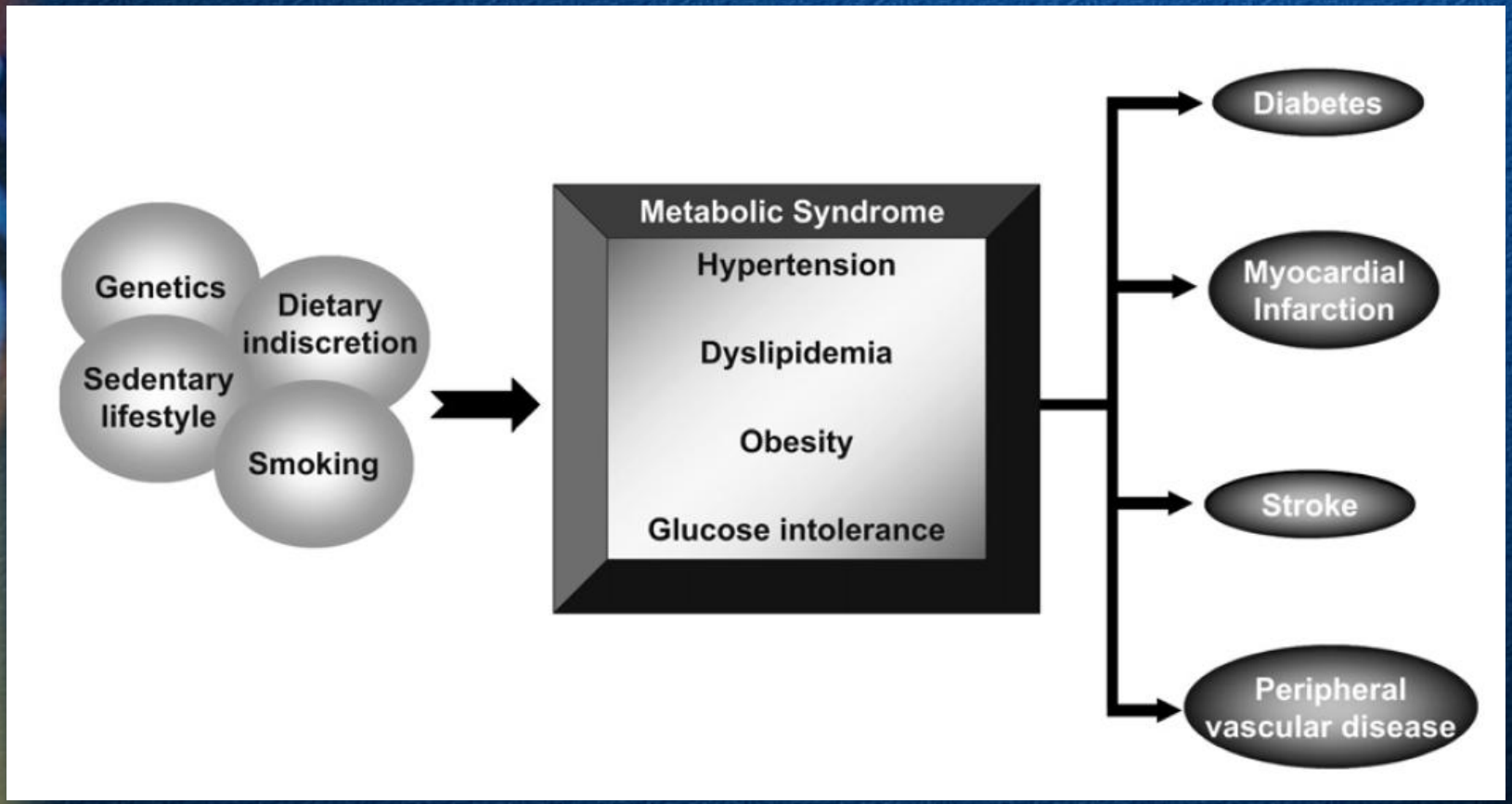
Gunnar & Quevedo, 2007

Neurobiological Organization of Stress Systems

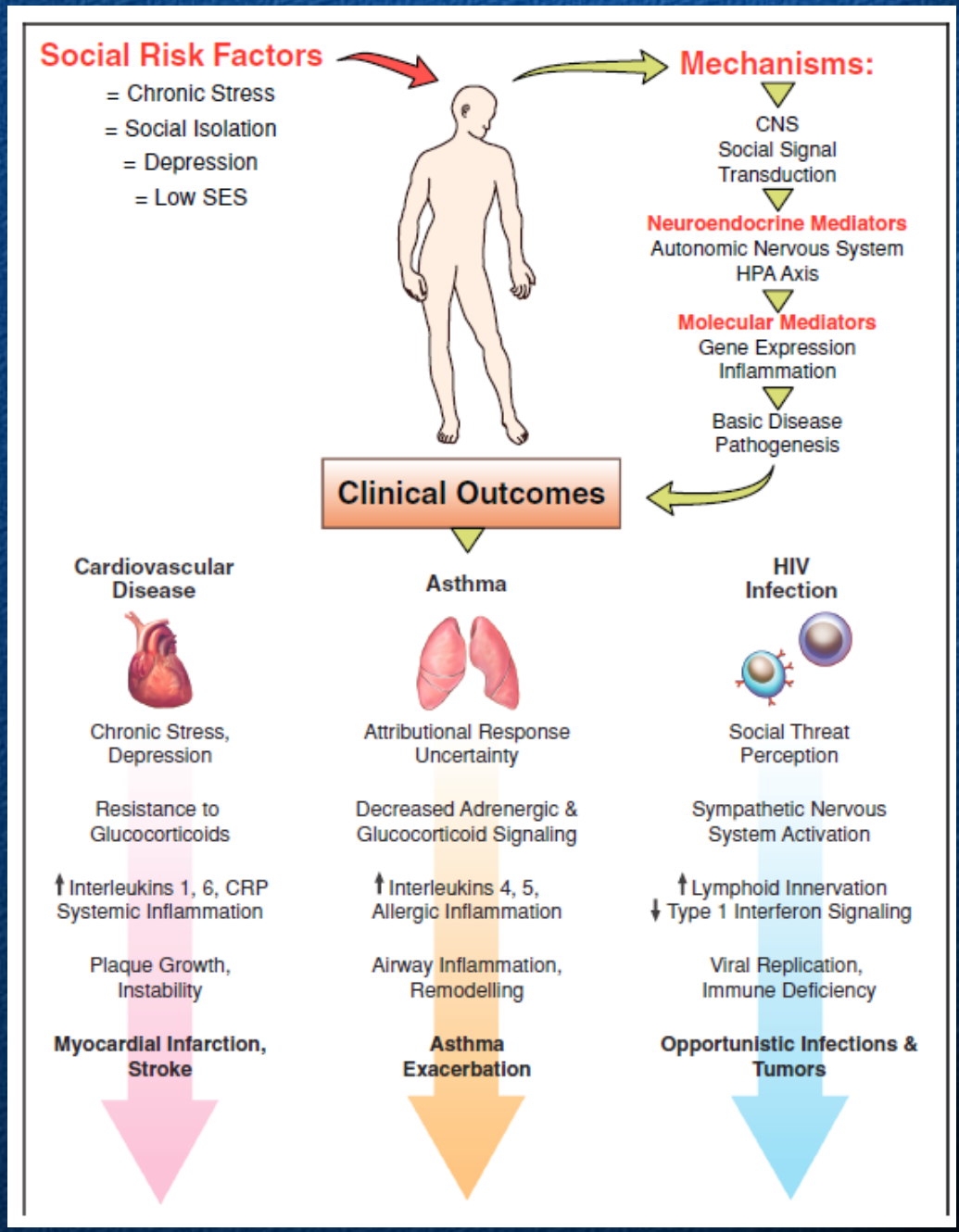


Gunnar & Davis 2003


Level 4
Level 3
Level 2
Level 1
Sweden
Germany
Switzerland
Netherlands
Canada
USA
Poland
Ireland
N Ireland
New Zealand
G Britain
1.5
1
0.5
0
-0.5
-1
-1.5
Effect Size
6
7
8
9
10
11
12
13
14
15
16
17
Parents' Level of Education


Genetics
Dietary indiscretion
Sedentary lifestyle
Smoking
Metabolic Syndrome
Hypertension
Dyslipidemia
Obesity
Glucose intolerance
Diabetes
Myocardial Infarction
Stroke
Peripheral vascular disease

Chain of events through which the social world *"gets inside the body"* to influence disease pathogenesis



Miller et al 2009