Chapter 26

Stress and Associated Problems

Stress

Over 40% of adults experience adverse effects from stress.

The History of Stress

- 1935 Hans Selye conducted studies to see if he could find a new sex hormone
  - He injected extracts from ovaries and placentas into rats
  - He hoped to induce a “tropic” effect
  - To then isolate a “new hormone” in the blood in response to the injections of the extracts

The History of our Concept of Stress

- He did not find a new hormone
- But to his surprise he observed three unexpected responses
  - Hypertrophy of the adrenal cortex
  - Atrophy of immune organs (spleen / thymus / lymph nodes)
  - Bleeding ulcers in stomach and small intestine

Selys's Next Investigative Step

- Injected animals to wide variety of different organ extracts /// also a variety of chemicals including poisons like formaldehyde
- Every time he observed the same changes in the experimental animals
  - Enlarged adrenal cortex
  - Shrunken lymphoid organs (spleen, thymus, lymph nodes)
  - Bleeding ulcers
  - He called this the "a triad"

Selye's Believed This Syndrome Represented a New Disease

- A syndrome is a set of signs and symptoms
  - They always occur together
  - They characterize one particular disease
  - Therefore…
    - Selye believed that he discovered a new disease // he called it "stress"

BOX 26-1 A Selection of Stress-Related Disorders

Gastrointestinal System
Peptic ulcer, stress ulcers
Ulcerative colitis
Regional ileitis
Nausea, diarrhea
Stomatitis, periodontitis

Nervous System
Multiple sclerosis
Seizures
Depression
CVA (stroke)

Respiratory System
Asthma

Musculoskeletal System
Rheumatoid arthritis

Cardiovascular System
Hypertension
Angina
Congestive Heart Failure

Skin
Herpes Simplex
Eczema
Acne

Urinary System
Acute renal failure
Cirrhosis due to alcohol abuse

Other
Cancer
Infection
Autoimmune Disorders
Obesity

c.

Selye's General Adaptive Syndrome

- Published paper in 1935 entitled, "A Syndrome Produced by Diverse Nocuous Agents"
- In 1956 follow up with his monumental technical treatise entitled, "The Stress of Life"
- These ideas were later summarized as the "General Adaptive Syndrome"
  - how the body is "alarmed" by stress
  - how the body copes and "resist" stress
  - how the body "exhaust" itself following chronic stress

Homeostasis & Stress

- Earlier // In 1914 Walter Cannon studied how the body regulates the internal environment
- He coined the term homeostasis to describe this dynamic equilibrium
- Mechanisms are regulated by negative feedback
- Cannon established the principle in physiology that a disease state occurs when homeostasis fails
- Cannon used the phrase “emotional stress” and established the principle in physiology that if homeostasis fails then a disease state occurs
- However, it was Selye who brought the concept of stress as a disease into mainstream medical practice

Stressors

- Selye called the *agents which caused the conditions stressors*
- Anything that causes stress is a stressor
- Physiologic or psychological
- Individuals react differently to stressors
- Individual's ability to cope with stressors will result in different outcomes

Five Generalizations About Stressors

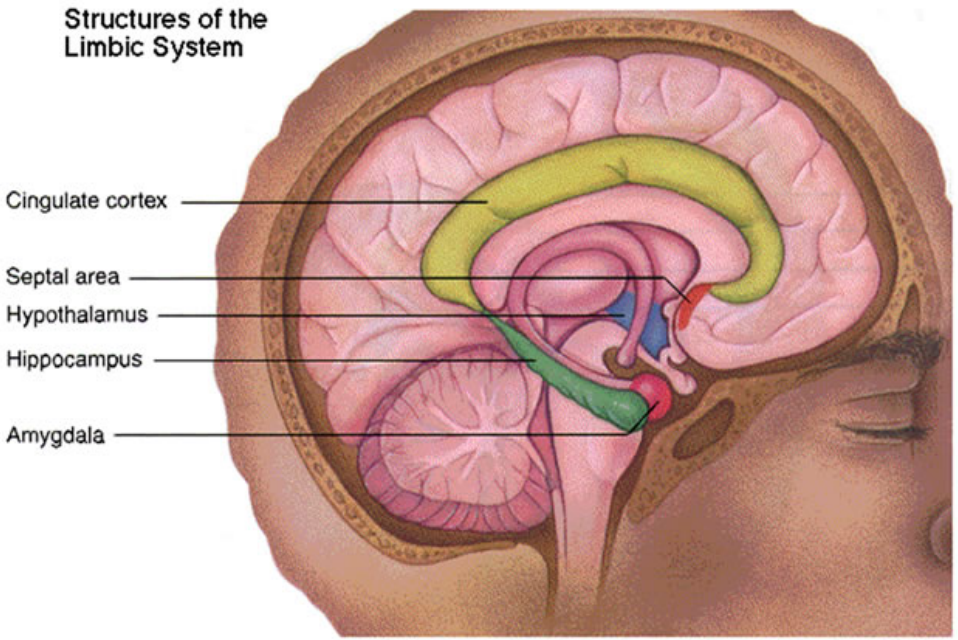
- (1) Stressors are extreme stimuli
  - individual's perception critical // too much or a deficient of a stimuli may both be a stressor
  - Extreme heat, extreme cold, loud sounds, over crowding, as well as solitary confinement are stressors
  - Anything in moderation tends to be a non stressor (soft music, cool temperatures)

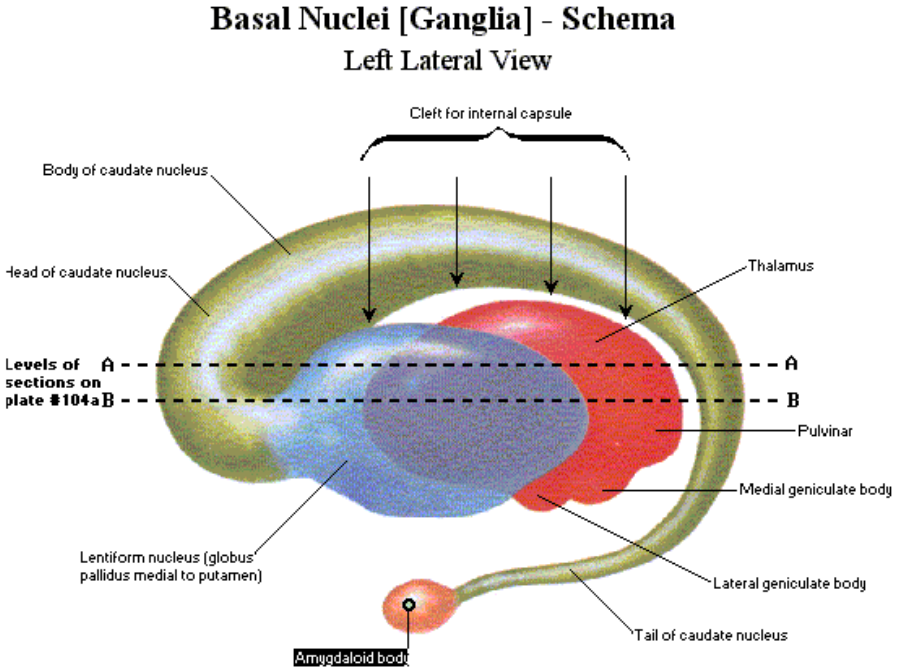
Five Generalizations About Stressors

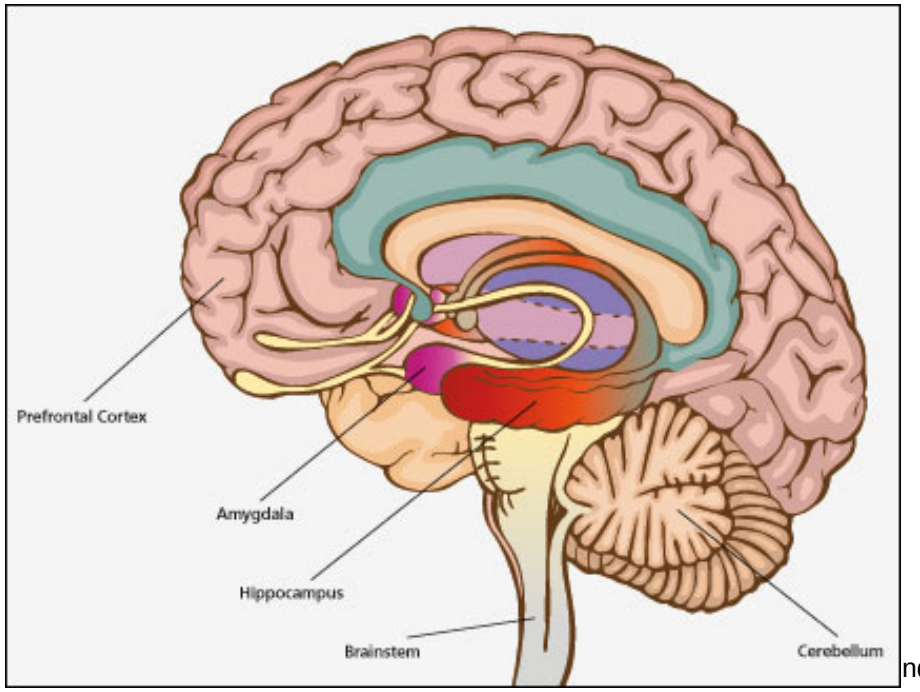
- (2) Stressors are often injurious, unpleasant, or painful stimuli
  - However, …. “a painful blow and a passionate kiss can be equally stressful”, Selye
- (3) A perceived threat (real or imagined) maybe a stressor // this can also includes grief!!!
- (4) Stressors differ for different individuals and in one individual at different times // a stressor today may not be a stressor yesterday or tomorrow

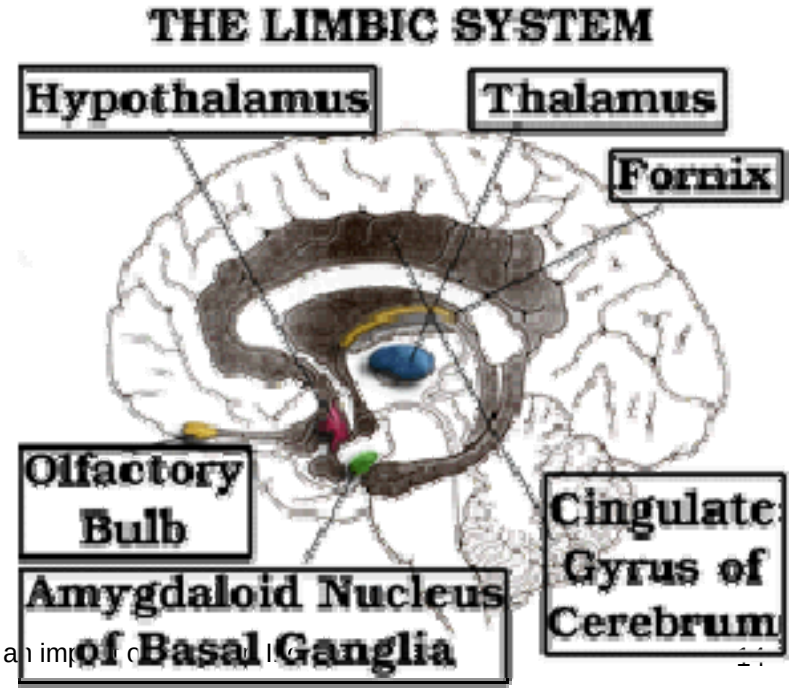
Five Generalizations About Stressors

- (5) Stress can occur even in a developing fetus (prenatal stress)
  - Lack of nutrients = stressor
  - Fetal alcohol syndrome = stressor
  - "biologic tradeoff" – risk danger of premature birth vs staying in environment with stressor
  - Stress also has profound developmental consequences for adolescents

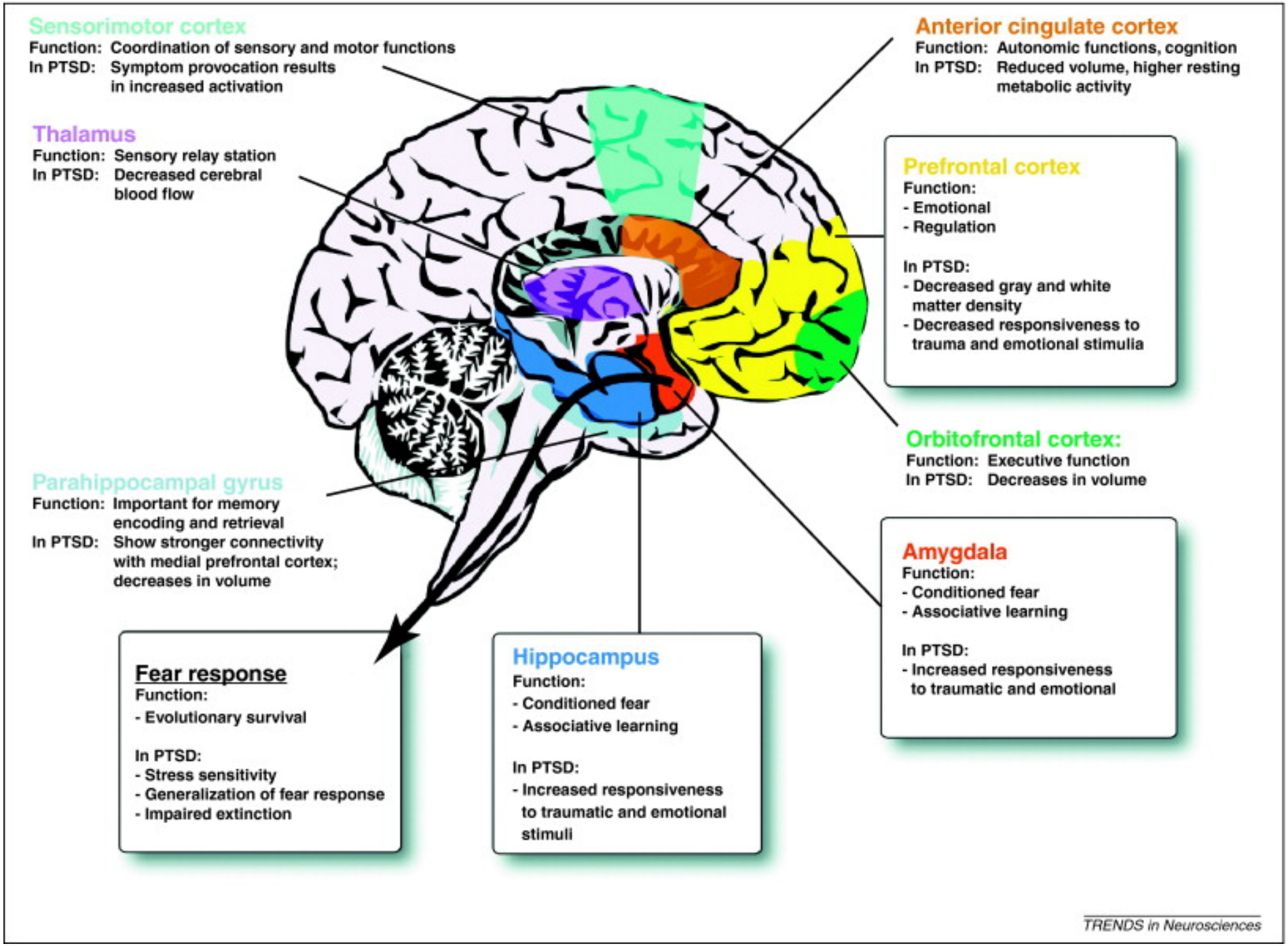

Structures of the Limbic System
Cingulate cortex
Septal area
Hypothalamus
Hippocampus
Amygdala


Basal Nuclei [Ganglia] - Schema
Left Lateral View
Cleft for internal capsule
Body of caudate nucleus
Head of caudate nucleus
Thalamus
Levels of sections on plate #104a
A
A
B
B
Pulvinar
Medial geniculate body
Lentiform nucleus (globus pallidus medial to putamen)
Lateral geniculate body
Tail of caudate nucleus
Amygdaloid body


Prefrontal Cortex
Amygdala
Hippocampus
Brainstem
Cerebellum


THE LIMBIC SYSTEM
Hypothalamus
Thalamus
Fornix
Olfactory Bulb
Cingulate Gyrus of Cerebrum
Amygdaloid Nucleus of Basal Ganglia

nders, an imp

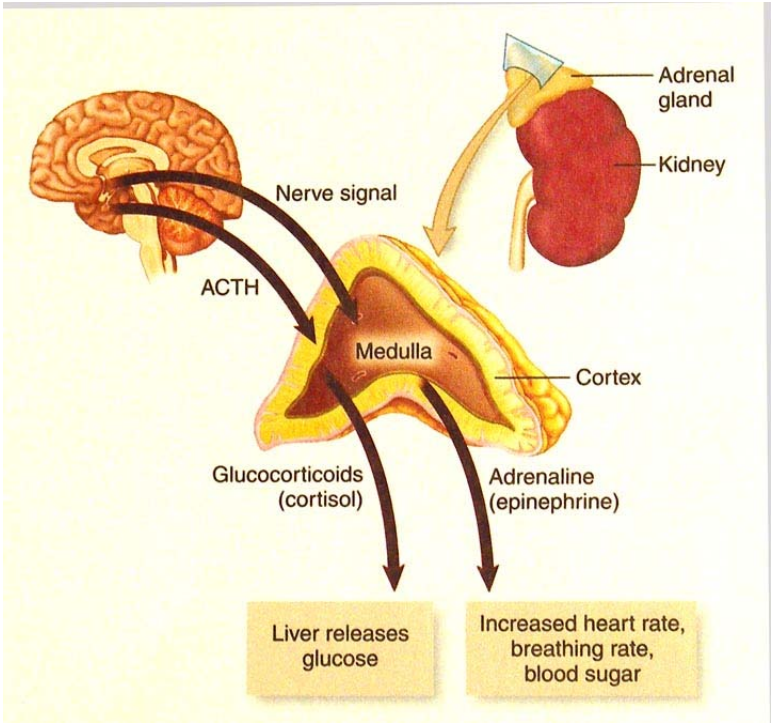

Sensorimotor cortex
Function: Coordination of sensory and motor functions
In PTSD: Symptom provocation results in increased activation
Thalamus
Function: Sensory relay station
In PTSD: Decreased cerebral blood flow
Parahippocampal gyrus
Function: Important for memory encoding and retrieval
In PTSD: Show stronger connectivity with medial prefrontal cortex; decreases in volume
Fear response
Function:
- Evolutionary survival
In PTSD:
- Stress sensitivity
- Generalization of fear response
- Impaired extinction
Hippocampus
Function:
- Conditioned fear
- Associative learning
In PTSD:
- Increased responsiveness to traumatic and emotional stimuli
Amygdala
Function:
- Conditioned fear
- Associative learning
In PTSD:
- Increased responsiveness to traumatic and emotional
Orbitofrontal cortex:
Function: Executive function
In PTSD: Decreases in volume
Prefrontal cortex
Function:
- Emotional
- Regulation
In PTSD:
- Decreased gray and white matter density
- Decreased responsiveness to trauma and emotional stimulia
Anterior cingulate cortex
Function: Autonomic functions, cognition
In PTSD: Reduced volume, higher resting metabolic activity
TRENDS in Neurosciences

General Adaptation Syndrome

- Selye summarized his findings as the General Adaptation Syndrome
- Syndrome is produced by only agents that have a general effect on large portions of the body
- Syndrome results in changes that makes it possible for the body to adapt (get away from the tiger!)
- *General adaptation syndrome = crucial part of the body's complex defense mechanism*

GAS Stages: Alarm – Resistance – Exhaustion

- A different syndrome characterized each stage
- The alarm stage = the stress triad



- Enlarged adrenal cortex
- Shrunken lymphoid organs (spleen, thymus, lymph nodes)
- Bleeding ulcers

Alarm Reaction

- Initial response mediated by
  - Norepinephrine and epinephrine from the sympathetic nervous system
  - lesser amount of aldosterone from the adrenal cortex

Alarm Reaction

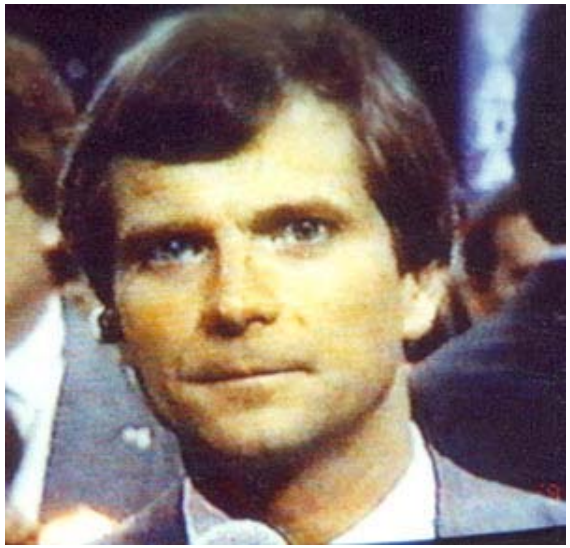
- Response to “fright” and prepares the body to either “fight or flight”
  - stored glycogen is catabolized (catecholamine)
  - increase in aldosterone and angiotensin levels
    - angiotensin helps raise blood pressure
    - aldosterone (mineralcorticoid) promotes sodium and water conservation
    - Why are these secretions appropriate?

Alarm Reaction

- After a few hours, glycogen reserves gone, but brain still needs glucose /// need to provide alternate fuels for metabolism
- This period of alarm stage now dominated by cortisol
- Hypothalamus responds by secreting corticotropin-releasing hormone (CRH)
- Pituitary secretes increasing amounts of ACTH
  - stimulates the adrenal cortex to secrete cortisol and to lesser extent mineralcorticoids
  - promotes the breakdown of fat and protein
    - glycerol, fatty acids, and amino acids – for gluconeogenesis

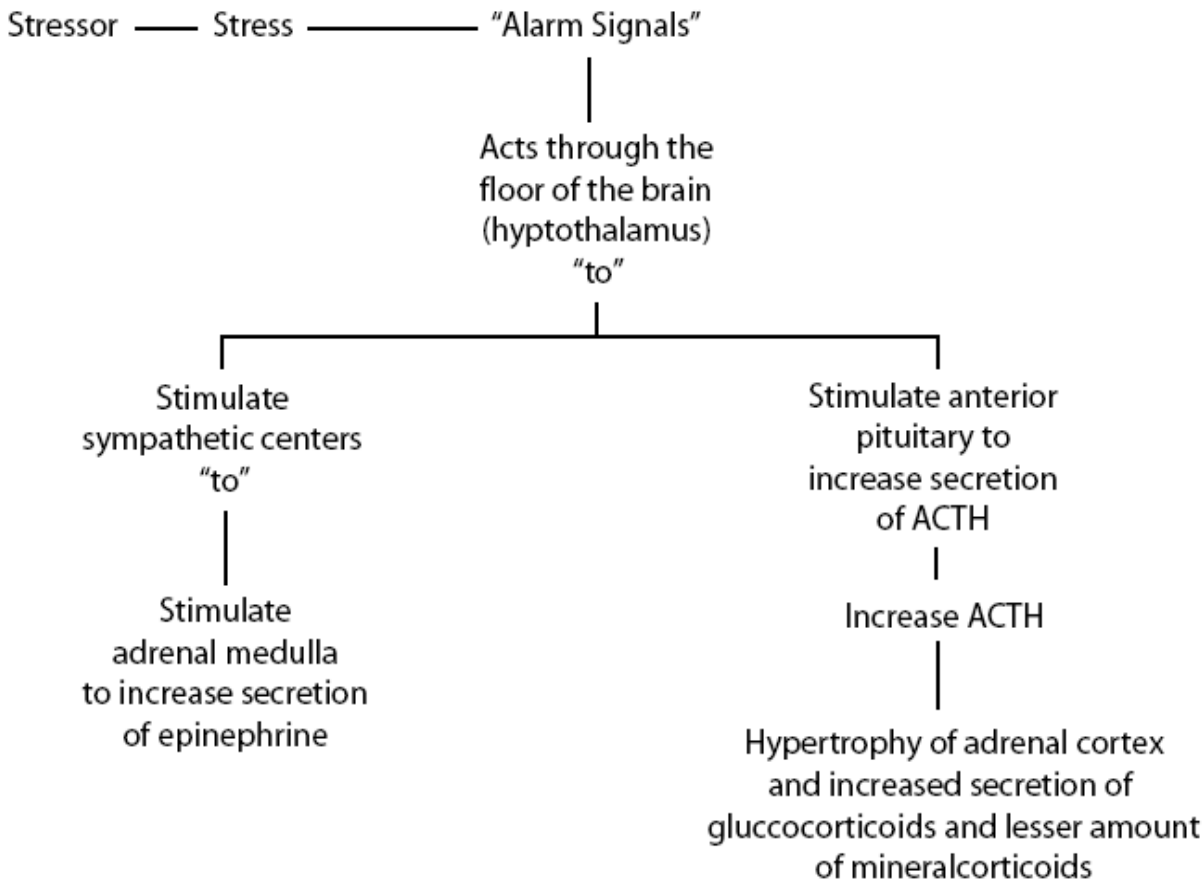
Alarm Reaction

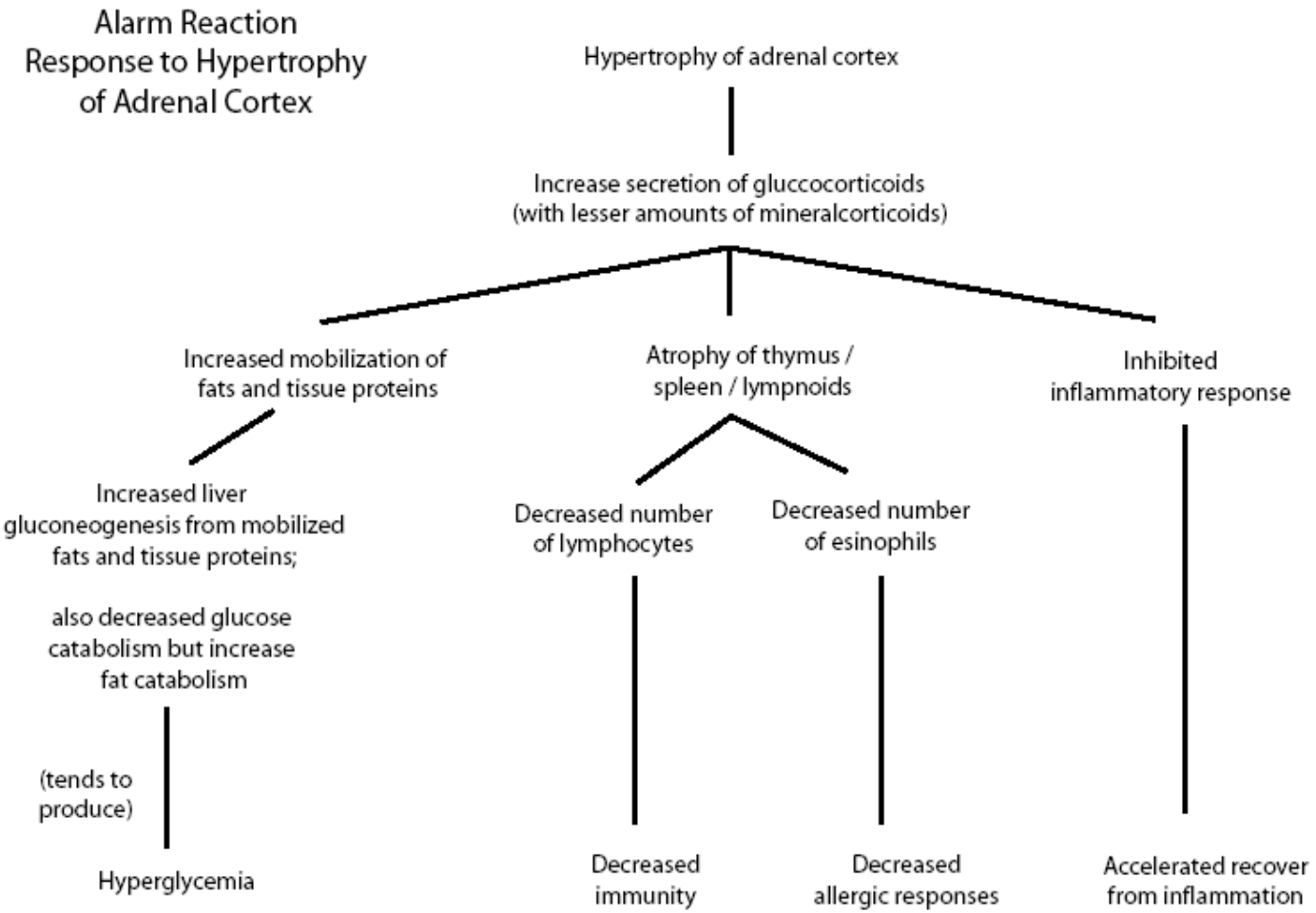
- cortisol has glucose-sparing effect
  - inhibits protein synthesis /// spares amino acids for gluconeogenesis
  - adverse effects of excessive cortisol
    - depresses immune function
    - Increases susceptibility to infection and ulcers
    - lymphoid tissues atrophy, antibody levels drop, and wounds heal poorly
    - Repositions fat deposits in body (from limbs to face & back)
    - However, glucocorticoids resist initial response to inflammation (reverses vascular events)



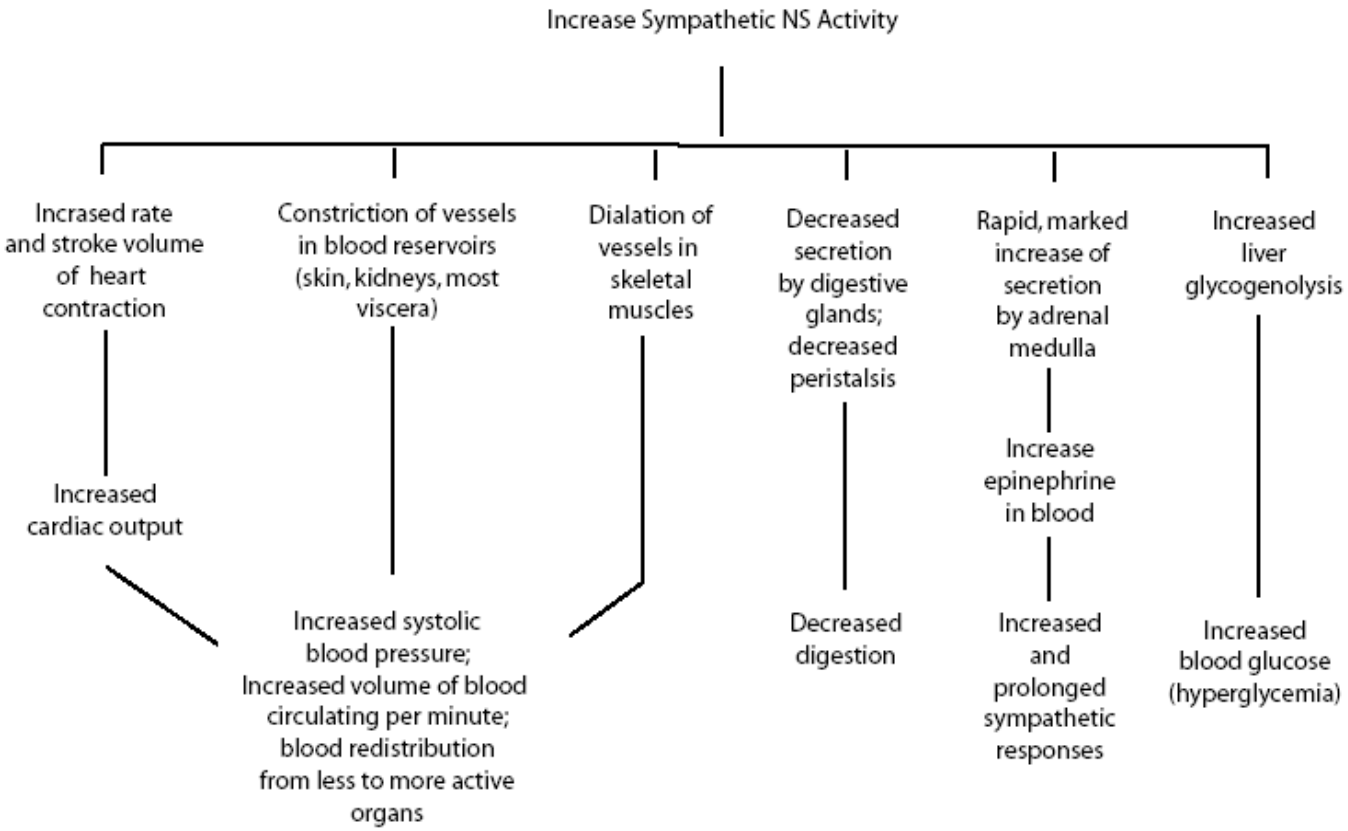
Lee Atwater

Hypothalamic - Pituitary - Adrenal - Axis




Alarm Reaction
Response to Hypertrophy
of Adrenal Cortex
Hypertrophy of adrenal cortex
Increase secretion of gluccocorticoids
(with lesser amounts of mineralcorticoids)
Increased mobilization of
fats and tissue proteins
Atrophy of thymus /
spleen / lympnoids
Inhibited
inflammatory response
Increased liver
gluconeogenesis from mobilized
fats and tissue proteins;
also decreased glucose
catabolism but increase
fat catabolism
Decreased number
of lymphocytes
Decreased number
of esinophils
(tends to
produce)
Hyperglycemia
Decreased
immunity
Decreased
allergic responses
Accelerated recover
from inflammation

Alarm Reaction
Response to Stimulation of Adrenal Medulla



GAS Stages: Alarm – Resistance – Exhaustion

- Resistance stage occurs when the individual is able to adapt (to cope) with the stressor
- We experience stressors all the time (daily) and the alarm stage is initiated but within minutes we cope // resistance to stressor
- Secretions from adrenal cortex and medulla return to normal // this is the resistance stage

Stage of Exhaustion

- If we can not “resist” then stress continues for prolonged period (weeks or months)
  - fat reserves are gone
  - protein breakdown results in muscle wasting
  - homeostasis is overwhelmed // electrolytes imbalanced
  - Physiology now marked by rapid decline
- Furthermore, associated with loss of glucose homeostasis because adrenal cortex stops producing glucocorticoids

End Stage of Exhaustion

- Aldosterone continues to promoted water retention and hypertension
  - conserves sodium and hastens elimination of K^+ and H^+
  - hypokalemia and alkalosis will ultimately leads to death
  - death results from heart and kidney failure or overwhelming infections

Coping with Stress

- Ensure adequate rest and a healthy diet.
- Use creative solutions to minimize stressors and adapt quickly to stressor.
- Regular moderate exercise
- Engage in distracting activities.
- Counseling and support services
- Relaxation techniques

Stress and Disease: Specific Problems

- Headache // May develop during or after stress response
- Stomatitis (ulcers in the mouth) and necrotizing periodontal disease
- Prolonged vasoconstriction // Can impair function or necrosis in gastrointestinal tract or kidneys
- Precipitating factor
  - Chronic infections
  - Physical and/or emotional distress

Potential Effects of Prolonged or Severe Stress

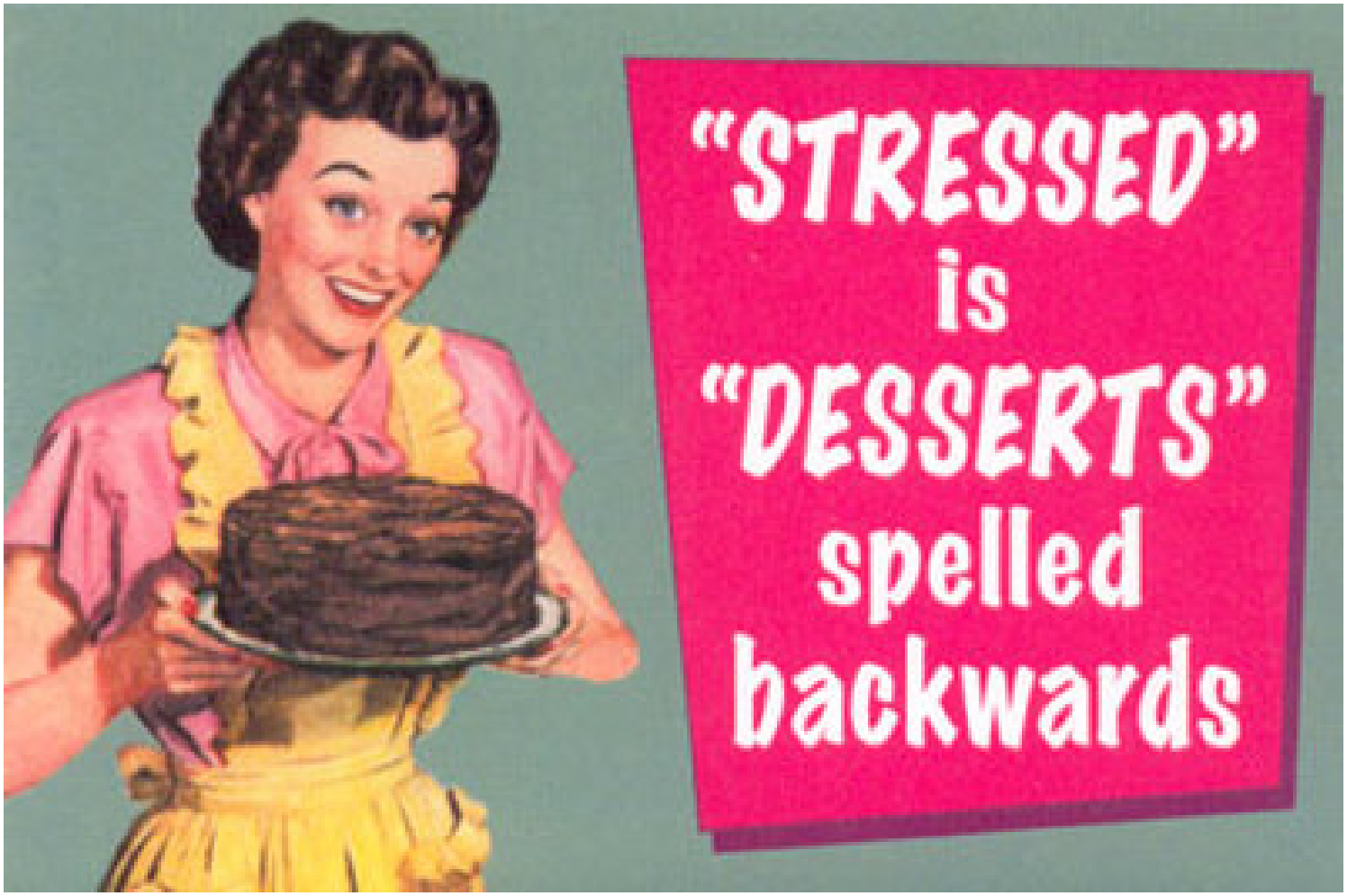
- Renal failure
  - Prolonged severe vasoconstriction
  - Ischemia causes cell damage.
- Stress ulcers
  - Vasoconstriction and glucocorticoids
  - Decrease in mucosal regeneration and mucus production
- Infection // Depression of the inflammatory and immune responses

Potential Effects of Prolonged or Severe Stress

- Slowed healing
  - Following trauma or surgery
    - Increased secretion of glucocorticoid - reduction in protein synthesis and tissue regeneration
    - Increased catecholamine levels - vasoconstriction, reduced nutrients and oxygen to the tissue

Potential Effects of Prolonged or Severe Stress

- Post-traumatic stress disorder
  - Serious consequence of major disaster or personal threat
  - Usually occurs within 3 months of event // May cause symptoms years later
  - High risk of developing dependence on drugs and/or alcohol



Some may look for relief from stressors in food while others may turn to alcohol or other substance abuse!

PROCESS

Stress Response