Introduction to Medical Psychology
Lecture 7: Stress

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https://youtu.be/RtbvK35c53I

Lecture video at above link.

Today: Stress

Stress

- The concept of stress
- Neurobiology of the stress response
- Effects of chronic stress on health
- Stress and peptic ulcers
- Relaxation techniques

Rate your stresses

What is stressful for you?

Undergradate Student Stresses
Severity out of 4 (most stressful)

Death (of a close person)	3.97
Lots of tests/finals week	3.62
Applying to graduate school	3.59
Victim of a crime	3.59
Assignments due on same day	3.57
Breakup with girl/boyfriend	3.45
Girl/boyfriend cheated	3.45
Lots of deadlines	3.41
Property stolen	3.41
Hard upcoming week	3.31
…	
Death of a pet	3.21
…	
Traffic ticket	3.10
…	
Sat through a boring class	1.66

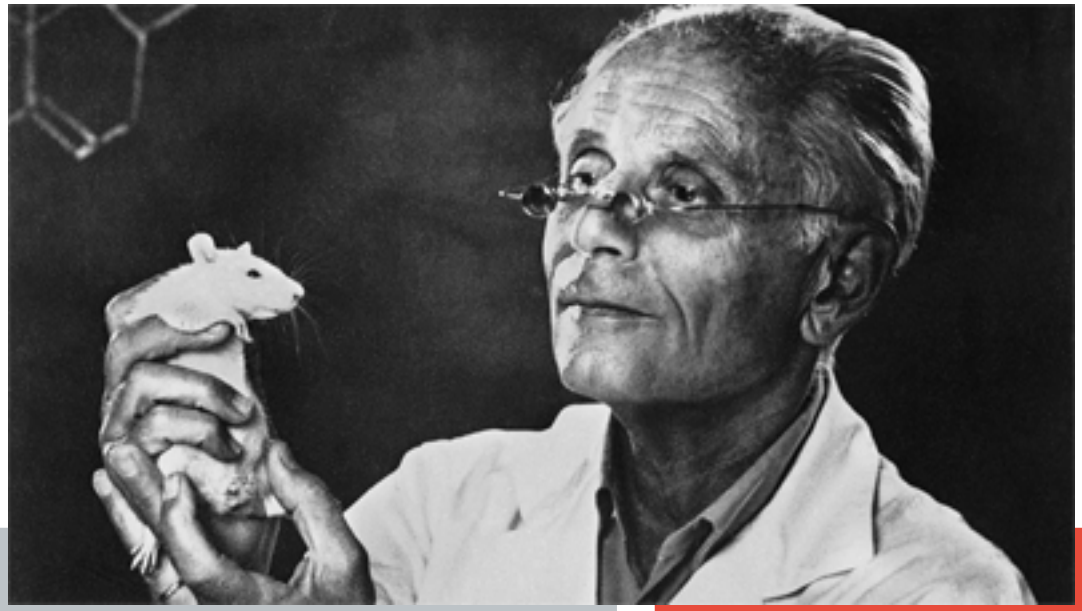
Crandall, J. Behav. Med., 1992

Hormones and Stress

In the 1930, Hans Selye studied hormonal communication in the rat and injected them with ovarian extracts daily. After several months, the rats had peptic ulcers (painful stomach sores), enlarged adrenal glands and shrunken immune tissues (lymph nodes, thymus).

When he found similar results in his control group (salt injections), he concluded that it was his “stressing” the rats during injection that caused the health decline.

Hans Selye (1907-1982)



Effects of Stress on Body

Similar effects of stress were seen when Selye stressed the rats by exposure to high/low temperature, forced exercise, immobilization, etc.

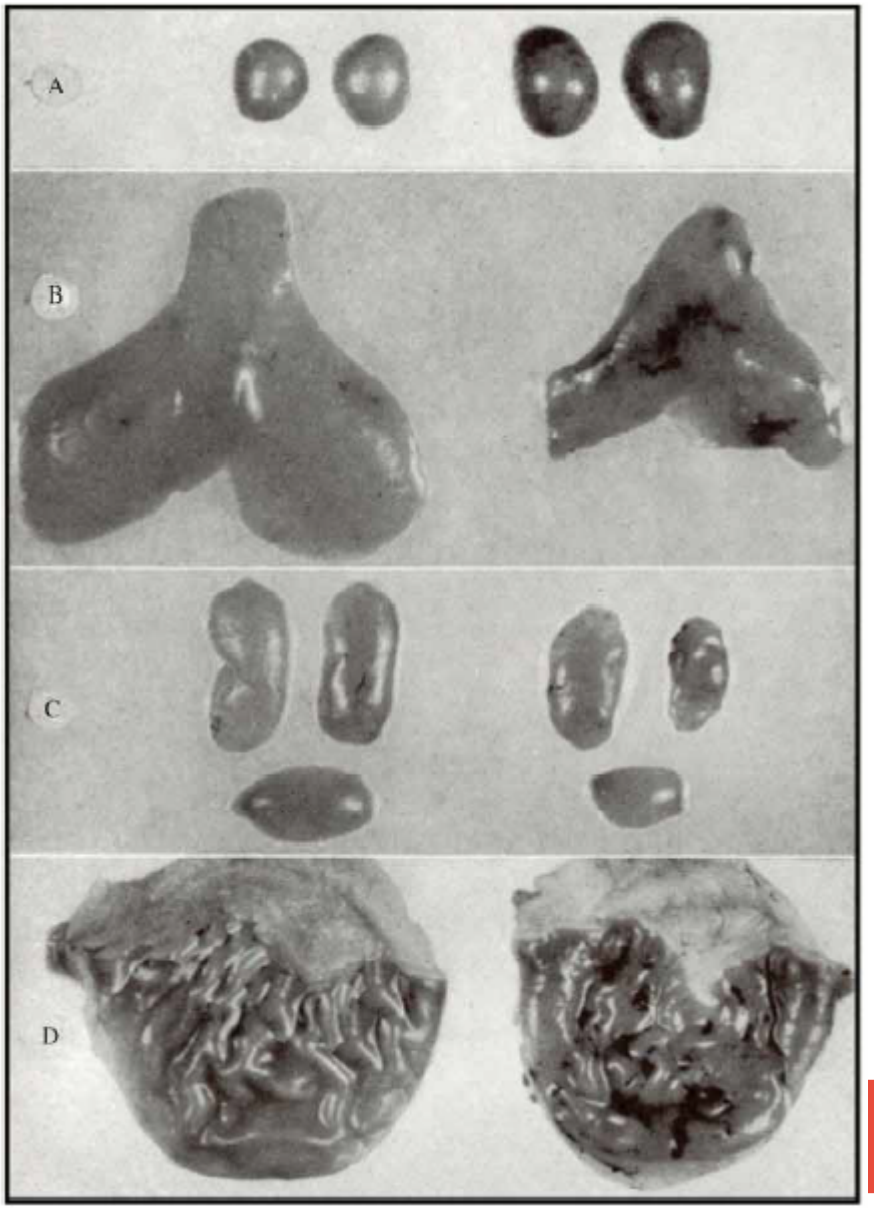
Normal rat Stressed rate (immobilized)

Adrenal glands

Thymus

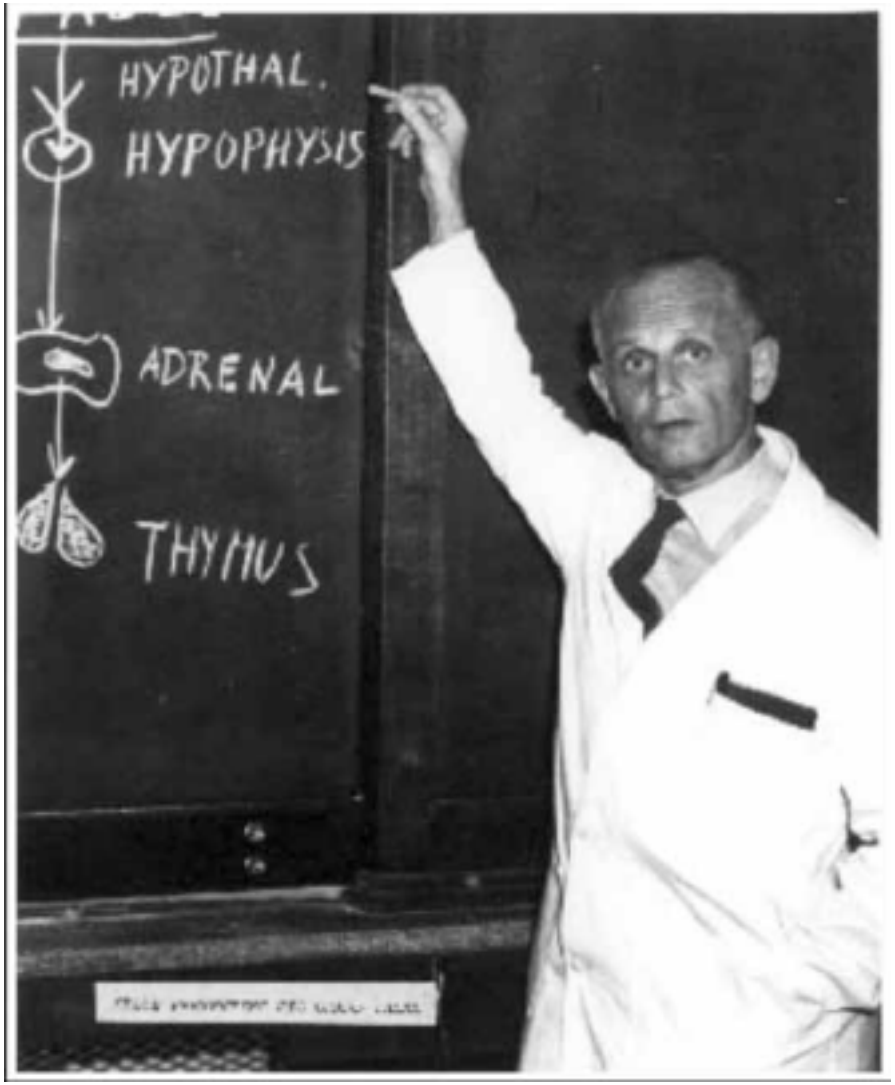
Lymph nodes

Stomach



Szabo, Stress, 2012

Stress and the Body



From these findings, Selye concluded that:

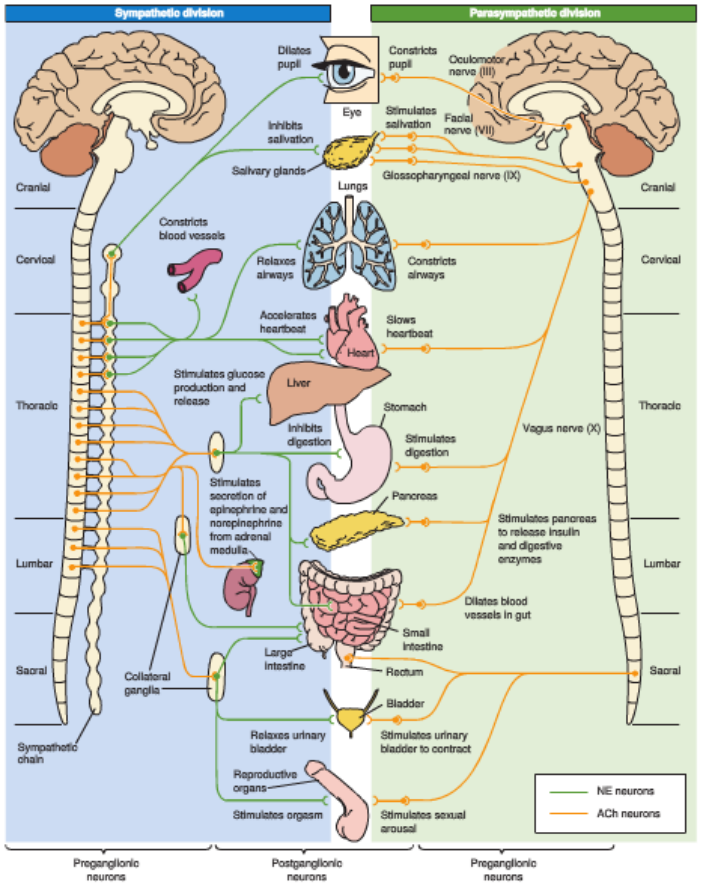
- The body reacts to various stressors in a similar way: with a stress response (general adaptation syndrome)
- Long-lasting stress results in sickness

Szabo, Stress, 2012

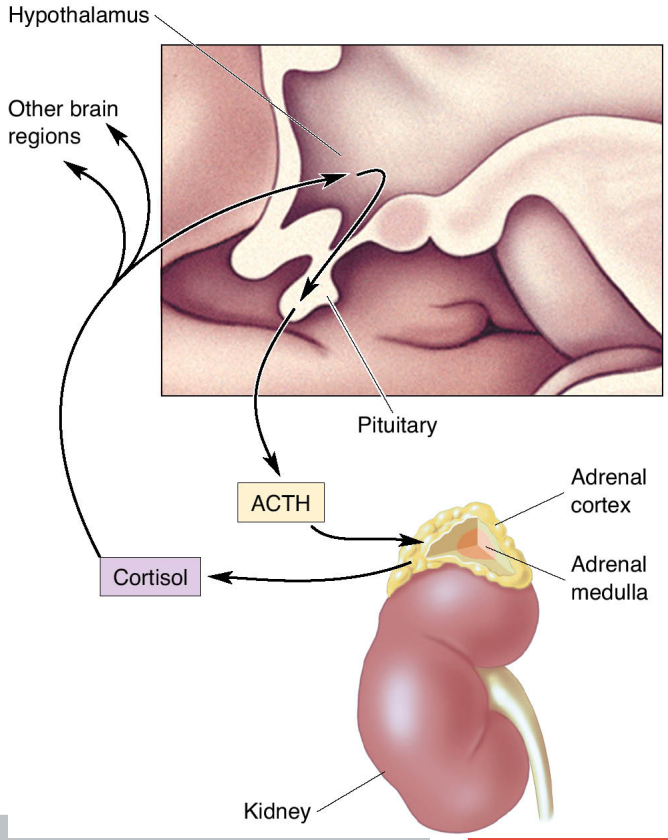
Mechanisms of Stress: Stress Response

The stress response involves two main pathways:

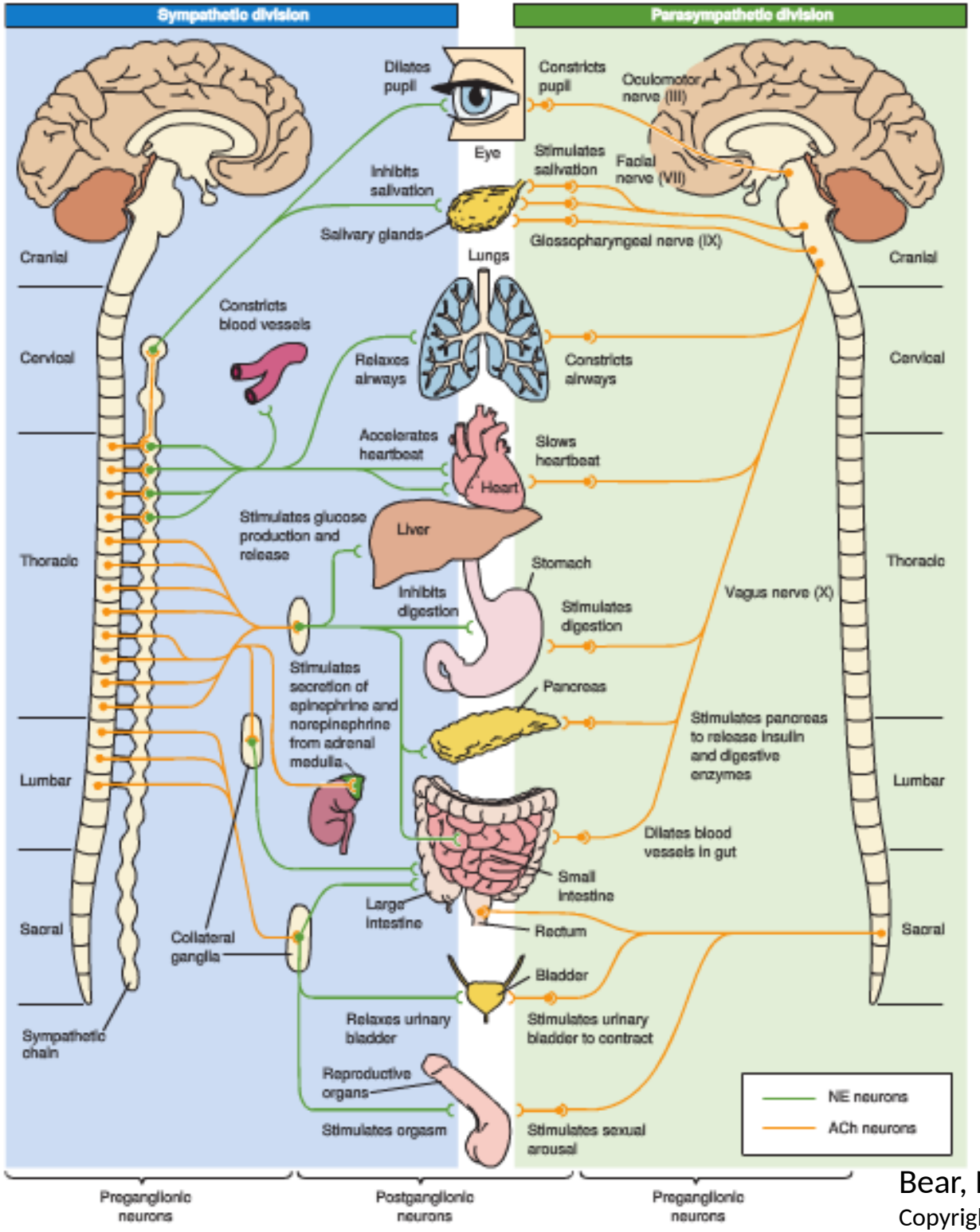
The autonomic nervous system (activation of the sympathetic nervous system in response to stress)



The hypothalamus-pituitary-adrenal (HPA) axis



Bear, Neuroscience

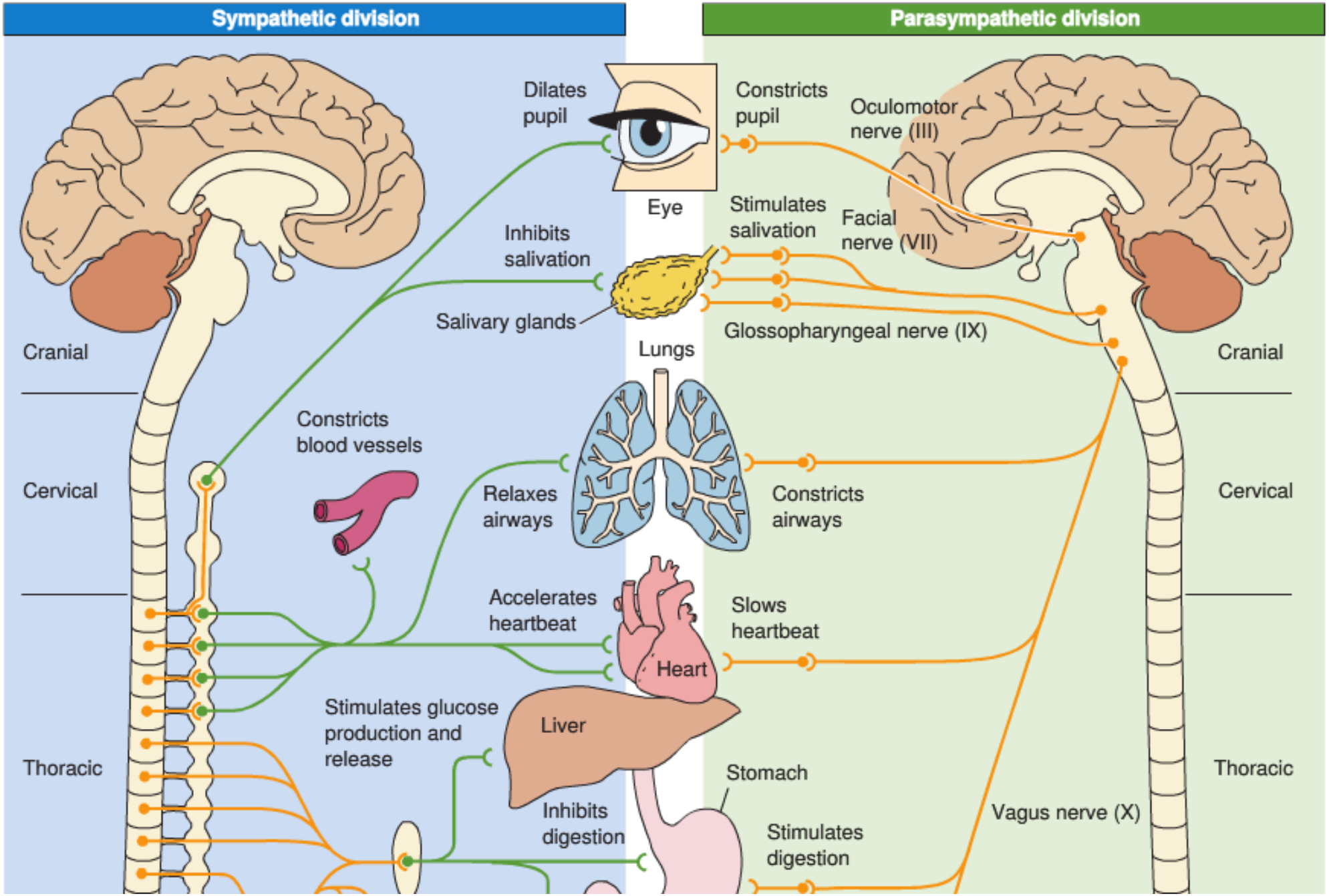


The Autonomic nervous system (ANS) is divided into two parts:

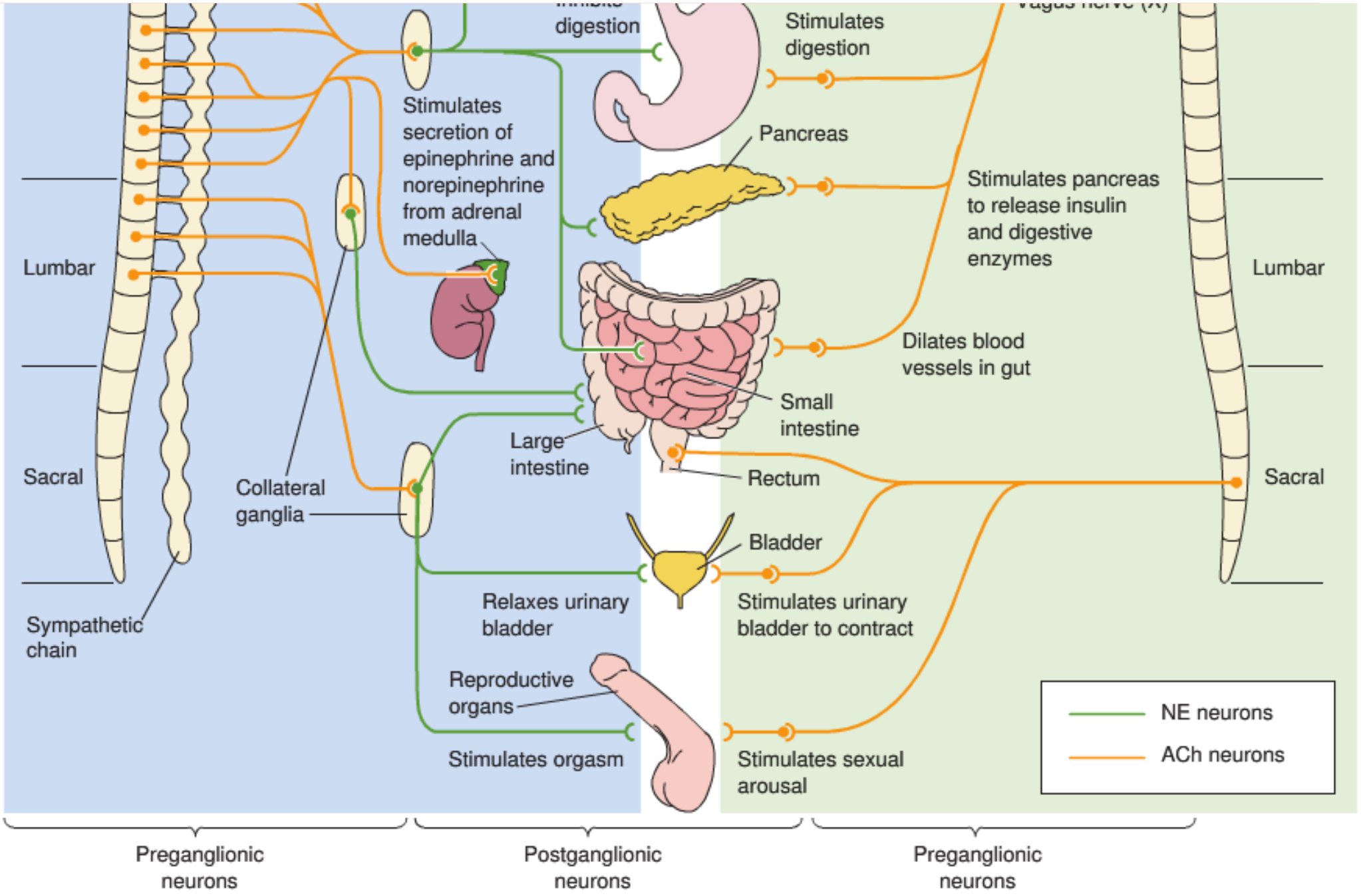
Sympathetic division: activated in crisis, i.e., Fight, Flight, Fright, Sex (orgasm)

Parasympathetic division: relaxation, digestion, sexual arousal

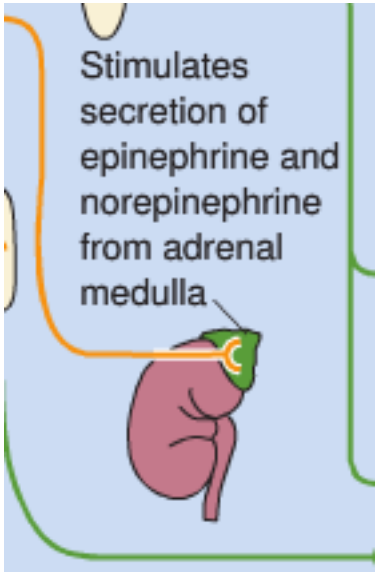
Bear, Neuroscience



Bear, Neuroscience



Autonomic Nervous System: Stress Response

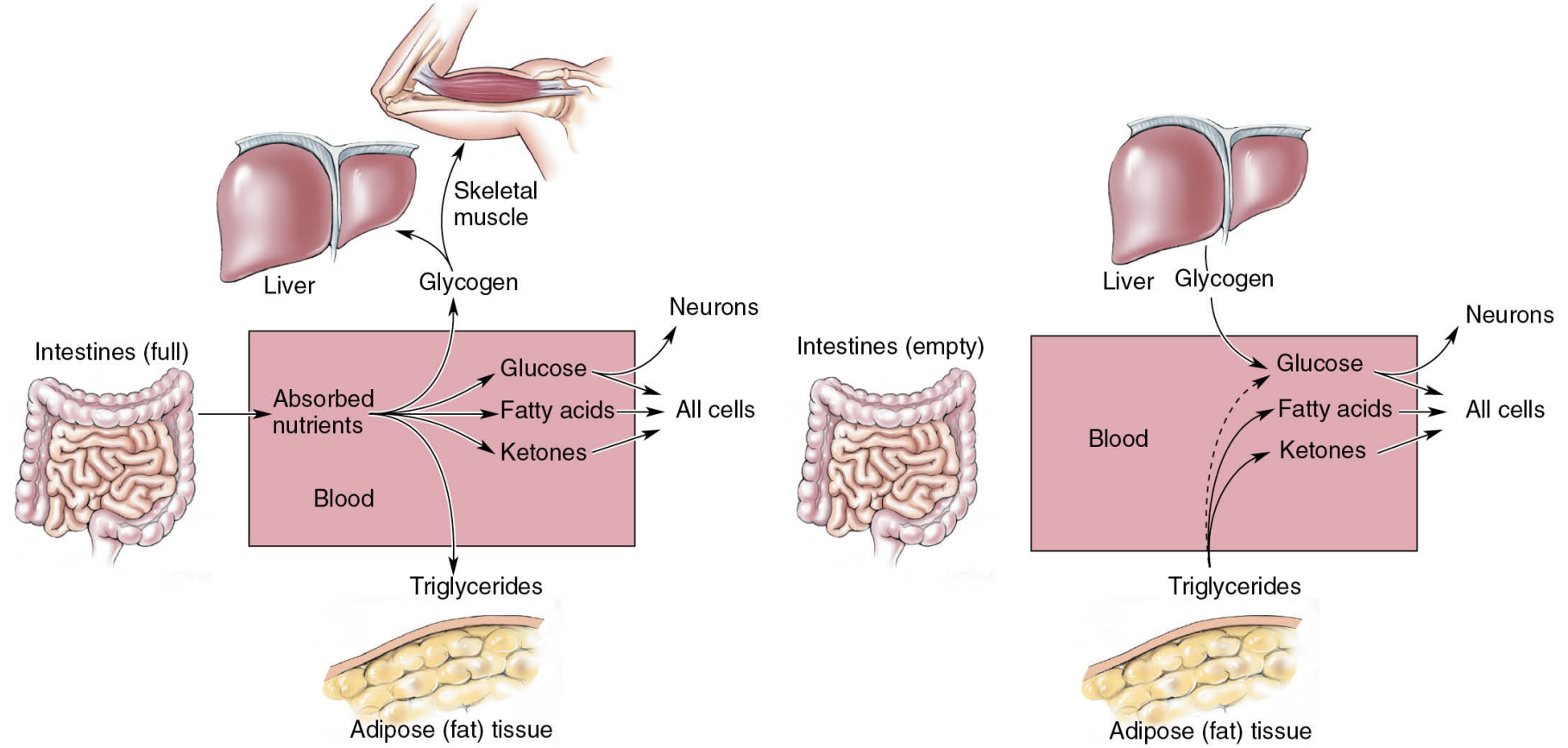


Sympathetic activation occurs within seconds.
It leads to secretion of the hormones epinephrine (UK: adrenalin) and norepinephrine (UK: noradrenalin) from the medulla (inner part) of the adrenal glands.

These two hormones help to provide energy for a stress situation:

- release of fatty acids from fat storages
- increase of blood sugar level (glucose)
- increase of blood pressure
- constriction of some blood vessels
- widens airways

Detour: Metabolism

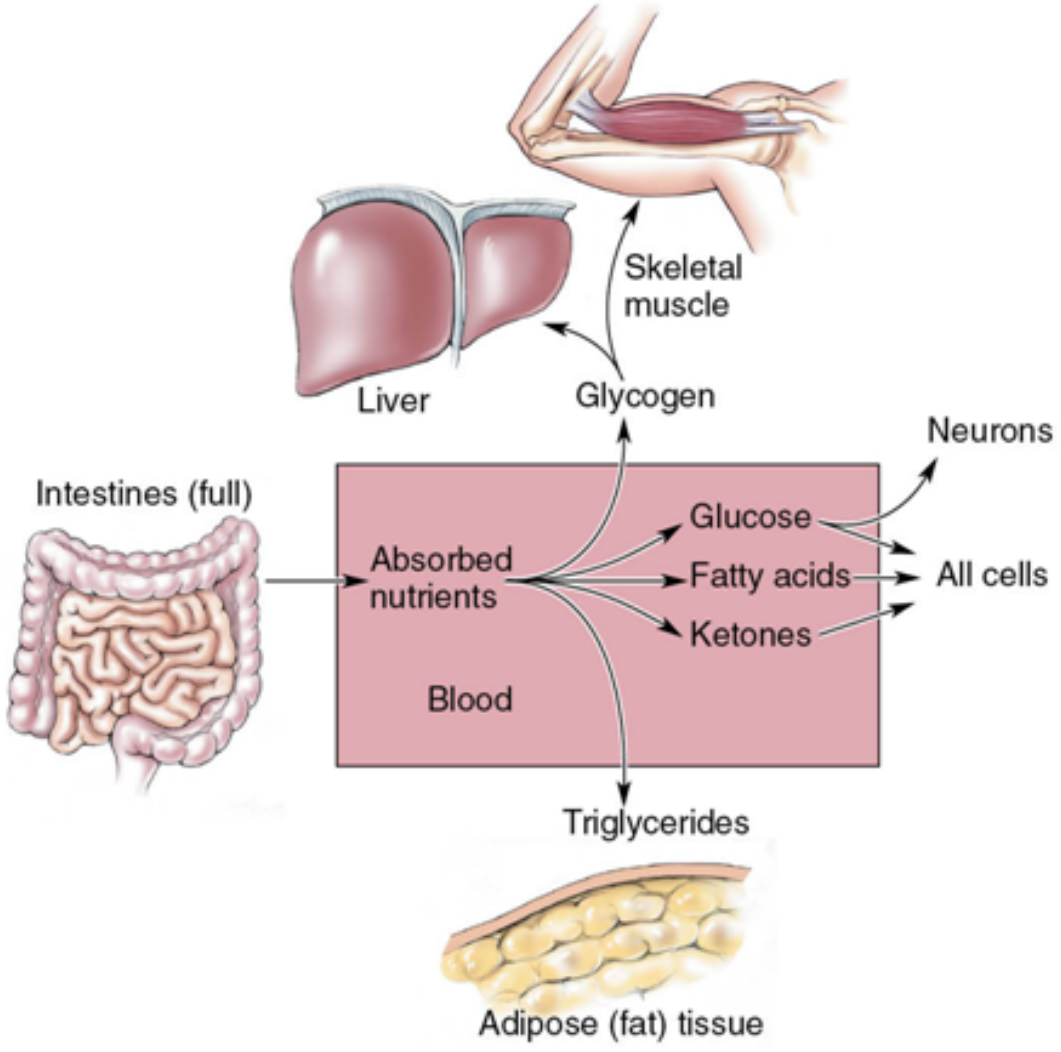


(a) Anabolism during the prandial state

(b) Catabolism during the postabsorptive state

Nutrients: Proteins → Amino acids; Fat → fatty acids, glycerol;
Carbohydrates, sugars, starch → glucose

Metabolism 1:
Anabolism (net positive nutrients)

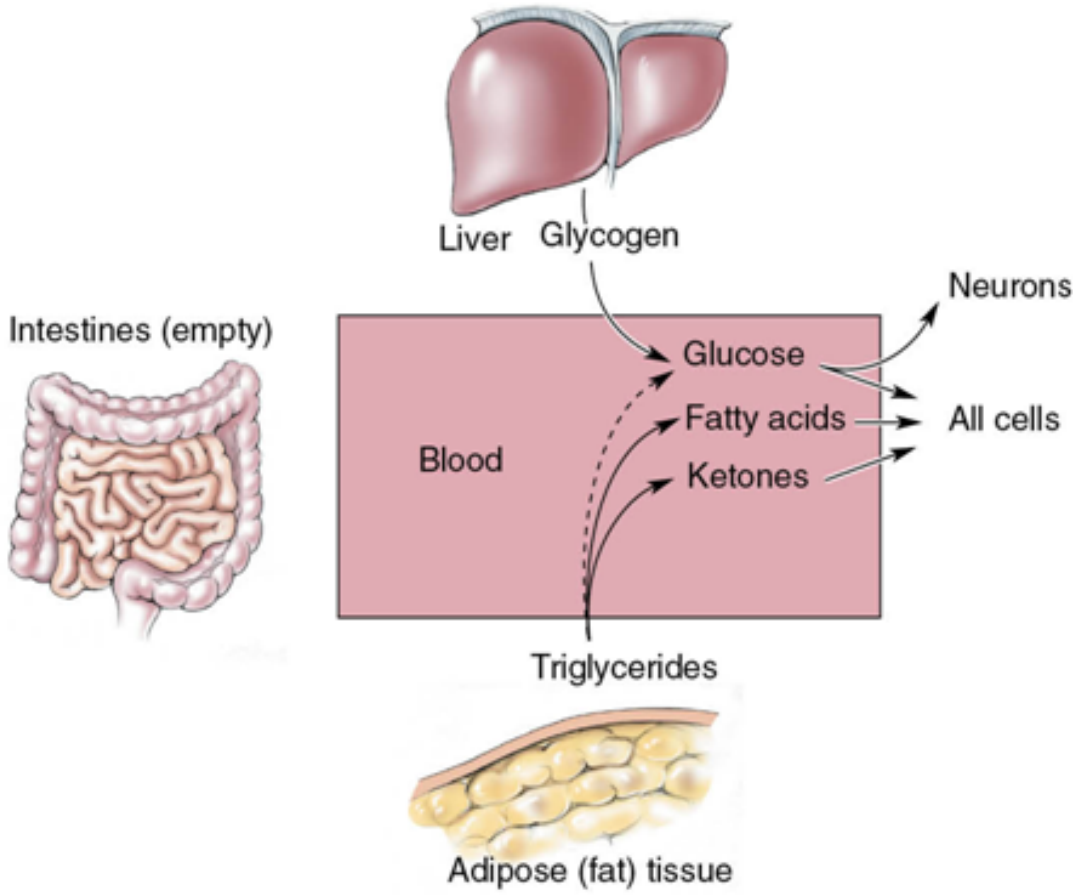


(a) Anabolism during the prandial state

Anabolism:
Nutrients come in and are stored as glycogen and triglycerides.

This is regulated by insulin, a hormone secreted from the pancreas in response to high blood glucose (sugar) levels.

Metabolism 2:
Catabolism (net negative nutrients)

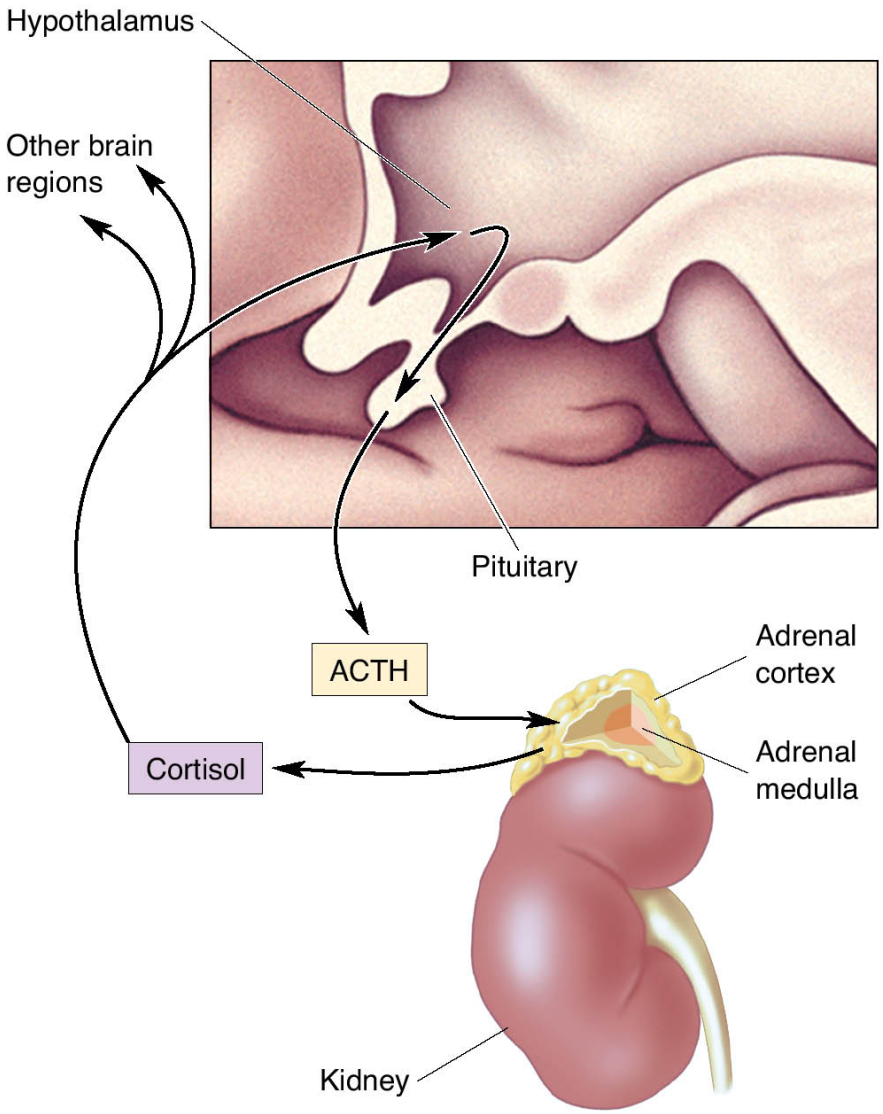


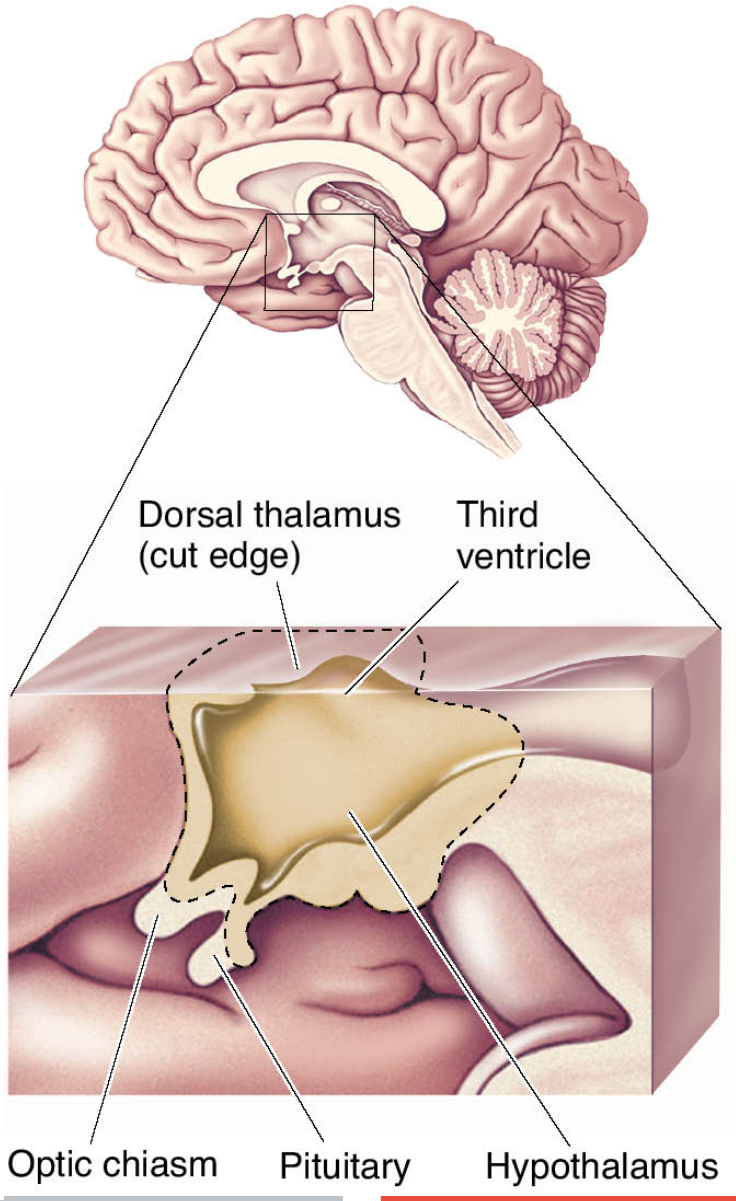
(b) Catabolism during the postabsorptive state

Catabolism:
The body needs energy and takes it from stored glycogen and triglycerides. They are broken down and enter the blood as glucose and fatty acids.

This is regulated by glucagon (pancreas), epinephrine, norepinephrine, and cortisol.

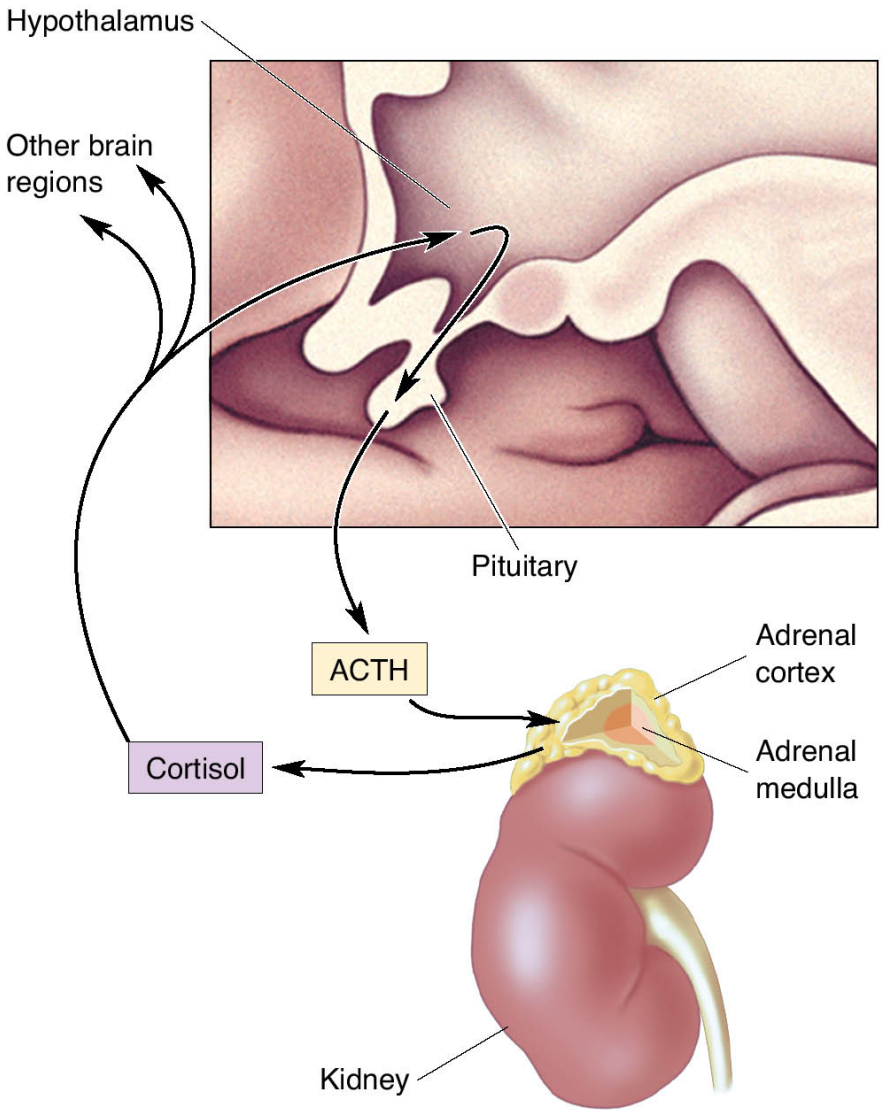
Hypothalamus-Pituitary-Adrenal (HPA) axis





Bear, Neuroscience

HPA Axis 1



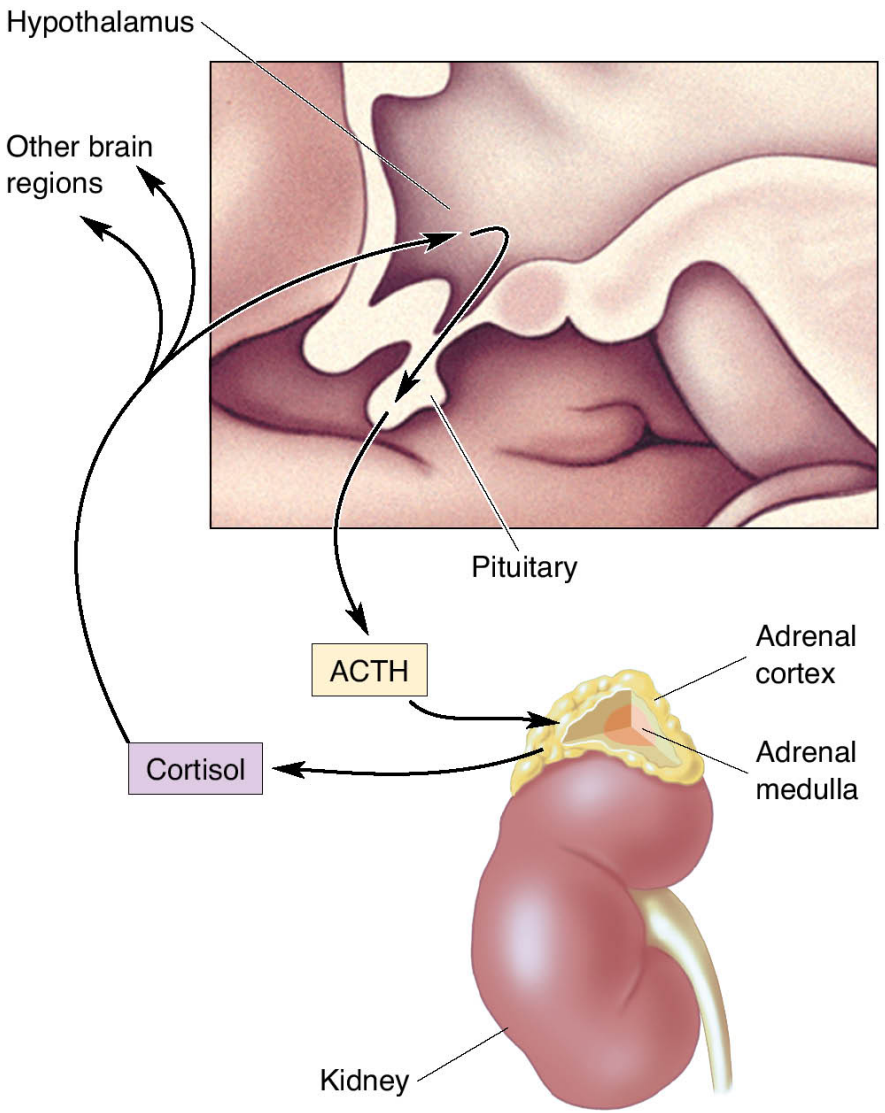
The HPA acts in response to stress over the course of minutes or hours.

Hypothalamus releases corticotropin releasing hormone (CRH).

This leads to a release of adrenocorticotropic hormone (ACTH) into the blood stream.

This in turn leads to a release of cortisol from the adrenal cortex.

HPA Axis 2

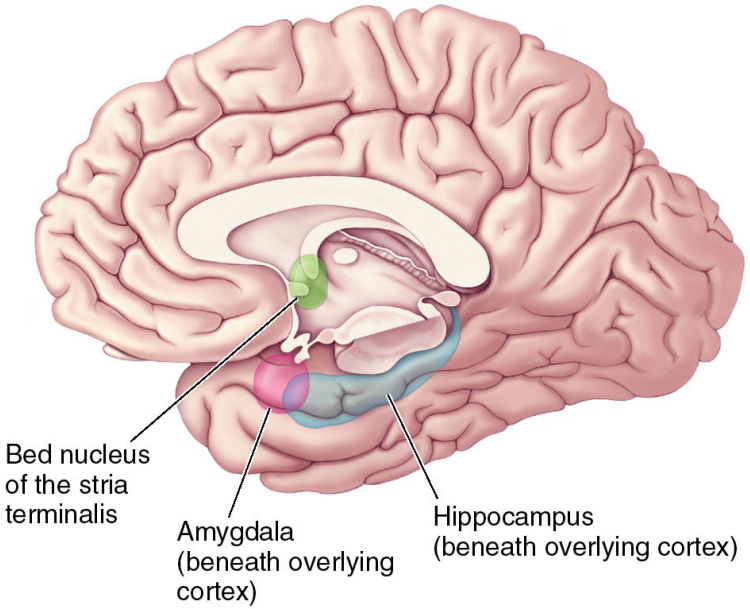


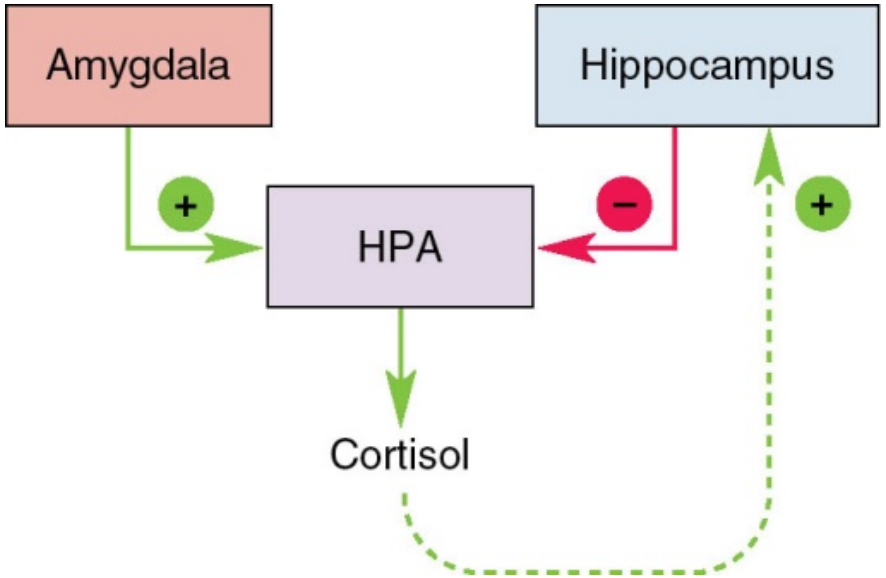
Cortisol increases blood glucose and fatty acids (energy for cells).

It also modulates immune function and wound healing (immune-enhancement for acute short-term stress, immune-suppression for chronic long-term stress).

Blood-borne cortisol can enter the brain and will inhibit the release of CRH from the hypothalamus (negative feedback).

HPA Axis, Hippocampus, Depression





Neurons in the hippocampus have glucocorticoid (cortisol) receptors and these neurons inhibit the HPA axis via the hypothalamus and lessen the secretion of CRH (negative feedback loop).

Patients with severe depression show increased blood levels of cortisol, possibly due to a low number of hippocampal glucocorticoid (cortisol) receptors and thus an impaired negative feedback system.

HPA Axis, Hippocampus, Depression

Robert Sapolsky investigated the effects of chronic stress in baboons, primates with a complex social order.

In one study, villagers have caged baboons together, also putting dominant and subordinate baboons into one cage. This meant that the subordinate baboons could not escape and many of them died soon.

Causes of death were not wounds or malnutrition, but stress-induced effects: gastric ulcers, colitis (colon inflammation), enlarged adrenal glands.

Their hippocampi were degenerated, possibly due to excessive activation by high cortisol levels.

Why have a stress response?
→ Important for survival

The stress-response helps to mobilize as much energy as possible and inhibit anything that is not so important at the moment, such as digestion, reproductive behavior etc.

However, long-term / chronic stress affects our health negatively.

Chronic stress → effects on cardiovascular system

Systolic blood pressure:
contraction phase of heart

Diastolic blood pressure:
relaxation phase of heart

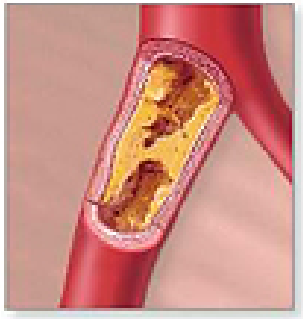
Norm: 120/80

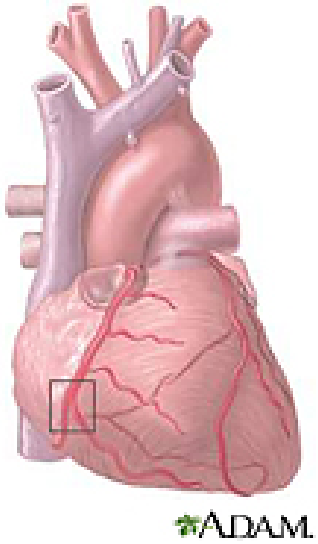
The stress response increases blood pressure, chronic stress can lead to a chronic increase of blood pressure, hypertension (>140/90).

The increased blood pressure means more work for blood vessels, they will increase their vascular muscles and become more rigid, which in turn increases blood pressure again. Hypertension increases force of blood flow and can be damaging to blood vessels → inflammation.

http://www.ncbi.nlm.nih.gov/pubmedhealth/

Chronic stress → effects on cardiovascular system





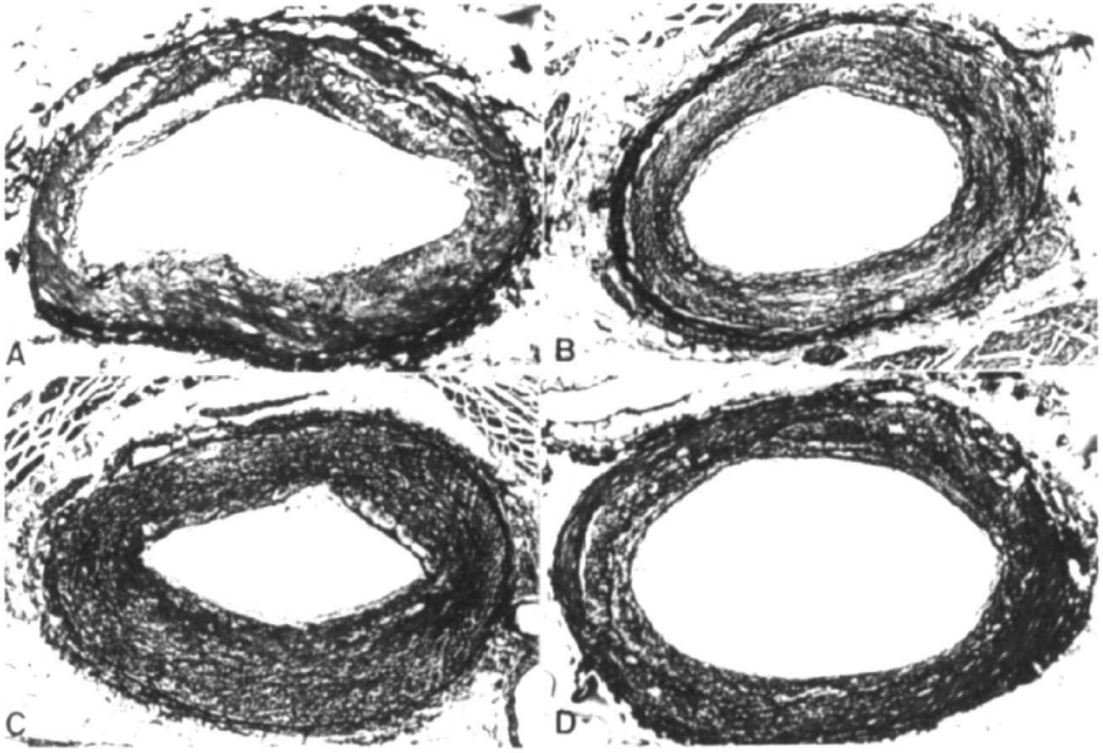
Atherosclerosis: plaques (fat, cholesterol, etc.) build up in arteries which harden and narrow them.
-> heart attack (occlusion of coronary arteries),

stroke

Cortisol releases glucose and fatty acids into the blood stream during the stress response. Chronic stress will increase the likelihood that plaques form, in particular in already damaged vessels (inflammations).

http://www.ncbi.nlm.nih.gov/pubmedhealth/

Chronic stress → effects on cardiovascular system



A: stable subordinate
B: unstable dominant
C/D: unstable subordinate

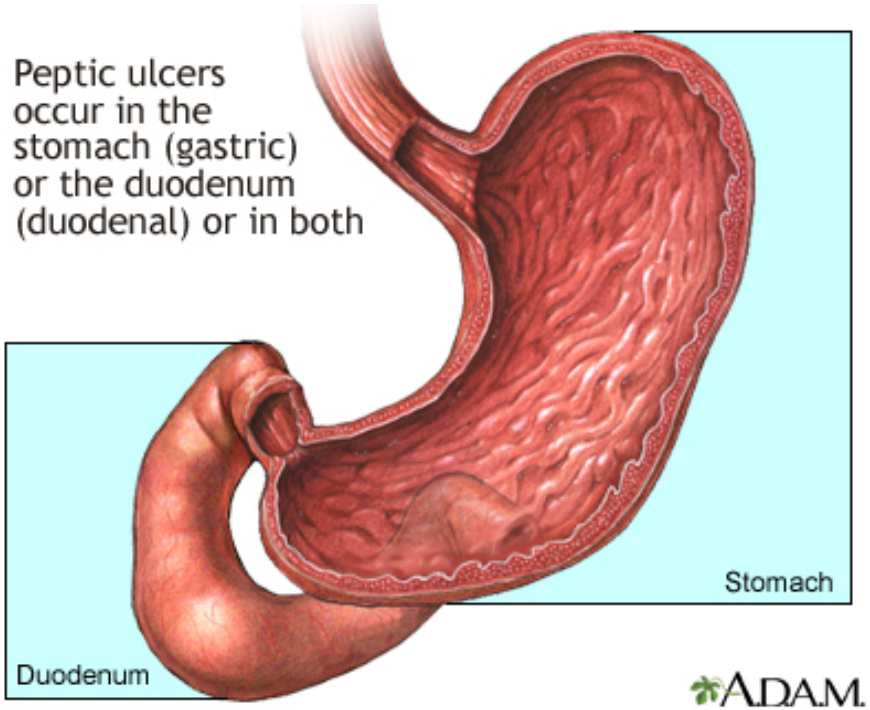
Atherosclerotic plaques are thicker in C and D.

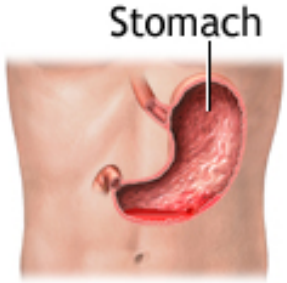
In this study, macaque monkeys were fed a diet that can lead to atherosclerosis (North American style, 43% fat). They were grouped into stable (always same peers) and unstable (new mix from time to time) social groups to induce stress. The animals stressed most (C/D) developed more atherosclerosis (after 22 months).

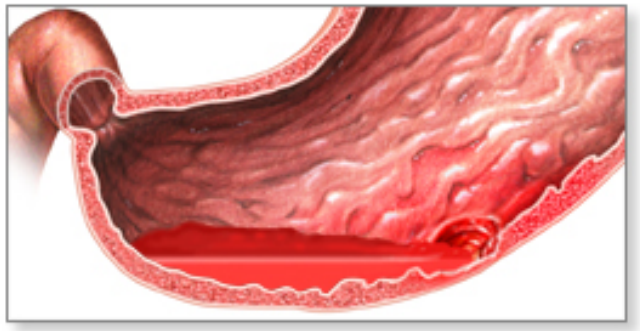
Manuck et al., Neuroscience and Biobehavioral Reviews, 1983

Stress and peptic ulcers

A peptic ulcer is a sore or a raw area in the lining of the stomach or duodenum.







Peptic ulcers may lead to bleeding, perforation, or other emergencies

A.D.A.M.

https://www.nlm.nih.gov/medlineplus/ency/article/000206.htm

Stress and peptic ulcers

After Selye's finding of peptic ulcers in rats, for a long time stress has been seen as a main factor for peptic ulcers.

However, in 1983 Robert Warren and Barry Marshall discovered the bacterium Helicobacter pylori that can live in the acid environment of the stomach.

Amongst other evidence, Marshall infected his own stomach with H. pylori, causing gastritis (which usually precedes an ulcer) and then cured himself with antibiotics.

Thus, H.pylori was established as cause for peptic ulcers (Nobel prize 2005).

Photo: Lars Engstrand, Christina Nilsson

Stress and peptic ulcers

Helicobacter pylori is very common, around 40% (numbers vary widely by region, age, and study) of the population are infected, but not all develop peptic ulcers.

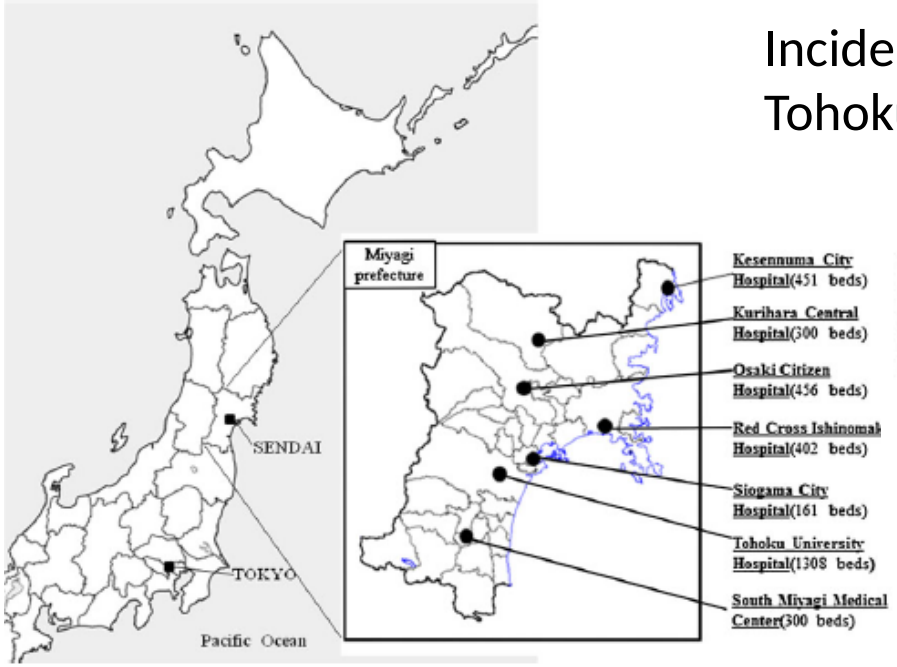
On the other hand, 16-31% of patients with peptic ulcers are not infected with H.pylori (Levenstein et al., Clinical Gastroenterology and Hepatology, 2015).

Thus, multiple causes in interaction might underlie peptic ulcer:

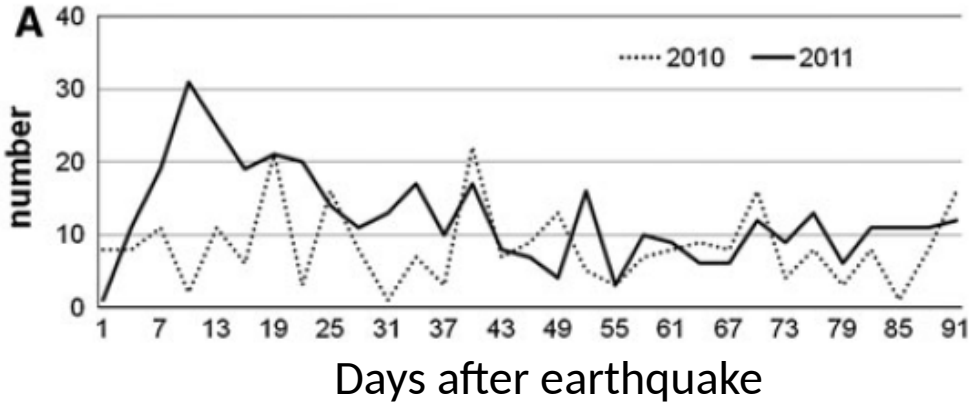
H.pylori
Alcohol
Smoking
NSAIDs (e.g., aspirin)

& **Stress**

Stress and peptic ulcers



Incidence of peptic ulcers after the May 2011 Tohoku earthquake:



Psychosocial stress might increase the risk for peptic ulcer due to an existent H.pylori infection (for example via immune modulation).

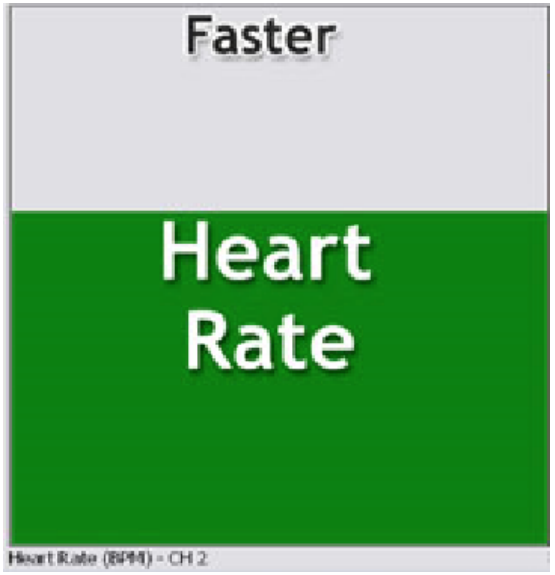
This study by Kanno et al. (2013) suggests that psychological stress alone can induce the development of peptic ulcer, because the incidence of peptic ulcer not related to NSAIDs or H.pylori increased from 13% (2010) to 24% (2011).

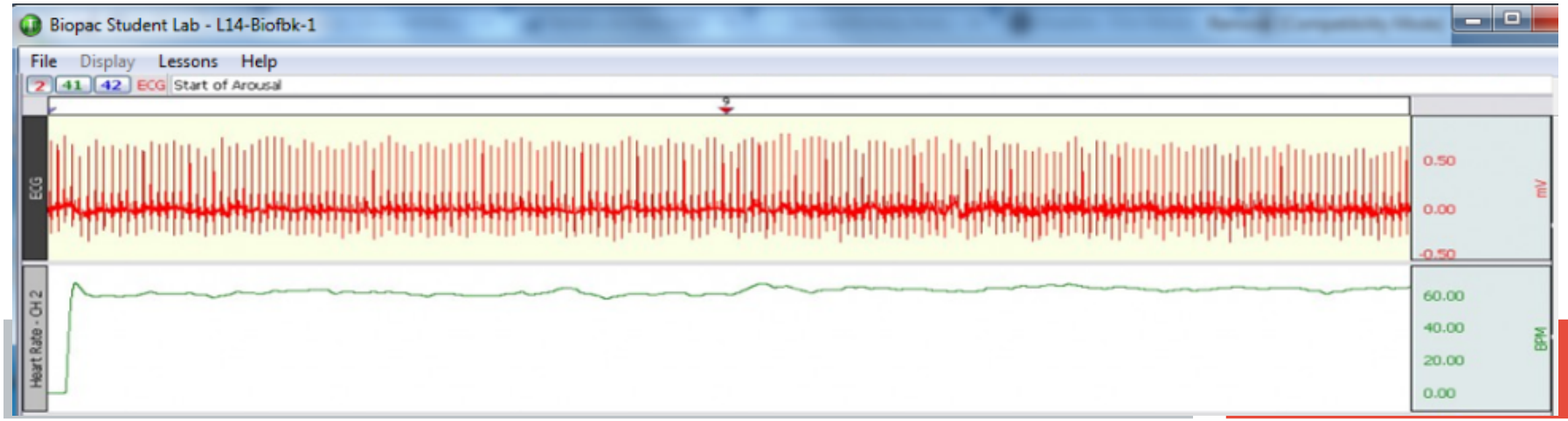
Kanno et al., J Gastroenterol., 2013

Counter-measures against “negative” stress

Bio-feedback:
We can measure sympathetic arousal for example with heart rate, palm sweating, breath rate.

This can be fed back to the patient who learns to control it (e.g., lower the green bar that signifies the heart rate).





Counter-measures against “negative” stress

<u>Progressive muscle relaxation</u> (Jacobson, 1938):

The idea of progressive muscle relaxation is to alternately tense and then relax muscles. Tension for about 5-10 sec, relaxation 25-60 sec.

Tension should not be too strong, one should focus on the tension and feel it.

During relaxation it is important to feel the difference between tension and relaxation.

The whole exercise involves muscles from forearms, face, neck, shoulders, abdominal muscles, legs, feet, and toes.

Summary: Stress

- Stress response is mediated by
  - Autonomic nervous system (ANS)
  - Hypothalamus-Pituitary-Adrenal (HPA) axis

- Important hormones are
  - Epinephrine, Norepinephrine (via ANS)
  - Cortisol (via HPA)

- Health effects of long-term stress occur via
  - increased blood pressure
  - increase of glucose and fatty acids in blood circulation
  - (immune system)
  - (insulin resistance)