STRESS
General mobilisation mechanisms

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General considerations

What is the stress ?

- **Stress** = acute or sustained challenge, which exceeds obvious ranges of homoeostasis reactions and requires critical adaptive response (neural, humoral, immunological, metabolic) to sudden, short lasting or long-term demands:
- **Stress reaction / response**– set of body compensatory or adaptive mechanisms (psychogenic, nervous, endocrine, immunological, metabolic etc.) initiated by stress to renew homeostasis (well being)
- encompasses compensatory (to momentary misbalance) and adaptation responses (to build up a resistance against next challenge)
- ***Stressor*** – apparent inductor of stress; often complex chain of several stressors;

Organismal/systemic stress

- Serve to maintain the organismal integrity
- is always created/ in the brain (CNS); stimuli must reach a brain and must arouse it
- not all stimuli are stressful; they have to be considered suprathreshold (alarming, interesting) (there is appraisal system)
- one part of the body/ tissues/ cells serve and sacrifice for higher principle

Cellular /tissue stress

- serve to maintain cellular or tissue integrity
- encompasses several intracelullar stress signalling cascades;
- Cell under stress either die or excessively multiply: part of chronic infllammation and tumorigenesis (scarring, metaplasia, dysplasia, carcinogenesis etc.)

There is no scientifically accepted definition of stress exists. ...stress can be practically anything that contributes to virtually any disease in humans

Stressors and forms of stress

- **Enviromental** – noise, cold, heat, moiscure, lack of light, pressure changes, (airplains, elevator),
- **Social** – relationships (family, love, friends), work (boss, corroborators, customers), not friendly, critical competitive
- **Institutional** – rules, restrictions, laws, time limitation, meetings
- **Major life events** – positive/ negative Marriage, divorce, birth of kid, new employment, resettlement, loss of work; disease, death of relatives, violence, military service, etc.
- **Minor life events** – irritating, frustrating: traffic accident /crash; looking for parking, waiting in queue, stupid persons, seeking for things defects of electronics, comps, soft, damage of dress, etc.

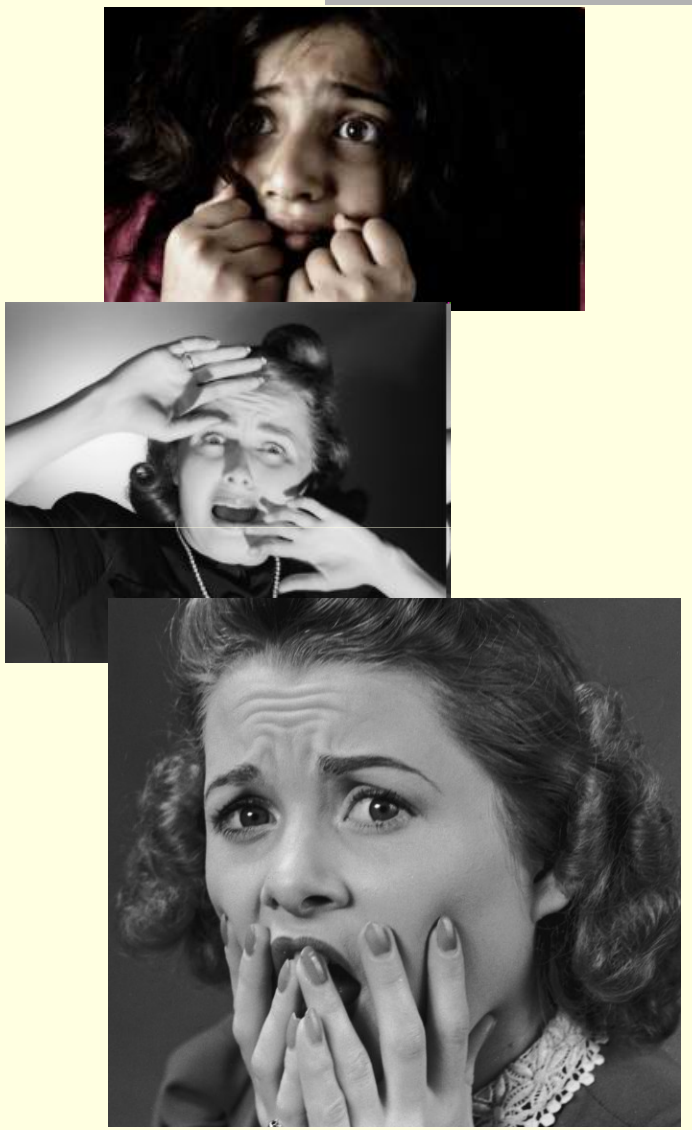
- ***Physiological stress (experimental)***
- Simple and well defined; repeatable structure; good prediction, non-specific reactions (withdrawal), e.g. electrical current, senzoric hyperstimulation, extinction, cold, heat, radiation, tiredness, etc.
- ***Biological stress (enviromental)***
- More complicated structure; less precice predictivity, specific responses, e.g. climatic changes, weather, biotope, food accessibility, sleep deprivation, seasonal effects, etc..
- ***Psychogenic (mental) stress***
- Complicated structure; from common to very individual,unique reactions; from good to weak predictivity and repeatability, e.g. isolation, loneliness, death in family, of partner, of friends, failure/ success in exam, break of marriadge, violence, work overload, etc.

Various forms of stress

- **Peracute stress –** violence, robery, bad news,
- **Acute stress** – motivating (eustres) or destructive (disstres)
  - daily hassles; "D" day (traveling, exam, terms)
- **Subacute periodic stress**
  - repeated acute stress`pesimistic views on the world
- **Chronic stress -** demotivating, blind circuit

Acute stress reaction (Shock)

- ***Occ:*** in anybody (if not present something is not correct)
- ***Cause:*** Sudden unpredictive situations which surprize and shock without anticipation: sudden awaking due to noise, violence, physical attack, robery, explosions, traffic accidents, death of relatives, traumas, acute pain etc.
- ***Sy:*** Peracute neurohumoral stress response (alpha-catechoamines, serotonin)....



Acute (episodic) stress

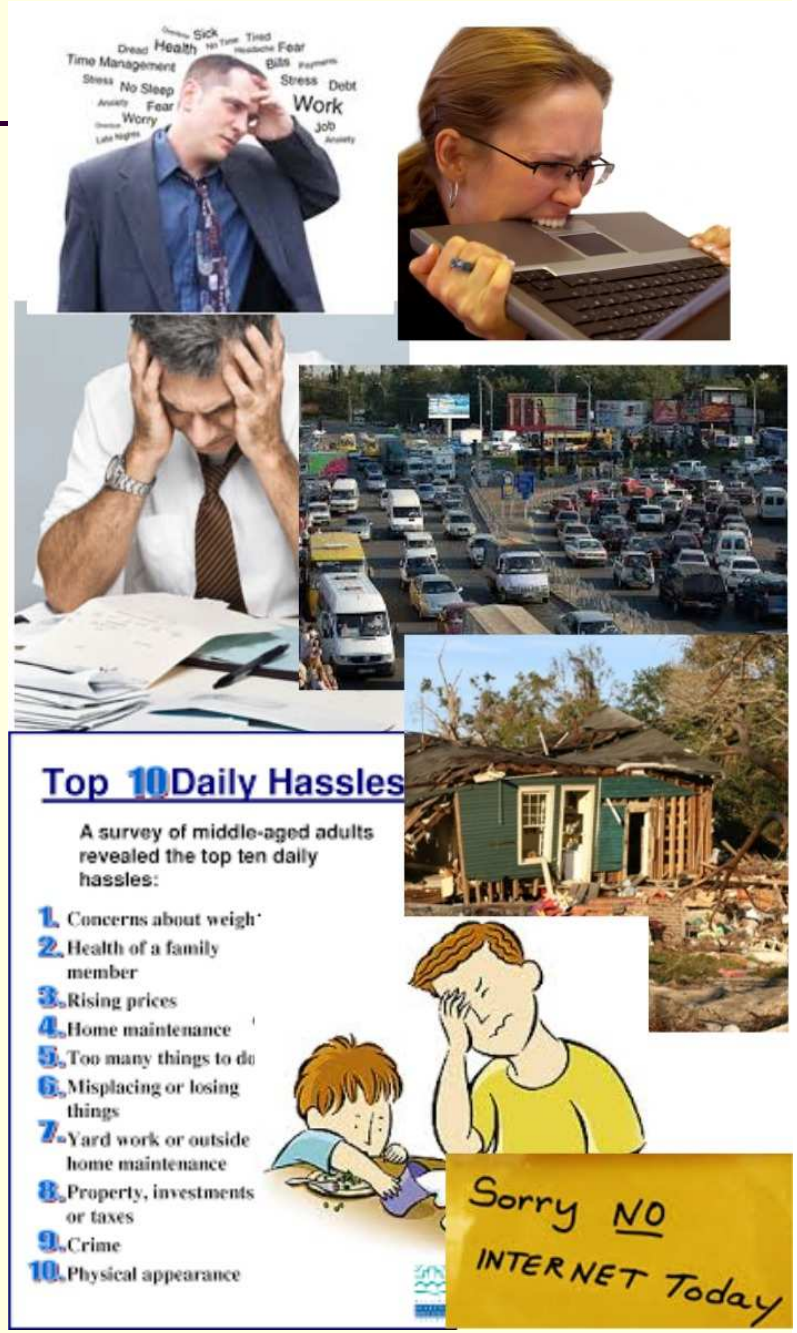
Occ: most common form of stress; present in everyone; stress can be a) ***positive,*** enpowering, exciting, motiva-ting, or b) ***negative***, depressing, demoti-vating, raging; Stress is well anticipated or will happen in near future

Etio: **Daily hassles** - heath problems, trubles with kids, rela-tives, morning wake up, public traffic, home maintenan-ce, physical beauty, overweight, too much to do, loosing misplacing things, breaking the things, stupid software, slow computers, internet, full elevators,

D days - traveling, terms of exams, dating, sport match, labor, wedding day, investments, tender, etc.

Sy:

- ***Affective and emotional instability*** – anxiety, tension, resignation, irritability, bad mood, anger, agressivity
- ***Somatovegetative reasponses*** (hypertension, tachycardia, palpitations, seating, dizziness, migrain, cold hands, feet, dyspnoea, chest pain, feeling gastric fullness, irritable bowel disease.



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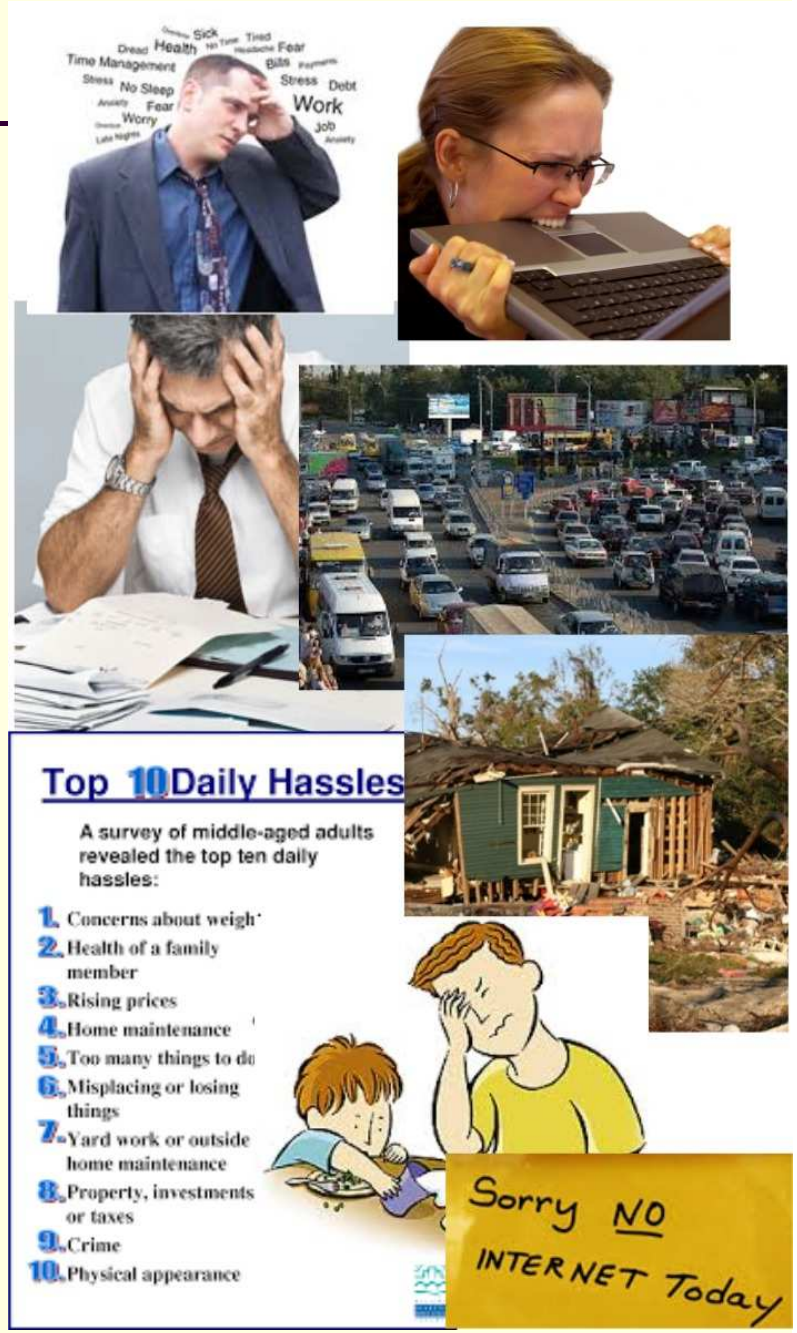

Lazarus: Daily Hassles & Uplifts…

Daily Hassles

Hassles

1. Concern about weight
2. Health of family member
3. Rising prices of common goods
4. Home maintenance
5. Too many things to do
6. Misplacing or losing things
7. Yardwork or outside home maintenance
8. Property, investment, or taxes
9. Crime
10. Physical appearance

Hassles

1. Troubling thoughts about the future
2. Not getting enough sleep
3. Wasting time
4. Inconsiderate smokers
5. Physical appearance
6. Too many things to do
7. Misplacing or losing things
8. Not enough time to do the things you need to do
9. Concerns about meeting high standards
10. Being lonely

Uplifts

Uplifts

1. Relating well with your spouse or lover
2. Relating well with friends
3. Completing a task
4. Feeling healthy
5. Getting enough sleep
6. Eating out
7. Meeting responsibilities
8. Visiting, phoning, or writing to someone
9. Spending time with family
10. Home pleasing to you

Uplifts

1. Completing a task
2. Relating well with friends
3. Giving a present
4. Having fun
5. Getting love
6. Giving love
7. Being visited, phoned, or sent a letter
8. Laughing
9. Entertainment
10. Music

Chronic stress

Occ: estimated up to 15 -25 % of people;

Etio: plenty of reasons: unfunctional family, unhappy partnership, protective mothers, divorced parents, missunderstandings, conflicts intolerance, even. agressivity (in family wife, kids, etc.); workplace: high demands, competitive team, chief, plenty of work, low income; permament overload (e.g. emergencies, police, etc.)

1. ***Repeating acute stress*** – recognizable; one knows when stress comes so can prepare; when stress come from time to time, or it is of one klind (e.g. work) one can adapt; problem of overloading of multiple stressors (e.g. employed mothers)
2. ***Permanent stress*** – unrecognizable; unresolvable; people live within stress; they survive from day to day; adaptation is demotivating, grindling, degradating,

Sy: (A) tiredness, sleep deprivation; emotional lability and irritability; bursts of rage, anger; reactive depression

(B) infarction, stroke, suicide, tumors etc.

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Concepts of stress

History of stress study

- W. B. Cannon (1929)
  - role of sympathetic nervous system
  - *„fight or flight“*
- Hess (1932, 1936)

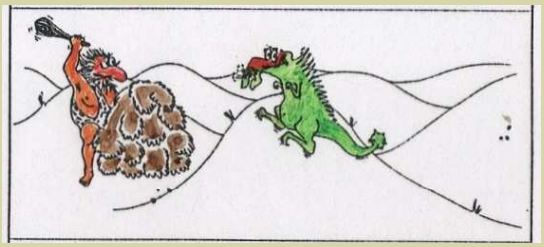
- H. Selye (1939,1950)
  - *General adaptation syndrome (GAS) - non-specific response*

- Friedman & Rosenman (1974)
  - A and B personality
- Mason (1977)
  - *Psychosocial stress*
  - *Biofeedback*
- Lazarus & Folkman (1978)
  - *Transaction model of stress*
- Fleming, Baum, & Singer (1984)
  - *Stress as postapraisal syndrome*

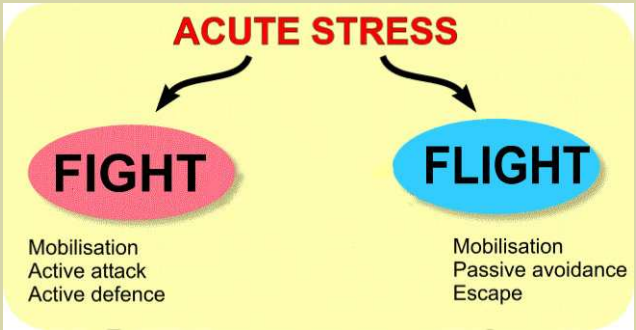
Walter Bradford Cannon

- (1871-1945) Harvard physiologist, – "homeostasis" and ***"fight or flight response***"
- Stress = phylologenetically old compensatory and adaptive response with many psychogenic, emotional and physiological accompanyments;
- Role of the vegetative nervous system – **sympathetic nerves** = principal role in compensatory responses;
- Role of catecholamines inlc.epinephrin
- Adrenergic metabolic response – tachycardia, hypertension, hyperpnoea, pupillary responses, metabolic responses – blood glucose

Face-off



Fight



Hans Selye – general adaptation syndrome

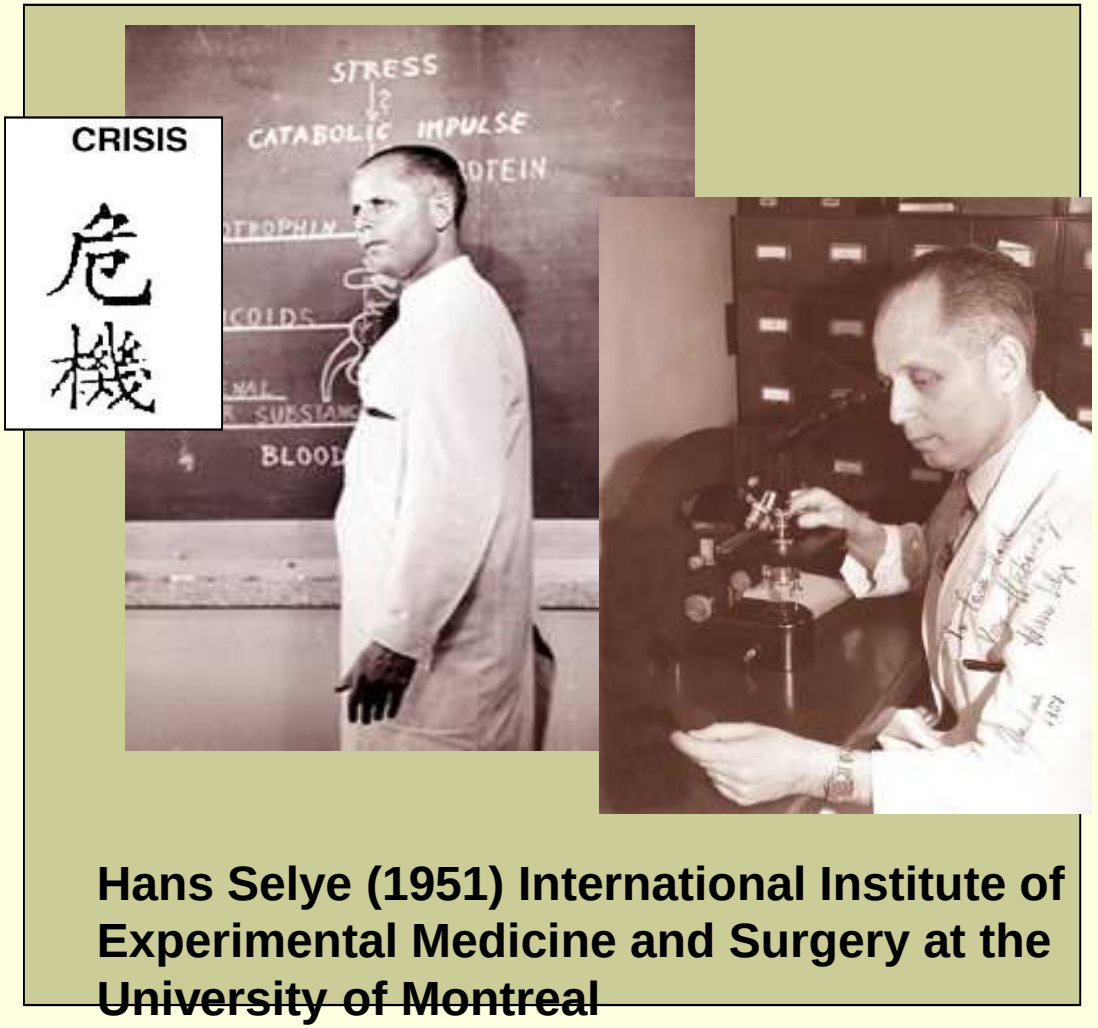
- *Komarom 1907, † Montreal 1982; studies in German Medical School in Prague; worked in Canada ; experimenter in endocrinology, steroid chemistry, experimental surgery and pathology; 40 books and over 1700 publications
- Selye introduced the terms:
  - **Stress** ="*the nonspecific response of the body to any demand*" (Selye, 1976) - state manifested by a specific syndrome which consists of all the nonspecifically induced changes in a biological system
  - **Stressor** = internal or external environmental factor disrupting homeostasis of an organism
  - **General adaptation response** = if we abstract all stimulus -related specific reactions in the body we get „common“ underlying neural, endocrine and metabolic adaptive reactions (non specific , general)
  - **General adaptation syndrome** = physical and biochemical findings in animals observed during general adpatation response

New York (1978):
The American Institute of Stress

Hans Selye – father of stress theory

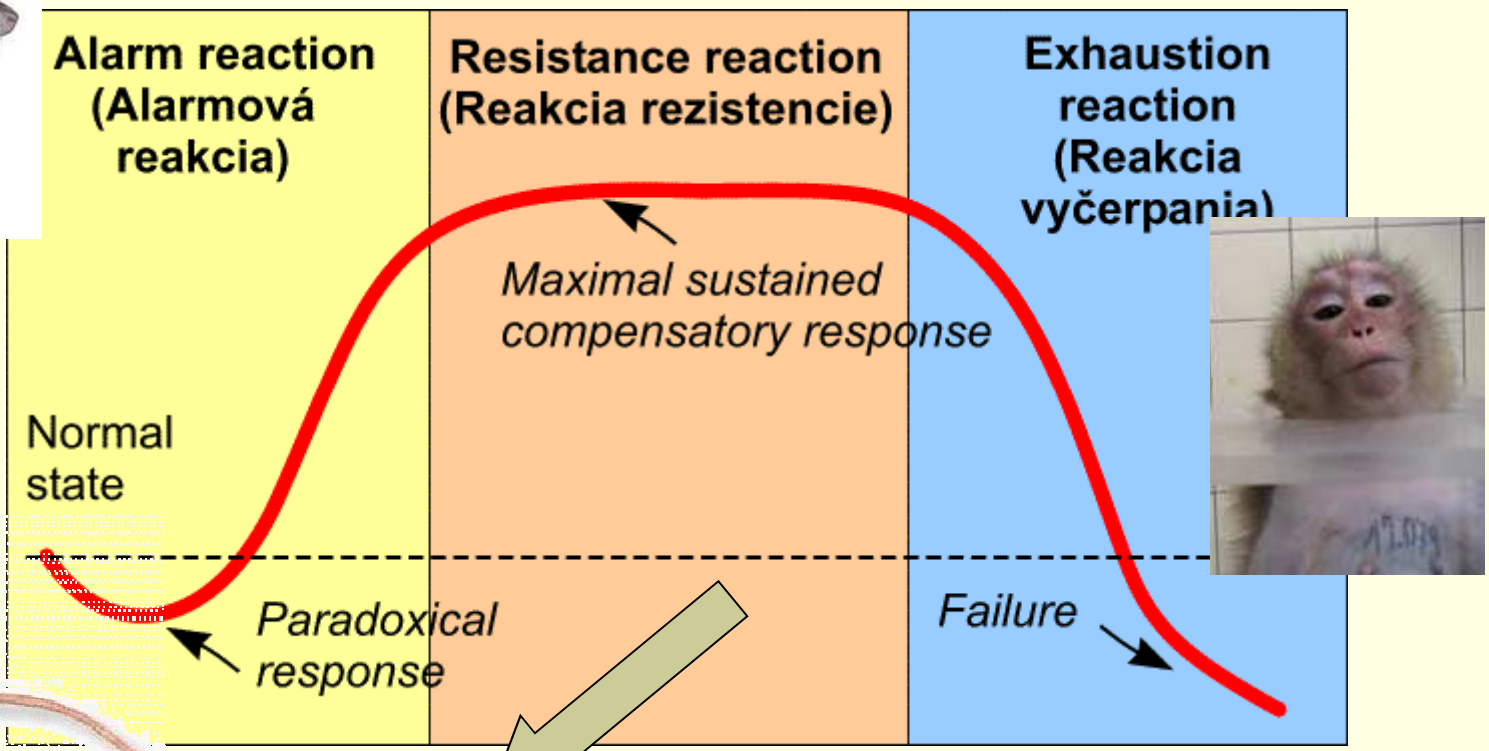
- "A Syndrome Produced by Diverse Nocuous Agents"

  1936 (*Nature)*.
  - used in physics
  - problem with translation
- non-specific response syndrome to various stimuli
- *Stress, le stress* (1946)
- ***Stressor***
- ***Eustress, Distress***



Hans Selye (1951) International Institute of Experimental Medicine and Surgery at the University of Montreal

General adaptation syndrome (GAS)



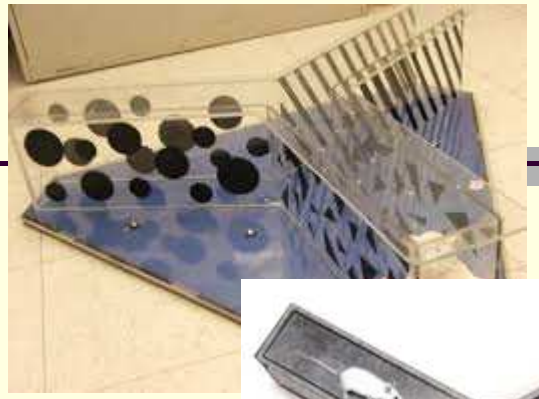
- Gastric ulcers
- Gastrointestinal bleeding
- Enlargement of thymus
- Enlargement of adrenals
- Hypertension, tachycardia
- Cortisolaemia
- Hypercatecholaminaemia
- Regression of lymph nodes

General adaptation syndrome (GAS)

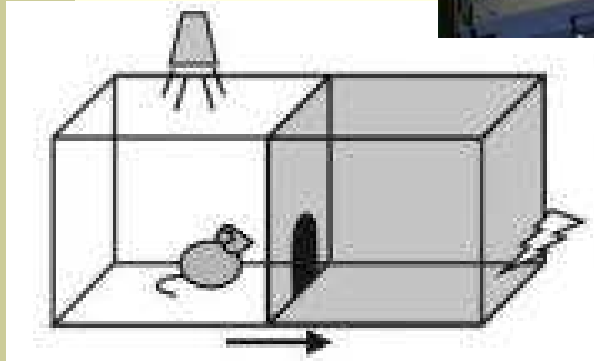
Changes in function	Alarm reaction		Stadium of resistence	Stadium of exaustation
	Shock	Contra-shock		
Diuresis	⇩	⇩	⇩ or no	⇩
Glycaemia	⇧⇧	⇩	⇧ or no	⇩⇩
Cl^-	⇩	⇩	⇧ or no	⇩ or no
Na^+	⇩	⇩	⇧ or no	⇩ or no
K^+	⇧⇧		⇩ or no	⇧⇧
Zn^{2+}	⇧	⇧⇧	no	⇧⇧
Uric acid	⇧	⇧⇧	⇧ or no	no
Leucocytes neutrophiles lymphocytes eosinophiles	⇧ ⇧ ⇧	⇧⇧ ⇩⇩ ⇩⇩⇩	⇧⇧ ⇩⇩ ⇩⇩⇩	⇩ ⇧ ⇩⇩
Sedimentation	⇧	⇩⇩	no	no
Thymus, lymphatic tissue	⇩	⇩⇩	⇩	⇩⇩⇩
Suprarenal gland enlargement lipide storage	⇩ or no ⇩	⇧⇧⇧ ⇩⇩⇩	⇧⇧ ⇧⇧⇧	⇧⇧⇧ ⇩⇩⇩
Vessels	capillary laesions	capillary laesions	atherosclerosis	atherosclerosis
Heart	tachycardia	tachycardia		
Sexual functions	no	⇩	⇩⇩	⇩⇩⇩

Tests

Avoidance experiments

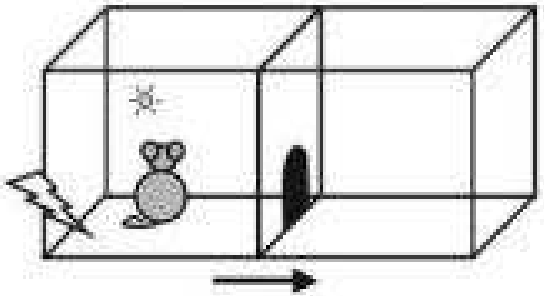


Maze experiments



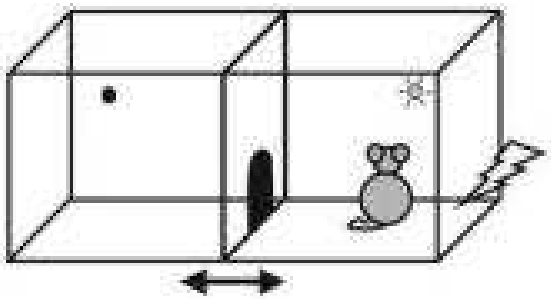
Passive Avoidance
Exploits a natural tendency of mice to enter dark environments.

Unidirectional: mouse goes from light to dark chamber.



Active Avoidance
Mouse learns to avoid shock based upon the presentation of a light cue.

Unidirectional: mouse is always shocked in the same chamber/location.



Shuttle Avoidance
Mouse learns to avoid shock based upon the presentation of a light cue which is dependent upon location of the mouse in the apparatus.

Bi-directional: mouse learns to monitor for cues in both chambers that predict shock.

Immobilisation experiment

Swimming experiment

Post-experimental stress; Stress in man

Animal stress model criticism

- Studies on stressful animals showing spontaneous escape behavior (rats, rabbit, mice)
- Stressors were simple variables while in man psychological stress prevails
- Stress is individual reaction
- Non- specificity of stress physiological systemic responses as well as consequences is limited

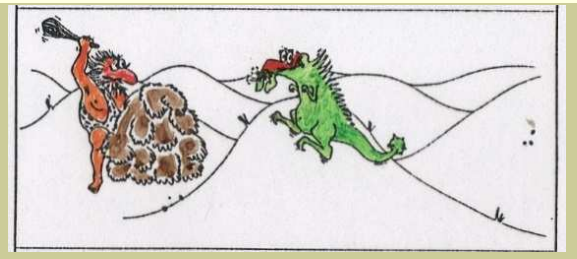
Henry J. P., Stephens, P. M. (1977)

- Cognitive evaluation of reasons leading to **fight-or-flight** → active response (via sympathetic-adrenal system)
- Loss of control over situation leads to resign - **fright** → activation of the serotonergic system and hypothalamus- hypophysis to secretion of ACTH and cortisol.

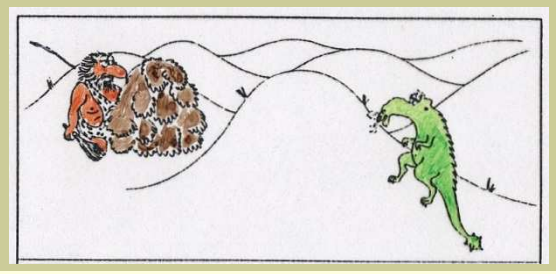
Henry, J. P., Stephens, P. M.: Stress, Health and the Social Environment, A Sociobiologic Approach to Medicine. 282 Seiten, Springer Verlag, New York, Heidelberg, Berlin 1977.

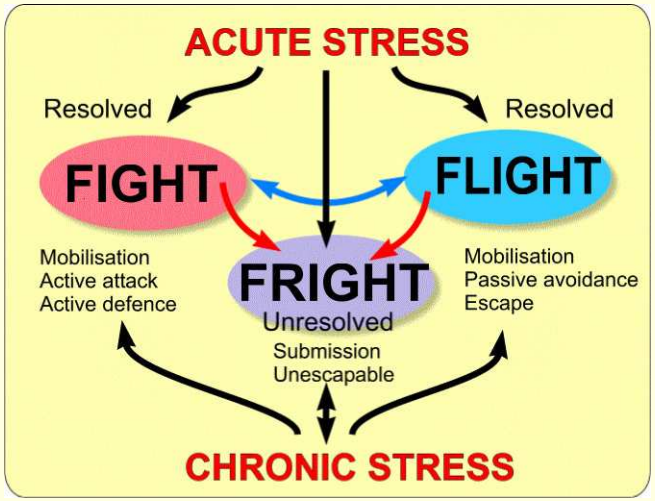
Weiner H. (1992)
interactive stress model

Face-off



Fright





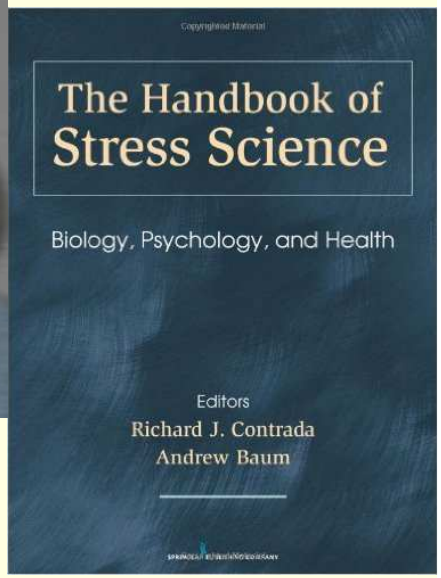
Psycho-Biologic concepts of stress

- **John L. Mason (1977)** – psychology of stress, stress coping; anti-stress education (Stress Education Center);
  - *Stress is specific and individual response;*
  - Stress is a process involving recognition of danger or awareness of whether the event is critical – „transaction stress concept":." blissful ignorance „
- **Fleming, Baum, & Singer (1984)** – social stress; work stress
  - Preparation of the stress reducing its negative consequences - "stress can be taught to live.".

John L.Mason

Jerome Singer

Andrew Baum



Fleming R, Baum A, Singer JE.: Toward an integrative approach to the study of stress.J Pers Soc Psychol. 1984 46(4):939-4

Baum A, Fleming R, Reddy DM. Unemployment stress: loss of control, reactance and learned helplessness. Soc Sci Med. 1986;22(5):509-16.

Psychology of stress

- **Lazarus & Folkman (1985)**
- Stress is the "continuous interaction between the environment and individuals,
- The adaptation occurs when a phenome-non essential to the survival exists
- ***„Entire life is a stress, each former episode is a preparation for the next one„***

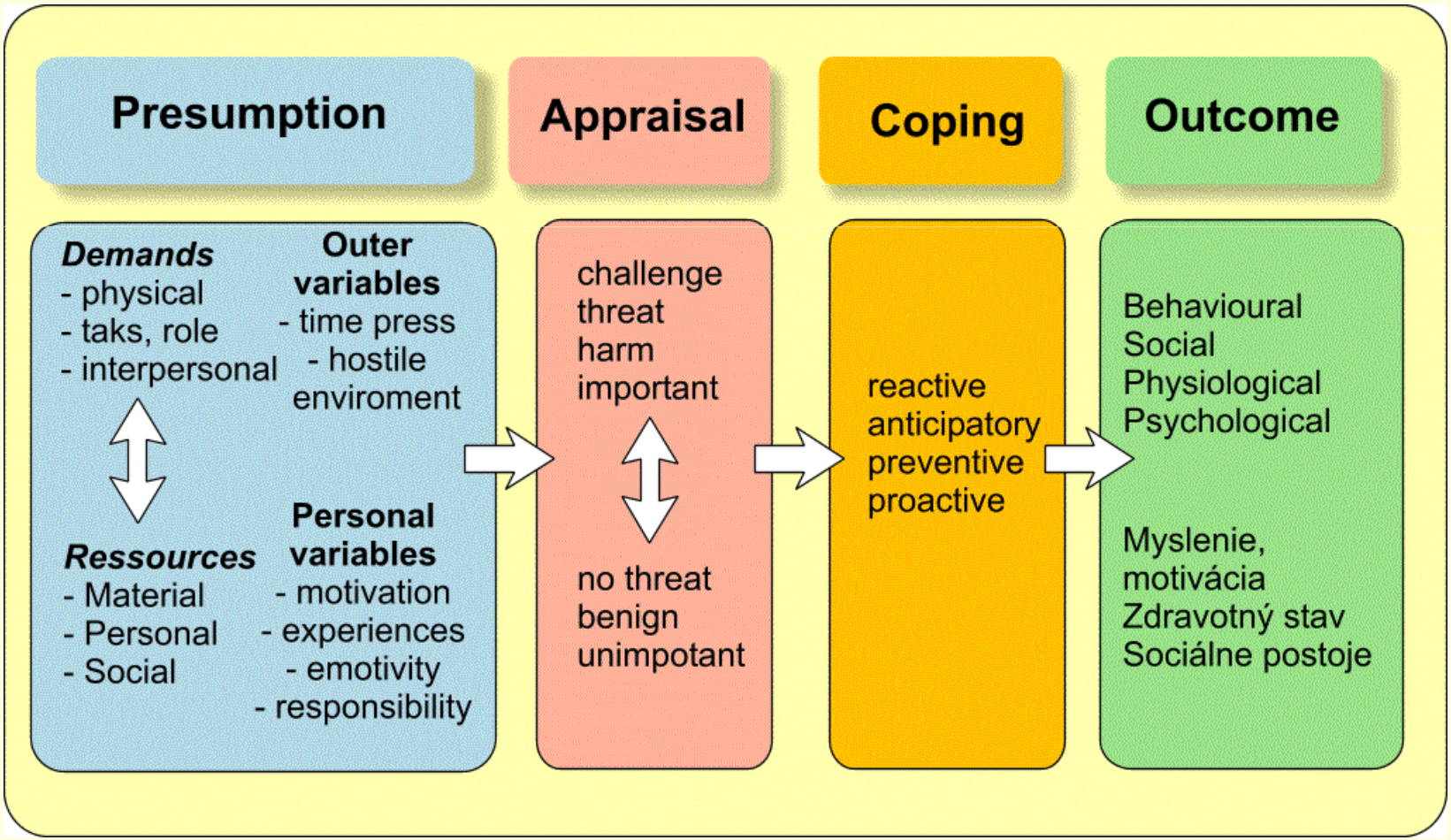
Richard Stanley Lazarus (1922 - 2002)

- strengthened importance of **cognitive determinants of stress**; stressor determines the character of stressful situations and response rates (Lazarus, 1966, 1993, 2000)
- developed the **appraisal concept od stress** based on „transaction concept of stress" of Mason);
- whether „Selye's stress response develops or not“ in a particular person depends on a **cognitive evaluation of any specific stressful situation by this specific person**

Primary assessment - transaction (not relevant / applicable) of the individuals with the environment; whether the situation is important for survival (?)
Secondary assessment – what is the possibility of coping + the choice of appropriate procedures
Tertiary assessment - change of thought process in relation to the stressor; next time this will not to be a stressor

Appraisal theory

- Suggestions are reviewed - the stress response occurs in situations for the individual critical - real or fictitious (exaggeration)
- The solution is successful - adaptation, or failed - maladaptation



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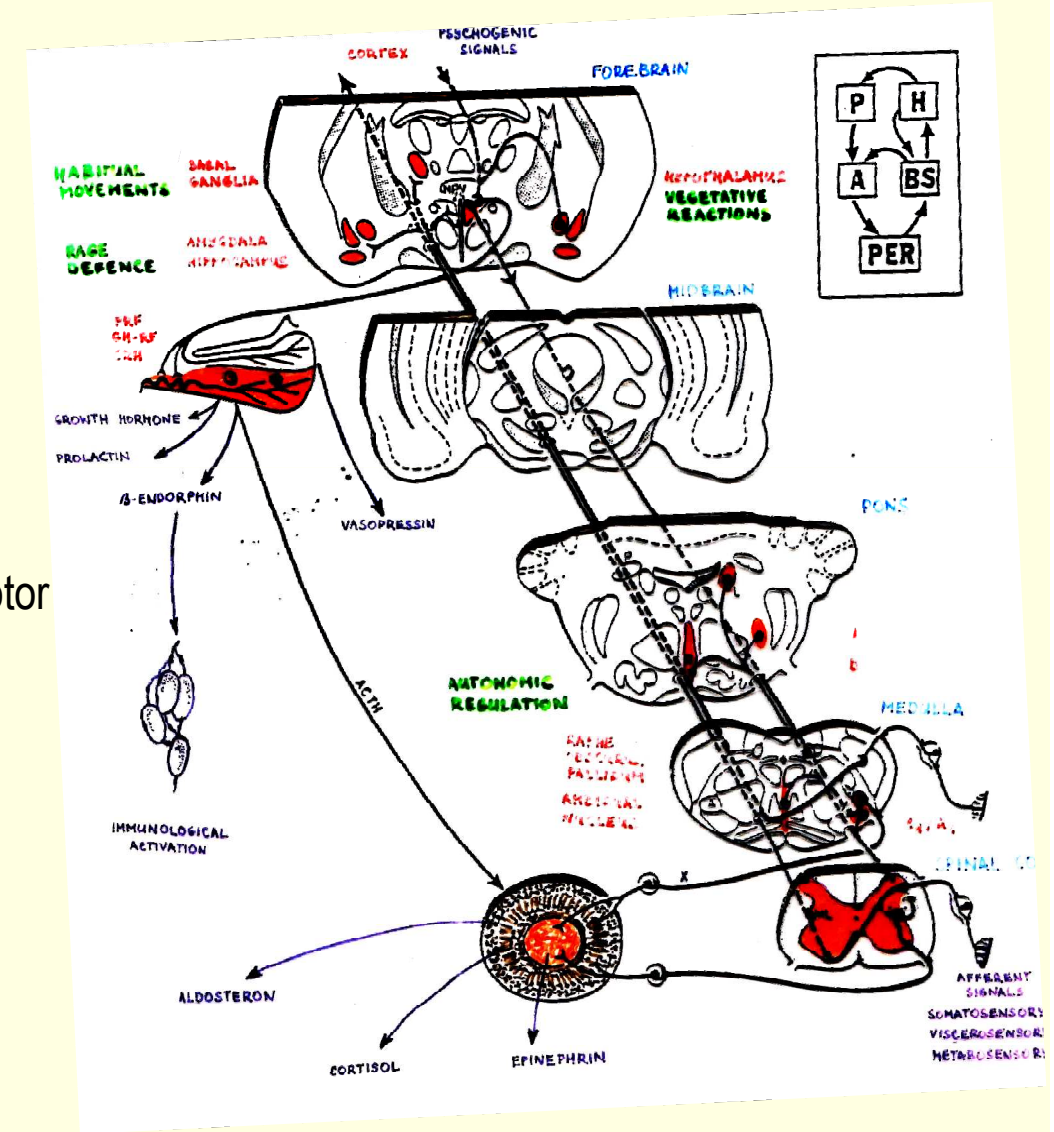
Execution of stress response

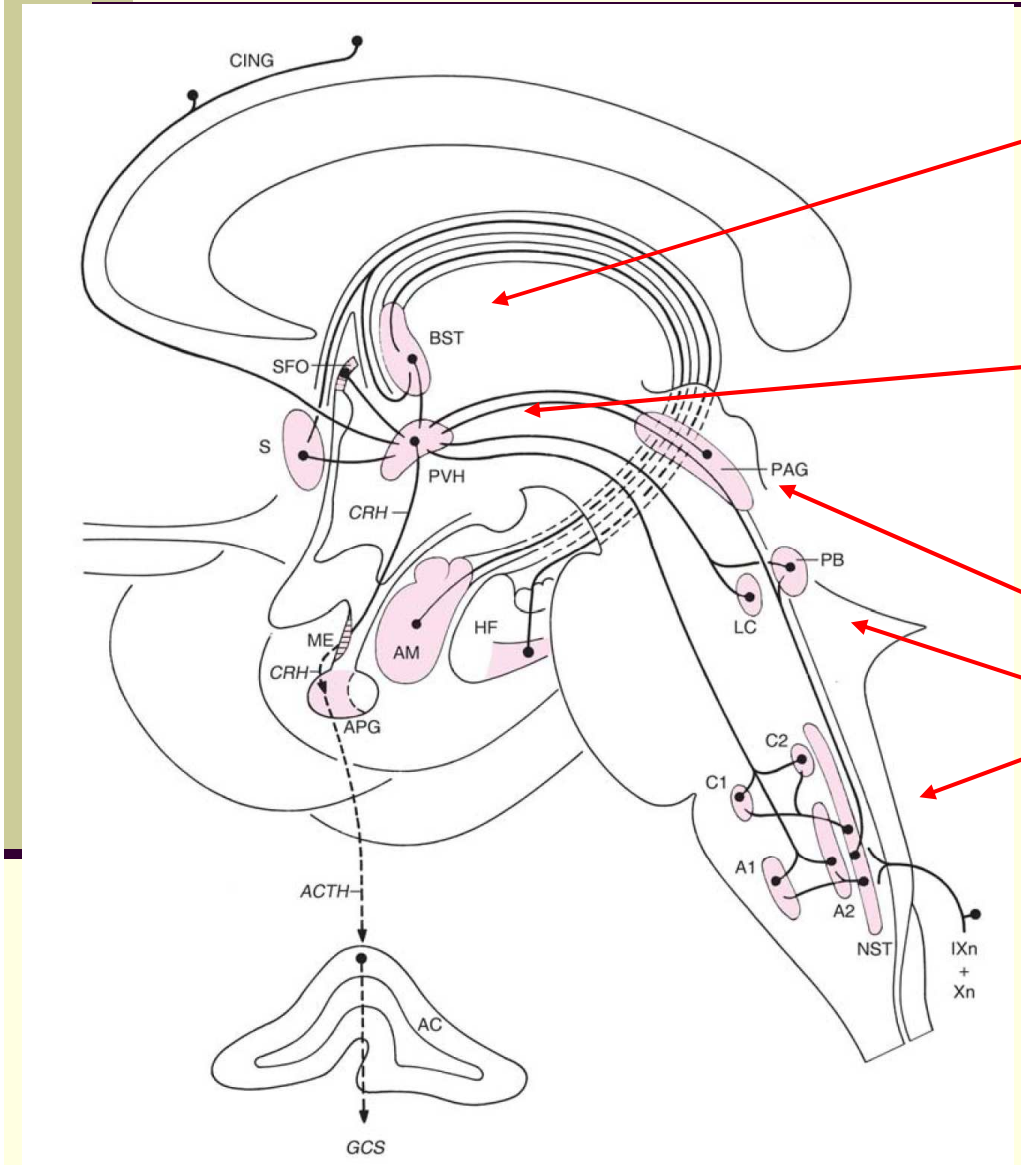
Nervous efferent pathways in stress

- **Afferent pathways**
- **Somatosensory** (e.g. thermoreceptors, nociceptors, mechanoceptors, ...)
- **Viscerosensory** (e.g. pressure sensors, chemosensors
- **Humoral** – metabolic, immune-derived
- **Psychological** – percieved by brain

- **Efferent pathways**
- Cognitive, emotional responses
- Neurogenous – somatomotor, visceromotor
- Humoral



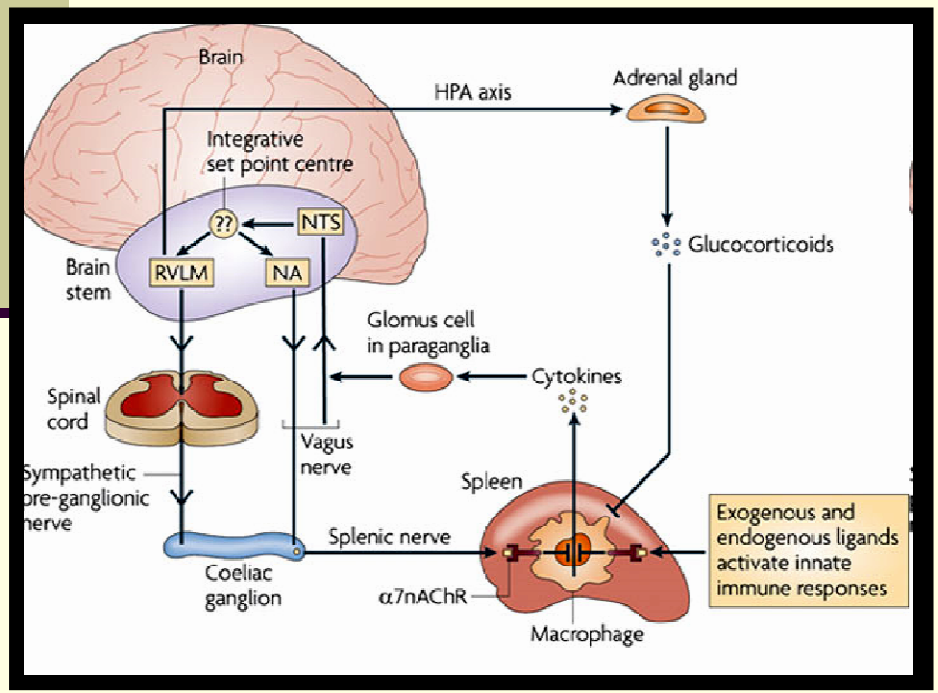
Circuitry subserving the stress response

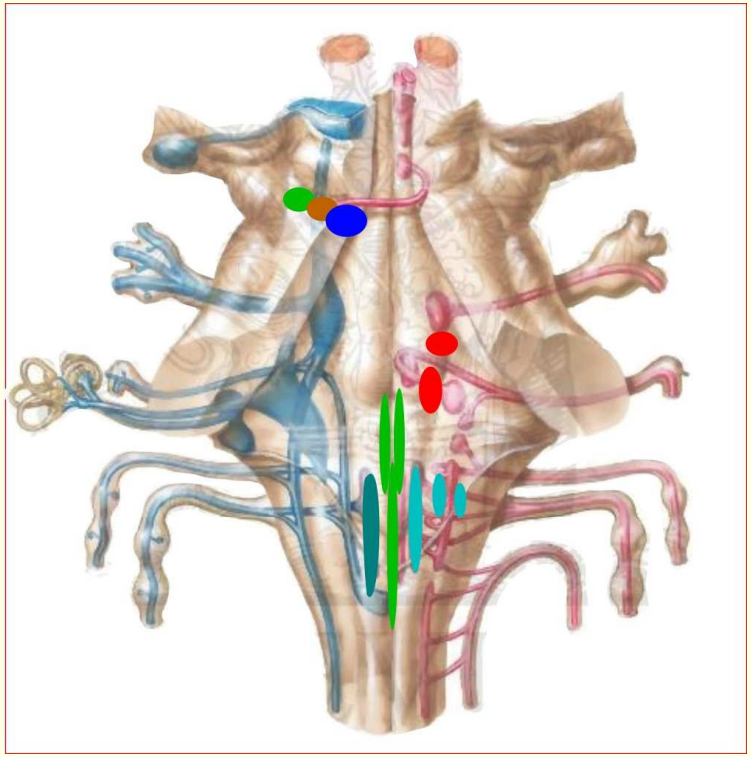


- **Structures signallinmg into PVH:** amygdala (AM),; BST, bed nucleus of stria terminalis, *BST, bed nucleus of stria terminalis; CING, cingulate cortex;* S, septal nuclei; SFO, subfornical organ; *HF, hippocampal formation;*
- **Hypothalamus** Nucl. periventricularis (releases CRH) releases CRH (corticotropin-releasing hormone) into *ME, median eminence; CRH* passes into anterior pituitary (APG) to produce ACTH; this stimul. product of GCS, glucocor-ticoids from AC, adrenal cortex
- **Brainstem -** PAG, periaqueductal gray; Nuclei synthetizing epinephrin (C1-2) & noradrenalin (A1,A2, A5 – locus coeruleus (LC)), 5-HT producing raphe nucl. (B1-3; not shown); Rostroventrolateral medulla (RVLM): circulation related structures (vascular tone, cardio-stimulatory centra), respiratory related structures (PreBotzinger, Nucl.ambiguus)
- **Viscero-sensory relay:** PB, parabrachial nuclei, NST, nucleus of the solitary tract;
- **Bulbo-spinal (presympathetic) – sympathetic**

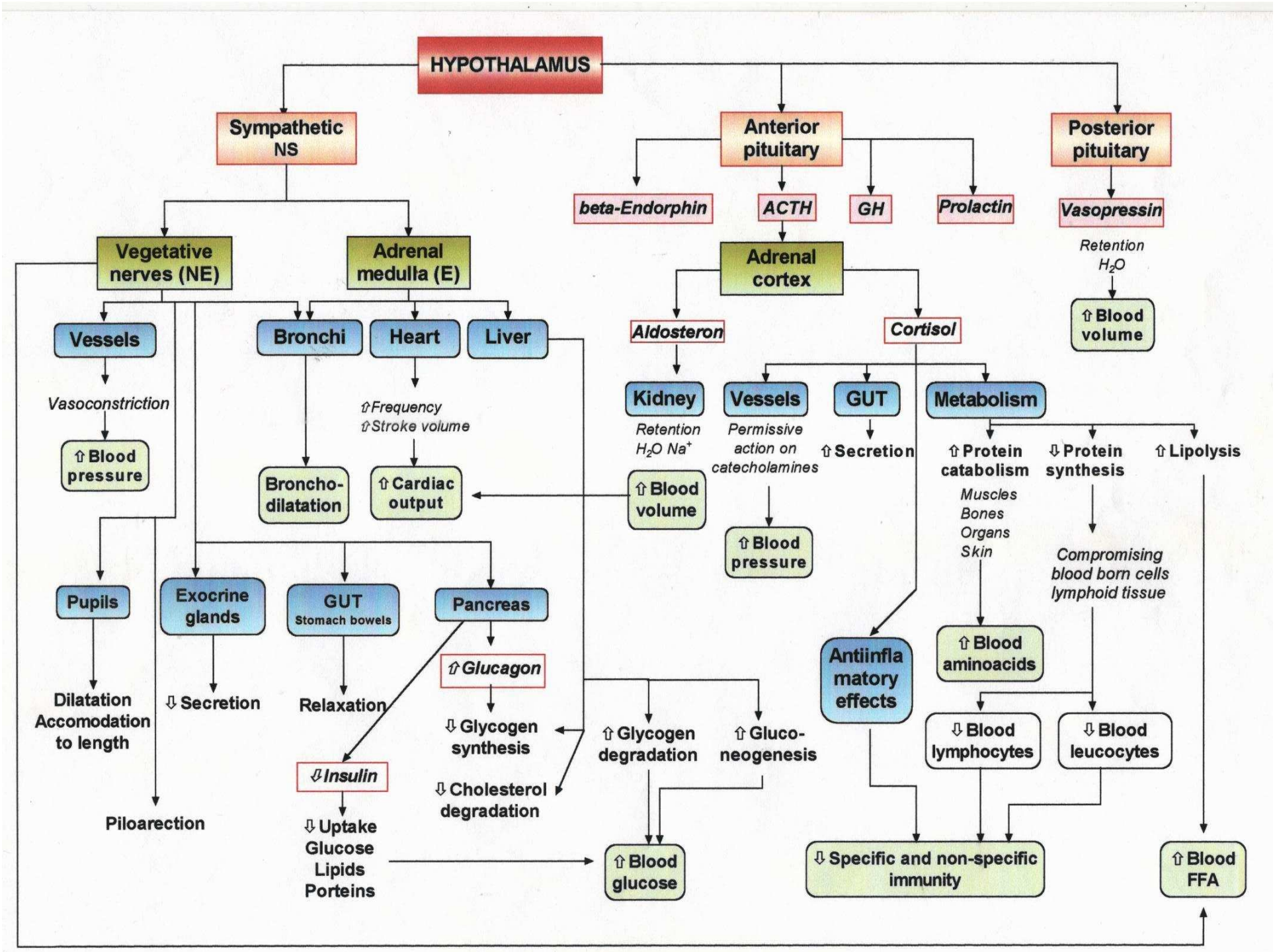
Central structures of ANS

- Visceral sensory relay in brainstem medulla - *nucl. tractus solitarii* pons - *nucll. parabrachiales et nucl. Kölliker-Fuse, locus coeruleus*; Visceral motoric nuclei: cranial nerves (III, VII, IX, X)



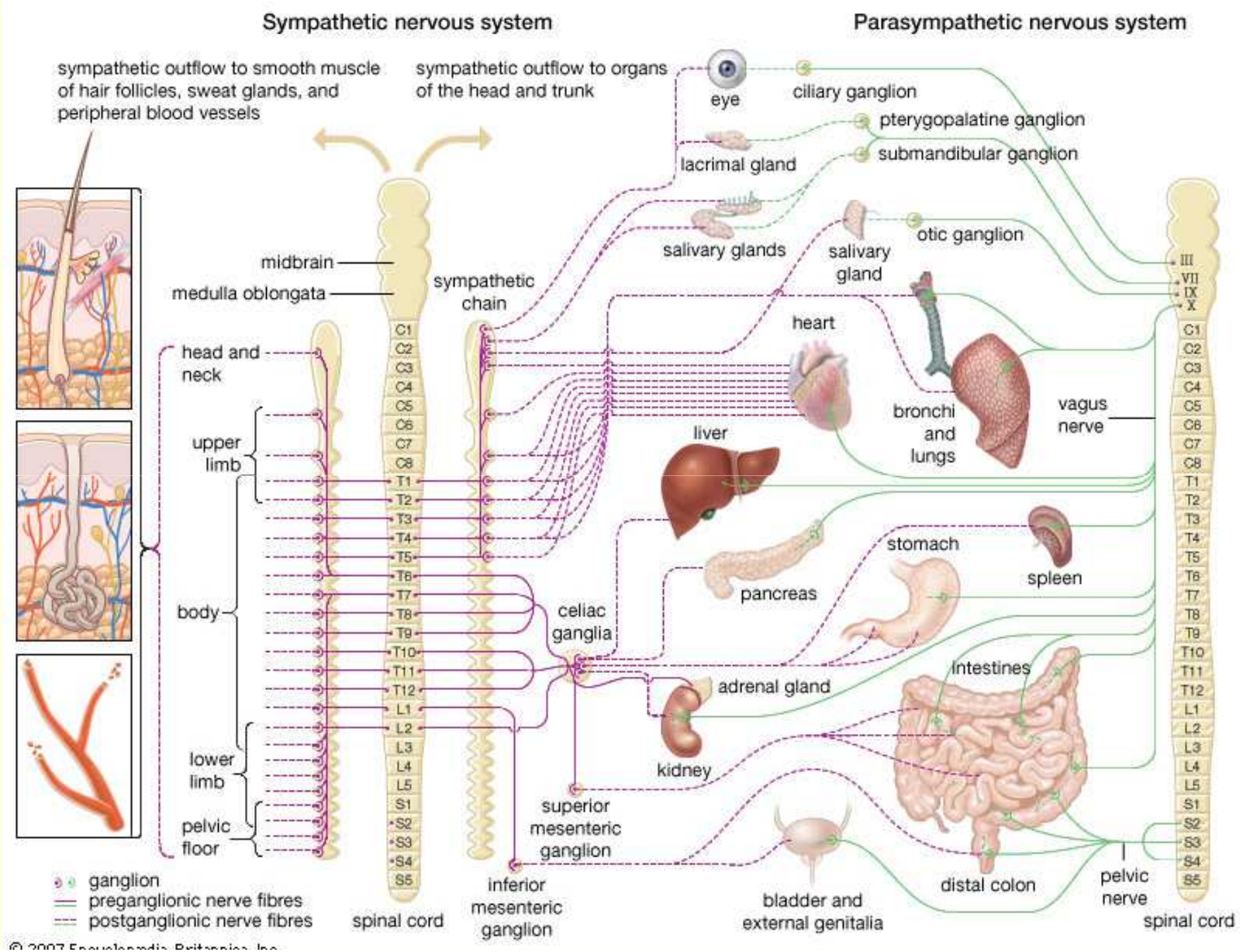


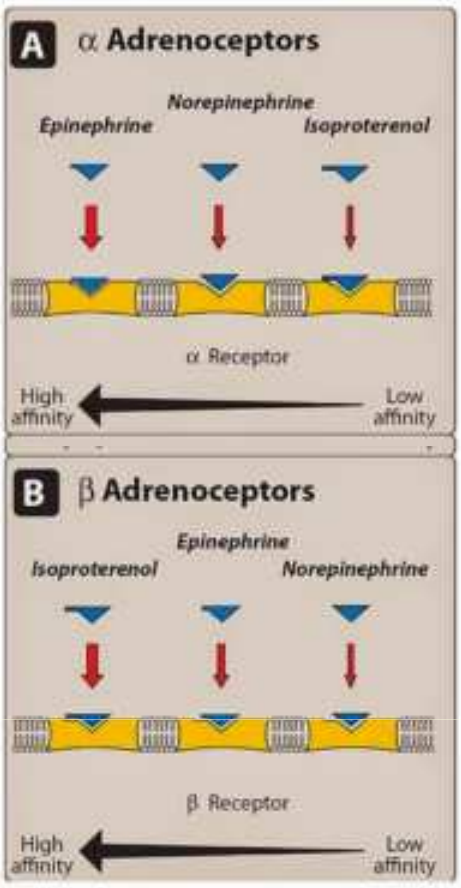
- Katecholaminerbé skupiny A, C; serotoninergné skupiny B, dopaminergné: RVLM, CVLM, kardiostimulačné, kardioinhibičné

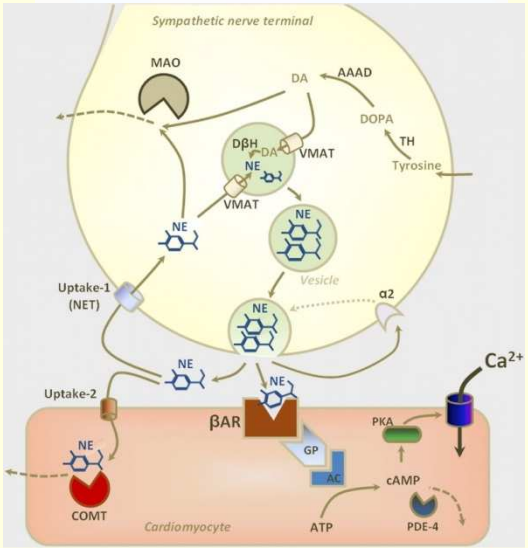

HYPOTHALAMUS
Sympathetic NS
Anterior pituitary
Posterior pituitary
beta-Endorphin
ACTH
GH
Prolactin
Vasopressin
Retention H_2O
⇧Blood volume
Vegetative nerves (NE)
Adrenal medulla (E)
Adrenal cortex
Aldosteron
Cortisol
Vessels
Bronchi
Heart
Liver
Vasoconstriction
⇧Blood pressure
⇧Frequency
⇧Stroke volume
Broncho-dilatation
⇧Cardiac output
Kidney
Retention H_2O Na^+
⇧Blood volume
Vessels
Permissive action on catecholamines
⇧Blood pressure
GUT
⇧Secretion
Metabolism
⇧Protein catabolism
Muscles
Bones
Organs
Skin
⇩Protein synthesis
Compromising blood born cells lymphoid tissue
⇧Lipolysis
Pupils
Exocrine glands
GUT
Stomach bowels
Pancreas
Dilatation
Accomodation to length
⇩Secretion
Relaxation
⇧Glucagon
⇩Glycogen synthesis
⇩Cholesterol degradation
⇧Glycogen degradation
⇧Gluco-neogenesis
⇩Insulin
⇩Uptake
Glucose
Lipids
Porteins
Piloarection
⇧Blood glucose
Antiinfla matory effects
⇧Blood aminoacids
⇩Blood lymphocytes
⇩Blood leucocytes
⇩Specific and non-specific immunity
⇧Blood FFA

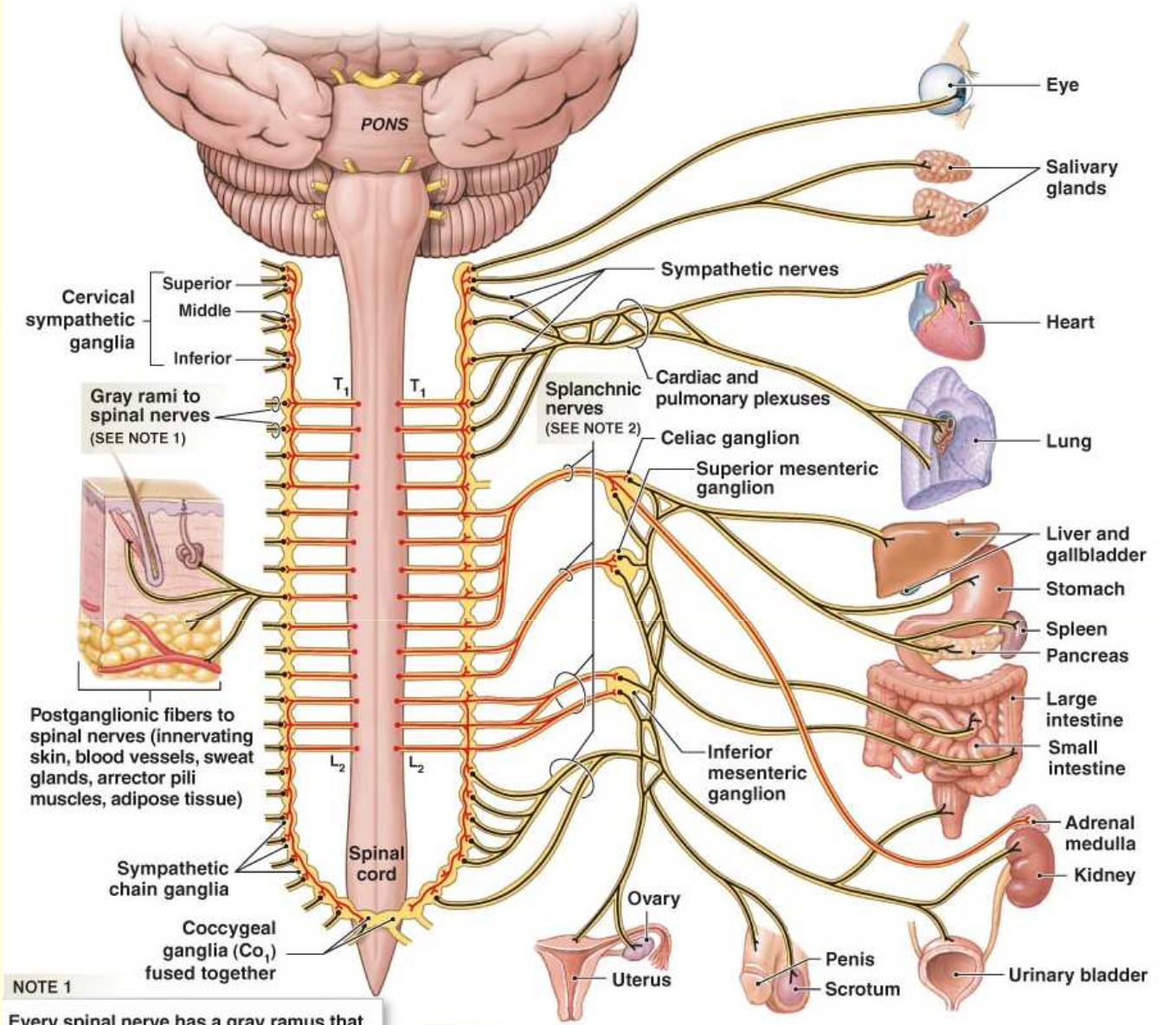
4

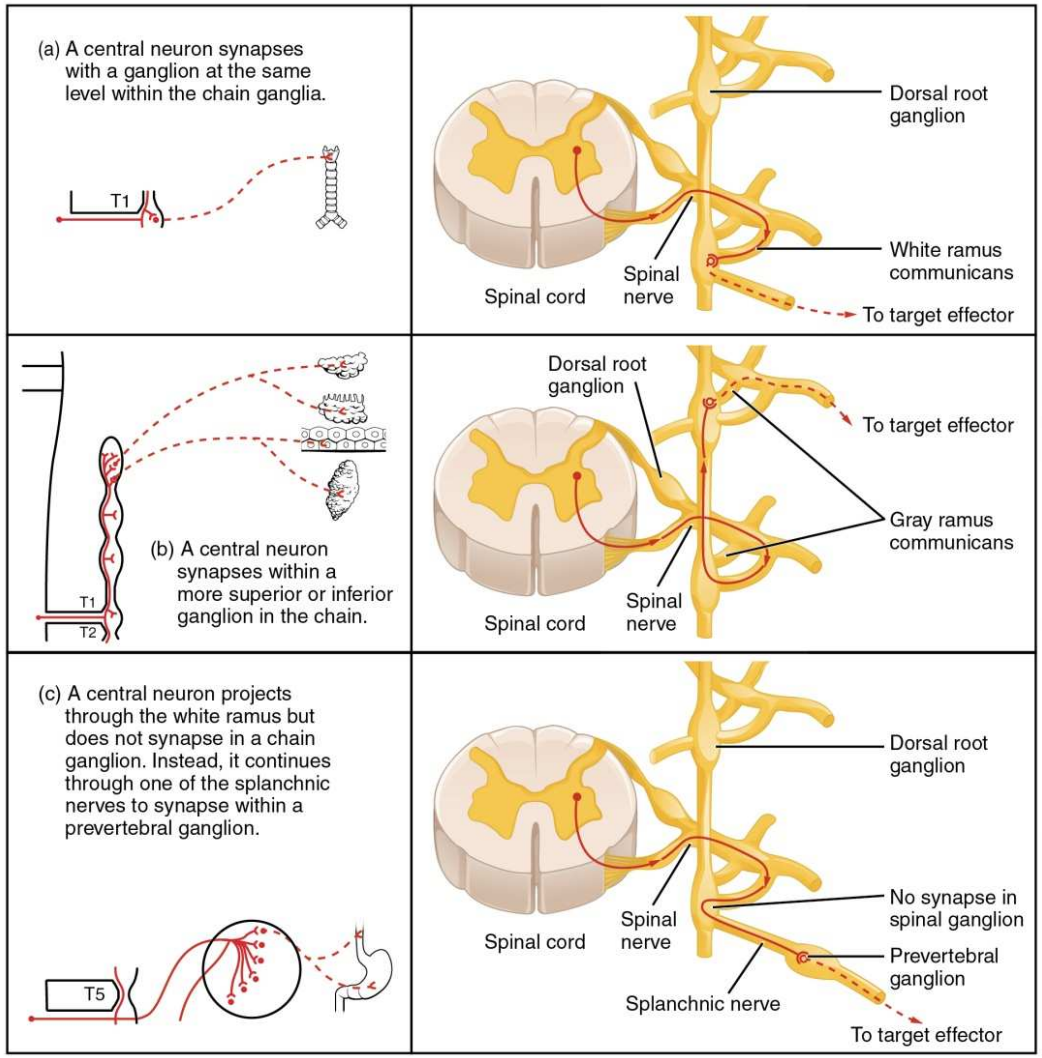
Neurogenic arm of the stress

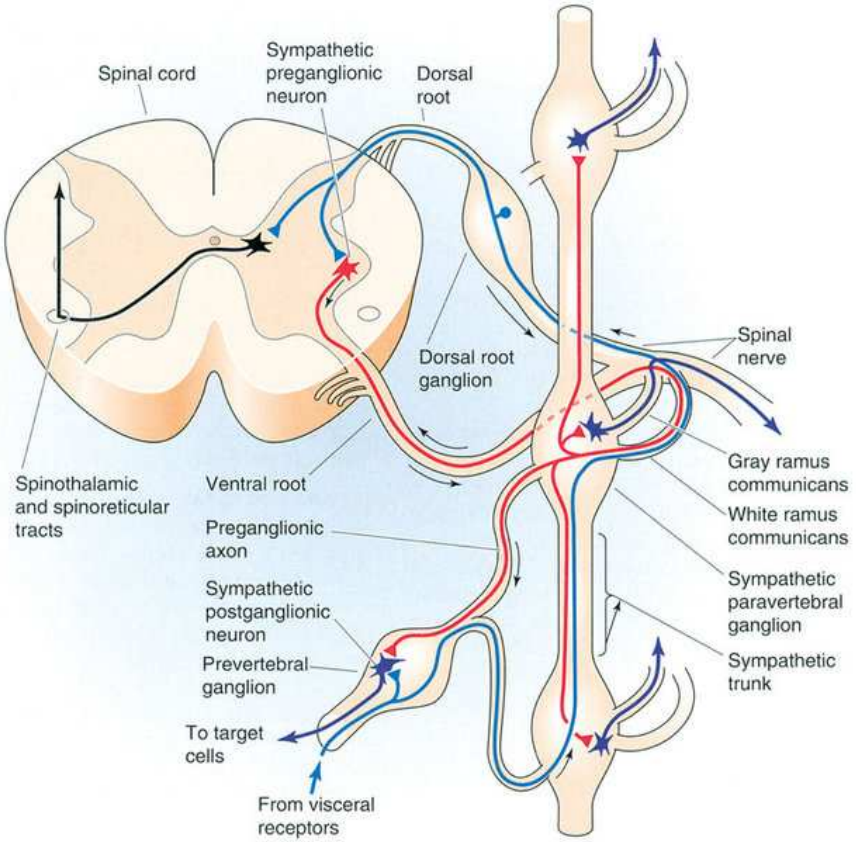


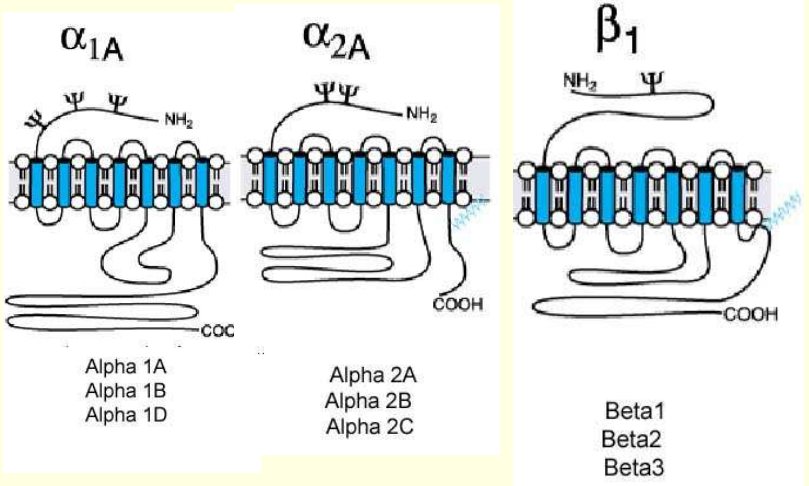

A α Adrenoceptors
Norepinephrine
Epinephrine
Isoproterenol
α Receptor
High affinity
Low affinity
B β Adrenoceptors
Epinephrine
Isoproterenol
Norepinephrine
β Receptor
High affinity
Low affinity

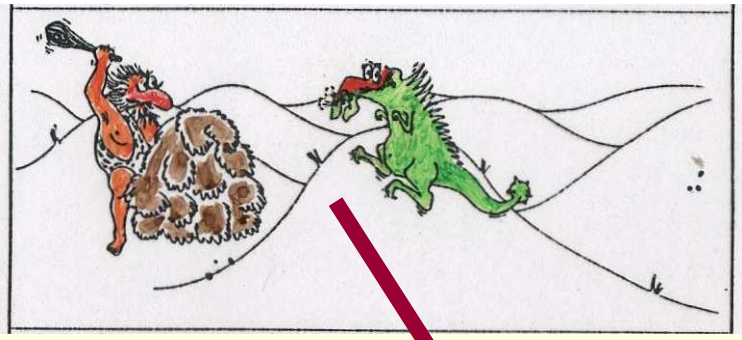

Sympathetic nerve terminal
MAO
DA
AAAD
DOPA
TH
Tyrosine
DβH
VMAT
NE
Vesicle
Uptake-1 (NET)
α2
Uptake-2
βAR
PKA
GP
AC
cAMP
ATP
PDE-4
COMT
Cardiomyocyte
Ca2+

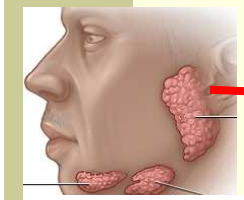

PONS
Eye
Salivary glands
Sympathetic nerves
Heart
Cervical sympathetic ganglia
Superior
Middle
Inferior
Gray rami to spinal nerves
(SEE NOTE 1)
T1
T1
Splanchnic nerves
(SEE NOTE 2)
Cardiac and pulmonary plexuses
Celiac ganglion
Lung
Superior mesenteric ganglion
Liver and gallbladder
Stomach
Spleen
Pancreas
Large intestine
Small intestine
Inferior mesenteric ganglion
Adrenal medulla
Kidney
Postganglionic fibers to spinal nerves (innervating skin, blood vessels, sweat glands, arrector pili muscles, adipose tissue)
L2
L2
Spinal cord
Sympathetic chain ganglia
Coccygeal ganglia (Co1) fused together
Ovary
Uterus
Penis
Scrotum
Urinary bladder
NOTE 1
Every spinal nerve has a gray ramus that carries sympathetic postganglionic fibers for distribution in the body wall and limbs. In the head and neck, postganglionic sympathetic fibers leaving the superior cervical sympathetic ganglia supply the regions innervated by cranial nerves III, VII, IX, and X.
NOTE 2
Preganglionic fibers on their way to the collateral ganglia form the splanchnic (SPLANK-nik) nerves. Postganglionic fibers innervating structures in the thoracic cavity, such as the heart and lungs, form bundles known as sympathetic nerves.
KEY
Preganglionic neurons
Ganglionic neurons

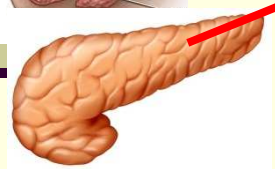

(a) A central neuron synapses with a ganglion at the same level within the chain ganglia.
T1
Dorsal root ganglion
White ramus communicans
Spinal cord
Spinal nerve
To target effector
(b) A central neuron synapses within a more superior or inferior ganglion in the chain.
T1
T2
Dorsal root ganglion
To target effector
Gray ramus communicans
Spinal cord
Spinal nerve
(c) A central neuron projects through the white ramus but does not synapse in a chain ganglion. Instead, it continues through one of the splanchnic nerves to synapse within a prevertebral ganglion.
T5
Dorsal root ganglion
No synapse in spinal ganglion
Spinal cord
Spinal nerve
Prevertebral ganglion
Splanchnic nerve
To target effector

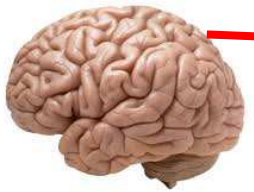

Spinal cord
Sympathetic preganglionic neuron
Dorsal root
Dorsal root ganglion
Spinal nerve
Gray ramus communicans
White ramus communicans
Sympathetic paravertebral ganglion
Sympathetic trunk
Spinothalamic and spinoreticular tracts
Ventral root
Preganglionic axon
Sympathetic postganglionic neuron
Prevertebral ganglion
To target cells
From visceral receptors


α_{1A}
α_{2A}
β_1
NH2
COOH
Alpha 1A
Alpha 1B
Alpha 1D
Alpha 2A
Alpha 2B
Alpha 2C
Beta1
Beta2
Beta3

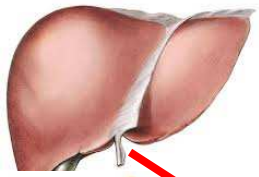


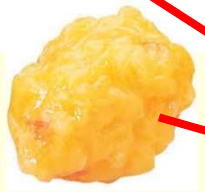


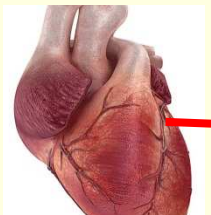


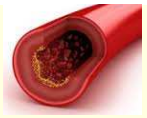


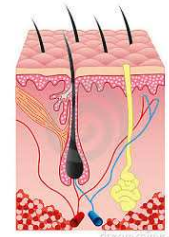
Tab. 2. Physiologic effects of vegetative control			
	Sympathetic		Parasympathetic
	alpha response	beta response	
Eyes			
m. dilatator pupillae	contraction α1	--	--
m.constrictor pupillae	--	--	contraction
pupila	mydriasis α1	--	miosis
m.cilliaris (akomodation)	--	relaxation β1 (acc. into distance)	contraction (acc. to near)
intrabulbar pressure	increase	--	decrease
Glands			
salivary (gl.parotis, submandibularis etc.)	dense mucous secretion	--	liquid serose secretion
pancreas	insulin α2	↑insulin, glucagon β2	secretion (exocrinne)
lacrimal, paranasal bronchial, stomach	--	--	secretion
sweet glands	↑ secretion	--	↑ secretion (apocrinnic)
suprarenal medulla	↑ secretion α1	--	--
macula densa (kidney)	renin release α1	↑renin β2	--
CNS			
cerebrum	stimulation	stimulation β2	?
cerebellum	--	stimulation β2	--
basal ganglia	stimulation	--	stimulation
thalamus	stimulation α2	--	stimulation



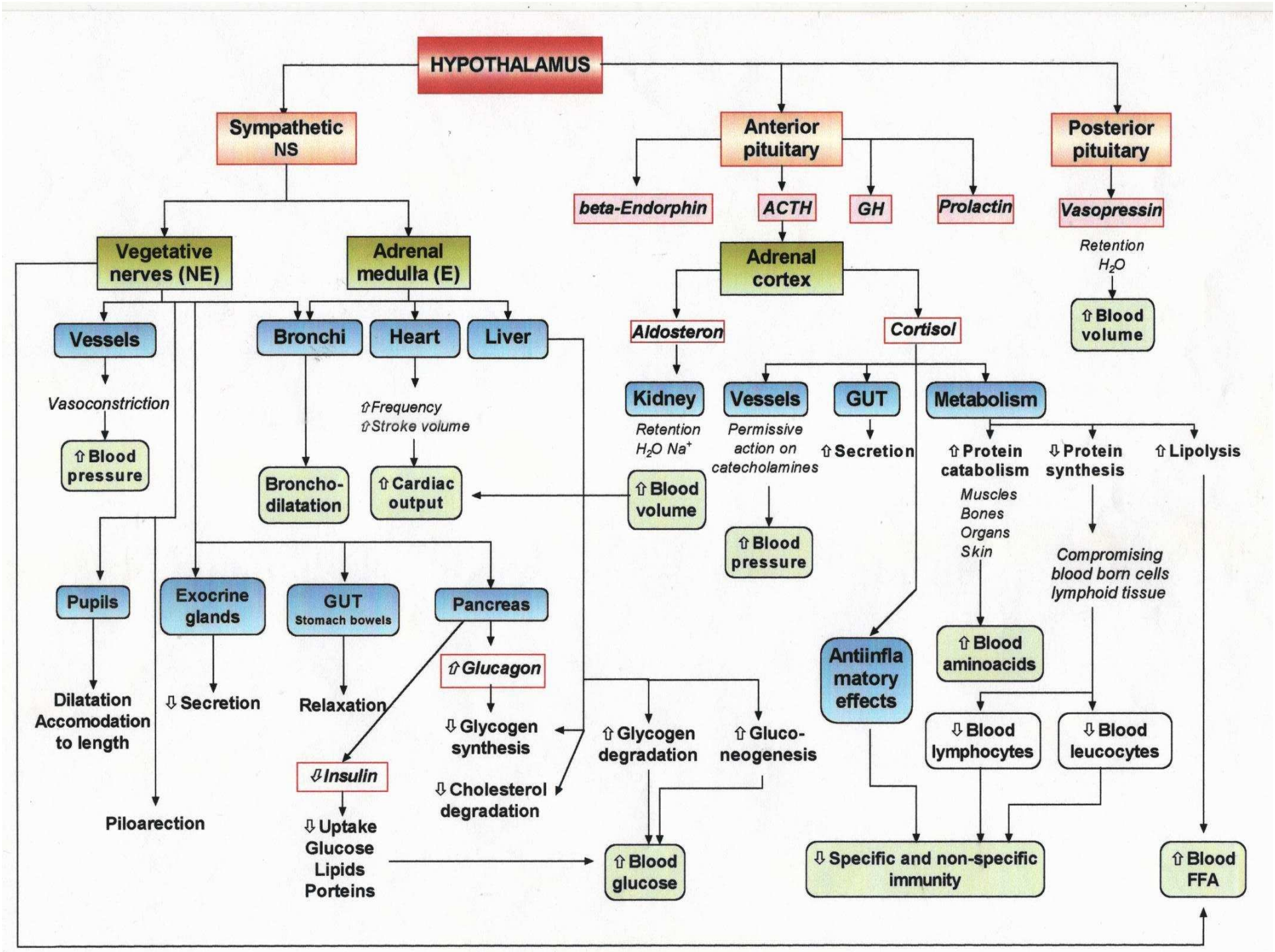








Tab. 2. Physiologic effects of vegetative control			
	Sympathetic		**Parasympathetic**
	alpha response	**beta response**	
Metabolism			
Liver	↑ glykogenolysis α1	↑ glykogenolysis β2 ↑ glukoneogenesis β2 ↑ lipolysis β2	--
Fat tissue	↓ lipolysis α2	↑ lipolysis β1	--
Muscles		↑ glykogenolysis β2	--
Global regimen		catabolic	anabolic
Heart			
sino-atrial node	--	↑ chronotrophy β1	↓chronotrophy
atrio-ventricular node	--	↑ chronotrophy β1	↓chronotrophy
conductive system - chambers	--	↑ dromotrophy β1 ↑ batmotrophy β1	↓ dromotrophy
atria	--	↑ inotrophy β1	↓ inotrophy
chambers	↑ contraction α1	↑↑ contraction β1	--
Vessels			
skin, mucosa, lung	constriction α1	--	dilatation
visceral organs	constriction α1	dilatation β1	?
skeletal muscles	constriction α1	dilatation β2	relaxation
coronary vessels	--	dilatation β2	relaxation
brain	--	--	dilatation
uterus	constriction α1/α2	--	--
kidney	constriction α2	--	dilatation ?
Smooth muscles - viscera			
holow organs (stomach, bowels,bronchi)	--	relaxation β2	contraction
sphincters,testes, ductus deferens	contraction α1	--	relaxácia
piloarectors (skin)	contraction α1	relaxation β2	--
uterus, tuba uterina	contraction α1	relaxation β2	--
parenchymatose organs	contraction α1	--	--

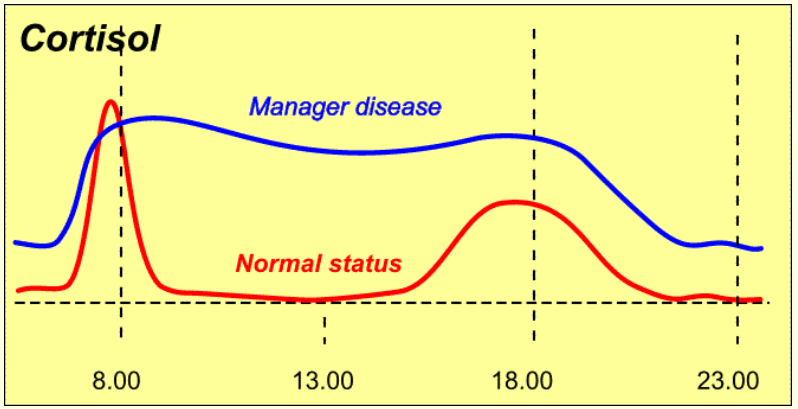

HYPOTHALAMUS
Sympathetic NS
Anterior pituitary
Posterior pituitary
beta-Endorphin
ACTH
GH
Prolactin
Vasopressin
Retention H_2O
⇧Blood volume
Vegetative nerves (NE)
Adrenal medulla (E)
Adrenal cortex
Aldosteron
Cortisol
Vessels
Bronchi
Heart
Liver
Vasoconstriction
⇧Blood pressure
⇧Frequency
⇧Stroke volume
Broncho-dilatation
⇧Cardiac output
Kidney
Retention H_2O Na^+
⇧Blood volume
Vessels
Permissive action on catecholamines
⇧Blood pressure
GUT
⇧Secretion
Metabolism
⇧Protein catabolism
Muscles
Bones
Organs
Skin
⇩Protein synthesis
Compromising blood born cells lymphoid tissue
⇧Lipolysis
Pupils
Exocrine glands
GUT
Stomach bowels
Pancreas
Dilatation
Accomodation to length
⇩Secretion
Relaxation
⇧Glucagon
⇩Glycogen synthesis
⇩Cholesterol degradation
⇧Glycogen degradation
⇧Gluco-neogenesis
⇩Insulin
⇩Uptake
Glucose
Lipids
Porteins
Piloarection
⇧Blood glucose
Antiinfla matory effects
⇧Blood aminoacids
⇩Blood lymphocytes
⇩Blood leucocytes
⇩Specific and non-specific immunity
⇧Blood FFA

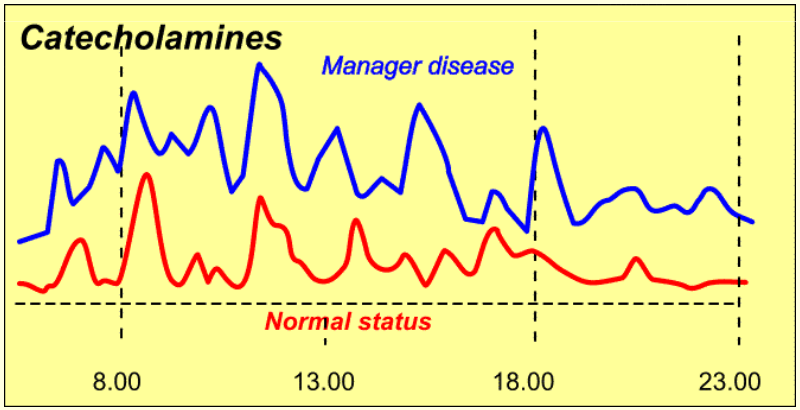
5

Humoral arm of the stress response

Humoral effectors of the stress system

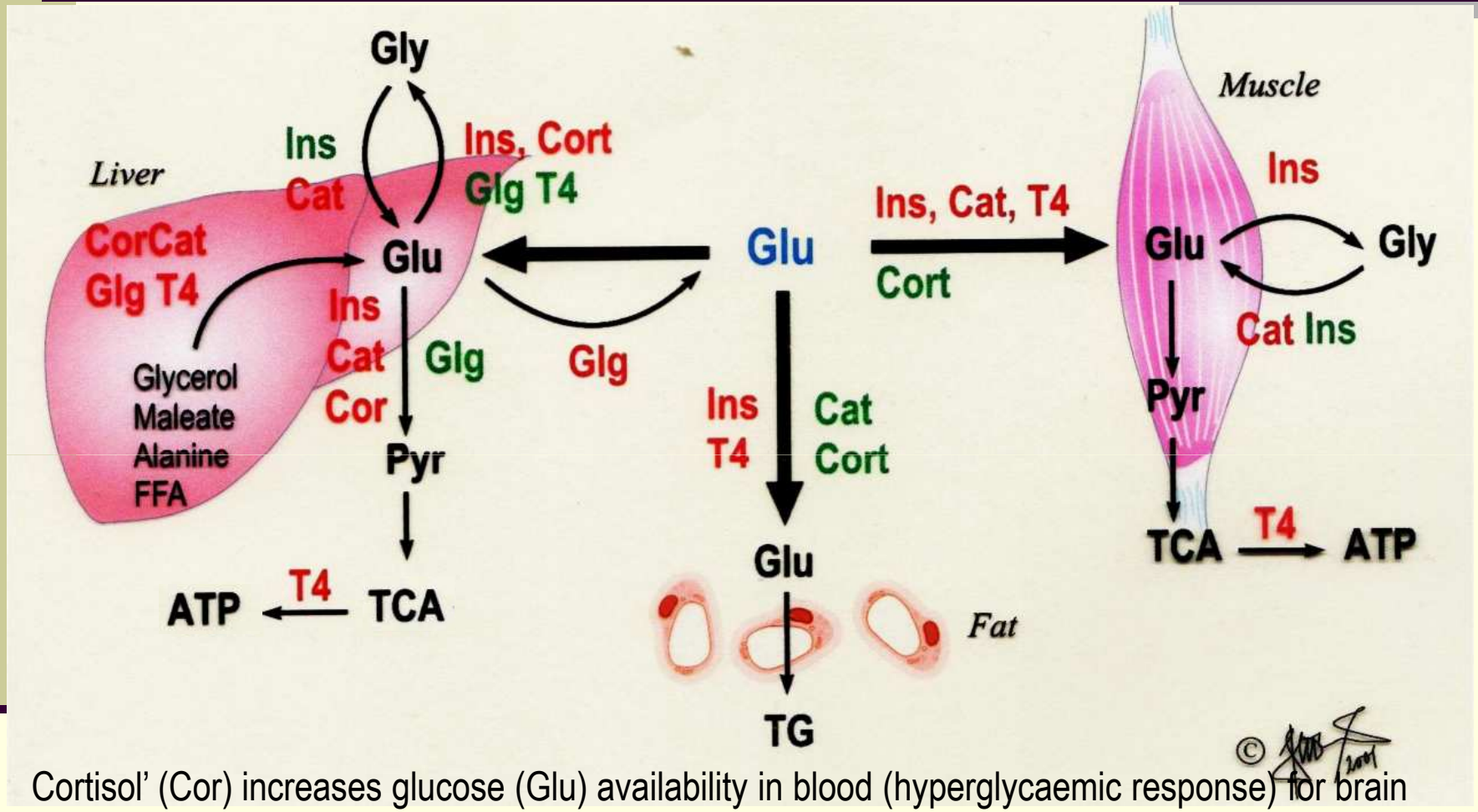
- *HPA axis:* hypothalamus (CRH), hypophysis (ACTH), supraren cortex glucocorticosteroids (cortisol, hydrocortison)+ sex hornones (androstendion, DH-epiandrostendione (DHAD)
- *HPT axis: hypothalamus (TRH, thyroid relaseing horm.)- pituitary (TSH, thyroid stimnulatimng h.) thyroid gland (thyroid hornones T3, T4)*
- *HPG axis: hypothalamus (GnRH), pituitary (LH, FSH), ovaries (estrogens), testicles (androgens)*
- Vasopressin (ADH) =
- GH (growth hornone), Prolactin
- Proopiomelanocortin (POMC) : MSH, END, ENK
- Adrenal catecholamines – epinephrine, DA





Susteined levels out of cyclic circadian variations

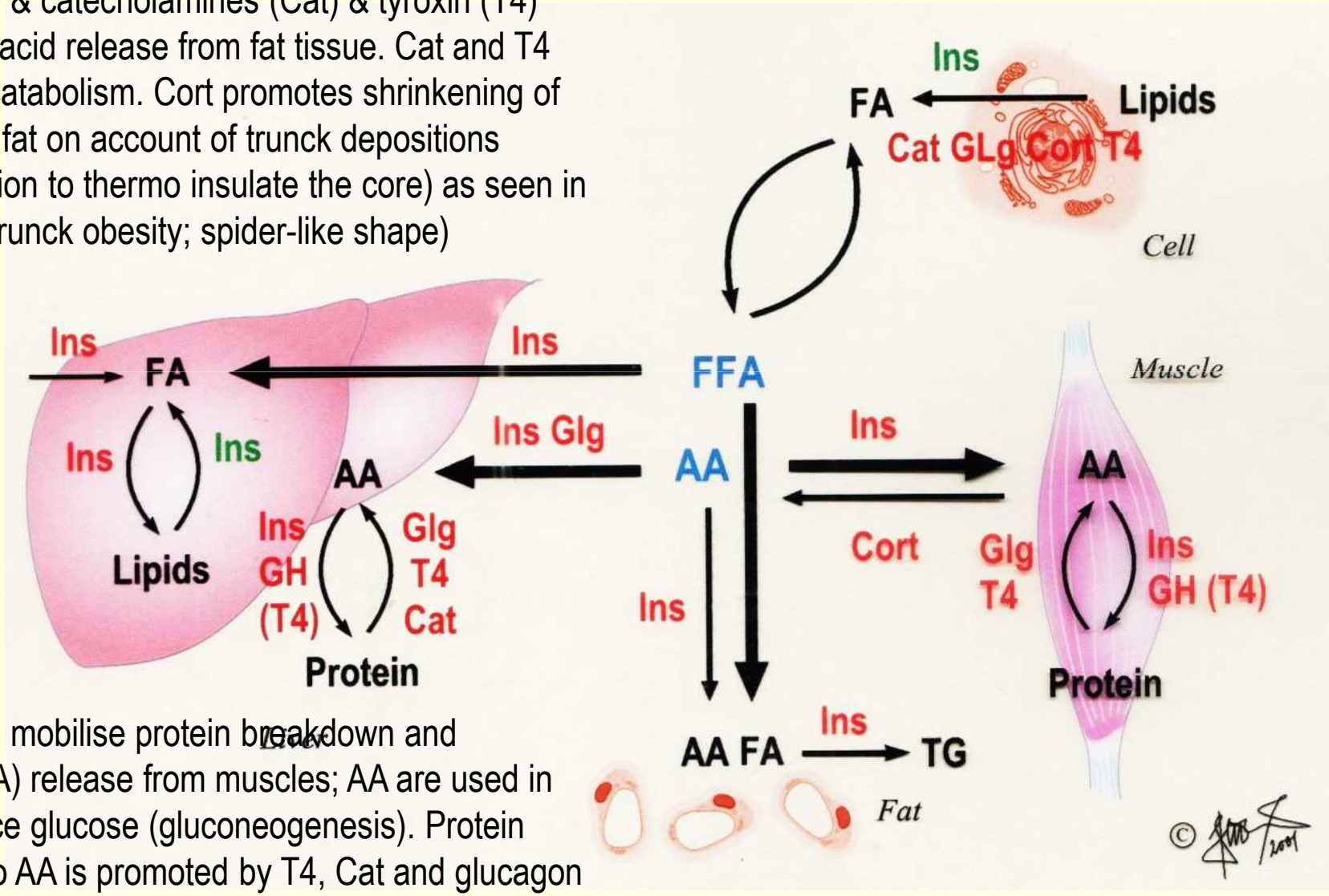
Catabolic regulation of metabolism 1



Cortisol' (Cor) increases glucose (Glu) availability in blood (hyperglycaemic response) for brain and liver through block of Glu intake to muscle and Glu storage in a fat. In liver, Cor promotes Glu mobilisation from non-glycogen (Gly) resources (e.g. aminoacids, free fatty acids.glycerol) along with catecholamines (Cat), thyroxin (T4) and glucagon (Glc). Together with insulin (Ins) and T4 Cor and Cat stimulate ulitisation of Glu into energy.

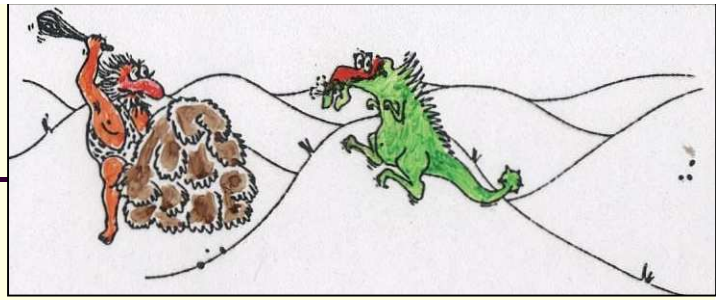
Catabolic regulation of metabolism 2

Cortisol (Cort) & catecholamines (Cat) & tyroxin (T4) mobilise fatty acid release from fat tissue. Cat and T4 stimulate fat catabolism. Cort promotes shrinkening of extremities of fat on account of trunck depositions (archaic reaction to thermo insulate the core) as seen in Cushing sy. (trunck obesity; spider-like shape)

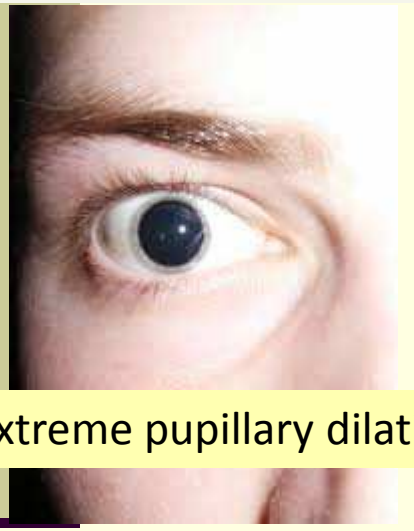


Cortisol (Cort) mobilise protein breakdown and aminoacid (AA) release from muscles; AA are used in liver to produce glucose (gluconeogenesis). Protein degradation to AA is promoted by T4, Cat and glucagon (Glc) in the liver

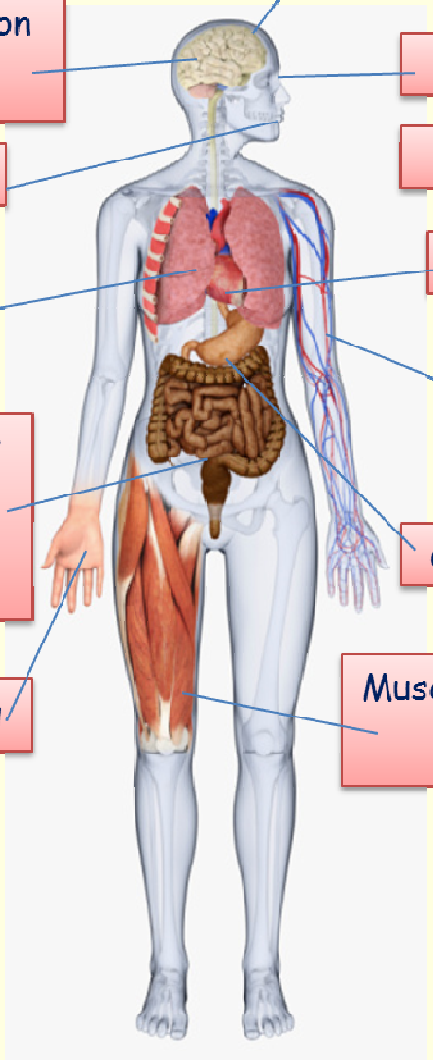
Acute fear response



Piloarection, gose skin



Extreme pupillary dilation



Feel dizzy

Rush of information to the brain

Pupils dilate

Dry mouth

Temperature fluctuation

Increased breathing expanding lungs

Heartbeat increases

Adrenaline races through the body

Digestive and urinary system slows down

can result in loss of bladder control

Churning stomach

Increase sweating

Muscles can feel weak or tense

2. Acute stress response – to prepared load

Increased blood flow to brain; Increased production of catecholamines (epinephrine, norepinephrine, dopamine) which help to facilitate cognitive performance

Pupils dilate/Peripheral vision is reduced

Heart rate increases

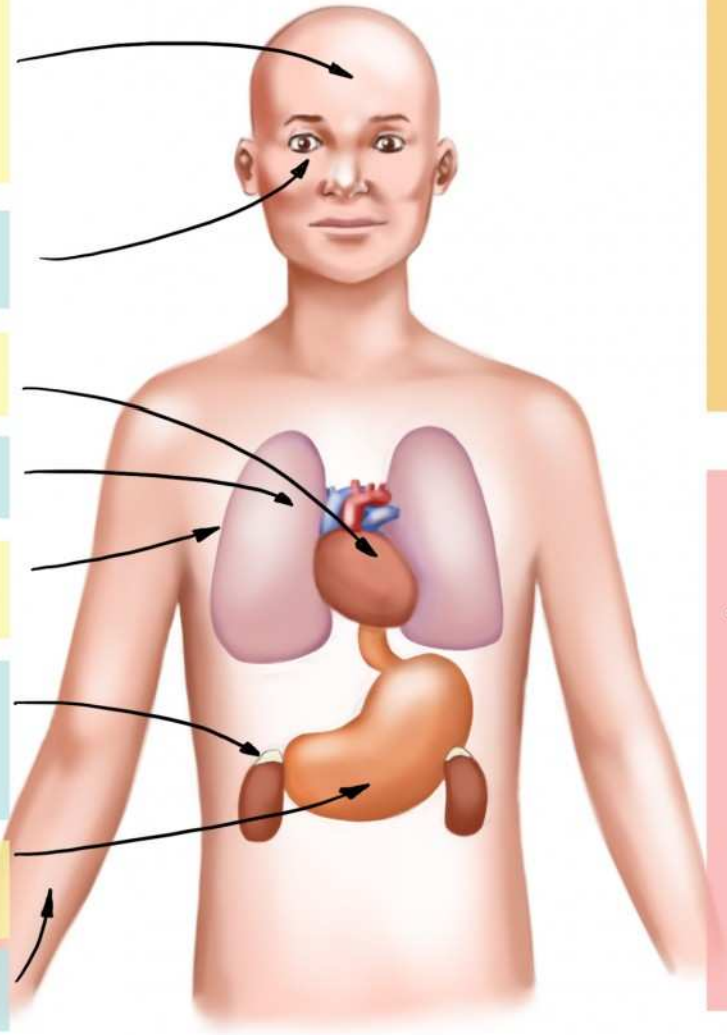
Faster, deeper breathing

Increased blood flow to large muscle groups

Adrenal hormones (cortisol and DHEA) released, resulting in increased energy mobilization

Digestion slows dramatically

Blood pressure increases

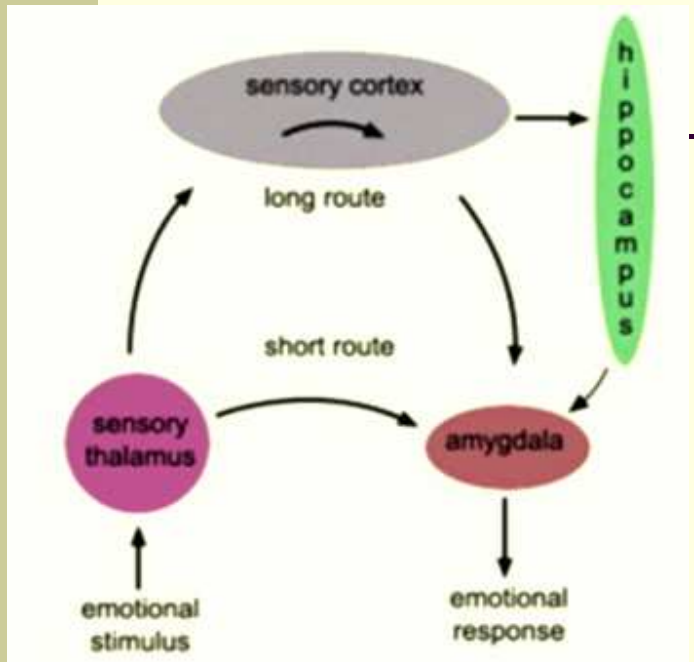


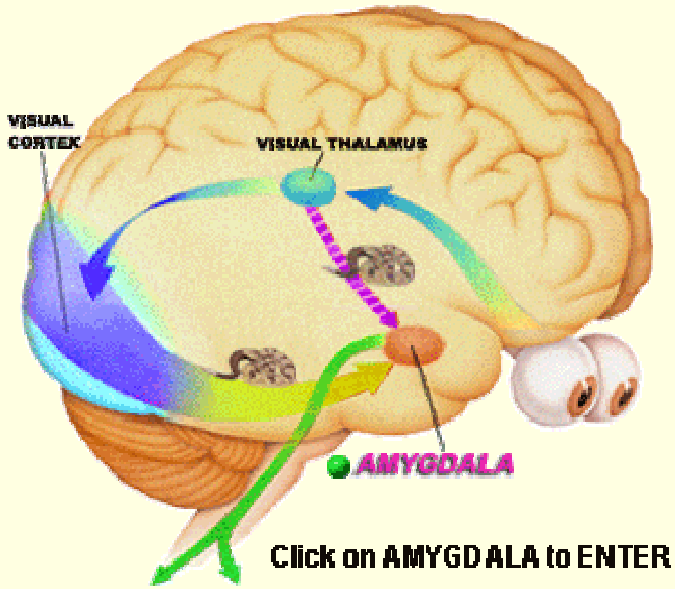
Reactions

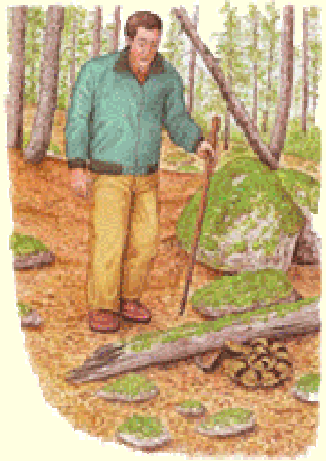
- Increased alertness
- Increased short term strength
- Increased ability to handle stress
- Heightened ability to focus
- Increased oxygen to the brain
- Faster, deeper breathing
- Heightened sense of smell
- Body and mind are hyper-alert

Other Responses

- Perspiration increases to cool body
- Muscle tension increases to prepare for "fight or flight"
- Saliva production decreases
- Metabolism speeds up considerably
- Inflammation increases
- Blood flow from skin surface is diverted to larger muscle groups & brain
- Body extremities can change temperature
- Blood pressure increases







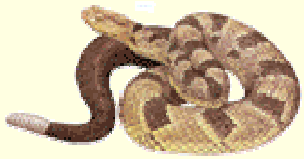
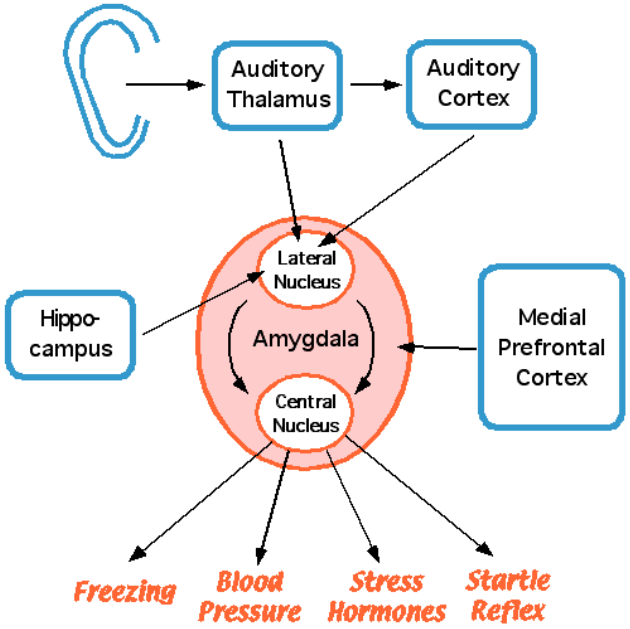
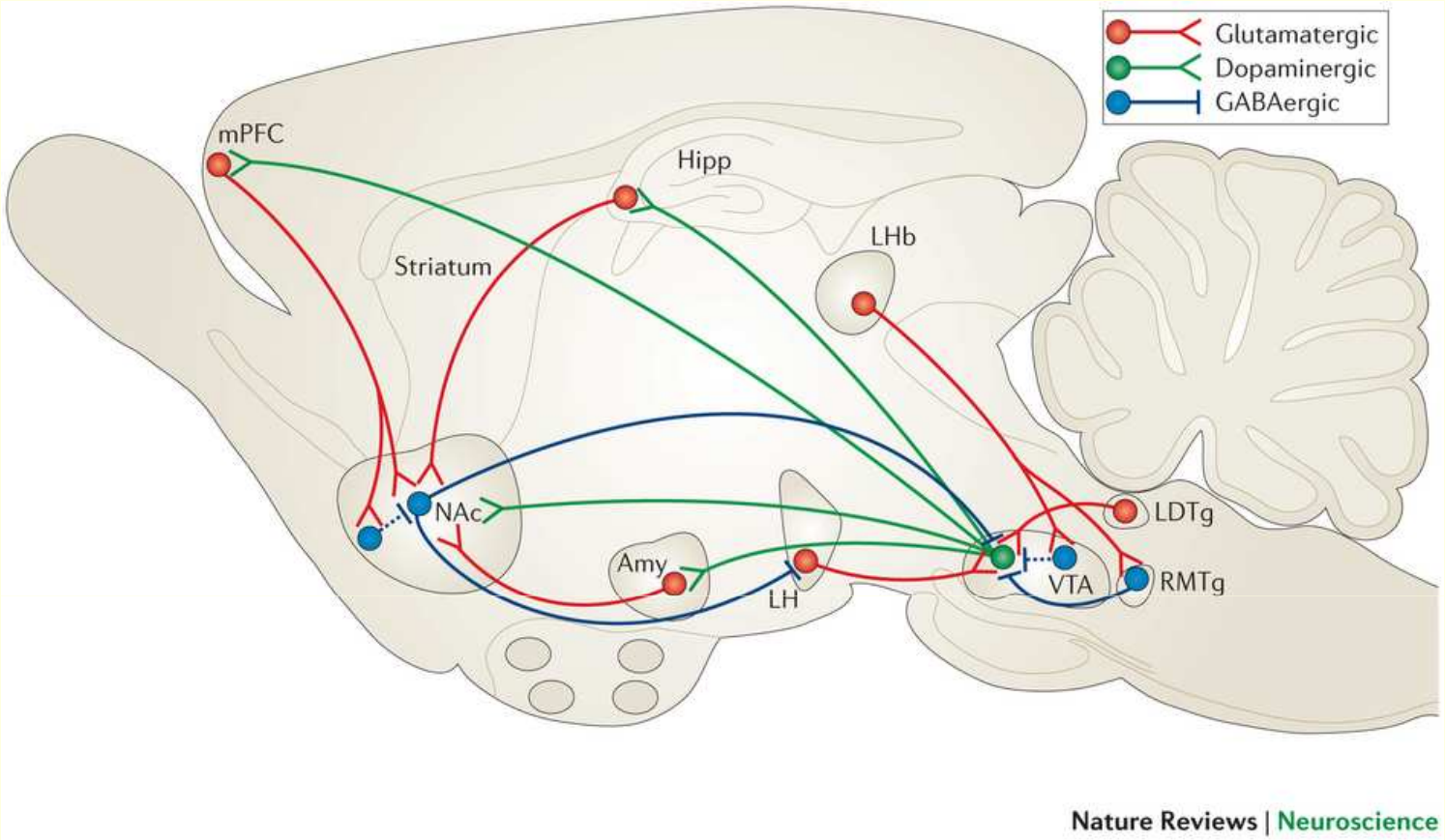


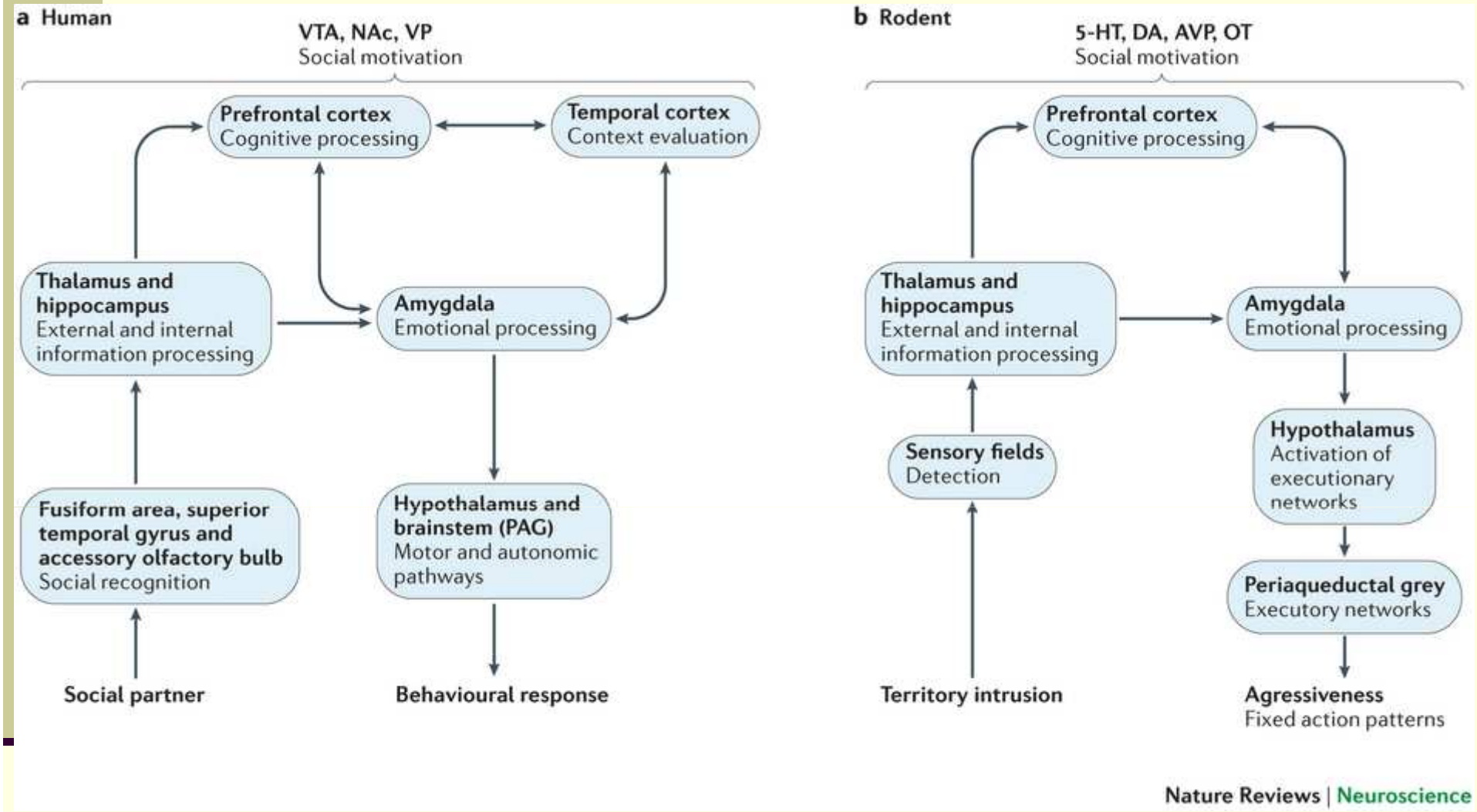
Illustration based on LeDoux JE (1994) Emotion, Memory, and the Brain. Scientific American.



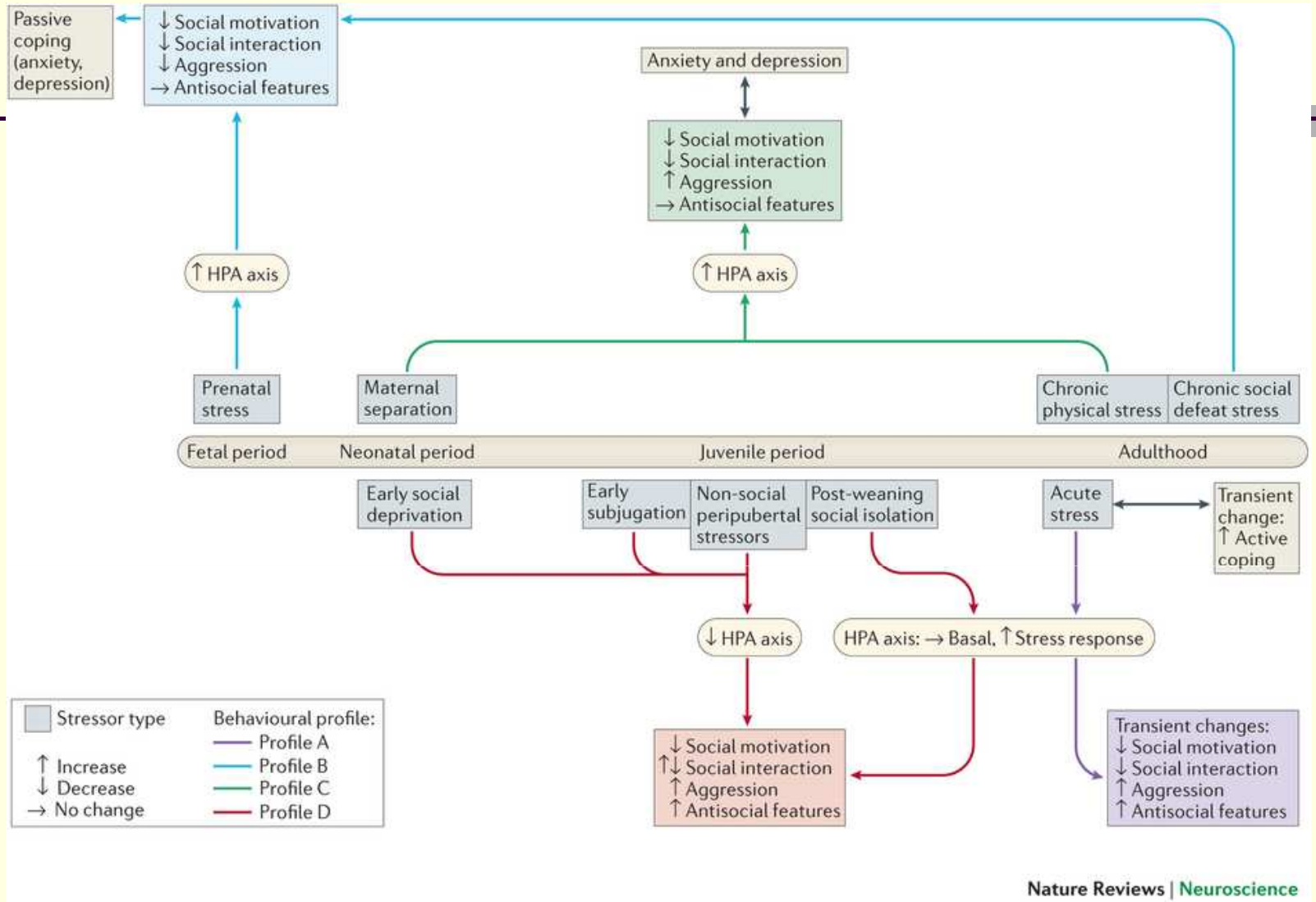
- **Freezing, Hypertension, Startle reflex**



A simplified schematic of the major dopaminergic, glutamatergic and GABAergic connections to and from the ventral tegmental area (VTA) and nucleus accumbens (NAc) in the rodent brain. The primary reward circuit includes dopaminergic projections from the VTA to the NAc, which release dopamine in response to reward-related stimuli (and in some cases, aversion-related stimuli). There are also GABAergic projections from the NAc to the VTA; projections through the direct pathway (mediated by D1-type medium spiny neurons (MSNs)) directly innervate the VTA, whereas projections through the indirect pathway (mediated by D2-type MSNs) innervate the VTA via intervening GABAergic neurons in the ventral pallidum (not shown). The NAc also contains numerous types of interneurons (Fig. 2). The NAc receives dense innervation from glutamatergic monosynaptic circuits from the medial prefrontal cortex (mPFC), hippocampus (Hipp) and amygdala (Amy), as well as other regions. The VTA receives such inputs from the lateral dorsal tegmentum (LDTg), lateral habenula (LHb) and lateral hypothalamus (LH), as well as both GABAergic and glutamatergic connections from the extended amygdala (not shown). These various glutamatergic inputs control aspects of reward-related perception and memory. The dashed lines indicate internal inhibitory projections. The glutamatergic circuit from the LH to the VTA is also mediated by orexin (not shown). Greater details of these monosynaptic circuits for NAc and VTA are shown in Fig. 2. RTMg, rostromedial tegmentum.



a | Brain regions that have become known as the 'social brain' in humans as a result of neuroimaging studies. b | Areas that constitute the 'aggressive brain' in rodents on the basis of stimulation, lesion and immunocytochemical studies79, 81, 109. Although the techniques used in identifying these brain areas were different, and the behaviours that they control are overlapping but distinct, similarities between the identified brain regions involved in the social brain in humans and the aggressive brain in rodents are noticeable. Arrows indicate the proposed flow of information between areas. 5-HT, serotonin; AVP, arginine vasopressin; DA, dopamine; NAc, nucleus accumbens; OT, oxytocin; PAG, periaqueductal grey; VP, ventral pallidum; VTA, ventral tegmental area



We can distinguish four different patterns of behavioural change that result from exposure to different types of stressor at different developmental time points. In profile A, acute stressors activate coping mechanisms and transiently promote agonistic behaviour (that is, any social behaviour related to fighting, including threats, displays, retreats, placating aggressors and conciliation). This profile is characterized by a transient shift towards aggressiveness ('fight or flight' changes). In profile B, prenatal stressors and chronic social defeat in adulthood promote passive coping mechanisms (including signs of anxiety and depression) along with a general reduction of social behaviours (asociality) without inducing abnormal forms of aggression. In profile C, maternal separation and chronic physical stressors administered in adulthood result in behavioural withdrawal in all contexts except for aggression, which increases (these animals are classified as hostile, anxious and/or depressed). In profile D, early social deprivation and stress experienced during the juvenile period induce a behavioural profile that is marked by different signs of antisociality. These animals are characterized by abnormal forms of aggression and model-dependent changes in other behaviours. HPA, hypothalamic–pituitary–adrenal.

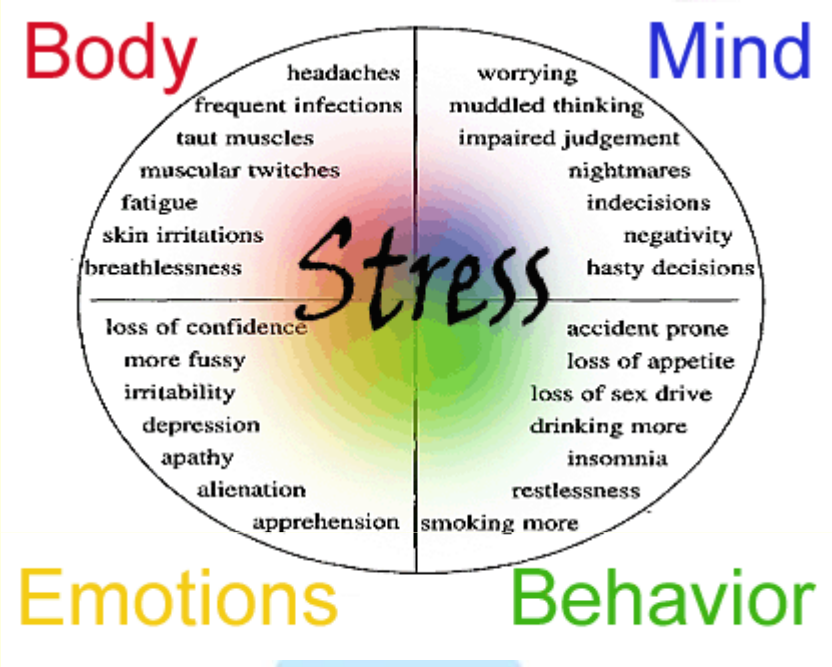
4

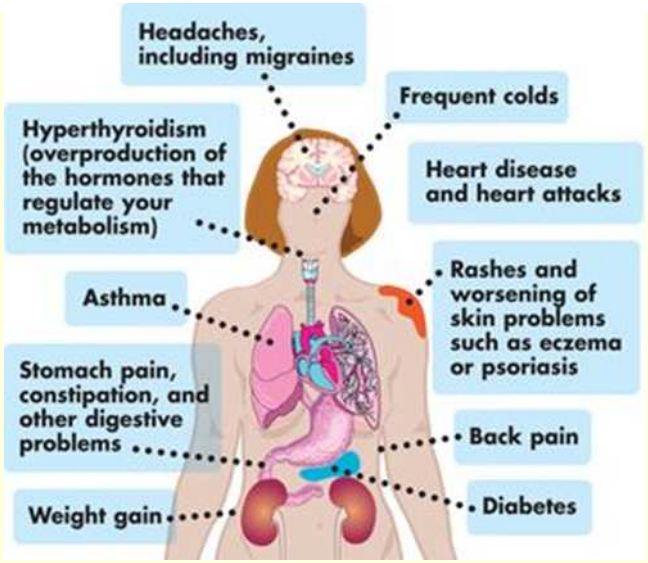
Stress – related diseases

Common manifestations of stress

- **Somatic signs and symptoms**
  - Headache, chest pain palpitations, grinding teeth, dyspnoea, nauzea, vomitus, diarrhoea, constipation, colitis, gastric ulcer,
  - Migrain, tremor, agitation, unrest, tiredness, weakness, sleep disorders, loss of appetite, common respirátory infections, asthma
  - Sweating, flushing, lactimation,

- **Mental and phychological symptoms**
  - Loss of concetration, forgetfulness, confusion
  - Anxiety, depresia,fear, pesimism, irritability, anger, frustration, apathy, loss opf interes and motivation
  - Smoking, alcoholism, nail biting etc.





Here are ways in which some key body systems react.

1 NERVOUS SYSTEM

When stressed — physically or psychologically — the body suddenly shifts its energy resources to fighting off the perceived threat. In what is known as the "fight or flight" response, the sympathetic nervous system signals the adrenal glands to release adrenaline and cortisol. These hormones make the heart beat faster, raise blood pressure, change the digestive process and boost glucose levels in the bloodstream. Once the crisis passes, body systems usually return to normal.

2 MUSCULOSKELETAL SYSTEM

Under stress, muscles tense up. The contraction of muscles for extended periods can trigger tension headaches, migraines and various musculoskeletal conditions.

3 RESPIRATORY SYSTEM

Stress can make you breathe harder and cause rapid breathing — or hyperventilation — which can bring on panic attacks in some people.

4 CARDIOVASCULAR SYSTEM

Acute stress — stress that is momentary, such as being stuck in traffic — causes an increase in heart rate and stronger contractions of the heart muscle. Blood vessels that direct blood to the large muscles and to the heart dilate, increasing the amount of blood pumped to these parts of the body. Repeated episodes of acute stress can cause inflammation in the coronary arteries, thought to lead to heart attack.

5 ENDOCRINE SYSTEM

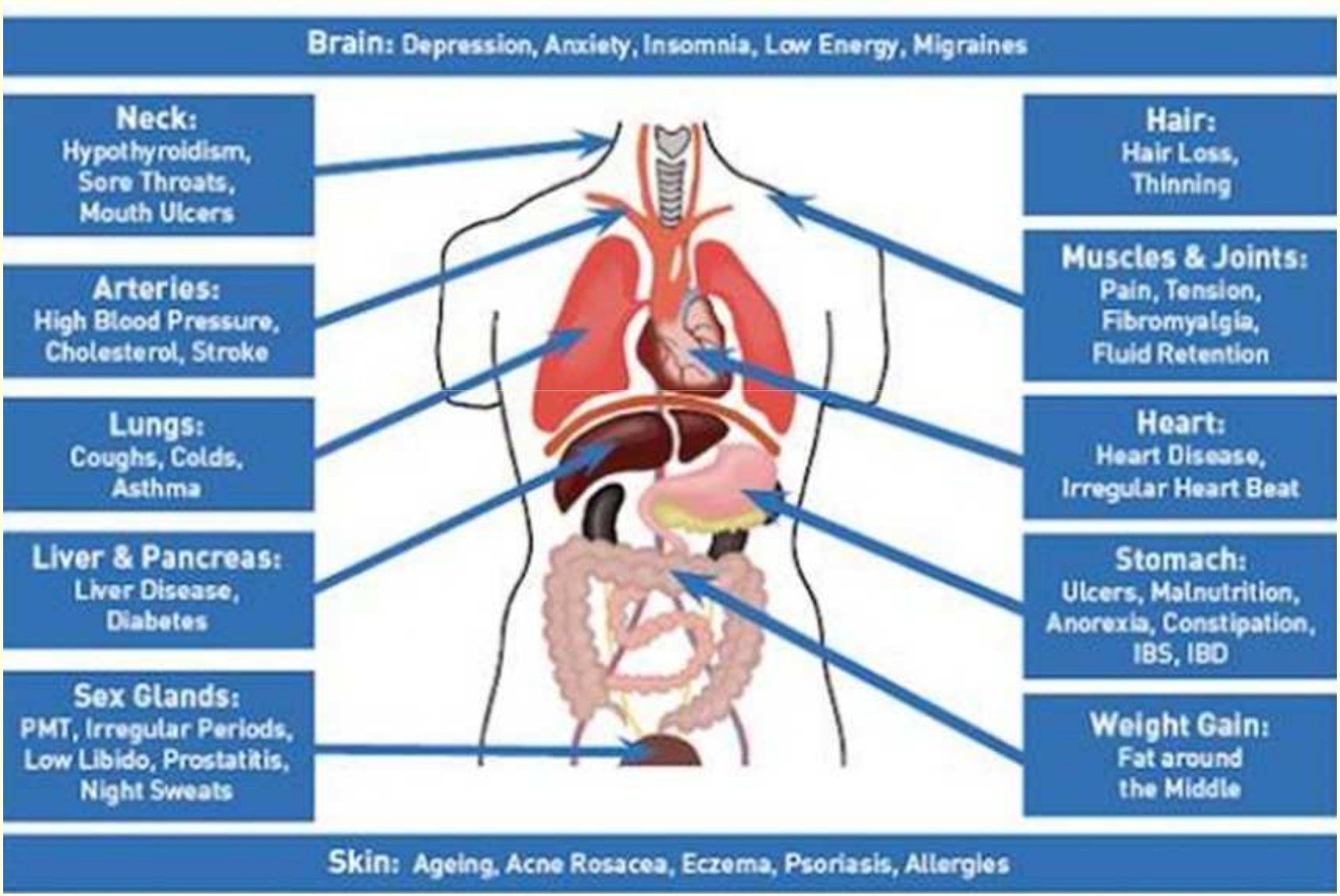
Adrenal glands

When the body is stressed, the brain sends signals from the hypothalamus, causing the adrenal cortex to produce cortisol and the adrenal medulla to produce epinephrine — sometimes called the "stress hormones."

Liver

When cortisol and epinephrine are released, the liver produces more glucose, a blood sugar that would give you the energy for

Manifestations of stress



Symptoms of stress

- **Physical**
  Headaches, chronic digestive problems, eating too much or "forgetting" to eat, grinding jaw, backaches, frequent illness, feeling exhausted, sleeping too much or too little
- **Emotional**
  Sadness, depression, bitterness, anger, anxiety, loss of spirit, loss of humor
- **Behavioral**
  Irritability, negativity, backbiting, acting out, aggressive, violence, substance abus
- **Cognitive**
  Diminished ability to concentrate, diffi
- **Self-Esteem**
  Expressed in negative self-talk

Stress- relates diseases

Organ	Disease, condition
Cardiovascular System	Coronary heart disease Hypertension Stroke Dysrhythmias
Pulmonary system	Neurogenic asthma, Hay fever
Gastrointestinal System	Ulcer, Irritable bowel disease, Diarrhea Nausea vomiting,
Genitourinary tract	Diuresis, Impotence, Frigidity
Skin	Eczema, Acne, Neurodermatitis
Endocrine system	Diabetes mellitus
CNS	Fatigue and lethargy, Overeating Depression, Insomnia
Immunological system	Autoimmune diseases Immunosupression
Connective diseases	Rheumatoid arthritis Colagenoses

Psychiatric dis. associated with stress

- *Post-traumatic stress disease (PTSD)*
- *Manager disease (MD)*
- *Burn-out syndrome (BS)*
- *Chronic fatigue syndrome (CFS)*
- *Emotional exhaustion (extinction)*
- *Reactive depression (mood disorders)*

Post-traumatic stress disease

Occ: about 1.4 to 8% of the population

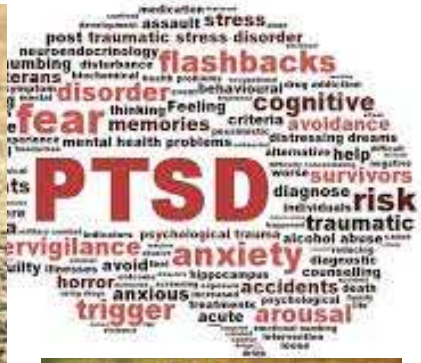
Etio: severe psychol./phys. trauma - war veterans, victims of racism, war genocide; roberry, rapes, criminal assault, domestic violence, abused children, etc.

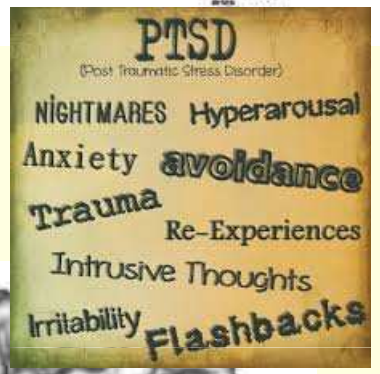
Sy: A)Psychol.: depressive mood, anxiety, lethargy, submissiveness, insomnia, nightmares, night terror, emotional blunting, memory dis., speech (stuttering, stammering)

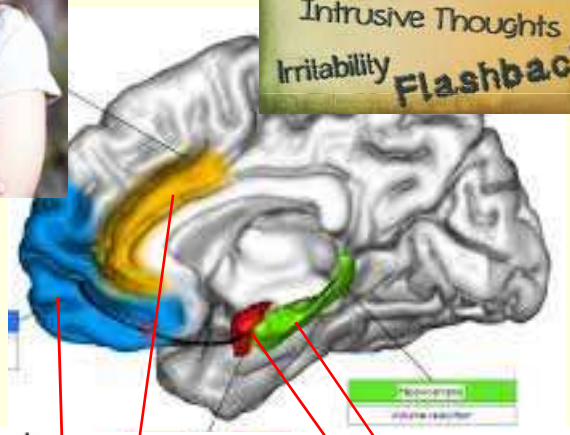
B) Somatic: nausea, vomiting, eating disorders (loss od appetite), headaches, palpitations - cardiac arrhythmia, sweating, tiredness ...

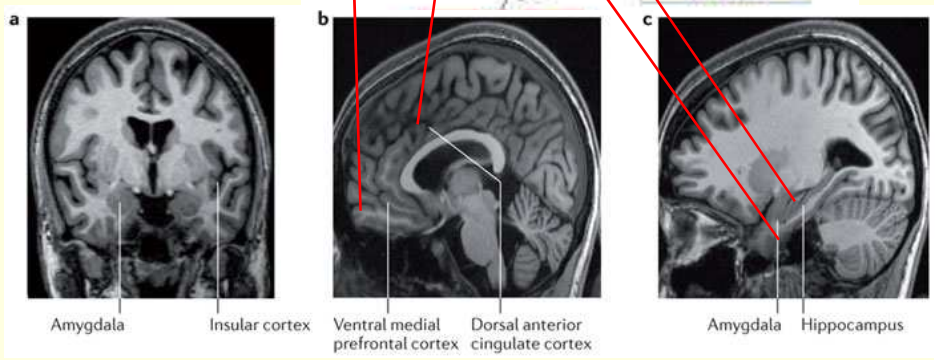
CT/ NMR: shrinkening of hippocampus, hyperactive amygala, insular cortex, anterior cigular & parahippocampal cortex

Pitman, R. K. et al.:: Biological studies of post-traumatic stress disorder. Nature Reviews Neuroscience 13, 769-787, 2012









Manager disease (MD)

- **Occ:** in 50s of the 20th century Germans claim high incidence of death from heart attacks among male managers (Managerkrankheit)
- *Later it was found as mistaken; actually significantly higher risk of heart attacks is in "lowest" professions + the risk is not higher among males) ??*
- **Etio:** long-term physical / mental switch in middle-aged men (40-60 years of age) in management positions;
- **Sy:**irritability, irritability, decreased concen-tration, flagging initiative, ignoring others depressed mood, sleep disturbances, anger, tendency to infarcion and stroke

Burnout syndrome (BS)

Syndrome of burning out, syndrome of aridity = even if working hard no real outcomes; cause people love smily nice stupidity

Occ: H. Freudenberger (1975) : occupations involving work with people and dependence on their assessment - teachers, practitioners, surgeons etc., loss of professional or personal interest

Sy: overall fatigue, emotional distress, cognitive exhaustion and "worn-out"; The actual burn is the result of a long gradual process, which has the following phases:

- 0, phase: individual works best, trying to, even though he feels that his work is not sufficiently reviewed
- Phase 1: the feeling that the individual is not fast enough to his work begins to lose system
- Phase 2: neurosis symptoms occur (eg. Anxiety); individual still has to do something, the result is a chaotic proceedings
- Phase 3: the feeling that something "must" be made to disappear; It replaces it with the opposite feeling - it does not have anything; the mere presence of other people Irritating individual, predominant fatigue, frustration and exhaustion

Emotional exhaustion (burnout)

Df: chronic state of physical and emotional depletion that results from excessive job and/or personal demands and continuous stress.

feeling of being emotionally exhausted by work.

Sy: both physical fatigue and a sense of emotionally "drained„

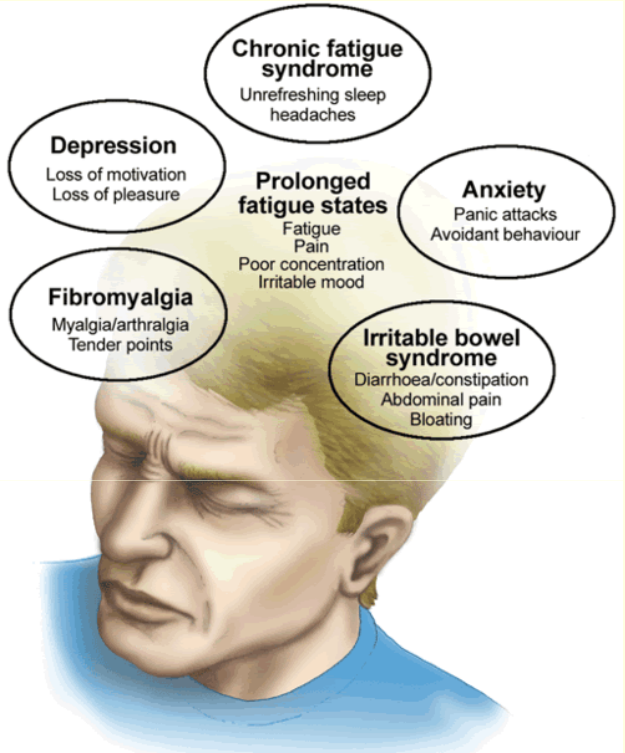
Maslach's and Jackson's three-component conceptualization of burnout. This model suggests burnout consists of three interrelated parts: emotional exhaustion, depersonalization, and diminished personal accomplishment.

Depersonalization, also called dehumanization, refers to a set of callous and insensitive behaviors displayed by a worker toward a client. Diminished personal accomplishment refers to negative evaluations of the self

Maslach C., Leiter M.P. (1997). The truth about burnout: How organizations cause personal stress and what to do about it. San Francisco, CA: Jossey-Bass. ISBN 0-7879-0874-6.

Chronic fatigue syndrome (CFS)

- Alternative names: systemic exertion intolerance disease (SEID), myalgic encephalomyelitis (ME), post-viral fatigue syndrome (PVFS), chronic fatigue immune dysfunction syndrome (CFIDS)
- long-term fatigue not due to ongoing exertion or disease, not much relieved by rest; seriously limit a person's ability to carry out daily activities; quality of life compromised
- **Occ:** 7 - 3,000 per 100,000 adults; ~ 1million US, ¼ million UK; more often in women than men, less common in children
- **Etio:** not understood; post-infective fatigue : viral / non-viral pathogens
- **Sy**:



- **A "flu-like illness„**: sore throat, headaches, painful, often slightly swollen lymph nodes, cardiac and respiratory problems.increased sensitivity to light, sounds and smells, digestive disturbances,
- **Physical muscular:** malaise after exertion; unrefreshing sleep, widespread muscle and joint pain, muscle weakness, problems standing upright,
- **Psychologic:** cognitive difficulties, chronic and severe mental and physical exhaustion, depression.