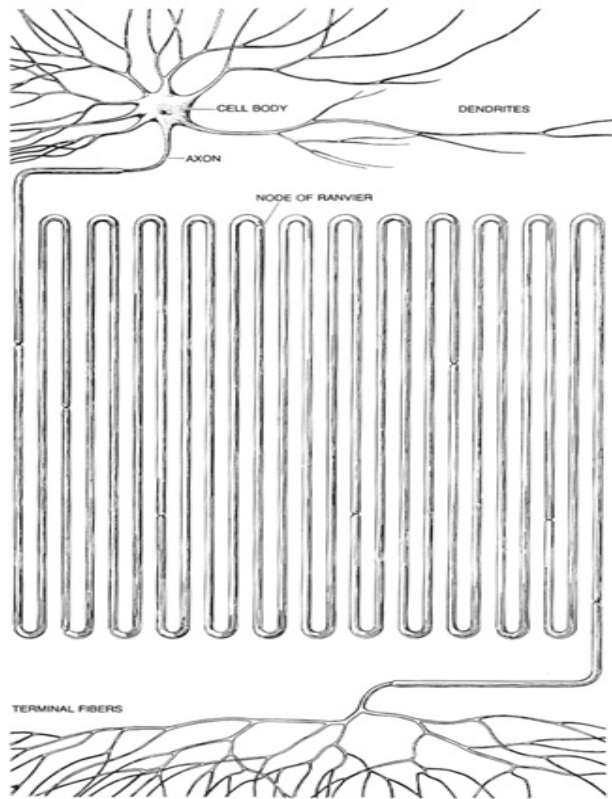
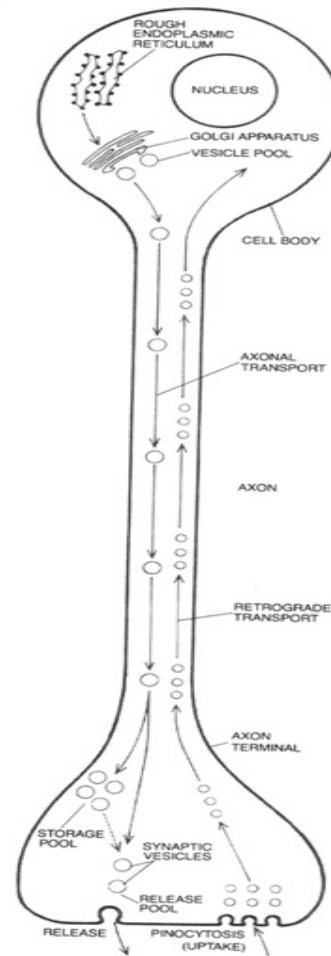


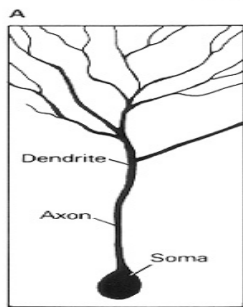
Prof. Š. Kujaník, MD, PhD: Comments to Central Nervous System



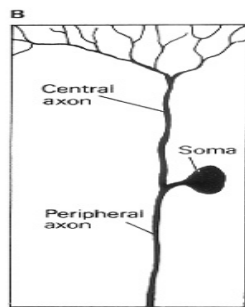
TYPICAL NEURON of a vertebrate animal can carry nerve impulses for a considerable distance. The neuron depicted here, with its various parts drawn to scale, is enlarged 250 times. The nerve impulses originate in the cell body and are propagated along the axon, which may have one or more branches. This axon, which is folded for diagrammatic purposes, would be a centimeter long at actual size. Some axons are more than a meter long. The axon's terminal branches form synapses with as many as 1,000 other neurons. Most synapses join the axon terminals of one neuron with the dendrites forming a "tree" around the cell body of another neuron. Thus the dendrites surrounding the neurons in the diagram might receive incoming signals from tens, hundreds or even thousands of other neurons. Many axons, such as this one, are insulated by a myelin sheath interrupted at intervals by the regions known as nodes of Ranvier.



unipolar Cells

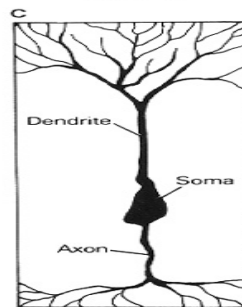


Invertebrate neuron



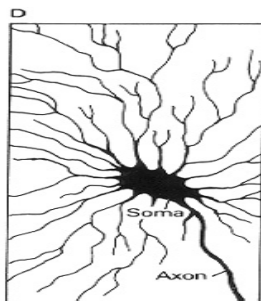
Dorsal root ganglion cell

bipolar Cell

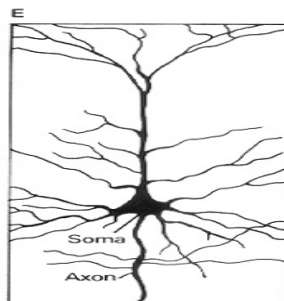


Retinal cell

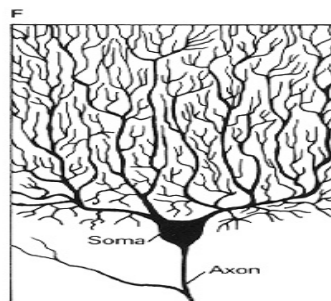
Multipolar cells



Spinal motor neuron

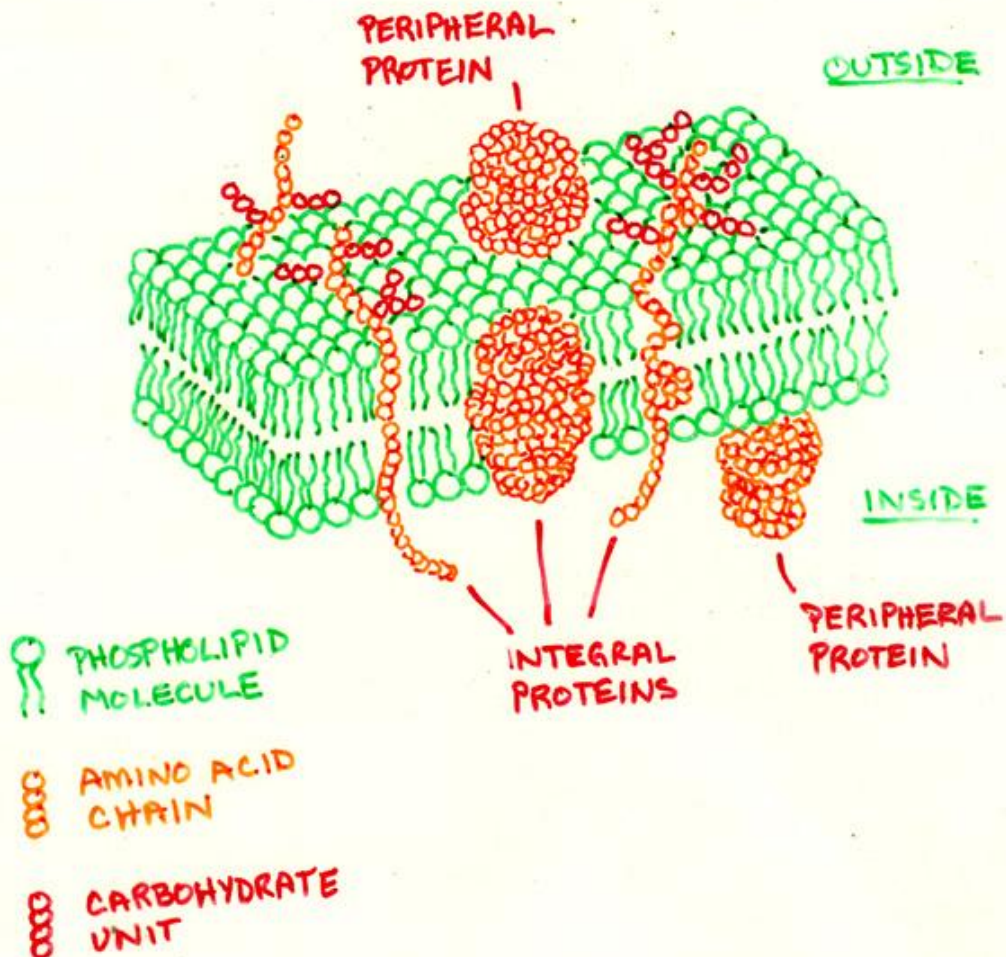


Pyramidal cell



Purkinje cell of cerebellum

FLUID MOSAIC MODEL OF CELLULAR MEMBRANE - LIPID BILAYER



RETICULAR FORMATION (RF)

RF is an important complex integrative functional system, influencing both the activity of the higher centres (included cerebral cortex) and the spinal cord. It collaborates with many central nervous structures. It is represented by diffused nerve cell bodies among the fibres in the MEDULLA OBLONGATA, PONS, MIDBRAIN, HYPOTHALAMUS, SUBTHALAMUS and cervical part of the SPINAL CORD. The typical nuclei are not present, it looks like a network. Connections with many other centres are mostly twosided. It has informations via collaterals from many ascendent and descendent pathways.

- RF CONTROLS AND COORDINATES many somatic and autonomic functions. Its network structure enables the convergence and divergence of informations. Some cells of the RF are able to produce impulses AUTOMATICALLY (centre of respiration, cardiac activity, vasomotorics, etc). However, under physiological conditions, its activity is

markedly influenced by other centres, particularly by the cerebral cortex, cerebellum, basal ganglia, vestibular apparatus and proprioceptors.

- The RF coordinates the somatic and autonomic functions, too. It influences also the activity of endocrine glands. In summary, the RF participates in control of almost all important functions of the body.

1. ASCENDING (ACTIVATING) SYSTEM OF RF (RAS) is activated by collaterals of the specific long sensory pathways. Input to the RF network without somatotopic localization produces loss of modality specificity => nonspecific system. So RAS bypasses the specific thalamic nuclei to project diffusely into the whole neocortex and to produce the conscious, alert state.

2. DESCENDING SYSTEM OF RF – acting on the spinal cord mostly by the reticulo-spinal tract. It ends on the spinal interneurons, alpha- and gamma-motoneurons and co-ordinates voluntary and involuntary movements. It includes two parts:

A) FACILITATORY PART is activated by statokinetic receptors (most important), vestibular cerebellum, collaterals of the specific sensoric pathways, and cerebral cortex. It increases excitability of spinal reflexory centres and increases the antigravitation muscle and extensors tone. Flexors tone is usually decreased. The facilitation effect is realized by interneurons. The facilitation region is important for upright body and head position.

B) INHIBITORY PART is activated by the spinal cerebellum, basal ganglia, and cerebral cortex (suppressor areas). The spinal reflexes and extensors tone are inhibited.

DECEREBRATE RIGIDITY: muscular rigidity produced experimentally by cutting the brain stem between the superior and inferior colliculi. It demonstrates the activity of higher centres of the CNS on the tone of antigravitation muscles. The cut between both colliculi removes the influence of higher CNS centres activating the descendent inhibitory part of the RF. Therefore the predominance of the facilitatory part and increased tone of extensors are produced. The extremities are extended (more in lower ones), the head is in position back.

THE HYPOTHALAMUS (HT)

HT – an important subcortical somatic and autonomic integrative centre.

Main functions of the HT:

1. THERMOREGULATION – here are situated the receptors for temperature of the flowing blood and maintaining the constant body temperature ($37 \pm 0.5^{\circ}\text{C}$). Temperature can be produced if it is cold (by chemical thermoregulation = chemical reactions producing heat – in the liver and kidneys, stimulation by epinephrine, norepinephrine and thyroid hormones) or released from the body if it is warm (by physical thermoregulation = physical mechanisms – conduction, convection, radiation mostly).
2. INTEGRATION of BEHAVIORAL REACTIONS – e.g. fight or flight reaction after stress, rage, punishment and reward reactions, (small animals in a cage with food but also in humans with aggressive or silent behavior), the collaboration of HT with the limbic system and cerebral cortex.
3. CONTROL of SEXUAL BEHAVIOR – to follow a sexual partner for reproduction and children, this is stimulated by sexual hormones (oestrogens in women or testosterone in men)
4. CONTROL of FOOD INTAKE – to maintain the constant body weight for a long time. In humans it must be under control of the cerebral cortex and voluntarily (to prevent obesity).

- a) SATIETY CENTRE is situated in the ventromedial HT nucleus dependent on the glucose blood level and perceived like a positive sensation after food
- b) HUNGER CENTRE is situated in the lateral HT nucleus, it has the permanent activity which is decreased for some time by stimulation of the satiety centre after food intake
- c) HYPOTHALAMIC GLUCOSTATIC NEURONS (glucostats) – the cells sensitive to the blood glucose level, participating in the glycaemia control

5. CONTROL of WATER INTAKE by osmoreceptors and volumoreceptors. Osmo-receptors are in the wall of the third brain chamber with the incomplete haemato-encephalic barrier. The increased osmotic pressure here stimulates secretion of antidiuretic hormone ADH from neurohypophysis and that stimulates permeability and reabsorption of water in the renal collecting ducts. Volumo-receptors are in the cardiovasc. system & increased blood volume blocks ADH production in the HT and stimulates excretion of abundant water in the renal tubules by urine. The definite urine has the specific weight 1003 – 1030.

6. CONTROL of ADENOHYPOPHYSIS (Anterior pituitary gland) – Releasing hormones RH (liberins) from the median eminence of the HT (somatoliberin, thyreoliberin, corticoliberin) stimulate production and secretion of the pituitary hormones (ACTH, growth hormone, TSH, etc). Inhibiting hormones (statins) (somatostatin, prolactostatin) block secretion of anterior pituitary hormones (growth hormone and prolactin).

7. CONTROL of NEUROHYPOPHYSIS (Posterior pituitary gland) – production of oxytocin and vasopressin in the supraoptic and paraventricular HT nuclei, production of other humoral agents by neurosecretion in the neurosecretory cells (neurons).

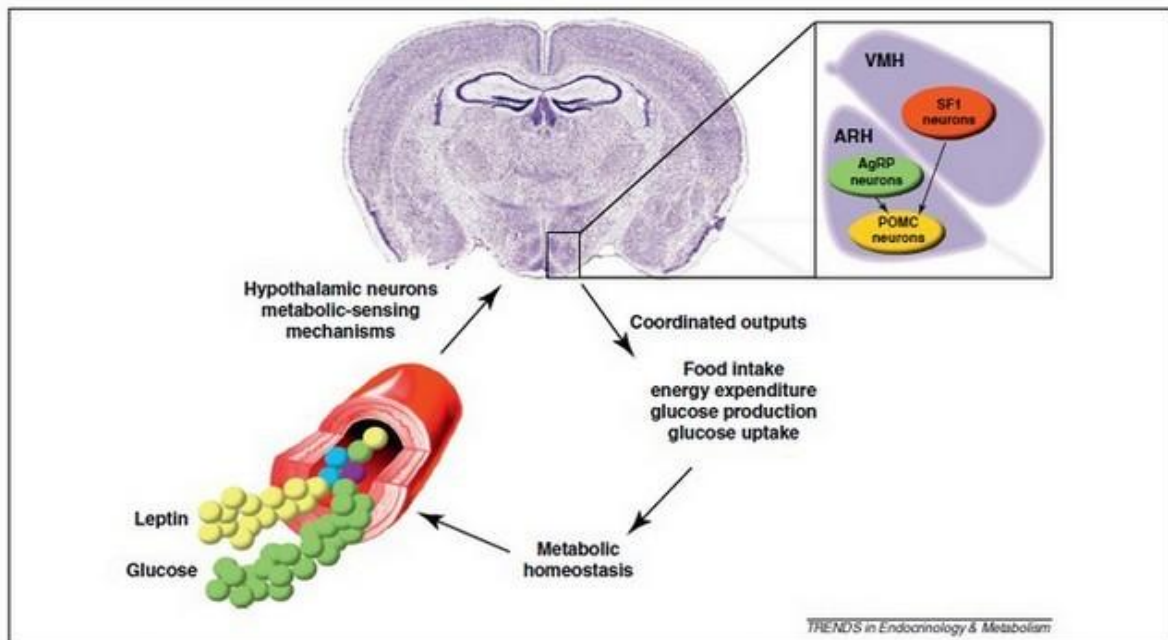


Figure 1. A model depicting hypothalamic-mediated control of metabolic homeostasis. AgRP and POMC neurons in the hypothalamic arcuate nucleus (ARH) and SF1 neurons in the ventromedial hypothalamic nucleus (VMH) are able to detect fluctuations in circulating levels of metabolic cues (e.g. leptin and glucose) and to coordinate responses (e.g. changes in food intake, energy expenditure, glucose production from the liver, and glucose uptake by the skeletal muscle) aimed at maintaining normal body weight and glucose balance. Projections from AgRP and VMH neurons to POMC neurons are also depicted.

AUTONOMIC NERVOUS SYSTEM (ANS)

AUTONOMIC NEUROTRANSMITTERS:

- a) preganglionic – SYMP – acetylcholine (via nicotinic N-receptors)
- PASYMP – acetylcholine (via nicotinic N-receptors)

- b) postganglionic – SYMP – noradrenalin (via adrenergic, α -, β -receptors)
 - PASYMP – acetylcholine (via cholinergic, muscarinic M-receptors)

Differences between the somatic and ANS

Somatic NS	Autonomic NS
1-neuron pathways	2-neuron pathways
31 spinal segments	22 spinal segments
nerve fibres of type A	nerve fibres of type B or C
short latency	longer latency
higher lability	lower lability
	summation (spatial or temporal) is typical
Neurotransmitter – acetylcholine	different neurotransmitters in the SYMP or PSYMP systems
fast EPSP	slow EPSP, present IPSP

Differences between the SYMP and PASYMP systems

SYMPATHETIC SYSTEM	PARASYMPATHETIC SYSTEM
Paravertebral or prevertebral ganglia	Terminal ganglia
Ganglia far from the effectors	Ganglia near the effectors
Short preganglionic fibres	Long preganglionic fibres
Long postganglionic fibres	Short postganglionic fibres
Large divergence 1:20	Small divergence 1:1
Effect is generalized	Effect is more localized
Sympatho-adrenal reaction	-----
Prolonged duration of effect	Shorter duration of effect
Postsynaptic neurotransmitter - NA	Postsynaptic neurotransmitter - ACH
NA has a longer effect	ACH has a shorter effect
NA is present in blood plasma	ACH is absent in blood plasma

AUTONOMIC REFLEXES: are not constant, can be unconditioned or conditioned, dependent on the autonomic tone, functional state of organism or effectors, SY-PASY tone

1. Viscero-visceral: gastro-colic, gastro-ileal, sinocarotic, orthostatic, clinostatic, Goltz
2. Viscero-motor: a sick visceral organ produces skeletal muscle spasm in some region
3. Viscero-cutaneous: changes in the skin (sweating, changed blood flow) during diseases of visceral organs
4. Cutaneo-visceral: stimulation of skin receptors produces changes in function of visceral organs (oculo-cardiac reflex, effects of cold or warm compresses)

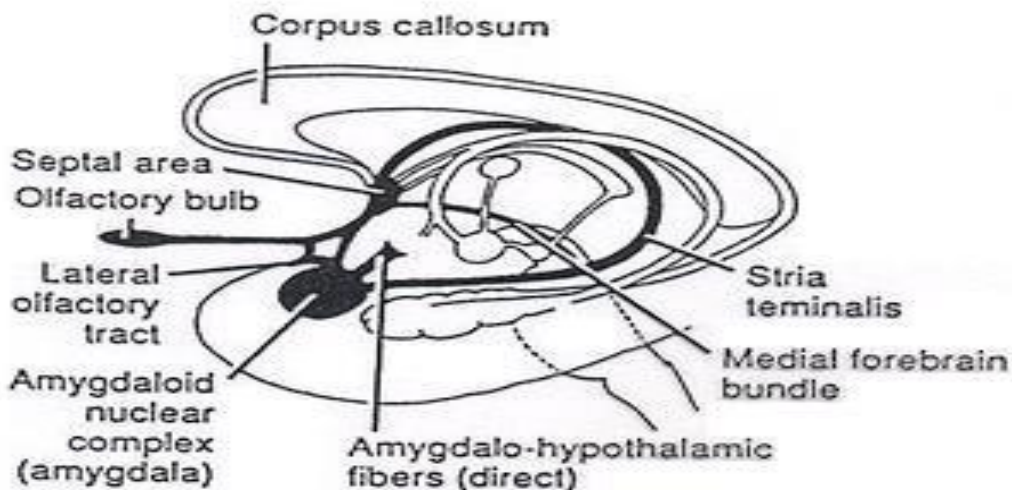
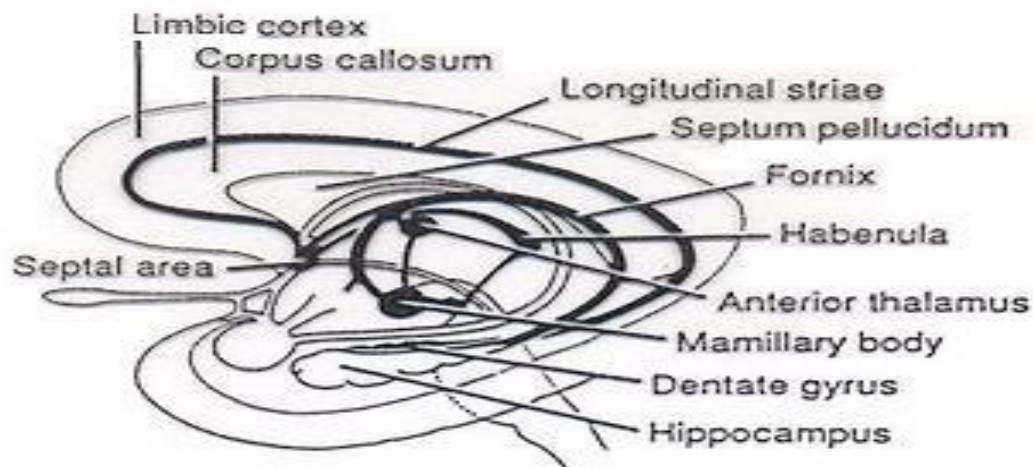


Figure 15–2. Principal connections of the limbic system. **Top:** Hippocampal system. **Bottom:** Olfactory and amygdaloid connections. (Reproduced, with permission, from de-Groot J: *Correlative Neuroanatomy*, 21st ed. Appleton & Lange, 1991.)

The schedule for movement is produced in associative cortical centres, from where it comes to the basal ganglia and cerebellum. Programmes for a fast fine aimed motorics are in cerebellum, the basal ganglia realize programmes for slow extensive movements. Programs input via thalamus the motoric cortical regions as a starting point from which a movement realization is controlled. Informations conducted in pyramidal tracts are modified by situation in effectors and by a system of complex feedbacks controlled by the cerebellum, basal ganglia and RF. Informations must be processed fastly – the nervous fibres are Aα.

ELECTRICAL ACTIVITY OF THE BRAIN

There are 4 types of the electrical activity of the brain:

(1) CELLULAR (UNITARY) ACTIVITY

a) spontaneous – action potentials of the nervous cells (resting potential -50 to -80 mV, amplitude 110-120 mV, duration 0.5-2 ms, negative and positive afterpotentials)

b) evoked potentials (EP)

- primary EPs (biphasic course after a short latent period, from receptors through the specific ascendent pathways to the primary cortical centre)
- secondary EPs (through the nonspecific ascendent system of the RF to the cerebral cortex diffusely)

(2) SUMMARY ACTIVITY – spontaneous or evoked

According to the site of recording:

- from the skull surface (EEG)
- from the surface of cerebral cortex or pia mater (ECoG)
- from the deep structures (deep recording)

According to the leads used:

- BIPOLAR recording (between 2 active electrodes) - most frequently
- UNIPOLAR recording (between 1 active and 1 indifferent electrodes)

(3) UNIDIRECTIONAL POTENTIAL - unipolar recording (+15-20 mV)

(4) IMPEDANCE (ELECTRICAL RESISTENCE) - reflects the extracellular conductivity. It can be changed during transmission of ions or pathological conditions

SLEEP

Sleep is a special kind of generalized internal inhibition in the cerebral cortex & some subcortical structures accompanied with expressed changes of electrical activity. Centres of the vital functions (breathing, cardiovascular activity) are not inhibited.

EEG rhythms:

- alpha (8-13/s, 30-50 μ V, at rest in the recumbent position with closed eyes, wandering mind)
- beta (14-30/s, 5-10 μ V, after opening of the eyes, during input of informations to the brain or during any activity)
- theta (4-7/s, 50 μ V, in small children also in consciousness)
- delta (1-4/s, 100-150 μ V, slow waves with a high amplitude, in small children also in conscious stage, typical for the deep sleep)
- gamma (35-40/s, 3-5 μ V, top exercise or experience)
- mu (μ) (8-10/s, 20-50 μ V, increase in attention)

DIVISION OF SLEEP – physiological (spontaneous), hypnotic, narcotic, pathologic

DURATION OF SLEEP – from 16 hours (newborns) till 5-6 hours (in elderly)

CHANGES DURING SLEEP:

- decrease in the heart rate, respiratory rate, blood pressure, metabolism, excitability of the nervous system
- increase in the blood flow in the brain stem, oxygen consumption, activity of some enzymes, RNA, ATP and protein production in the brain

2 TYPES OF SLEEP:

(1) rapid eye movements (REM, paradoxical, desynchronized, fast) sleep

(2) non-REM (NREM, slow-wave, orthodoxal) sleep

(1) Stages of NREM sleep:

1st stage - low amplitude & high frequency EEG, higher alpha-rhythm

2nd stage - relaxation, decrease in frequency (F) & increase in amplitude (A) of the EEG, alpha-like sleep spindles

3rd stage - decreased muscle tone, theta-rhythm, further changes of F & A

4th stage - delta-rhythm, the lowest F & highest A, synchronization (rhythmic slow waves), important for regeneration, somnambulism (parasomnia, sleepwalking)

(2) REM sleep: increased blood flow in the brain stem, dreams are present in this type, desynchronization, important for fixation of informations, waves similar to beta-waves

DESYNCHRONIZATION (arousal or alerting reaction) – replacement of the alpha-rhythm with irregular low-voltage activity, breaking of the synchronized activity, produced by a sensory stimulation

THEORIES of the CAUSES of SLEEP:

(1) passive – the decreased activity of RAAS

(2) sleep centres – the active inhibitory process from the centres below the midpontile level of the brain stem

(3) humoral – produced by several humoral compounds: delta-sleep producing peptide, muramyl peptide (experimental sleep), blockade of serotonin formation

(4) histological – produced by changes in the form of neurons

(5) sleep centre – stimulation of several regions in the diencephalon produces sleep (Hess)

(6) cortical (Pavlov) – generalized inhibition situated in the hemispheres

(7) electrophysiological – the most accepted theory recently, the REM and NREM sleeps are two different stages

COURSE OF SLEEP:

- 4-6 sleep cycles (60-90 min each) are during night, the further one is longer than the previous one
- successive prolongation of the REM sleep phase
- during falling asleep is REM sleep not present
- not all 4 stages of the NREM must be always expressed in each cycle
- after the last NREM sleep awakening arises without REM phase
- duration and depth of sleep usually decreases with age
- somnambulism (sleepwalking) in some persons

CONSCIOUSNESS (VIGILITY)

It is the dynamic communication between the organism and environment.

The most important STRUCTURES FOR MAINTAINING CONSCIOUSNESS:

- the reticular formation (RAS diffusely to the whole cerebral cortex)
- the thalamus
- the hypothalamus
- the limbic system
- the mesencephalon

- the rostral (anterior) parts of the brain
- serotonergic neurons (serotonin stimulates sleep, serotonin disorders inhibit sleep)
- the descendent systems securing excitability of many receptors

TRANSIENT PHASES BETWEEN CONSCIOUSNESS AND SLEEP

- (a) Equilibrical – the same effect of both strong & weak stimuli
- (b) Paradoxal – weak effect of the strong stimuli, strong effect of the weak ones
- (c) Ultraparadoxal – the positive conditioned stimulus inhibits, the negative one stimulates development of the conditioned reflexes (CRs)
- (d) Narcotic – ability of development of the CRs is decreased
- (e) Inhibitory – no CRs are developed

LOWER NERVOUS ACTIVITY

are the INBORN ASSOCIATIVE & INTEGRATIVE MECHANISMS of the CNS:

(1) Simple unconditioned reflexes:

- (a) reflexes inevitable for life and reproduction (suckling rfl, breathing, deglutition, micturition, defecation)
- (b) defensive reflexes – to avoid the dangerous & harmful influences (flight, to drag away the extremity after pain, vomiting, cough, sneezing)

(2) Reactions "drive" – stimulation to do something (to secure breathing, food & water intake, reproduction, etc.)

(3) Emotions and motivations

Emotions – pleasure, anger, rage, fear (centre the limbic system)

Motivations – reasons controlling our behaviour (motivation to learn, to have som hobby, to win in sport)

(4) Instincts – set of motoric activities & behaviour, typical for one species. They secure a better adaptation to changed conditions of life but sometimes they can be harmful (insect flies to the fire).

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HIGHER FUNCTIONS OF THE NERVOUS SYSTEM (HNA)

They are the functions bound with the cerebral cortex, reticular formation, limbic-hypothalamic circuit – learning, memory, judgment, language, based predominantly on the conditioned reflexes.

CONDITIONED REFLEXES (CR)

They develope after birth, their formation needs certain maturity of the nervous system (NS) (completed myelination & time) and several conditions. Most of reflexes are conditioned (CR)

CONDITIONS OF THEIR DEVELOPMENT:

- (1) existence of an inborn unconditioned reflex UR (the unconditioned stimulus and reflectory arch) or already existing CR
- (2) the conditioned stimulus CS which normally produces some other UR, indifferent for the first UR
- (3) the CS must be applied simultaneously with or immediately after the unconditioned stimulus (US)
- (4) repeated stimulation (CS + US) many times
- (5) development of the temporary connection between centres of both UR), usually in the cerebral cortex - then the new CS produces an effect of the first inborn UR
- (6) fastening (after some period since the development of the CR it is necessary to apply the CS & US together again)

SPECIAL CONDITIONED REFLEXES:

- DYNAMIC STEREOTYPES (walking, car or motorbike driving, sports, writing, painting, etc.)
- ACTION OF DRUGS (positive or negative effects)
- CONDITIONED AVOIDANCE REFLEXES (to avoid unpleasant events – insects, snakes, some food)
- FOOD AVERSION CONDITIONING (some food can elicit the conditioned vomiting – result of unpleasant influences in the past)
- CRs of HIGHER ORDER (on the basis of one CR other CR is developed)

THE DOMINANT CENTRE – a permanently active centre in the cerebral cortex which is able to attract informations (excitation) from surrounding cortex and support its activity. Dominant are usually the biologically important centres or pathologically (by long-lasting stress) arising centres.

INHIBITION OF CONDITIONED REFLEXES (CRs)

CRs can develop and later disappear. Disappearing (inhibition) has 2 mechanisms: internal and external.

1. INTERNAL (CONDITIONED) INHIBITION (ICI):

It is developing gradually & on the basis of the conditioned stimulus (CS).

4 types of ICI according to the development:

a) CS is not supported by the unconditioned stimulus (US) e.g. by food in salivary reflex and later it disappears

b) a longer pause between both stimuli (US and CS) – the reaction is after the US only, not after conditioned one (CS)

c) differential inhibition – after a similar (not the same CS) which is perceived like a new stimulus and inhibits the before developed CR

d) proper conditioned – with other (inhibitory) CS the development of inhibition is produced after 2 CS and no unconditioned stimulus (US)

2. EXTERNAL (UNCONDITIONED) INHIBITION (EUI):

External inhibition is inborn, not developing & arises immediately after the first application of the stimulus. It can be of three types:

a) an additional nociceptive stimulus can inhibit the development or manifestation of the functioning CR

b) that accessory stimulus is biologically unimportant, i.e. not necessary for development of a new CR

c) over-limit (protective EI) – after a very strong stimulus (also adequate) producing a very strong stimulation of the CNS with protective inhibition of the CNS structures

THE FIRST AND SECOND SIGNAL SYSTEMS

THE FIRST SIGNAL SYSTEM (FSS) – the collection of CORTICO-SUBCORTICAL MECHANISMS securing development of the CRs to CONCRETE SENSORY STIMULI from the external environment (visual, auditory, tactile, smell, taste, pain). FSS is common for animals & humans and necessary for analysis and synthesis of the direct (concrete) signals of those sensory stimuli. They produce impressions, sensations, and concepts of the external environment. FSS is typical for animals & small children – important for sensory recognition of things, to get food, nutrition and reproduction. In adults its activity is under control of the second signal system.

THE SECOND SIGNAL SYSTEM (SSS) – the collection of cortical mechanisms securing the development of the CRs to ABSTRACT STIMULI (words in heard or written form – secondary signals). They are the abstract signals of concrete signals, present in our mind only). SSS is characteristic for humans only and is accompanied with development of speech and writing – recognition by the psychical activity (abstract thinking, memory, learning, writing and generalization in our mind).

COLLABORATION OF SEVERAL CORTICAL CENTRES in speech:

- The Broca motoric centre of speech (in the dominant hemisphere) – in the frontal gyrus, an integrative function
- The Wernicke sensory centre of speech situated near the auditory centre (border of parietal and occipital lobe), an integrative function

- The differentiation centre in the associative parietal cortex
- The proprioceptively-logesthetic area (perception of word understanding)
- The proprioceptively-graphesthetic area (perception of written word understanding)
- The graphomotoric area (for movements of muscles in writing)
- The visual cortical area (in the occipital lobe – the calcarine area)
- The auditory cortical area (in the gyruses of Heschl)

The IMPORTANCE OF SIGNAL SYSTEMS for:

- (1) DEVELOPMENT OF CRs after abstract signals important since schoolchildren
- (2) MEMORY – learning by means of the concrete & abstract signals
- (3) ABSTRACT THINKING – generalization (speech and writing) without concrete signals (already preschool children start to differentiate general concepts and concrete things)
- (4) COMMUNICATION AMONG PEOPLE – speech and writing

TYPES OF HIGHER NERVOUS ACTIVITY (HNA)

There are several typologies of the higher nervous activity:

- (1) HIPPOKRATES and later Galenos – according to the predominance of one of body fluids (blood, white bile, black bile, phlegm) – SANGUINIC, CHOLERIC, PHLEGMATIC, MELANCHOLIC TEMPERAMENTS or types
- (2) Russian academician I. P. PAVLOV (the Nobel prizier) – according to the powerful, balance & mobility of the nervous processes (excitation, inhibition) and development of CRs
 - (a) according to powerful – intensity of E and I in the CNS (STRONG & WEAK)
 - (b) according to their balance – relation between E and I (EVEN-TEMPERED or BALANCED and IMBALANCED)
 - (c) according to their mobility – ability of exchange of E to I (MOVABLE & IMMOVABLE)

By combinations of those nervous processes – FOUR BASIC TYPES OF HNA:

- weak (small intensity of E and I, often protective = overlimit inhibition) = melancholic temper
- strong imbalanced (intensive E and I, predominance of E, explosive type) = choleric temper
- strong balanced movable (intensive both E and I, they are in equilibrium, rapid exchange) = sanguinic temper
- strong balanced immovable (intensive both E and I, they are in equilibrium, slow exchange, slow adaptation) = phlegmatic temper

=> division is similar to Hippokrates + Galenos, but the causes are absolutely different !!!

- (3) OBRAZTSOVAYA – she had been a follower of Pavlov and extended his division into 4 variants according to the powerful, 3 ones according to balance, and 10 ones according to mobility => 120 types together are finally available

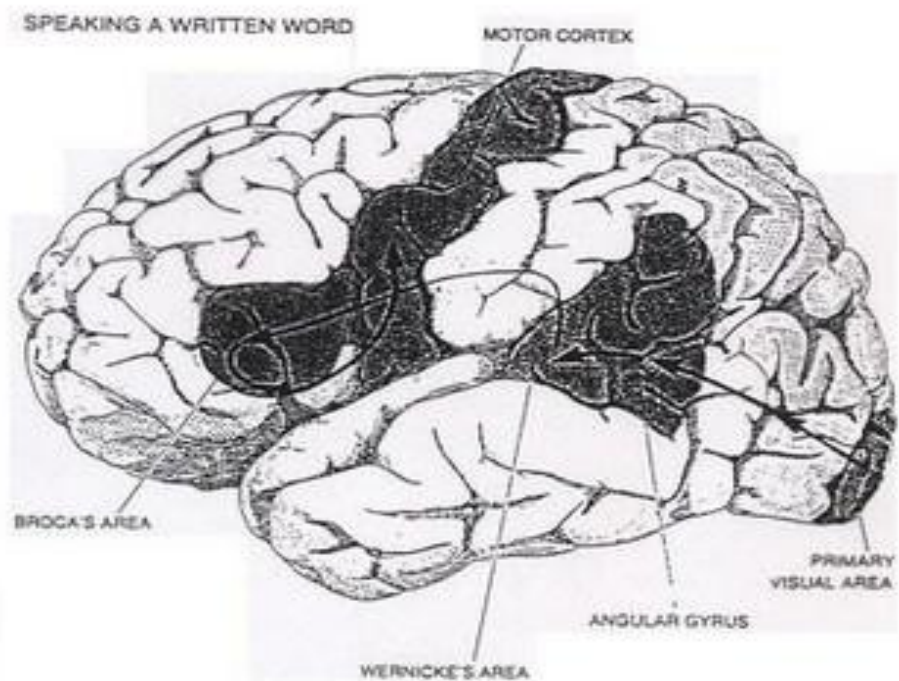
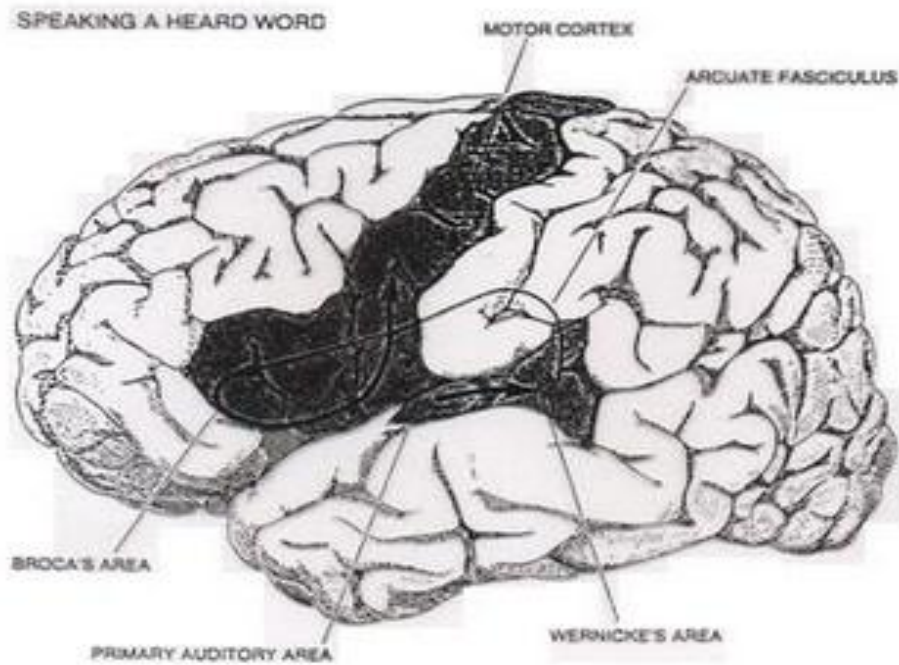
- (4) ACCORDING TO RELATION BETWEEN 1st & 2nd SS:

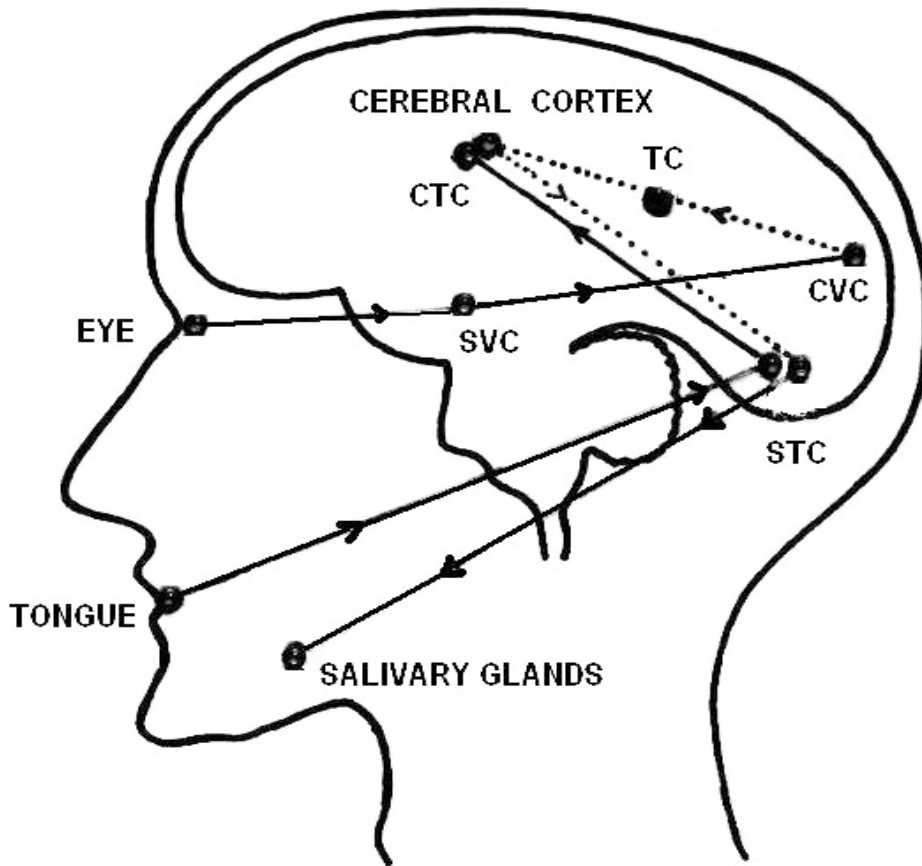
- artistic type (prevailing the 1st SS) – the concrete signals are characteristic (artists) for them

- scientific type (prevailing the 2nd SS) – the abstract thinking is typical (scientists) for them

- mixed type (equilibrium of the 1st & 2nd SS) – most of people are this type

(5) SKINNER CONDITIONING (according to the American psychiatrist) – a more active adaptation of the experimental animal to the conditioned in the rat box. Solution of the problem how to get the food despite the electrical stimulation of the rat on the way (step) before food.





The conditioned reflex of salivation (Practical lessons)

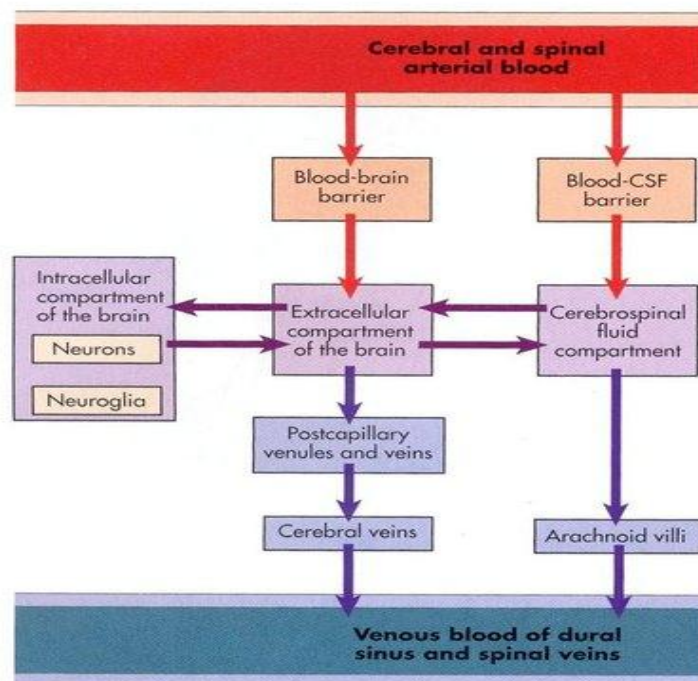


FIGURE 6-4. Structural and functional relationships involved in the blood-brain and blood-CSF barriers. Substances entering the neurons and neuroglial cells (i.e., intracellular compartment) must pass through the cell membrane. Arrows indicate the direction of fluid flow under normal conditions.

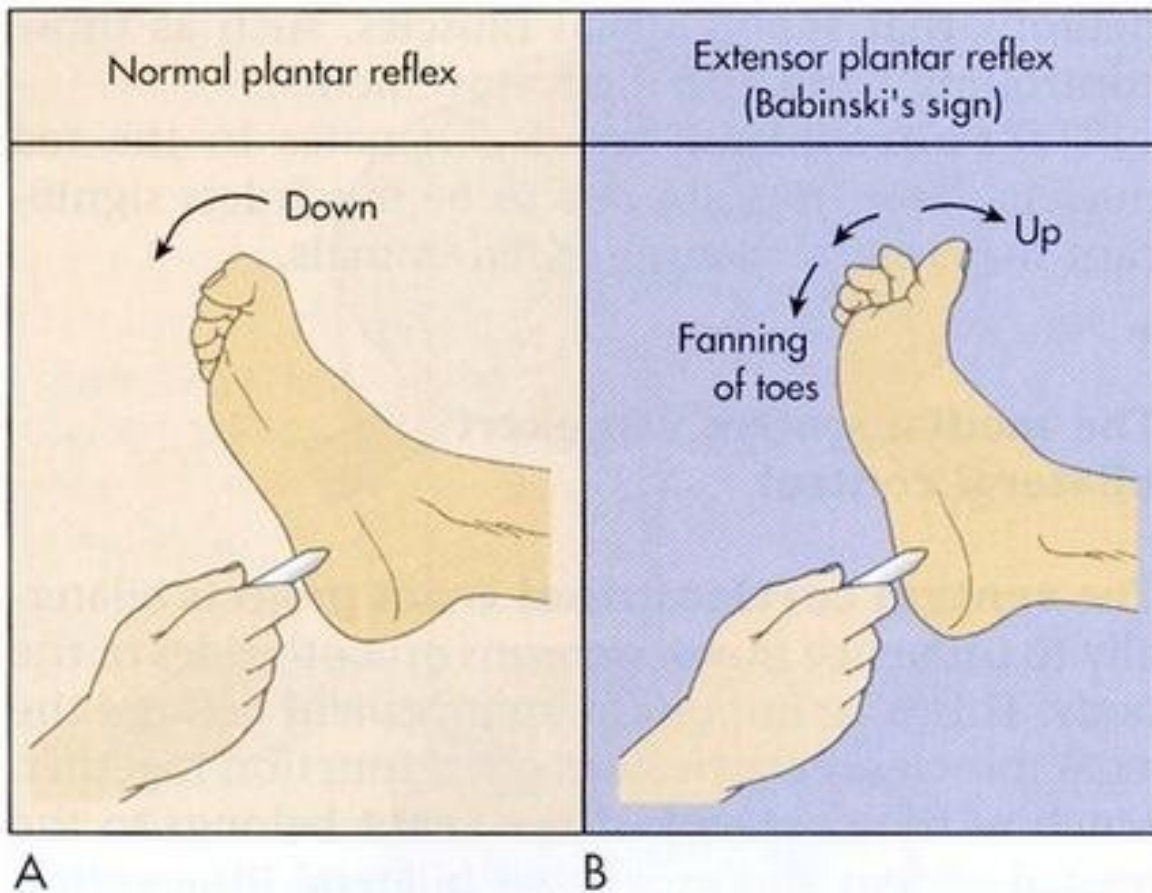
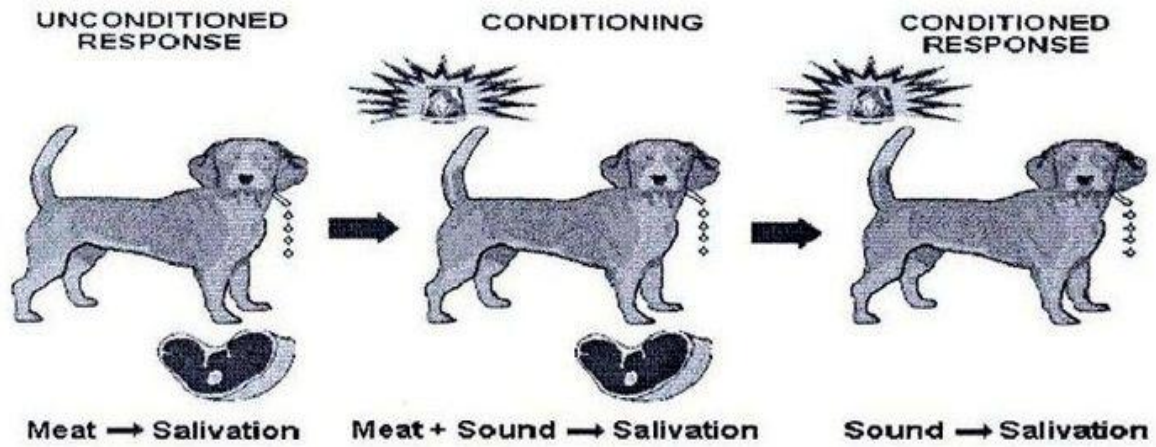


FIGURE 9-16. Babinski's sign. **A**, The normal response to stroking the plantar surface of the foot. **B**, Babinski's sign (extensor plantar reflex) in a person with interruption of the corticospinal tract.