Other senses: taste, smell, touch

Senses – general information

receive specific kind of stimuli (information):

- from the external environment by **exteroceptors**
  - smell, taste, vision, hearing, touch and pain
- from the internal environment by **interoceptors**
  - proprioception, pain, internal environment
- on the border of both – balance
  - perception of body movement is based on interoceptors and on the use of inertial forces in the inner ear

general classification:

- **primary** (receptor is directly a neuron)
- **secondary** (epithelial – receptor is an epithelial cell underlain with a dendrite)

Primary receptors

neuroepithelial

- smell
  - receptor: oflactory cells of olfactory epithelium of nasal cavity
- vision
  - receptor: rods and cones of retina of eyeball

neuronal

- touch, pain(nociception), proprioception
  - receptors: free nerve endings of skin, joints, fasciae, organs OR encapsulated nerve endings of skin (tactile corpuscles), tendons (Golgi tendon organs) and muscles (muscle spindles)
- internal environment – free and encapsulated nerve endings, nerve cells bodies
  - chemoreceptors
    - monitoring: blood acidity (pH), oxygenation level (partial pressure of CO_2 and O_2), glucose blood level, hormones blood levels, ions urine level
  - osmoreceptors
    - monitoring: blood osmolality
  - baroreceptors
    - monitoring: blood pressure

Secondary receptors

- hearing
  - hair cells of membranous cochlea of internal ear
- balance
  - hair cells of membranous labyrinth of internal ear
- taste
  - gustatory cells of gustatory buds of papillae on tongue and palate

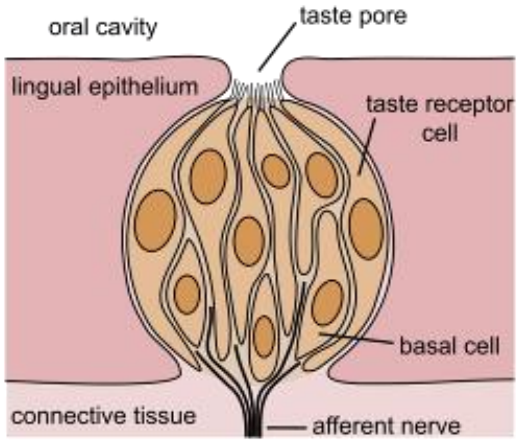
Taste (*Gustus*)

Greek: **geusis**

Organum gustatorium
Gustatory organ

- secondary receptors
- receptor cell has a synapse with peripheral process of 1-order neuron of gustatory pathway
- in mucosa of 8-12 papillae vallatae of tongue
  - arranged in a shape of letter V just in front of sulcus terminalis linguae
- also in mucosa of papillae fungiformes et foliatae of tongue
- also in mucosa of soft palate, posterior wall of pharynx, plicae glossoepiglotticae and epiglottis
- also free nerve endings can function as gustatory receptors

Organum gustatorium
Gustatory organ



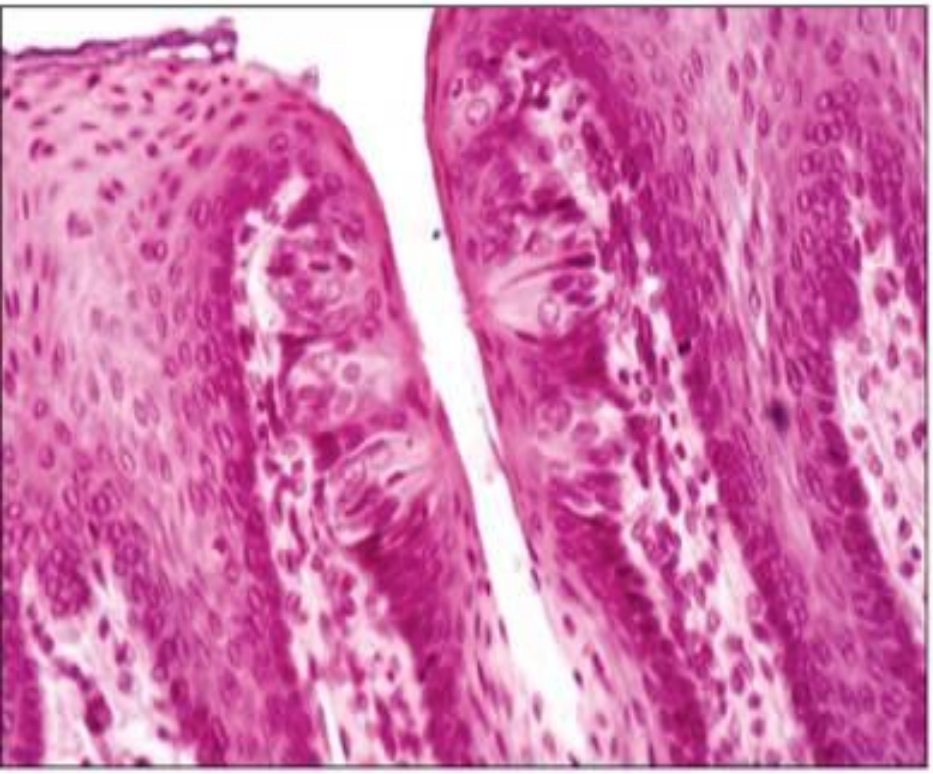
- vallate papilla (*papilla vallata*)
  - 1-2 mm wide
  - ***vallum papillae*** – outer wall (rampart)
  - ***sulcus papillae*** – circular groove around papilla, its wall contain gustatory buds
  - salivary glands open into the floor of sulcus papillae

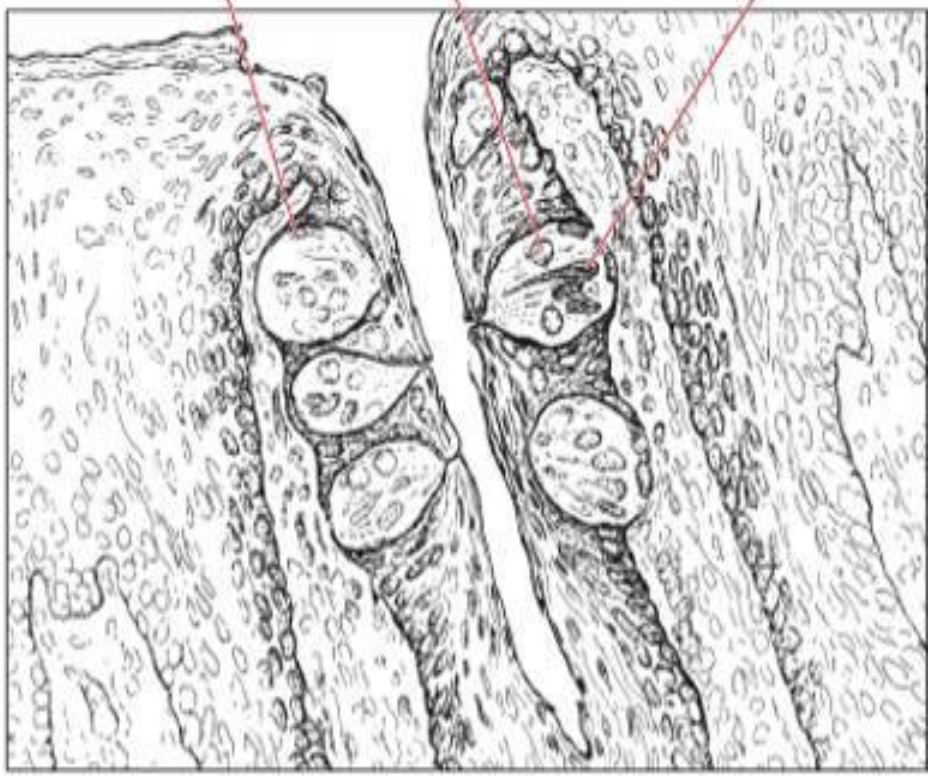
- **gustatory bud** (*gemma gustatoria, caliculus gustatorius*)
  - 50-150 cells (70 x 40 μm)
  - 5000 buds on tongue (250 in papilla vallata)
- gustatory pore (*porus gustatorius*)
  - superficial pit is the access into the bud


Stratified squamous epithelium non-keratinized
Trench
Taste buds
Connective tissue
Nerve fibers
Serous glands of von Ebner

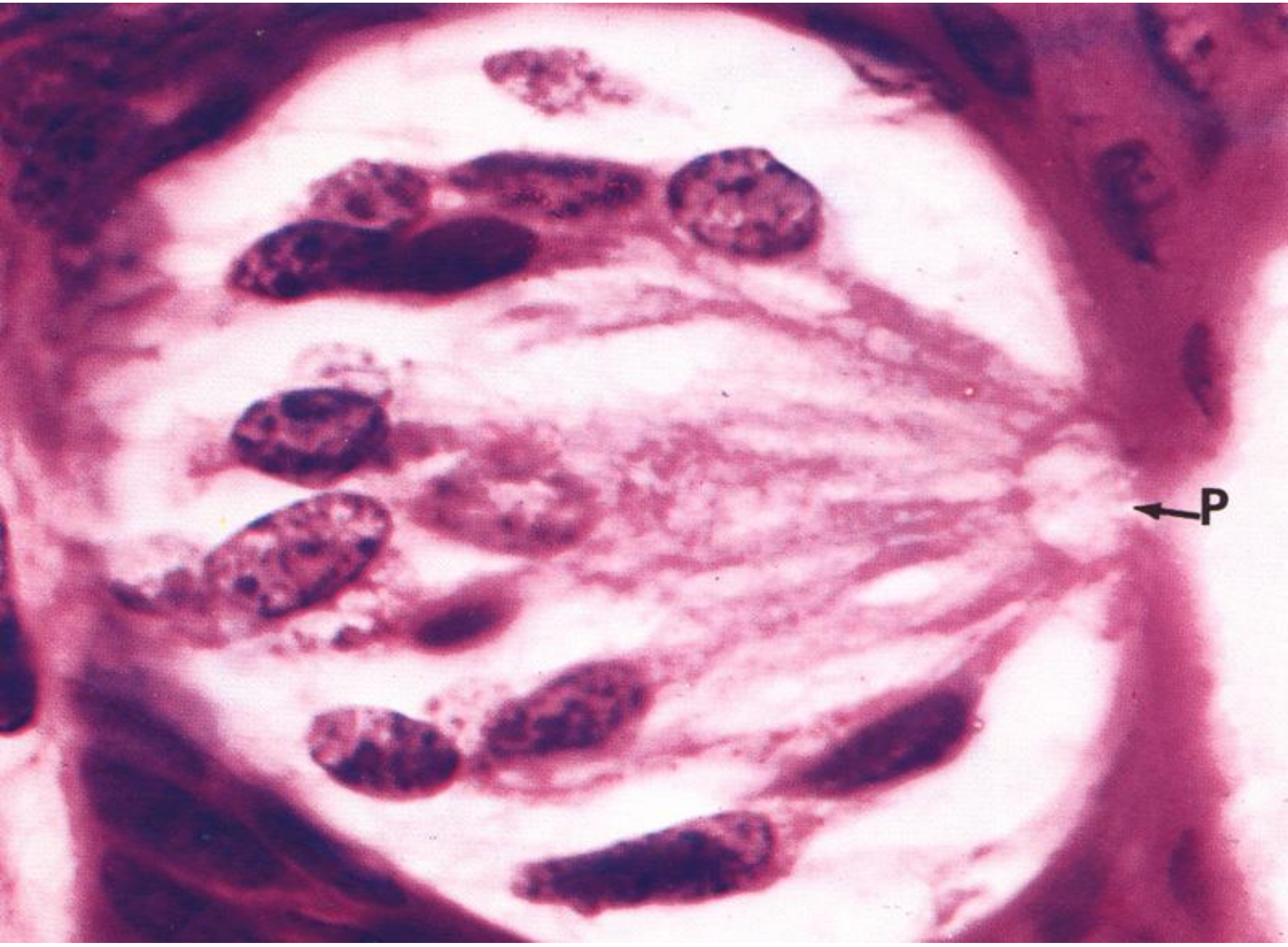
Gemma gustatoria
Gustatory bud

- development: Week 11–13
  - cells come from chorda tympani, n. IX, n. X
  - reaction by accelerated swallowing and facial movements (Week 26)
- 4 cell types – together 100–150 cells
  - gustatory cells (*epiteliocytus gustatorius*)
    - microvilli
    - chemoreceptors, secondary receptors (type I)
  - supporting cells (*epiteliocytus sustenans*)
  - basal cells (*epiteliocytus basalis*)




Basal cell
Gustatory cell
Sustentacular cell


T

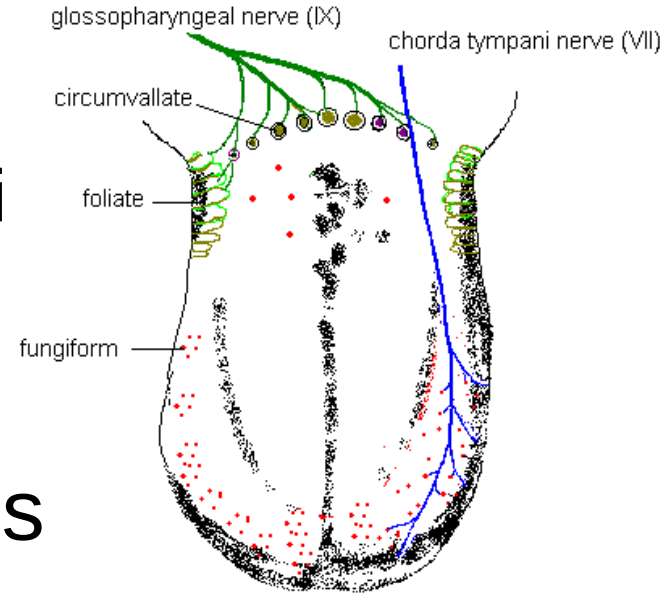

P

Accessory stucture of gustatory organ

- **glandulae gustatoriae *von Ebneri* (*pars profunda glandulae lingualis posterior*)**
  - fine serous salivary glands adjacent to papillae vallatae
  - compound branched tubulous to tuboalveolar gland
  - product contains enzymes starting introductory cleavage of nutrients (lingual lipase, acid phosphatase, nonspecific esterase, salivary amylase)
  - cells contain secretory granules with peroxidase → reduced number of bacteria around papillae → no infection
  - ducts open into floor of grooves round papillae vallatae
  - saliva dissolves substances perceived by taste and rinsed out the gustatory buds

Taste = *Gustus*

- basic kinds of taste
  - sweet, salt, bitter, acid, umami (natrium glutamate)
  - others (fat)
- each gustatory bud perceives all kinds of taste
  - located on papillae **vallatae,** fungiformes et foliatae



Projection → Ascending → Sensory

GUSTATORY PATHWAY

3-neuronal pathway, decussated and non-decusated

1.N: via cranial nerves

- soft palate → nn. palatini minores → ggl. pterygopalatinum (not synapsed!) → n. petrosus major → ggl. geniculi → n. intermedius → n. VII → nuclei tractus solitarii
- anterior 2/3 of tongue (= dorsum linguae) → n. lingualis → chorda tympani → n. intermedius → n. VII → nuclei tractus solitarii
- posterior 2/3 of tongue (= radix linguae) + papillae vallatae → n. IX → ganglion inf. et sup. n. IX → nuclei tractus solitarii
- epiglottis, aditus laryngis → n. X → ganglion inf. et sup. n. X. → nuclei tractus solitarii

Projection → Ascending → Sensory

GUSTATORY PATHWAY

2.N: **nuclei tractus solitarii** → tractus tegmentalis centralis (along tr. trigeminothalamicus posterior) → ncl. **VPM thalami**

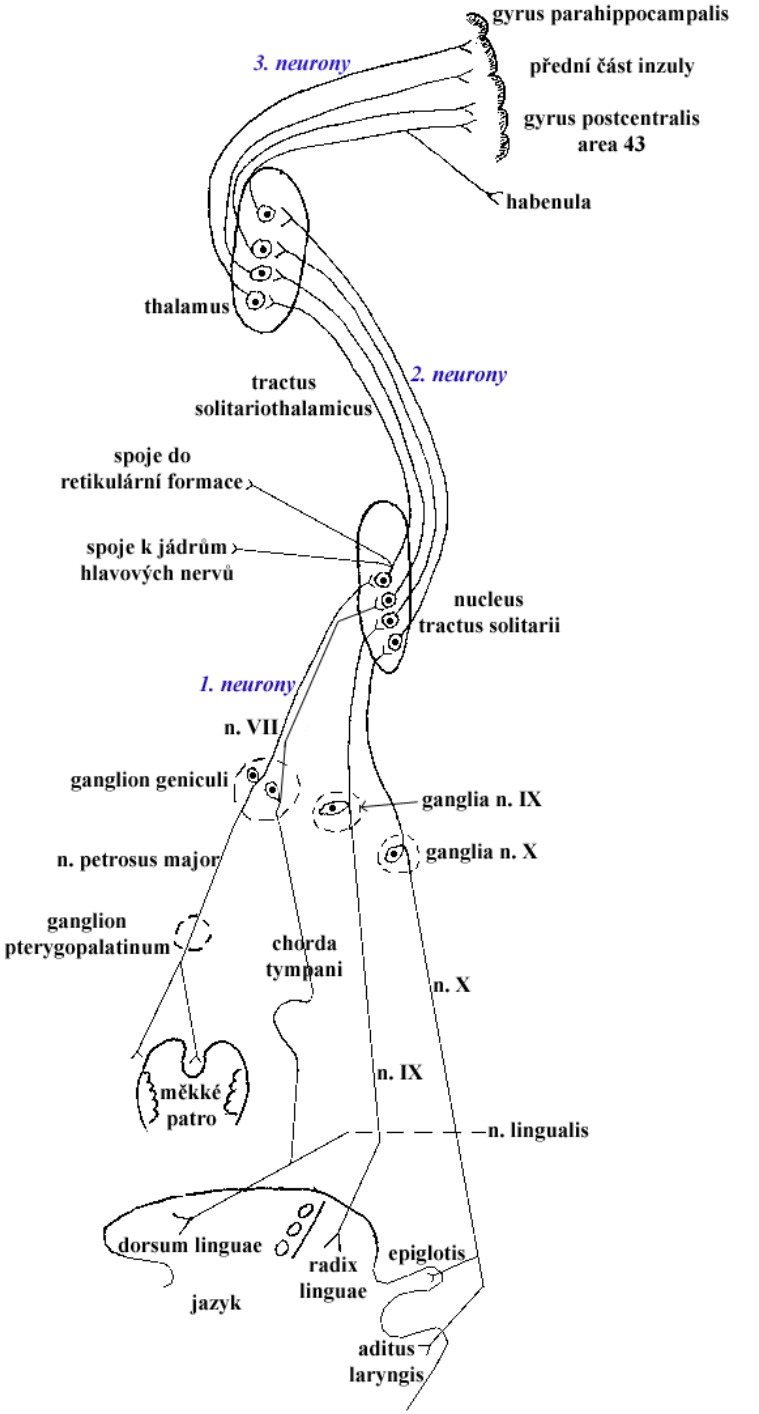
collaterals to motor nuclei of cranial nerves and to RF

3.N: thalamus → cerebral cortey – lobus parietalis, gyrus postcentralis (**area 43**) and anterior part of insula

collaterals to gyrus parahippocampalis

- collaterals to hypothalams, corpus amygdaloideum and cerebral cortex via **ncll. parabrachiales** bypasses thalamus

antigenic properties of nutrition (immunity) + taste aversion


gyrus parahippocampalis
3. neurony
přední část inzuly
gyrus postcentralis
area 43
habenula
thalamus
2. neurony
tractus
solitariothalamicus
spoje do
retikulární formace
spoje k jádrům
hlavových nervů
nucleus
tractus solitarii
1. neurony
n. VII
ganglion geniculi
ganglia n. IX
n. petrosus major
ganglia n. X
ganglion
pterygopalatinum
chorda
tympani
n. X
n. IX
měkké
patro
n. lingualis
dorsum linguae
radix
linguae
epiglotis
jazyk
aditus
laryngis

Smell / Olfaction (*Olfactus*)

Greek: osmé = odour

Olfactory organ
Organum oflactorium

- olfactory mucosa in nasal cavity
  - ceiling, concha superior and lateral walls at level of concha nasalis superior
- 3-5 cm^2 in one half of nasal cavity
- smell = *olfactus*
- perceiving of chemical substances (odorants) dissolved in air or water, usually in very low concentrations = **smell/scent/odour**
- primary receptor
- olfactory epithelium
- olfactory pathway (n.I)

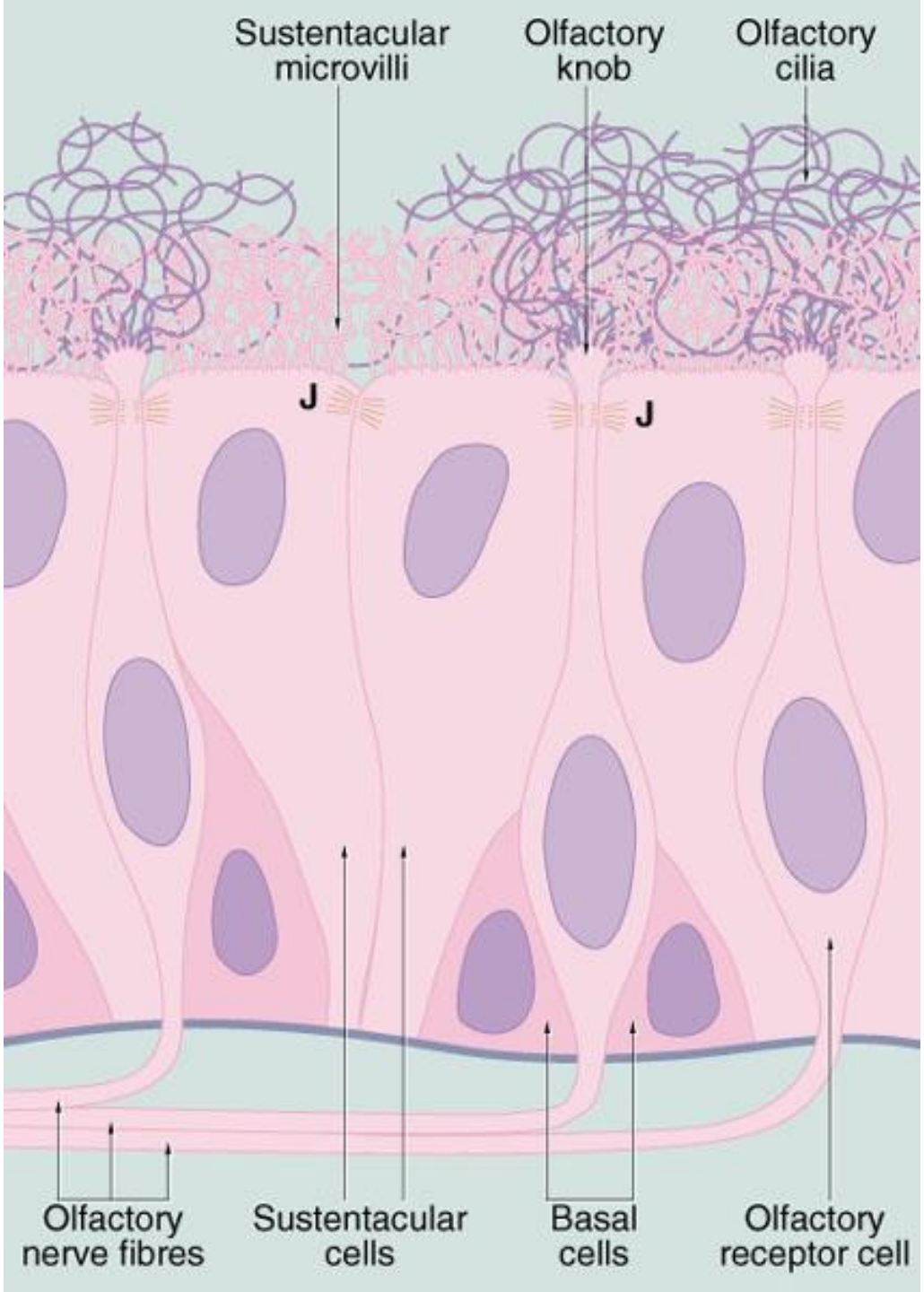
Nerves of Nasal Cavity

Distribution of Olfactory Mucosa

Olfatory epithelium = *Epithelium olfactorium*

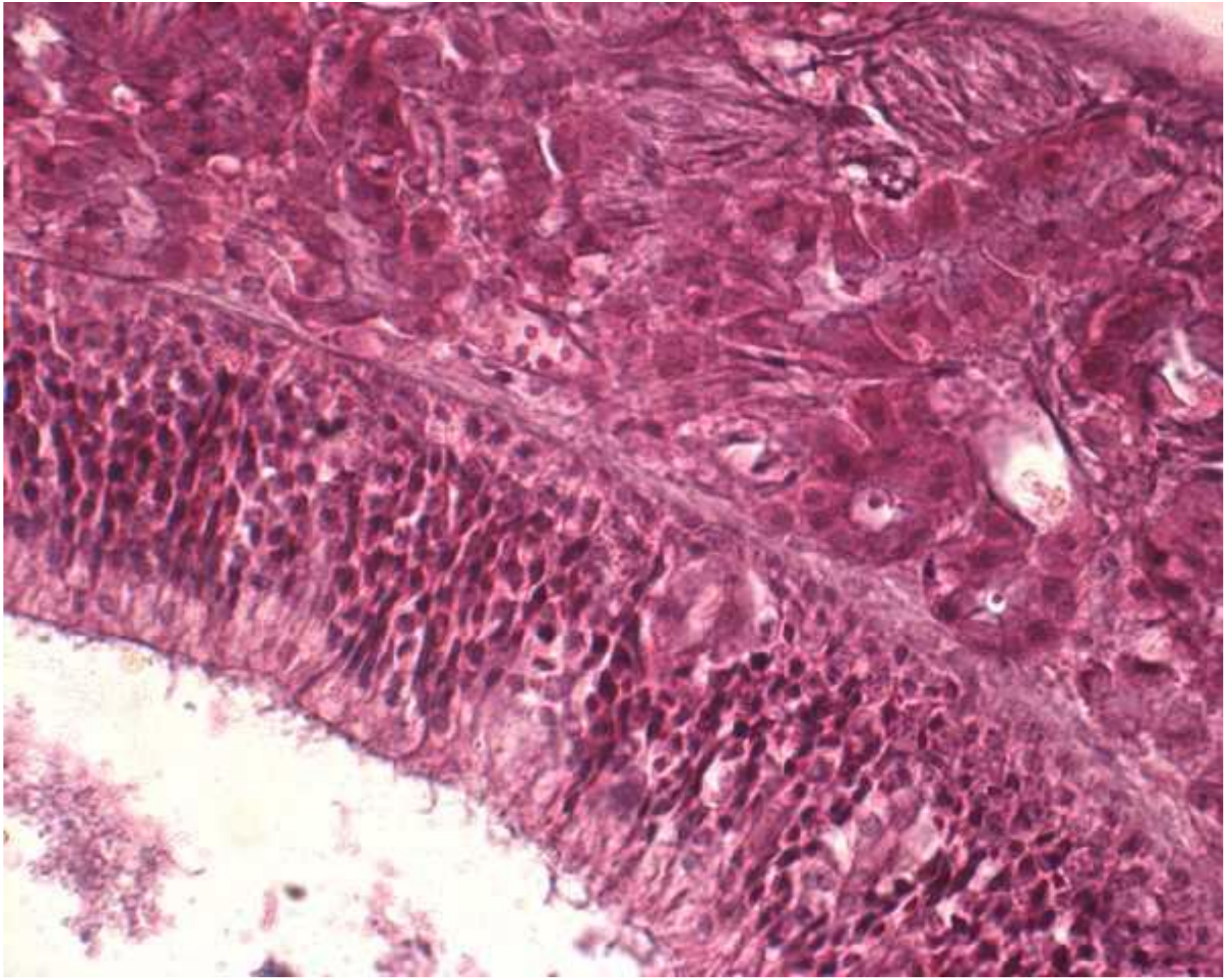
specialized pseudostratified columnar epithelium (100 µm high) with modified (immobile) cilia

- **olfacotry cells**(*epitheliocyti neurosensorii olfactorii*)
  - bipolar neurons, life expectancy 30-60 days
  - highly polarized cells, flask-shaped
  - apical end (dendrite) with button-like termination (*bulbus dendriticus*) contains 10-20 modified (immobile) cilia (and low border of microvilli)
  - cilia feature odorant receptors on their surface
  - nuclei located in the middle of epithelial height
  - basal end (axon) surrounded by cytoplasmic processes of glial cells (0,2 µm thick ranks it among the thinnest nerve fibers)
  - relatively quickly multiplying neurons neurons (major exception in neural tissue)


Sustentacular microvilli
Olfactory knob
Olfactory cilia
J
J
Olfactory nerve fibres
Sustentacular cells
Basal cells
Olfactory receptor cell

Olfatory epithelium = *Epithelium olfactorium*

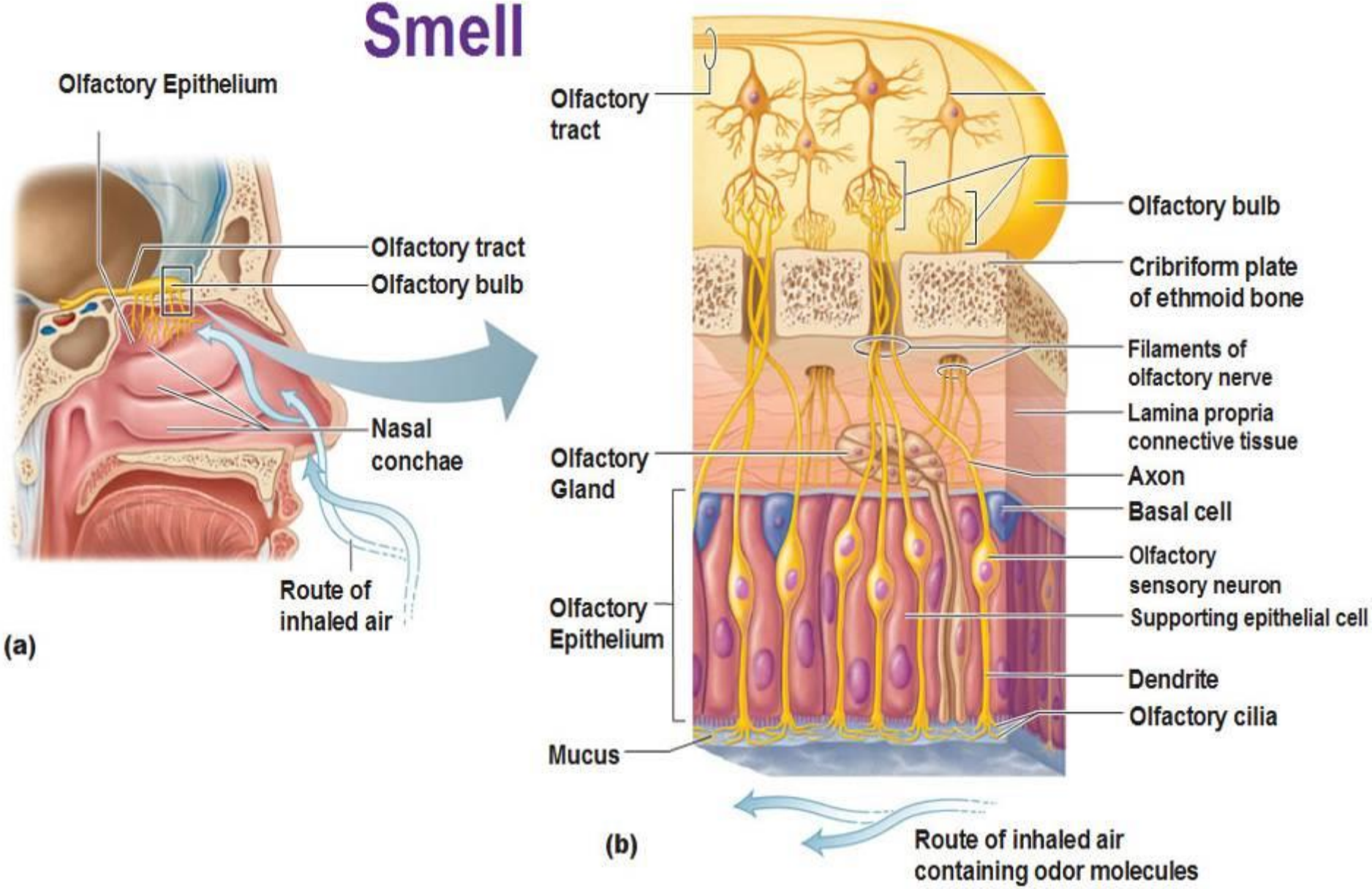
- **basal cells** (*epithelocyti basales*)
  - mitotically active stem cells/neurons with nuclei located basal at lamina basalis epithelii
- **supporting cells** (*epithelocyti sustenantes*)
  - mirror shape to olfactory cells
  - apically located nucleus
  - tight junctions with olfactory cells
  - long microvilli on apical surface
  - basally located lipofuscin granules (number increasing with age), long-living cells (life expactancy 1 year)
- immature olfactory cells = globose cells
  - intermediate stage between basal and olfactory cells
  - their apical end do not the epithelial surface yet

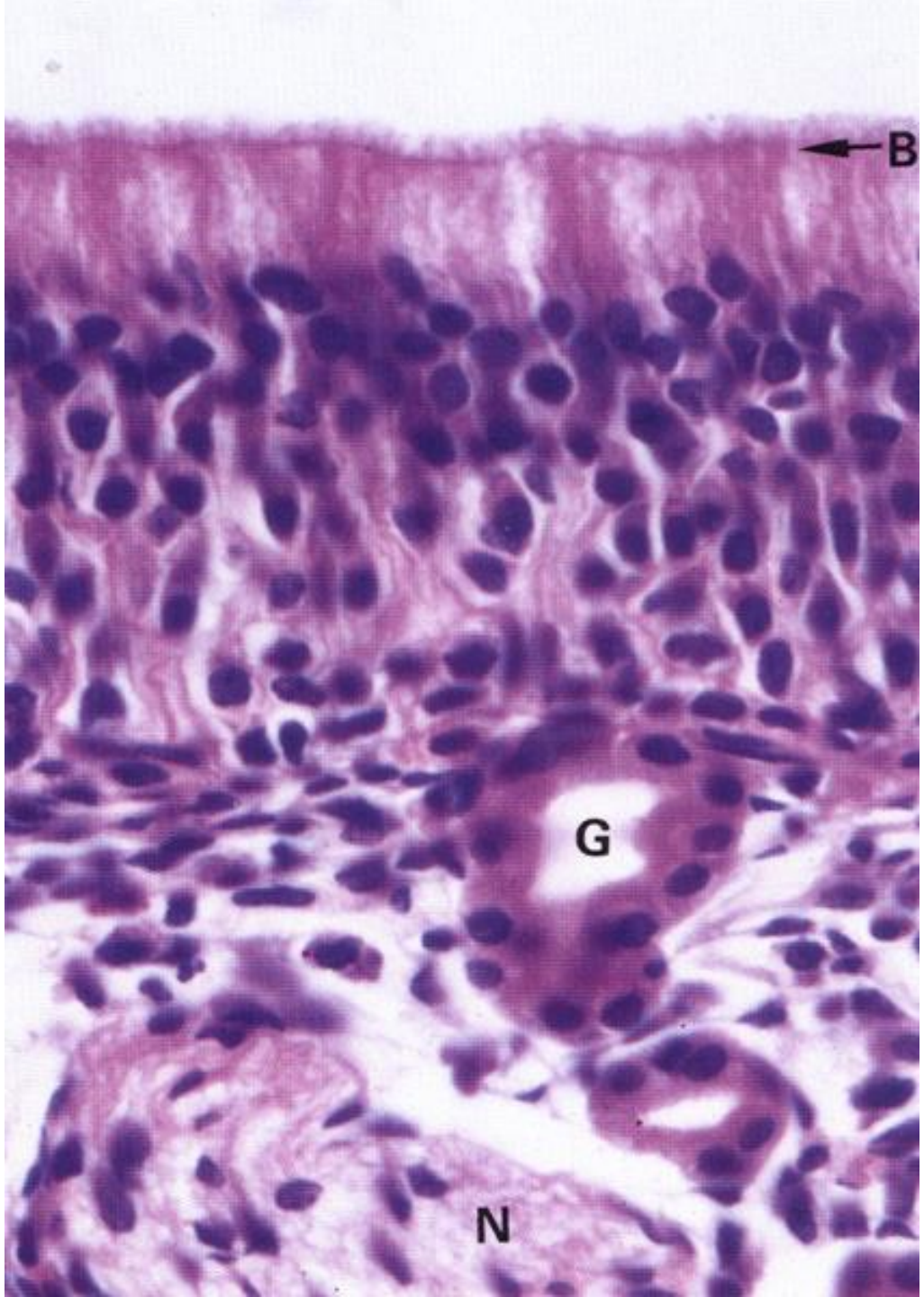


Olfatory epithelium – other parts

- **fila olfactoria**
  - bundles of unmyelinated axons of olfactory cells
  - pass via lamina cribrosa ossis ethmoidalis into cranial cavity to bulbus olfactorius
- **olfactory glands** (*glandulae olfactoriae Bowmani*)
  - simple branched tuboalveolar
  - serous secretion → concentrates and dissolves odorants and then rinsed them away
  - secretion contains odorant-binding protein (OBP) with high affinity to large scale of odorant molecules, and also lysosyme, lactoferrin and immunoglobulin A
- **olfactroia glia** (*glia olfactoria*)
  - fine cells encompassing unmyelinated olfactory fibers in v lamina propria mucosae
  - derived from olfactory placode (from superficial ectoderm)

Smell


Olfactory Epithelium
Olfactory tract
Olfactory bulb
Nasal conchae
Route of inhaled air
(a)
Olfactory tract
Olfactory bulb
Cribriform plate of ethmoid bone
Filaments of olfactory nerve
Lamina propria connective tissue
Olfactory Gland
Axon
Basal cell
Olfactory sensory neuron
Olfactory Epithelium
Supporting epithelial cell
Dendrite
Olfactory cilia
Mucus
(b)
Route of inhaled air containing odor molecules


B
G
N

Bulbus olfactorius

- 2-order-neuron of olfactory pathway
- olfactory glomerules (*glomeruli olfactorii*)
  - axons of olfactory cells form synapses with dendrite of mitral cells (and basket and periglomerular cells)
- axons of mitral cells (*neura mitralia*) pass as tractus olfactorius to olfactory cortex (*paleocortex*) and other olfactory centers

Projection → Ascending → Sensory

OLFACTORY PATHWAY

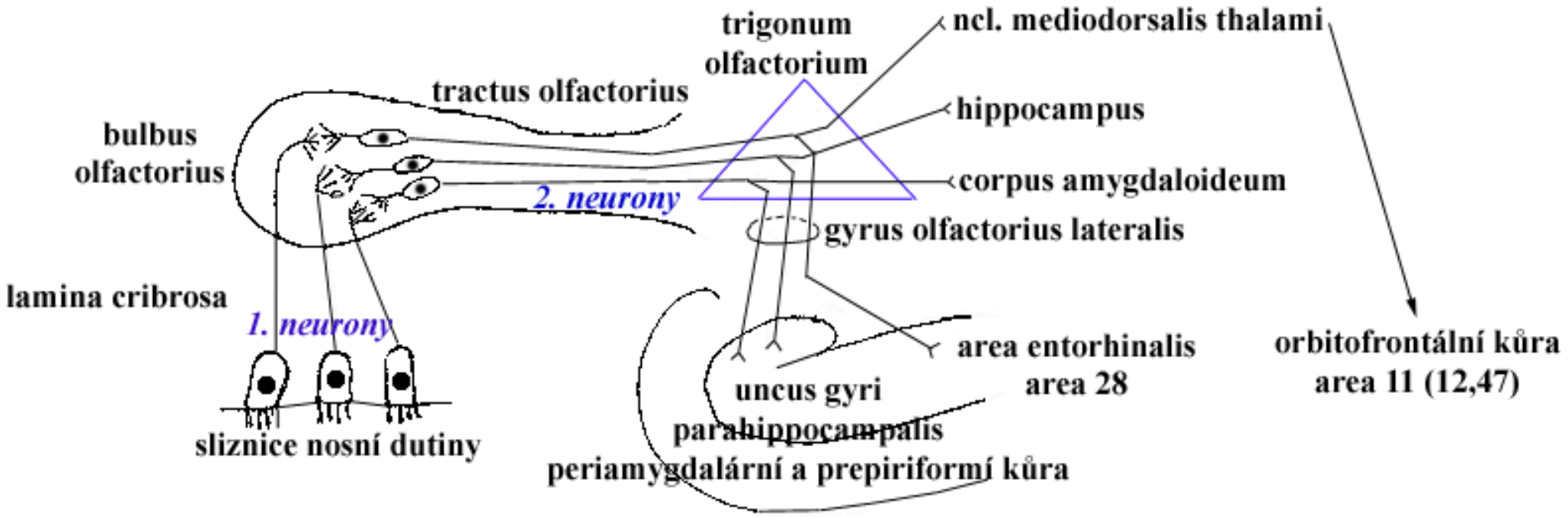
2-neuronal pathway

1.N: neuroepithelial cells in pars olfactoria cavitatis nasi → fila olfactoria → lamina cribrosa ossis ethmoidalis → fossa cranii anterior → bulbus olfactorius

2.N: mitral cells in bulbus olactorius → tractus olfactorius → trigonum olfactorium → stria olfactoria med. et lat. → **limbic system**

- cortex piriformis – anterior pole of lobus temporalis
- uncus and anterior end of gyrus parahippocampalis
- area entorhinalis (area 28)
- cortical part of corpus amygdaloideum

- hypothalamus, corpora mammillaria
- *highest olfactory center* – orbitofrontal cortex (11,12,47)


trigonum
olfactorium
ncl. mediodorsalis thalami
tractus olfactorius
hippocampus
bulbus
olfactorius
corpus amygdaloideum
2. neurony
gyrus olfactorius lateralis
lamina cribrosa
1. neurony
area entorhinalis
area 28
orbitofrontální kůra
area 11 (12,47)
uncus gyri
parahippocampalis
sliznice nosní dutiny
periamygdalární a prepiriformí kůra

Touch (*Tactus*)

Touch = *Tactus*

touch (tactus) involves discrimination, pressure, tension, vibrations

pain (*dolor*) **= nociception**

- somatosensory endings in skin
  - generally all receptors perceive all kinds of modalities (based on the stimulus intensity)
- somatosensory endings in joint capsules, muscles, tendons, fasciae
- viscerosensory endings in organs („inner touch“)
  - Head‘s zones
- areae nervinae x areae radiculares
- sensory components of cranial and spinal nerves
- ascending projection pathways

Skin receptors

- free nerve endings
- nerve endings connected with epidermal structures
  - within dermis, connected with structures derived from epidermis
  - nerve endings connected with hair follicle – **lanceolate nerve corpuscles**
  - nerve endings connected with epidermal cell – **Merkel‘s discs**
- encapsulated nerve endings (corpuscles)
  - group of corpuscles of different size, shape and location
  - always contain a dendrite (peripheral process) ensheated with unexcitable cells
  - Vater-Pacini‘s, Meissner‘s, Ruffini‘s corpuscles, Golgi‘s tendon organs, muscle spindles

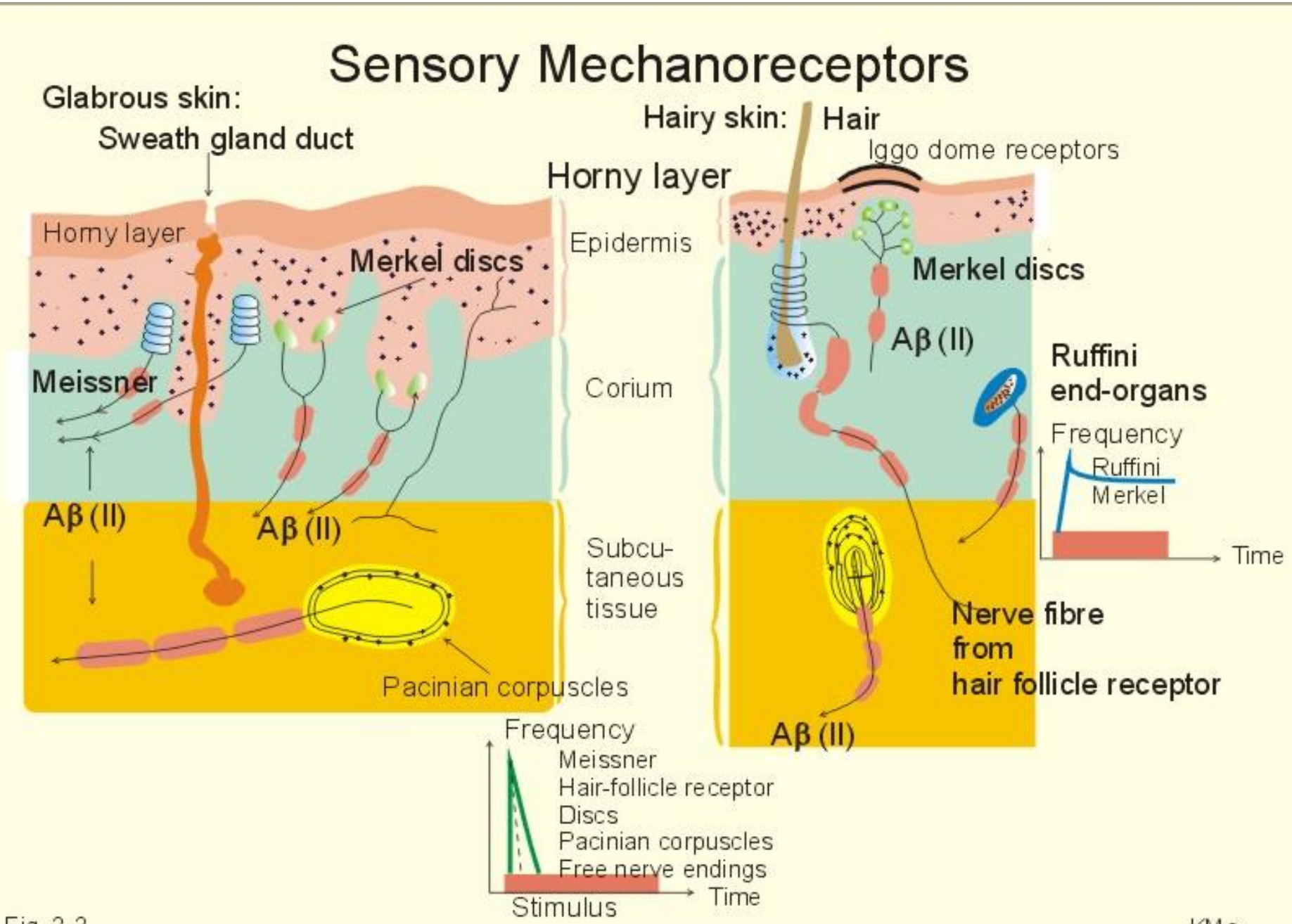

Sensory Mechanoreceptors
Glabrous skin:
Sweath gland duct
Horny layer
Epidermis
Merkel discs
Meissner
Corium
Aβ (II)
Aβ (II)
Subcu-
taneous
tissue
Pacinian corpuscles
Hairy skin:
Hair
Iggo dome receptors
Horny layer
Merkel discs
Aβ (II)
Ruffini
end-organs
Frequency
Ruffini
Merkel
Time
Nerve fibre
from
hair follicle receptor
Aβ (II)
Frequency
Meissner
Hair-follicle receptor
Discs
Pacinian corpuscles
Free nerve endings
Time
Stimulus

Fig. 3-3

KMc

Free nerve ending
Terminatio neuralis libera

- sensory nerve ending, branched into plexuses
- epidermis (stratum basale et spinosum), cornea, hair follicle, around sweat glands
- all connective tissues (dermis, fasciae, organ capsules, ligaments, tendons, vessel adventitia, meninges, joint capsules, periosteum, perichondrium, osteons, parietal peritoneum, endomysium of all kinds of muscles)
- epithelia (skin, cornea, conjunctiva, mucosa of cheeks, respiratory and digestive systems and their glands) and dentine
- acting as termoreceptors, mechanoreceptors, unimodal and polymodal nociceptors

Merkel‘s discs
Meniscus tactilis / dendriticus

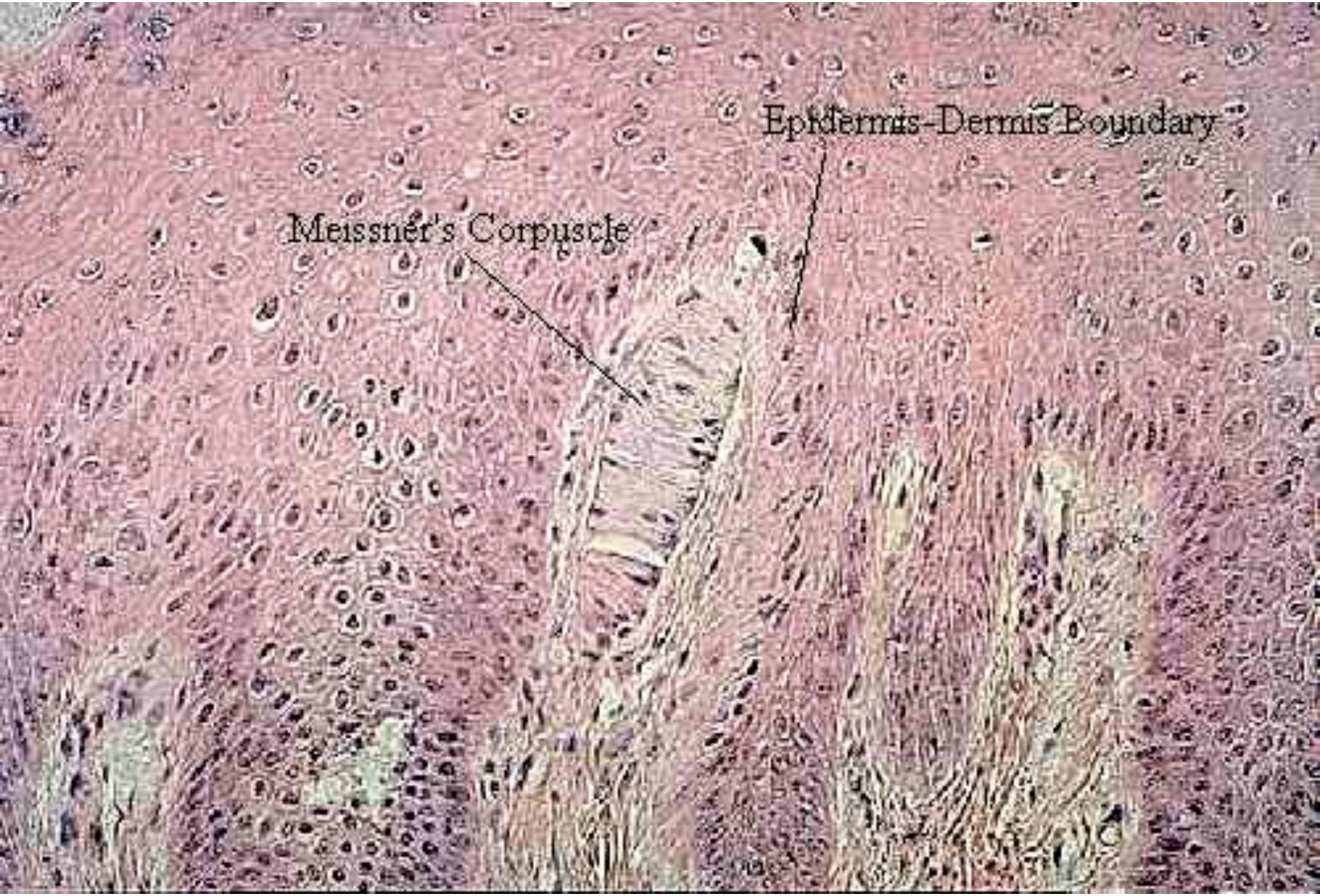
- flattened epithelial cells (*epitheliocytus tactilis*; Merkel‘s cells)
  - in deeper layers of epidermis form functional connections with branching of afferent nerve – A-beta fibers (*complexus epithelliales tactus*)
- in hairy skin: groups of corpuscles linked to one nerve fiber
- in bald skin: ratio of discs and fibers in equal
- very sensitive to perpedicular movements of skin and hair deflection

Lanceolate corpuscle
Corpusculum nervosum lanceolatum

- linked to hair follicle
- nerve fibers approaches right below the sebaceous gland
- then it loses its myelin sheath and branches up to 4 lanceolate endings
- rapidly adapting receptor
- sensitive to hair deflection

Meissner‘s (Wagner-M.) corpuscle *Corpusculum ovoideum / tactile*

- modified Schwann‘s cell layered across the corpuscle encompasses a central nerve fibers
- capsula fibrosa – encloses the corpuscle and transmits forces from the surroundings
- located in stratum papillare dermis within papillae right below the epidermis
- occurrence: over the whole body, densest on fingertips, less on palms, soles, preputium, lips and in oral cavity
- size: 50 µm x 100 µm

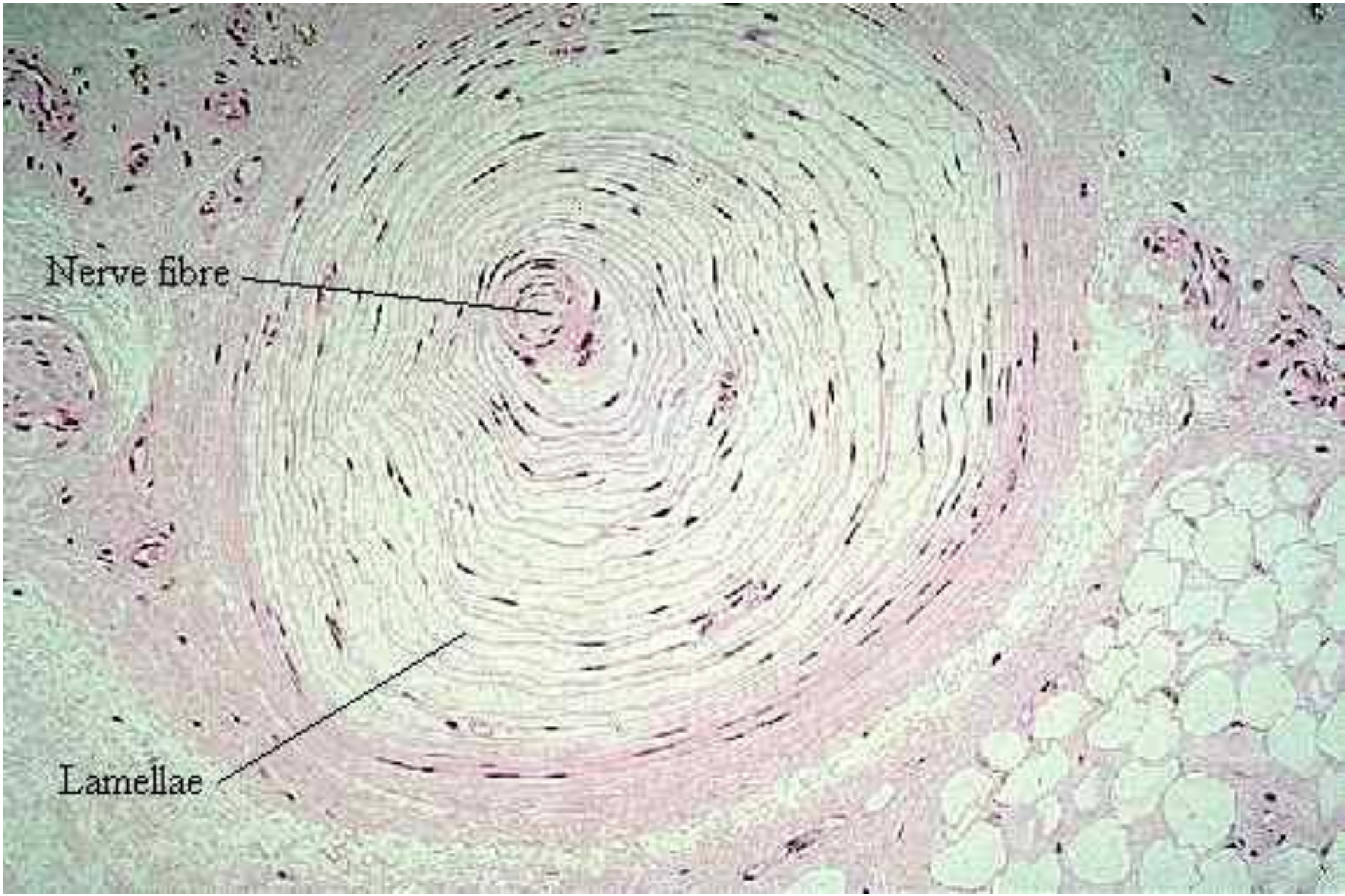

Epidermis-Dermis Boundary
Meissner's Corpuscle

Ruffini‘s corpuscle
Corpusculum sensorium fusiforme

- cylindrical encapsulated corpuscles (several lamellae), similar structure to perineurium
- branched nerve fibers intermingle with collagen fibers inside (transmission of mechanical forces from the surroundings to the collagen and then to nerve fibers) → large receptive field
- located in stratum reticulare (deep in dermis at the transition to hypodermis) and in hypodermis
- occurrence: over the whole body, also in gingiva, glans, joint capsule and tendon insertions
- size: 0,5 mm x 2 mm

Vater-Paccini‘s corpuscle
Corpusculum lamellosum

- most complex and largest encapsulated corpuscle
- up to 2.5 mm long, large receptive field
- central myelinated nerve fibers, enclosed by 30 lamellae of Schwann‘s cells
- capsula fibrosa – formed by 60 lamellae of perineural cells (*capsula perineuralis / bulbus externus*)
- onion appearance on transverse section (based on lamellae of Schwann‘s and perineural cells)
- fluid between lamellae – provides incompressibility and rapid transmission of pressure and vibration to dendritic zone of nerve fiber
- located deep in dermis (at border of dermis and hypodermis) and in hypodermis
- occurrence: skin (on palms, soles, fingers, toes, external genitals, arms, neck, nipples), periosteum, interosseous membranes, joint capsule, mesenterium of a cat ☺
- rapidly adapting receptors, sensitive to vibration with higher frequency


Nerve fibre
Lamellae

Other tactile corpuscles for lovers of histology☺

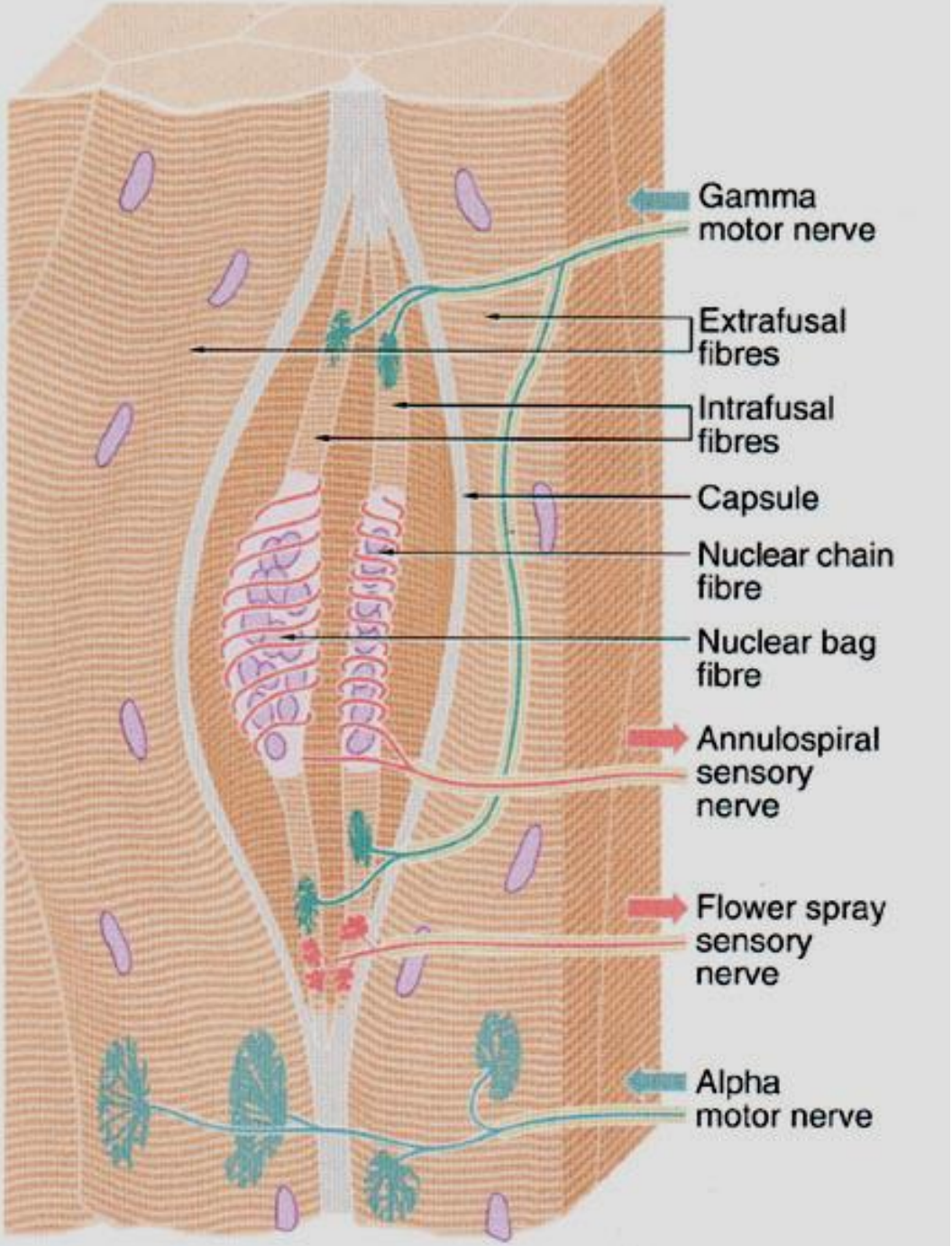
- **Golgi-Mazzoni‘s corpuscle**
  - in hypodermis of fingertips
  - thinner capsule and thicker nucleus than VP‘s corpuscle

- **Krause‘s corpuscle („end-bulb corpuscle“)**
  - in dermis (stratum papillare), conjunctiva, lips and tongue, epinerium of nerve trunks
  - group in 2-6 = **Dogiel‘s genital corpuscles** (penis, clitoris)
  - joint capsule (hand)
  - cylindrical or oval encapsulated
  - 50 µm x 150 µm

- Herbst‘s corpuscle – tongue of a duck ☺
- Grandry‘s corpuscle – beak and tongue of birds

Muscle spindle
Fusus neuromuscularis

- striated muscles
  - few in extraocular muscles, no in tongue muscles
- length: 0,8–5 mm
- capsule (*capsula*) – fusiforme fibrous cover
  - *lamina externa* – flat fibroblasts and collagen fibers (corresponds to perineurium)
  - *lamina interna* – fie tubules around individual fibers
  - between a gelatinous fluid with glycosaminoglycanes
- intrafusal muscle fibers (*myofibrae infrafusales*)
  - differ from usual (extrafusal) muscle fibers by significantly shorter length and thinner zone of myofibrils around then nucleus


Gamma motor nerve
Extrafusal fibres
Intrafusal fibres
Capsule
Nuclear chain fibre
Nuclear bag fibre
Annulospiral sensory nerve
Flower spray sensory nerve
Alpha motor nerve

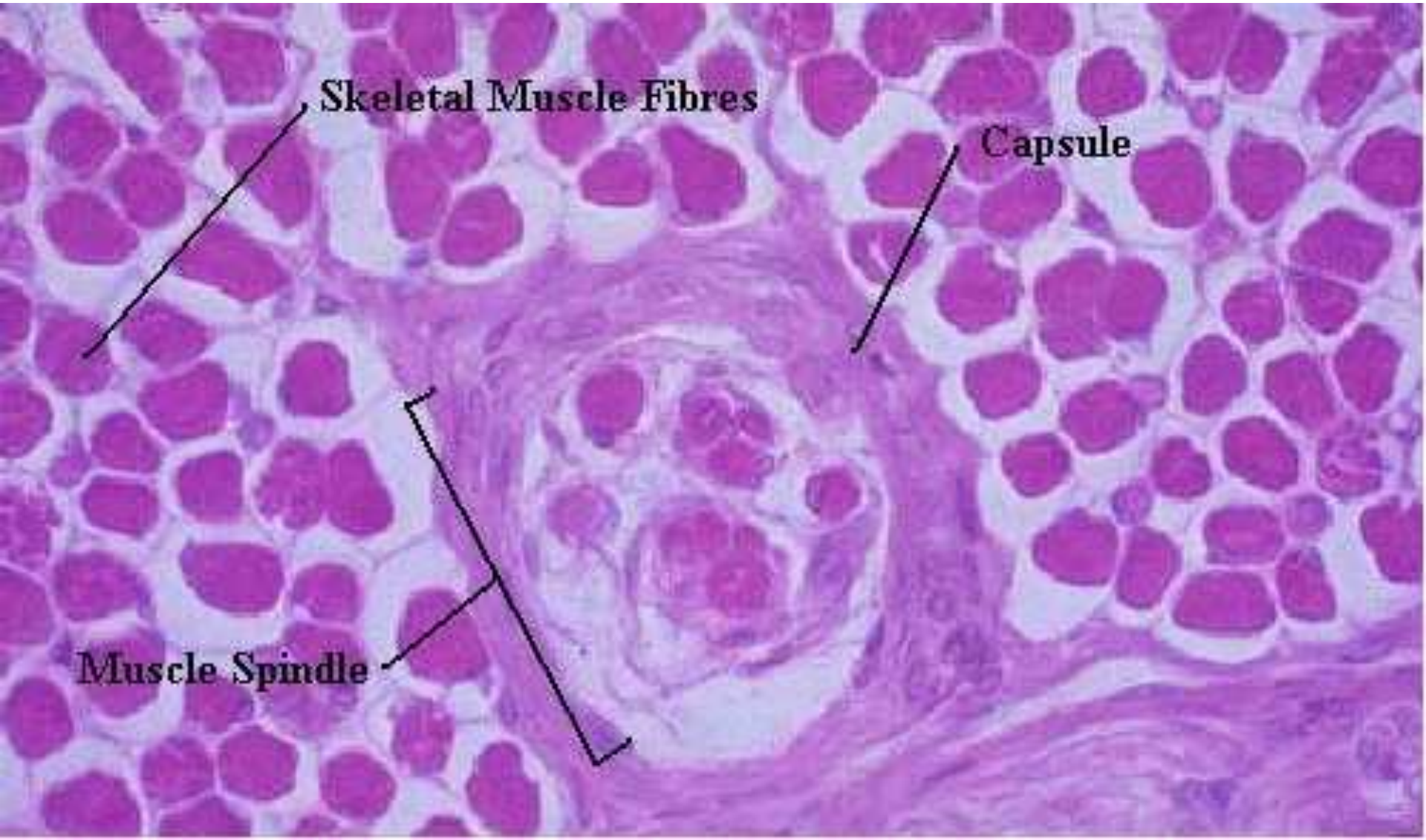
Muscle spindle – nerve endings

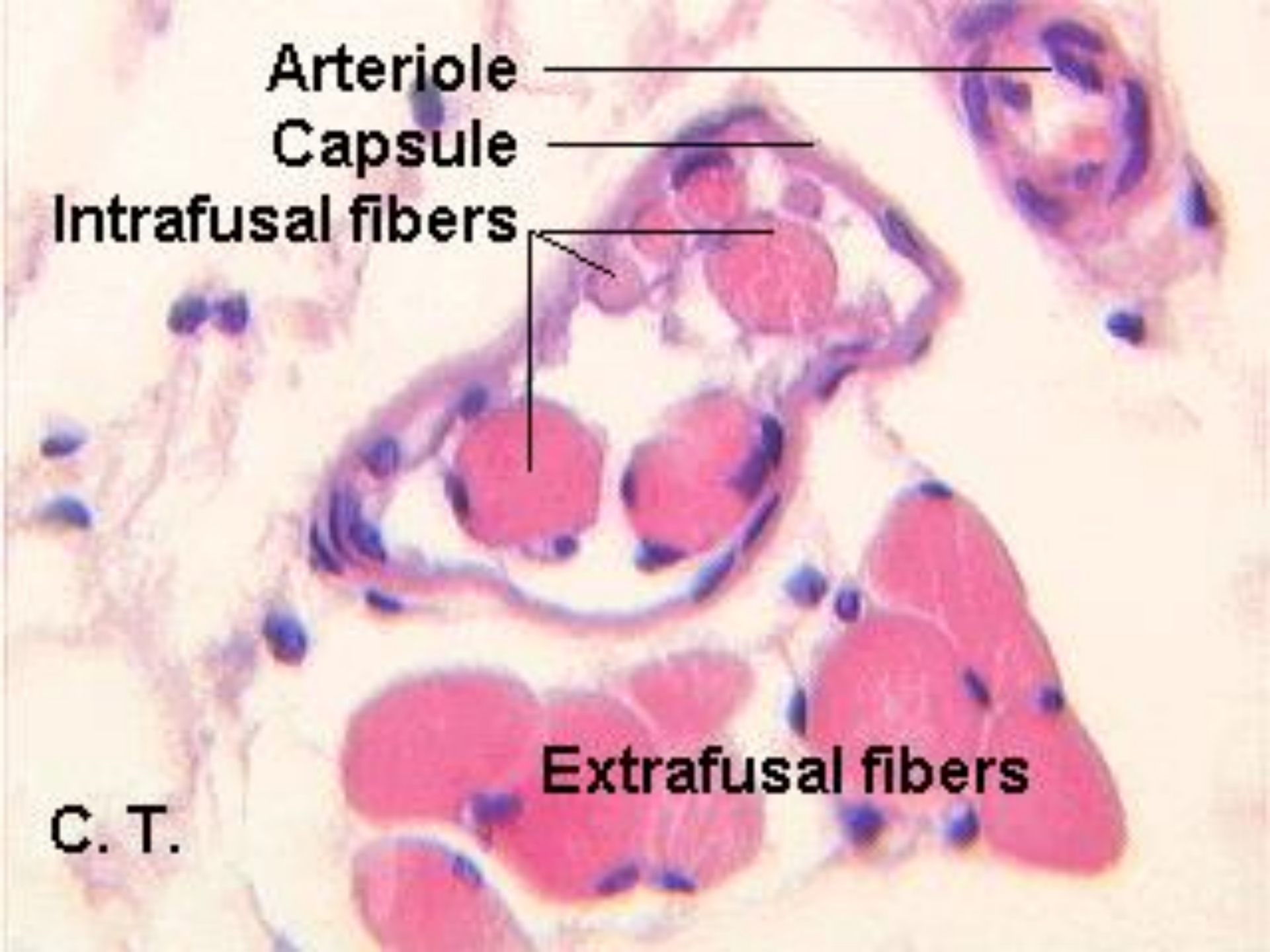
- anulospiral (primary) ending (*terminatio neuralis anulospiralis*)
  - spirals around nuclear area
  - rapidly adapting endings of sensory nerves
- flower spray (secondary) ending (*terminatio neuralis racemosa*)
  - branched with beaded ends
  - slowly adapting endings of sensory nerves
- neuromuscular plate
  - motor nerves endings (gama-motoneurons nd collaterals of alfa-motoneurons)

Muscle spindle – function

- provides information on the tension of extrafusal fibers at rest and during contraction or relaxation
- perceives isometric contractions (tension changes without stretching)
- the sensitivity is controlled by gamma-motoneurons, which select the pretension of intrafusal fibers
- it is possible to set the sensitivity with which the muscle spindles function as a centripetal component of motor reflexes and thus affect the muscle tone
- monitors muscle conditions and sends this information to the CNS to compare between intended and actual movements

Muscle spindle
Fusus neuromuscularis




Arteriole
Capsule
Intrafusal fibers
Extrafusal fibers
C. T.

Tendon (Golgi‘s) organ
Organum sensorium tendinis

- small bundles of tendon fascicles (*fasciculi intrafusales*) covered with a thin capsule
- over 50 tendon organs at each musculotendinous junction
- 1 tendon organ is in relation to a group of up to 20 muscle fibers, inserted a tendon bundle enclosing the tendon organ
- size: 500 x 100 μm
- slow adaptation
- provides proprioceptive information on muscle and tendon tension, thereby supplementing the proprioception of muscles and joint capsule

Projection → Ascending → Sensory → Direct:

TRACTUS SPINOBULBOTHALAMOCORTICALIS

= *lemniscal system* (lemniscus medialis)

= *posterior/dorsal column-medial lemniscus pathway*

- 3-neuronal pathway, decussated in medulla oblongata
- fine touch, vibrations, deep pressure, tension, proprioception from joints, tendons and muscles
- disorder: sensory ataxia (*sclerosis multiplex, tabes dorsalis*) – tabetic dissociation of sensitivity

Projection → Ascending → Sensory → Direct → Anterolateral system:

TRACTUS SPINOTHALAMICUS

- part of *anterolateral system* (neospinothalamic tract)
- 3-neuronal pathway, decussated in spinal cord one (segment above entering the spinal cord)
- fast (acute pain), heat and cold (lat.) and crude touch (ant.)
- as lemniscus spinalis within brainstem
- from Rexed‘s zone I,V,VII,VIII
- *disorder: syringomyelia* – syringomyelic dissociation of sensitivity
- *stimulation / chordotomy in severe pain*

Projection → Ascending → Sensory → Direct → Anterolateral system:

SOMATOSENSORY PATHWAY OF CRANIAL NERVES

- analogous to both previous pathways
- fine touch + proprioception (tr. trigeminothalamicus post.), crude touch and pain (tr.t-th ant.) from head
- n. V, IX, X
- lemniscus trigeminalis (lateral to lemniscus medialis et spinalis)

Baroreceptors

- usually branched, knobby, twisted and intertwined myelinated nerve endings of n. IX + n. X.
- in heart located subendocardially and are nmyelinated
- **high-pressure baroreceptors**
  - at beginning of a. carotis interna (*sinus caroticum*)
  - at origin of a. subclavia (*glomus subclavium*)
  - in arcus aortae (*glomera supracardiaca*)
  - in the wall of left ventricle
- **low-pressure baroreceptors**
  - in the wall of vv. cavae and vv. pulmonales at their ends into atria
  - in the wall of heart atria
  - in the wall and at bifurcation of truncus pulmonalis (*glomus supracardiacum*)

Sinus caroticus

= widened origin of a. carotis interna

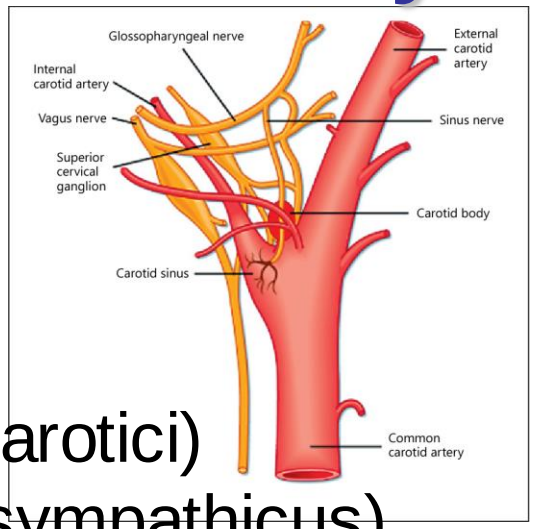
- thinned tunica media
- thickened tunica adventitia
- nerve endings of n. IX (ramus sinus carotici)
- baroreceptor
  - arterial blood pressure
  - receptor for one of principal reflexes of blood pressure regulation

Chemoreceptors

- **peripheral**
  - glomus caroticum
  - glomus subclavium + glomera supracardiaca (aortica) = aortal bodies
    - in arteries of 4th and 6th aortic arch
    - can serve as baroreceptors as well (similar to sinus caroticus)
  - macula densa of distal tubule of nephron
    - level of ions in urine

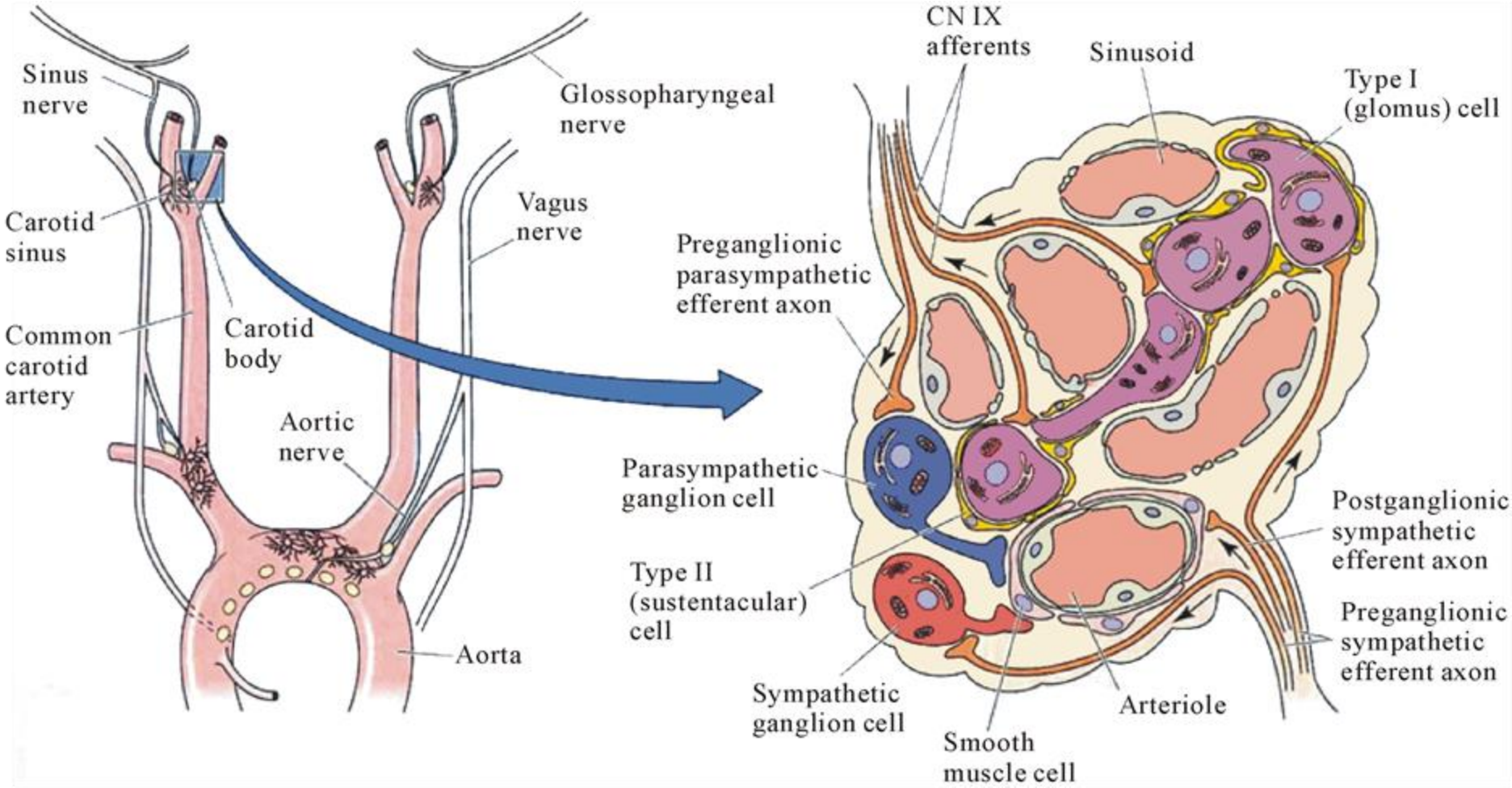
- **central**
  - **area postrema**
    - circumventricular organ
    - sensitive to various toxins brought by blood
    - sensitive to PH changes of cerebrospinal fluid by means of modified ependym cells
  - chemoreception zones for detecting various substances
    - level of glucose and fat (center of hunger and satiety in hypothalamus)
    - level of hormones in hypothalamus and other areas
      - estrogenes, gestagenes, thyroid gland hormones, mineralocorticoids and glucocorticoids) – feedback regulation
        - » effect of hormonal anticonception

Glomus caroticum = Carotid body



- arterial chemoreceptor
- at bifurcatio carotidis
- oval, red-brown corpuscle
- with or at tunica adventitia (6 x 3 cm)
- viscerosensory fibers of n. IX (n. sinus carotici)
- visceromotor fibers of n. X and truncus sympathicus)
- stimulated by hypoxia mainly (low partial pressure of oxygen), less by hyperkapnia and lowered pH
- response: reflex higher breathing frequency and volume (caused by stimulation of breathing centers of RF in brainstem)
- structurally belongs to sympathetic paraganglia
- develops from ectomesenchyme of the 3rd pharyngeal arch (derived from neural crest cells)

Glomus caroticum



Glomus caroticum – structure

- **fibrous capsule** (*capsula fibrosa*)
  - *septa*
  - *lobuli*
- **glomus cells** (*paragangliocyti, glomocyti*)
  - function as dopaminergic interneurons
- supporting cells (*epitheliocyti sustenantes*)
- ganglionic cells
- **fenestrated capillaries**
- unmyelinated nerve fibers are the actual chemoreceptors

Other receptors

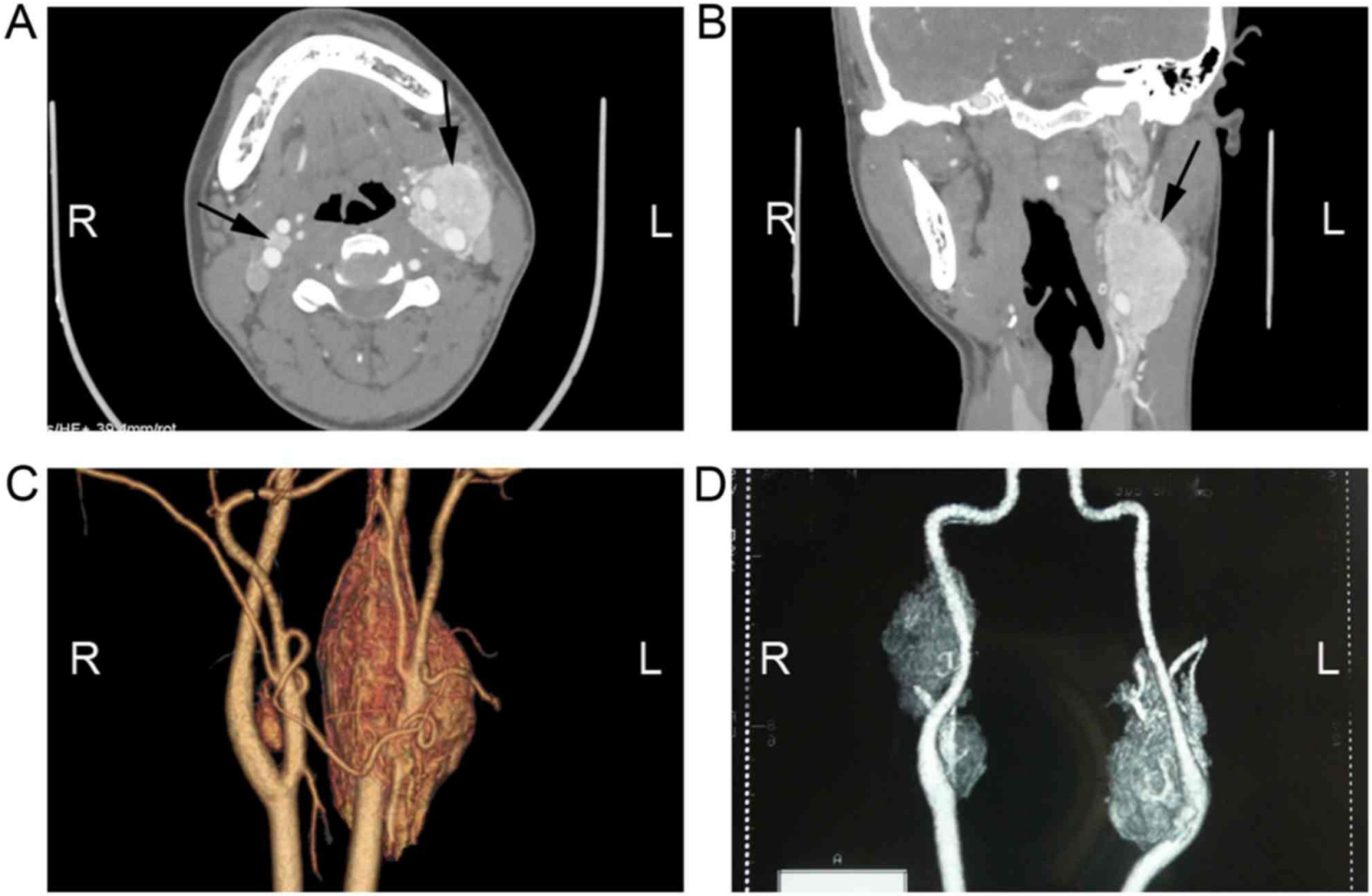
- **osmoreceptors**
  - chemoreception zones for osmolality of cerebrospinal fluid
  - organum vasculosum laminae terminalis + organum subfornicale
    - for level of angiotensin II to induce a feeling of thirst and secretion of ADH
  - osmolality of blood
    - center of thirst and „non-thirst“ in hypothalamus and secretion of ADH

- **thermoreceptors**
  - hypothalamus – center of cold and heat

Case report

- woman, 22 years
- 4 year history
- intermittent pain in cold, foreign body feeling
- palpable resitance on the neck
- *ultrasound*
- *CT + angiography*

Bilateral tumour of glomus caroticum



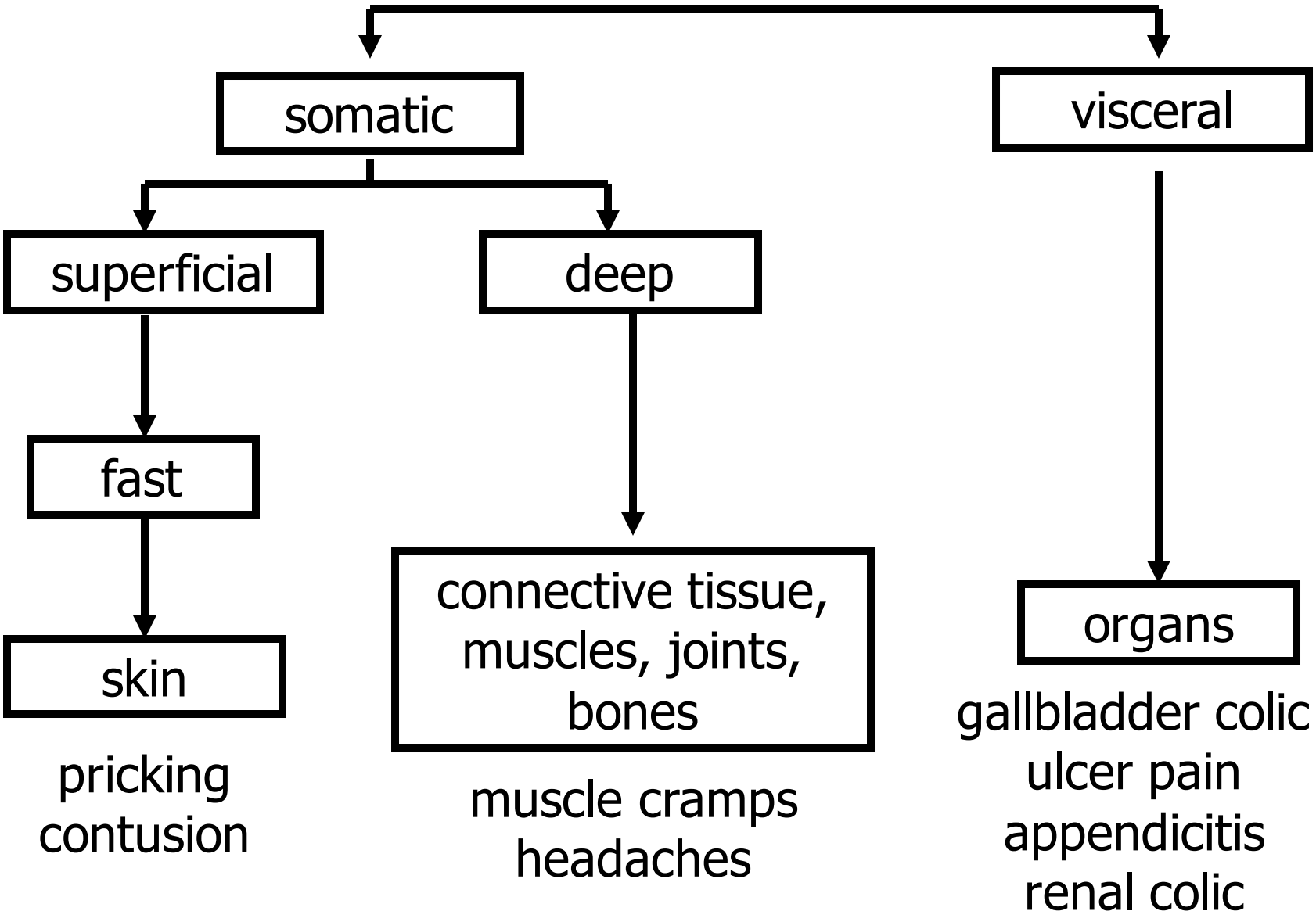
Pain (*Dolor*)

Pain – definition

„ An unpleasant sensory and emotional experience associated with real or potential tissue damage or described by terms for such damage. Pain is always subjective.“

- independent entity = specific nociception system
- relationship „impulse intensity = perception intensity“ does not always apply

PAIN


somatic
visceral
superficial
deep
fast
skin
connective tissue, muscles, joints, bones
organs
pricking
contusion
muscle cramps
headaches
gallbladder colic
ulcer pain
appendicitis
renal colic

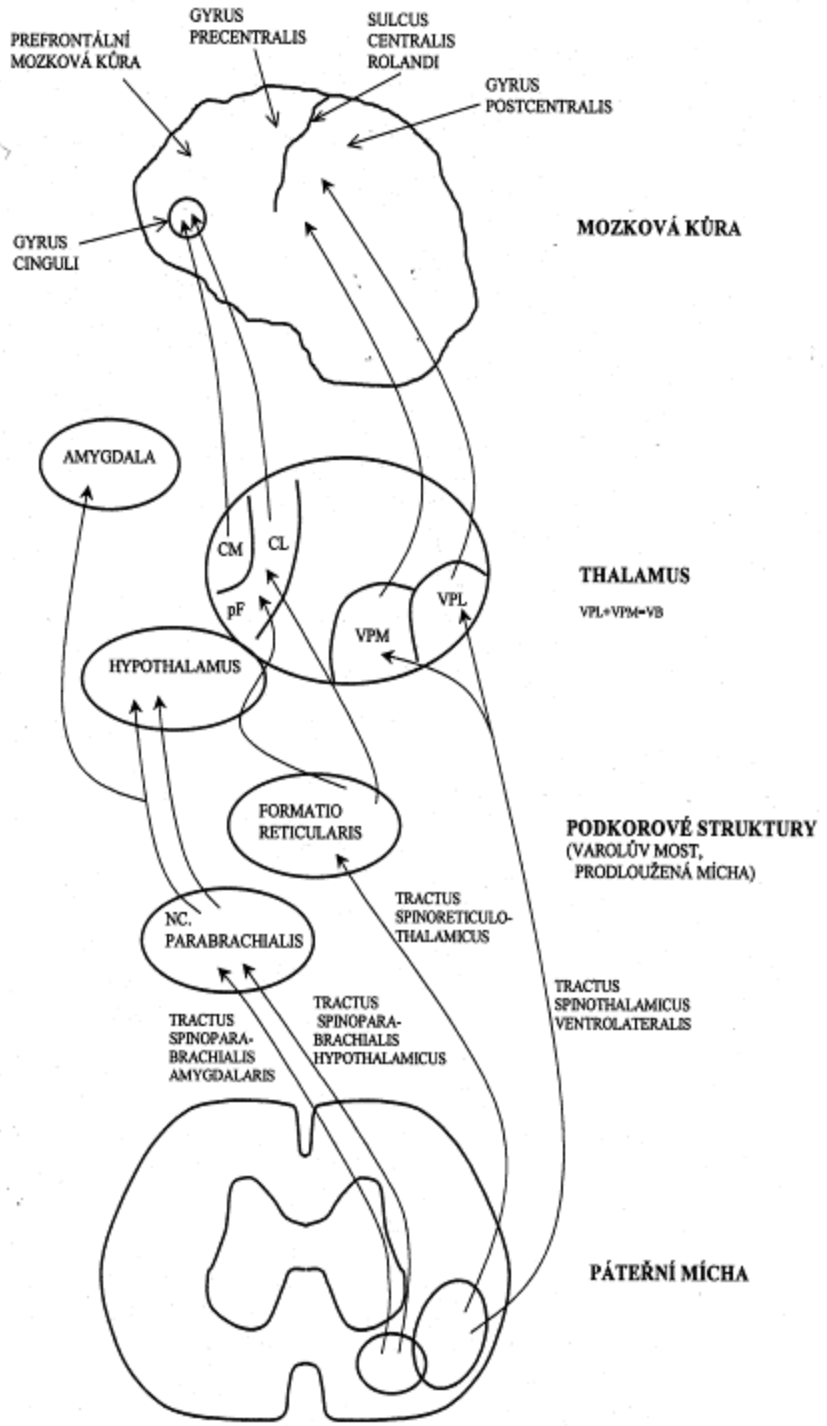
Nociceptors = Nocisensors

- do not adapt
- skin, mucosa of internal organs, striated muscles, joint capsules, periosteum, adventitia of small vessels, lymph vessels,
- CNS (cornu posterius medullae spinalis, medulla oblongata, hypothalamus, thalamus)
- *not within cerebral cortex*

3 types of nociceptors

- free nerve endings
  - thickened ends (boutons terminaux) with receptors
  - only react under very intense painful stimulation (stone movement, overeating) = **silent nociceptors**
- polymodal nociceptors
  - only in skin
  - react to temperature below 10°C and above 45°C
- high-level mechanoreceptors
  - tension, pressure, pain
  - Vater-Paccini‘s corpuscles
  - stroking with hand x kicking with foot

Scheme of transmission of painful stimuli from receptor to CNS



Pain pathways – ascending

- anterolateral system
  - **tr. spinothalamicus ant. + lat.** (neospinothalamic tract) – acute/fast pain
  - **tr. spinoreticulothalamicus** (paleospinothalamic tract) – chronic/slow pain
    - tr. spinoparabrachialis (tr. spinomesencephalicus) – affective-emotional component of pain
- (tractus spinobulbothalamicus)
- (tractus spinocervicalis)
- (tractus spinotectalis)
- ((tractus spinothalamicus secundarius))

Acute/fast/somatic pain

- weakly myelinated fibers Aδ (7-14 m/s)
  - somatic (lateral) afferentation

→ nociceptive-specific neurons of Rexedo‘s lamina I,II

→ decussation at spinal cord level (commissura alba anterior)

→ tractus spinothalamicus ant. + lat. (*glutamate*)

→ ncll. ventrobasales thalami (ncl. VPL + VPM)

→ somatosensory cortex (area 3,1,2) – gyrus postcentralis

Visceral/slow/chronic pain

- unmyelinated fibers C (0,5-3 m/s)
  - visceral (medial) afferentation
- multireceptive neurons in ncl. proprius columnae post. = Rexed‘s lamina III-V (VIII,X)

→ tractus spinoreticulothalamicus → RF → ncll. intralaminares thalami (ncl. centralis medialis, centralis lateralis, parafascicularis)

→ prefrontal cortex (area 6,9) + gyrus cinguli, insula – *pain expectation*

Affective-emotional component of pain

tractus spinoparabrachialis

→ ncll. parabrachiales → tractus longitudinalis posterior → *emotional and motivation centers*

- tr. spino-parabrachio-hypothalamicus → hypothalamus → limbic system
- tr. spino-parabrachio-amygdalaris → corpus amygdaloideum

RF – descending inhibition of pain

substantia grisea centralis mesencephali = (PAG)

enkefalins

↓

ncll. raphes (ncl. raphe magnus, dorsalis) medullae oblongatae

serotonin

↓

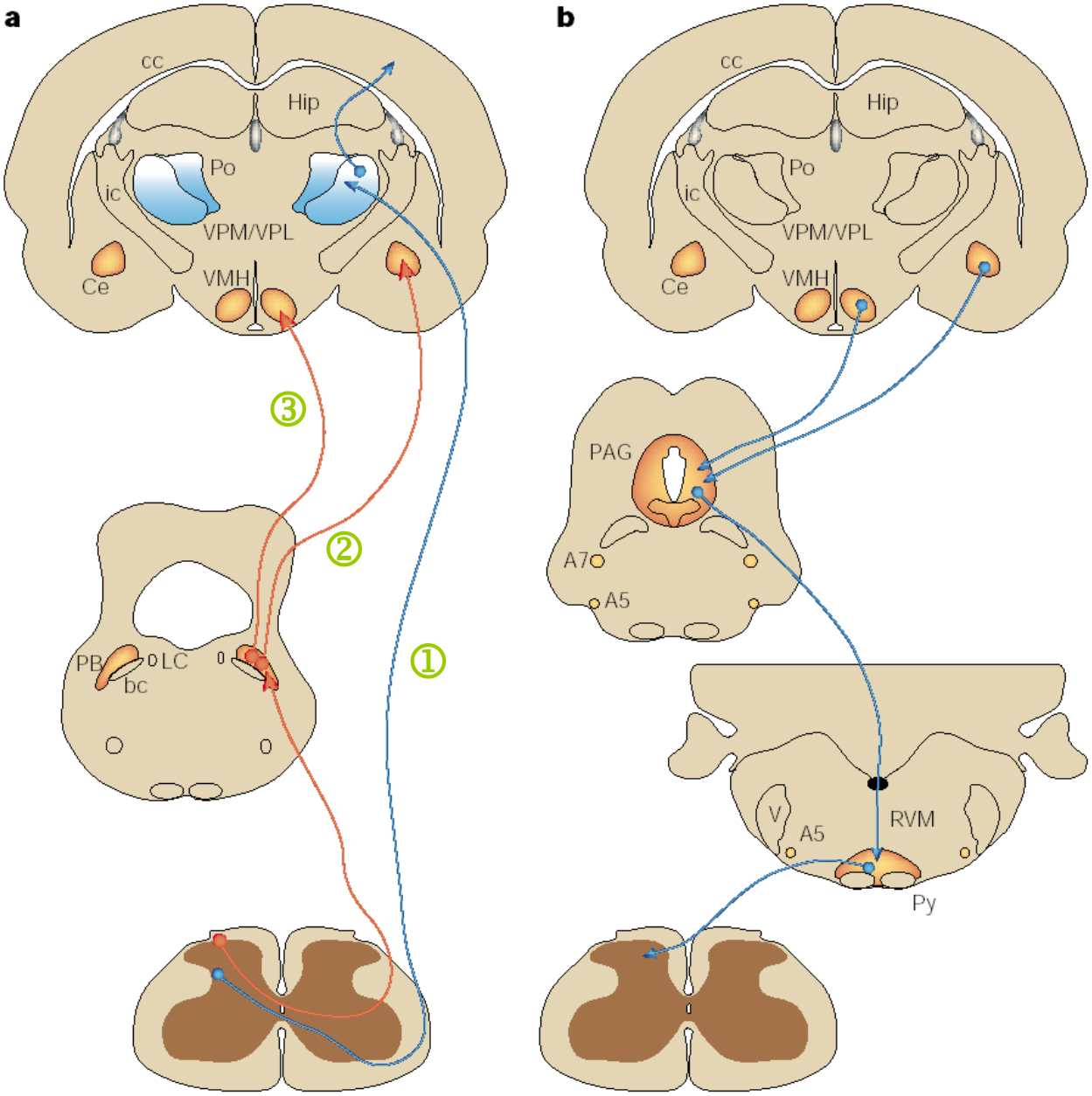
fasciculus posterolateralis (Lissaueri)

↓

Rexed‘s lamina II – presynaptic inhibition

block of Ca^{2+} channels ➔ block of substance P

subnucleus caudalis ncl. spinalis n. V



Ascending and **descending** pain pathways

① tr. spinothalamicus

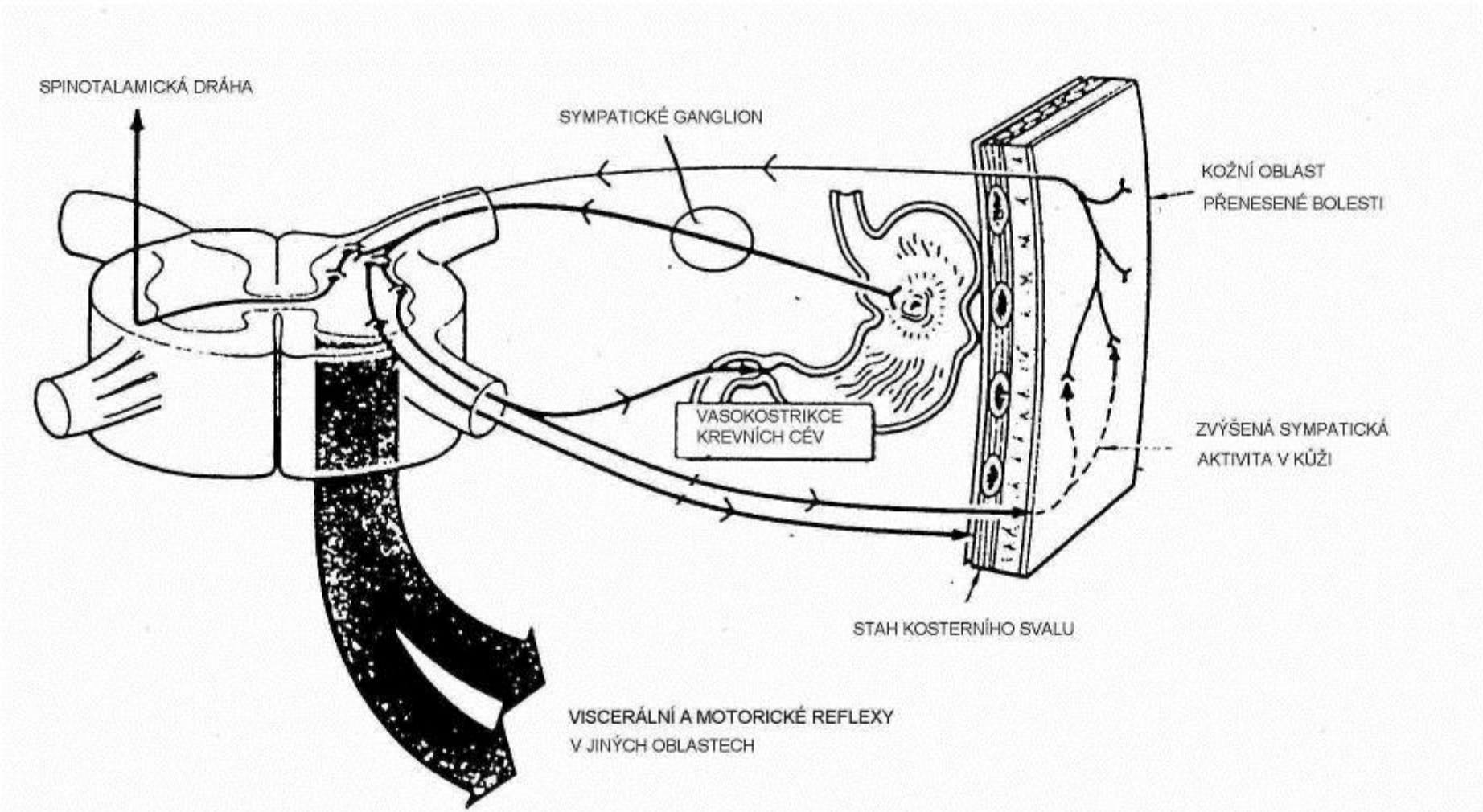
② tr. spino-parabrachio-amygdalaris

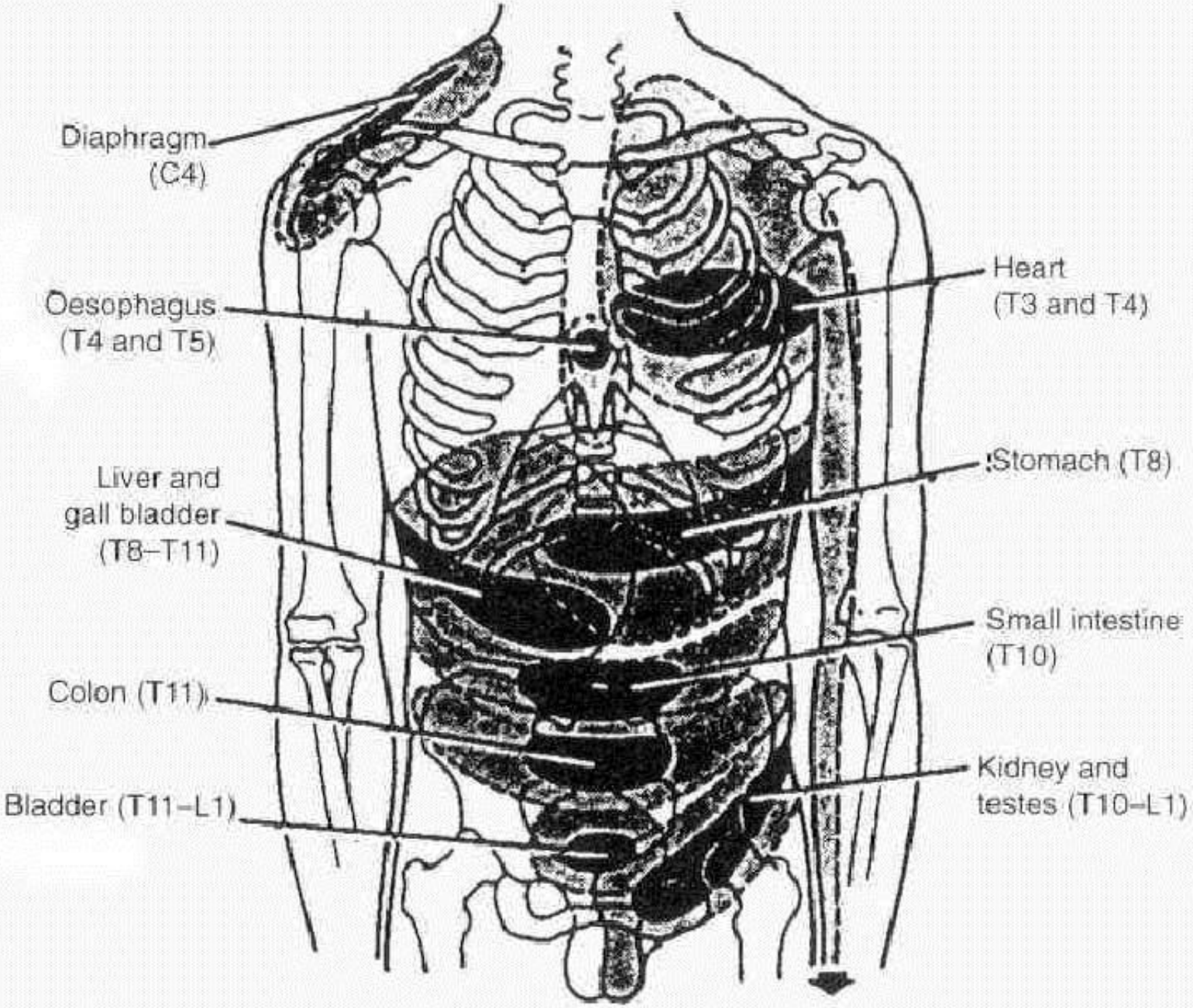
③ tr. spino-parabrachio-hypothalamicus

Referred pain

- Head‘s zones
- pain in the trunk (back) or on other parts of the body surface, the origin of which is from more distant organs – heart, pancreas, stomach, etc.
- convergence of viscerosensory afferents from internal organs and somatosensory afferents on common spinal interneurons

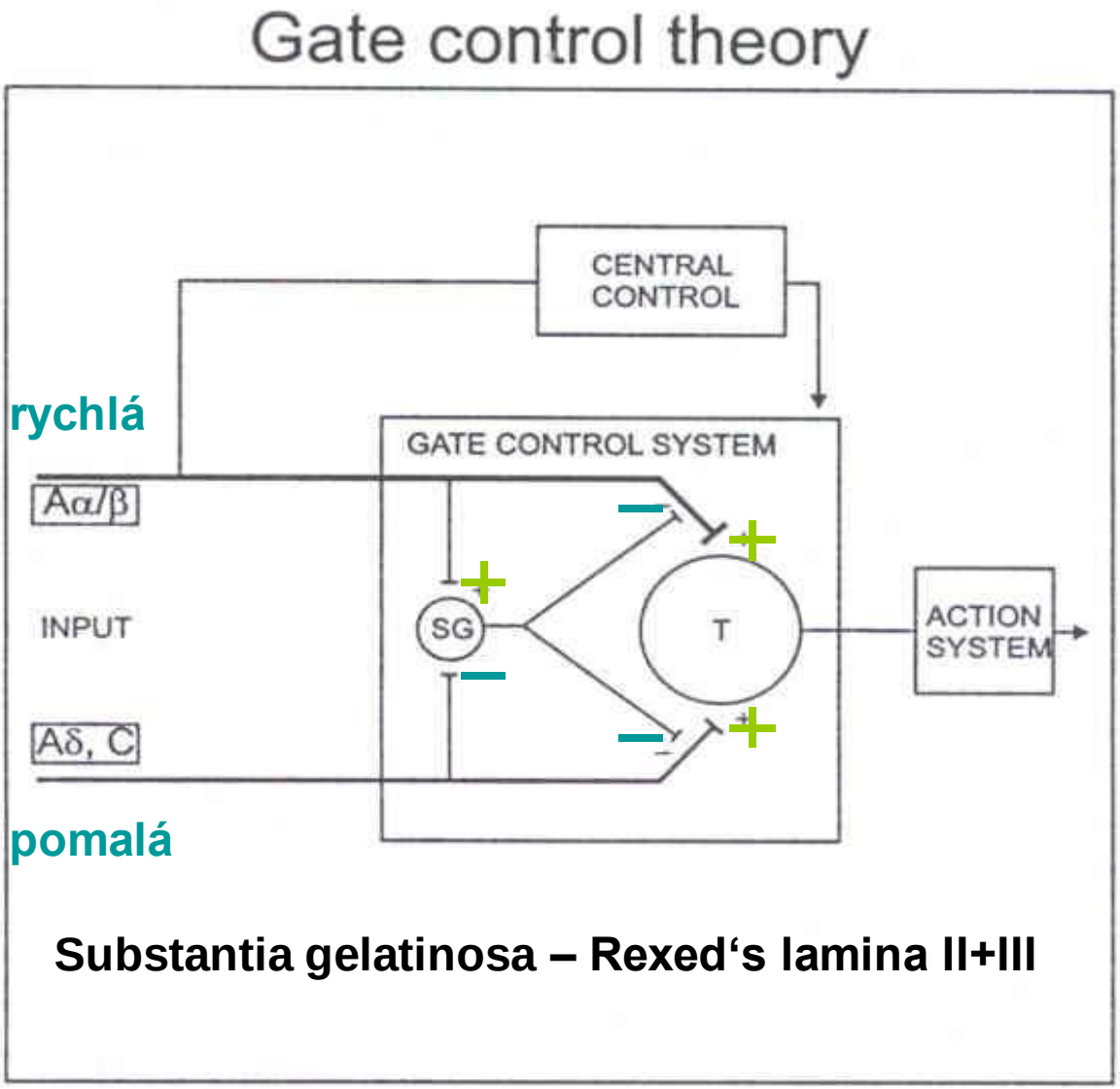
Reffered pain creation
Head‘s zone




Diaphragm (C4)
Oesophagus (T4 and T5)
Liver and gall bladder (T8–T11)
Colon (T11)
Bladder (T11–L1)
Heart (T3 and T4)
Stomach (T8)
Small intestine (T10)
Kidney and testes (T10–L1)

Classical gate control theory

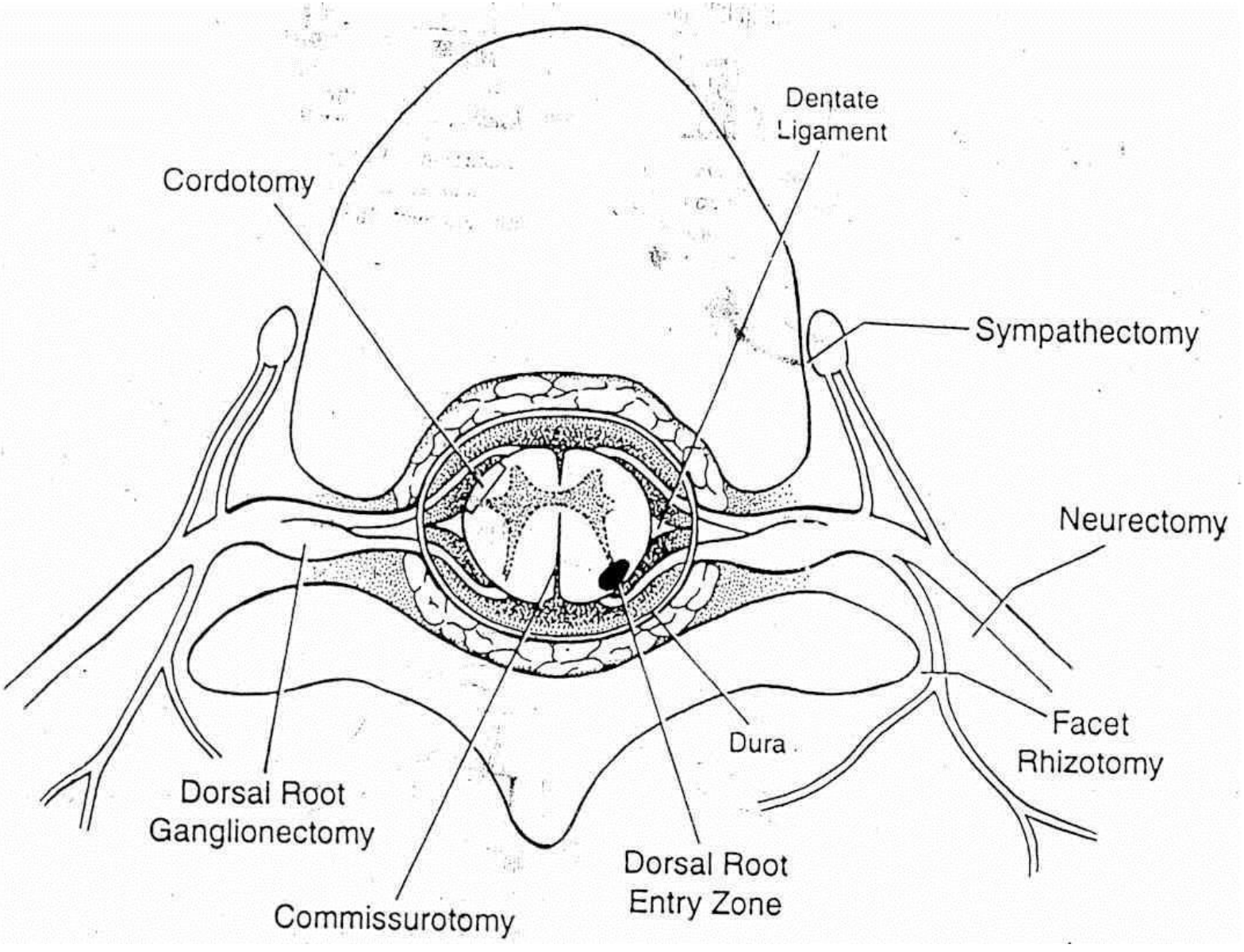
today considered obsoletee



Algorithm of pain treatment

- physical therapy, rehabilitation, acupuncture
- pharmacotherapy – non opioid analgetics
  - ASA, NSA
- pharmacotherapy – opioid analgetics
  - codeine, morphine, fentanyl
- psychotherapy
- invasive methods
  - spinal neuromodulation
  - DREZ (dorsal root entry zone)
  - cortical stimulation

Invasive treatment of pain



Invasive treatment of pain – DREZ

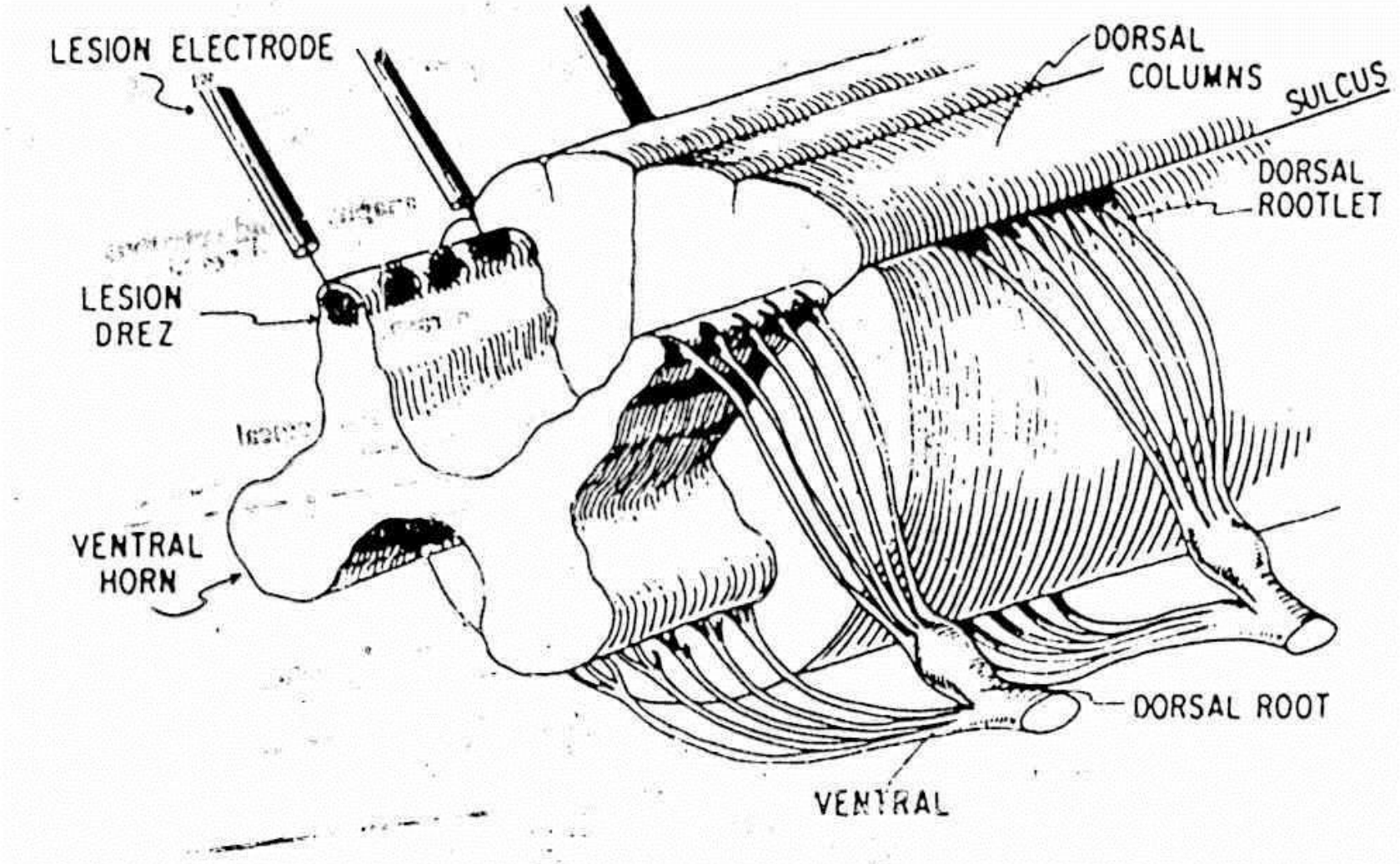


Fig. 58.1 Nashold's diagram of location of his lesions in dorsal root entry zone. (From Nashold & Ostdahl 1979)

Basic types of pain

Acute (fast) pain

- is triggered by identifiable stimuli
- is short-termed
- it ceases when the tissue injury that caused it has healed
- usually does not repeat

Chronic (slow) pain

- lasts longer than 6 months
- the causes may not always be identifiable
- the intensity of the pain is always higher than the intensity of the stimulation
- causes great physical and mental suffering
- worsens the quality of life

Neuropathic pain

- it does not start at nociceptors but at primary afferent fibers
- hypersensitivity of C and Aδ fibers
- remodeling of neural responses arrangement
- canalopathy (sodium, calcium and potassium channels)

Neurotransmitters of pain

- excitatory aminoacids – **glutamate** (Glu)
  - receptors: kainate, AMPA, NMDA
- **substance P** (NK1 receptor, $\Downarrow K^+$ conductivity)
- **CGRP** (calcitonin gene-related peptide)
  - glutamate causes rapid and short-term depolarization
  - peptides cause long-term discharges

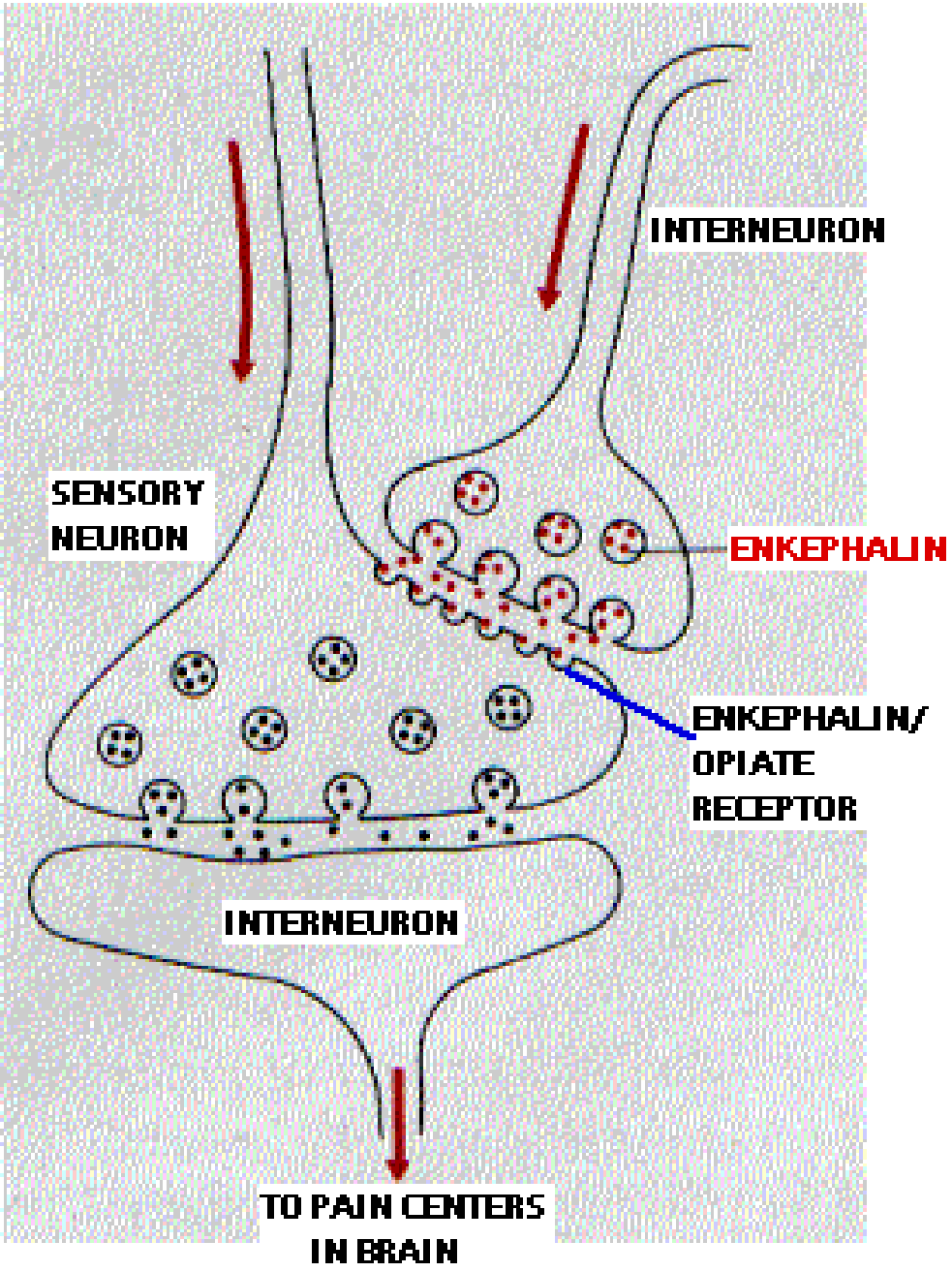
Primary hyperalgesia*

- occurs at the site of injury
- peripheral sensitization – lowering the threshold of nociceptors
  - activation of TTX-R sodium channels
  - increased TTX-R expression (e.g. by NGF)
  - redistribution of TTX-R from the perikarya to the periphery
  - redistribuce TTX-R z těla neuronů na periférii

Secondary hyperalgesia*

- occurs in undamaged tissue around the injury
  - e.g. repeated stimulation of C fibers or intradermal application of capsaicin
  - increased sensitization of spinal neurons, their permanent depolarization
  - wind-up phenomenon
  - activation of NMDA receptors
  - enlargement of receptive fields

Pain inhibition*



Met-enkephalin
(Tyr-Gly-Gly-Phe-Met)

Leu-enkephalin
(Tyr-Gly-Gly-Phe-Leu)

Opioid system*

- nigrostriatal (A9) + mesolimbic (A10) dopaminergic
  - influences motor skills and the reward system
- hypothalamo-hypophysial
  - modulates hormonal secretion
- ascendening and descending tracts
  - pain modulation
  - ascending – medulla spinalis, thalamus
  - descending – PAG, ncll. raphes

Endogenous opioids*

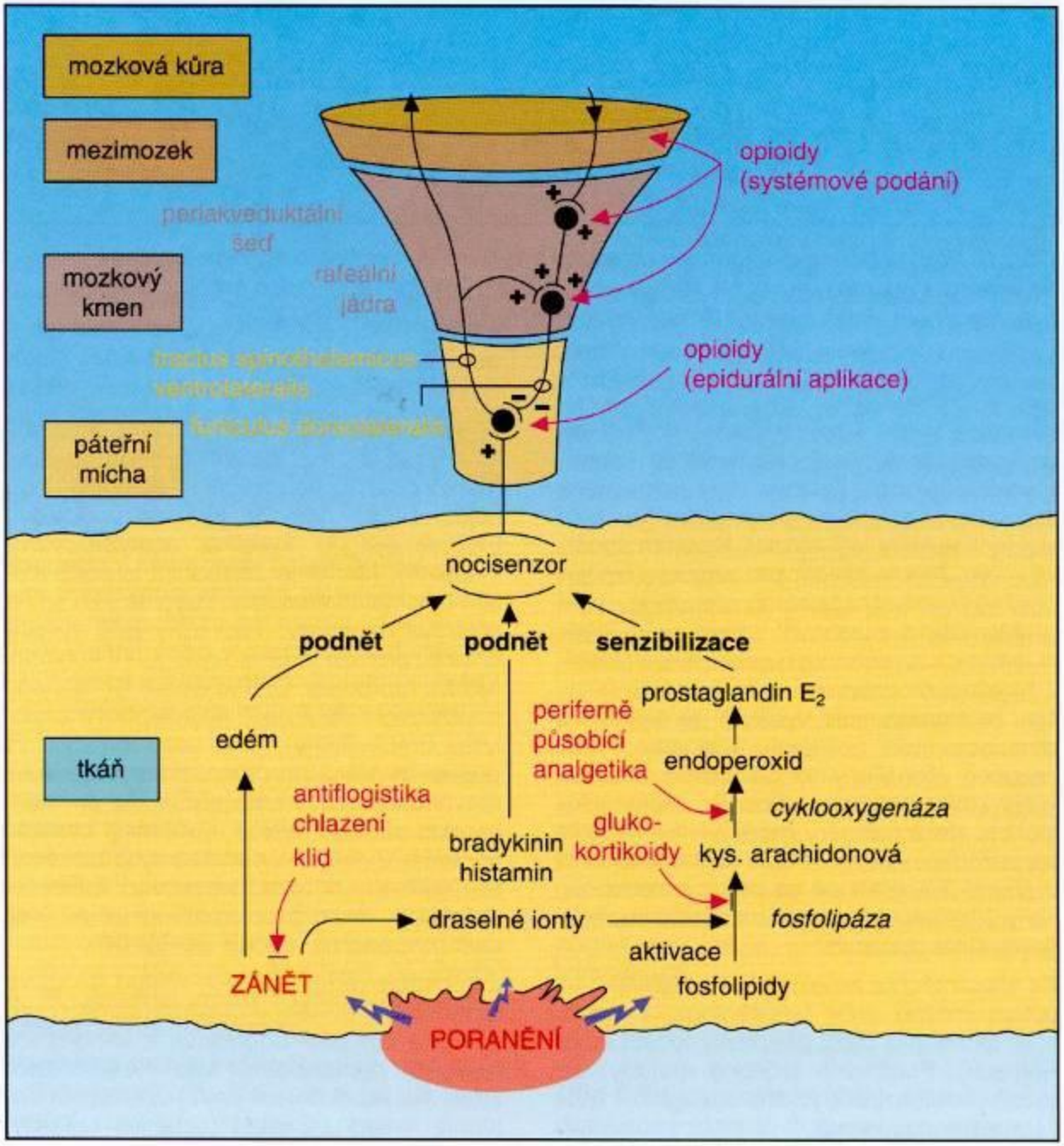
- β-endorfin (31 aminacids) - **μ, δ, κ**
- endomorfin (4 aminacids) - **μ**
- Leu-enkefalin (5 aminacids) - **δ**
- Met-enkefalin (5 am aminacids inokyselin) - **δ**
- dynorfin (A 1-8, B 1-17) - **κ**
- nociceptin/orfanin

Endogenous opioids*

- presynaptic receptors
  - inhibition of neurotransmiters release
  - ↓ Ca^{2+}
- postsynaptic receptors
  - ↑ K^{+} conductivity – hyperpolarization of membrane

Endogenous canabinoids*

- amids and esters of fatty acids
- anandamid
- palamitoyletanolamid (PEA)
- receptors: CB1, CB2
  - CB1 in PAG and RVM, sensory neuron
  - CB2 in structure of immune system
- FAAH – hydrolase of fatty acids amids


mozková kůra
mezimozek
mozkový kmen
páteřní mícha
periakveduktální šeď
rafeální jádra
tractus spinothalamicus ventrolateralis
fasciculus dorsolateralis
opioidy (systémové podání)
opioidy (epidurální aplikace)
nocisenzor
podnět
podnět
senzibilizace
tkáň
edém
antiflogistika
chlazení
klid
bradykinin
histamin
periferně působící analgetika
prostaglandin E_2
endoperoxid
cyklooxygenáza
gluko-kortikoidy
kys. arachidonová
draselné ionty
aktivace
fosfolipáza
fosfolipidy
ZÁNĚT
PORANĚNÍ