Patho-physiology of Nervous System Talk 1 – Pain and Motor disorders

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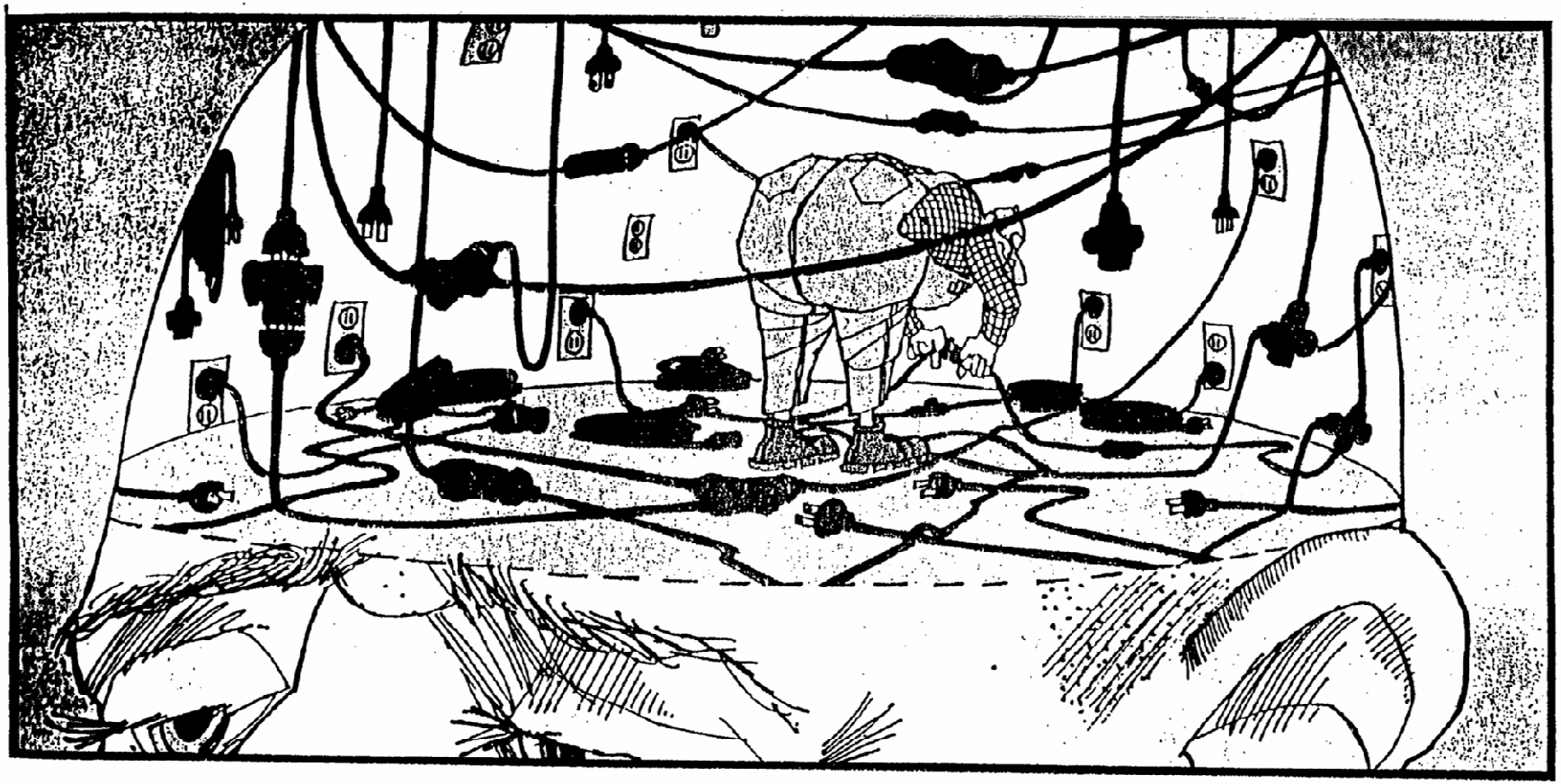


How the brain works.

Talks on NS

Talk 1 - This - Pain and Motor disorders

Talk 2 - Syndromes in neurosciences

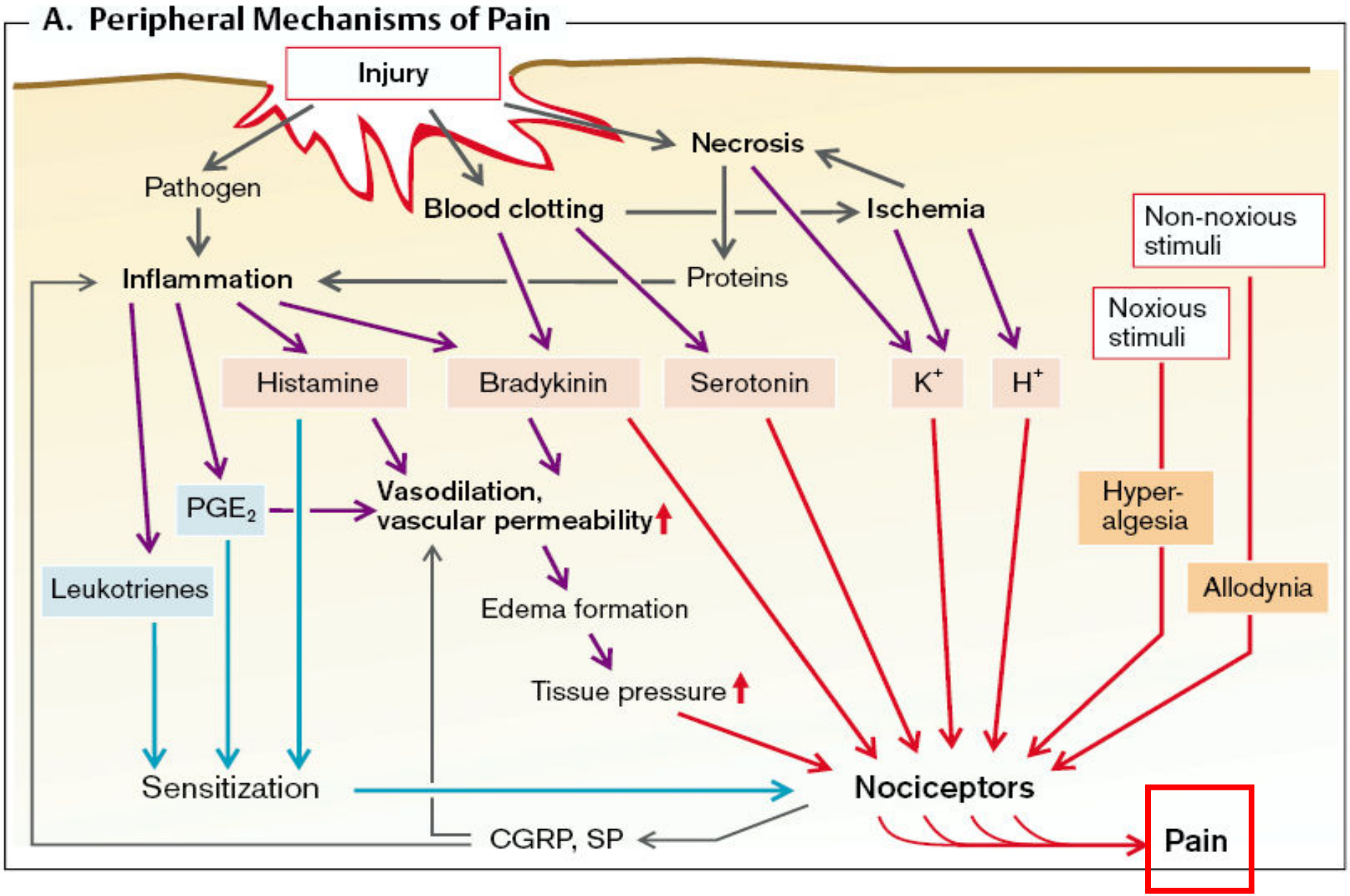
Talk 3 - Disorders of special senses

Talk 4 - Cognitive functions, dementias, etc.

Outline

- Pain
- Motor disorders

Pain



CGRP (Calcitonin-gene related peptide), SP (Peptide substance)

Tissue injury leads to painful sensation

Pain:
1 is a warning that something goes wrong
2 helpful to diagnostics and localization pathologies
3 can be pathologic, anoying beyond the purpose

Psychological pain components
Algothymic component is its emotional context
Algognostic component says, where, what and how much it gets wrong

Pains, which lose the warning purpose are **…neuralgic pains**
neurologic investigation shows no deviation from norm.

Psychophysics: - no relation between stimulus intensity and percept intensity
- there is continuous transition between various touch and pain sensations
tickling, sharp point touch, warm, cold vs.
itching, puncture, scalding (opaření), congelation
what itches, we scrub (scrape) (?), [Fenistil – antihistaminic, antipruriginous drug]

Pain is modified by…

- previous experience, expectations
- instruction, suggestion
- emotions, especially fear and anxiety
- concurrent activation of other sensory inputs
- diversion/ redirection of attention

Pain leads to activation of…

- sympathetic n.s.

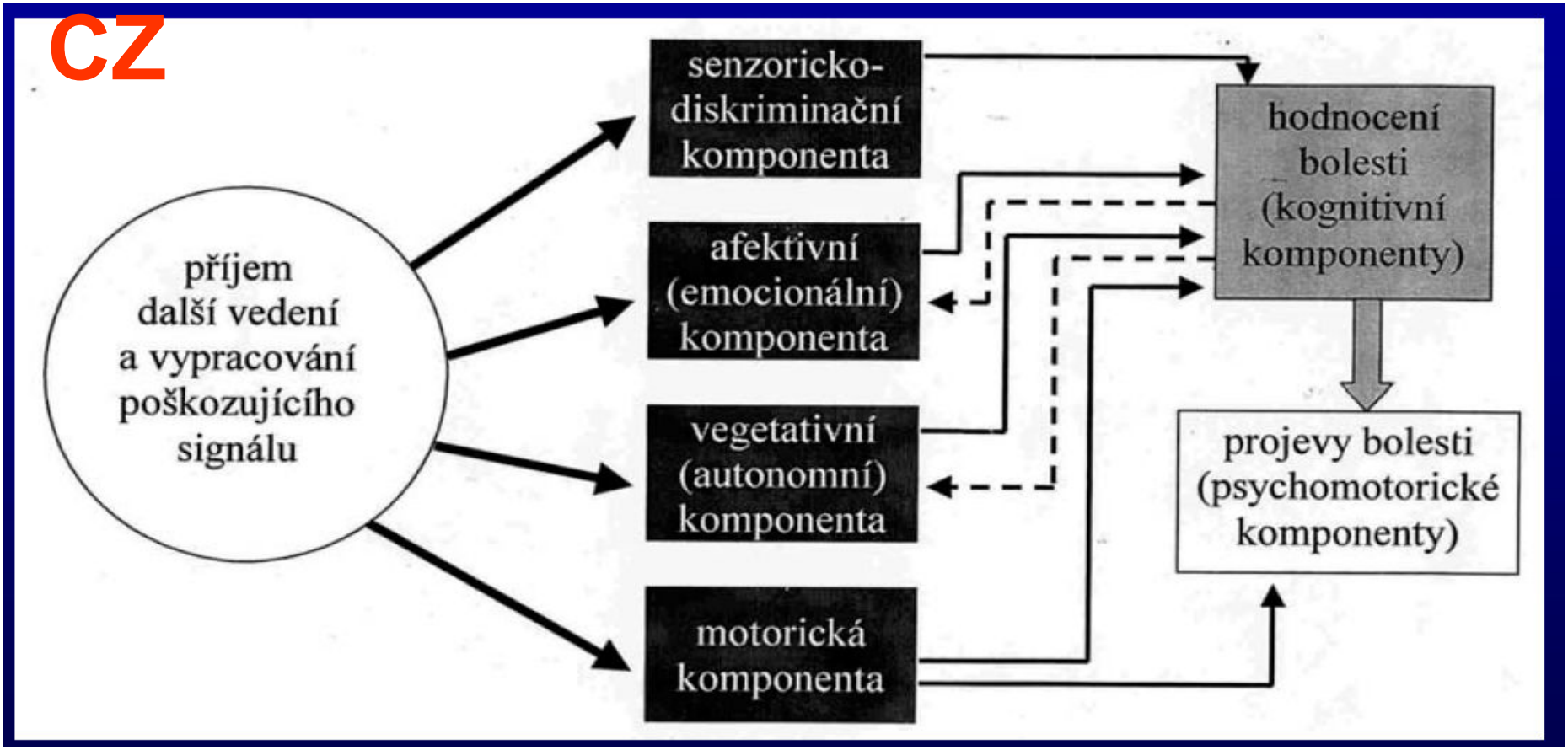
vasoconstriction, hypertension, tachycardia, sweating, paleness, goose flesh, mydriasis

- parasympathetic n.s.

hypotension, bradycardia, nausea/ vomiting

- motor response
- conscious response

CZ



Types of pain, phenomenology

Patho-genetic classification of pain

- •receptive (nociceptive)
- •peripheral neurogenous (neuropathy)
- •central neurogenous
- •originating in autonomous nervous system (Sympathetic n.s.)
- •visceral
- •pain of psychical origin

Acute pain

-cause can be identified

-short term

-disappears when the original cause is cured

-usually does not recurr

Chronic pain

-longer than 6 months

-cause may not be identified

-intensity higher than expected to known stimulus

-causes high physical and psychical stress

-annoying in daily life

Nociceptors, pain receptors = dedicated receptors, ion channels and free nerve endings

- They are sensitive on the **pH changes** (pH in acute abscess, phlegmona reaches 5,8 = pain, pH in chronic abscess is normal, without pain)

- Nociceptors register the **ratio K^+:Ca^{2+}**
  (treshold for pain is lower in the lower Ca^{2+} level in ECV)
- evoking inflammation are (permeability of vessel wall, oedema) histamin, bradykinin, serotonin

- direct influence of free-nerve endings:
  potassium, histamin, bradykinin serotonin

- sensitisation of nociceptors:
  prostaglandins, esp. PgE_2, interleukin-1, interleukin-6, cyclooxygenases (COX-1, COX-2)

- From activated free nerve endings P-substance is released.
  It influences vessel wall (vasodilation, permeability of vessel wall, oedema) and mast cells (release of histamin after degranulation).

Fibres conducting nociceptive stimuli

- **C-fibres** – without myelin sheets, action potentials are convected slowly, fibres convect deep, nonaccurate localized, diffuse pain
- **Aδ-fibres** – with thin myelin sheet, fibres mediate fast conduction of sharp, accurate localized pain
- **Aα/Aβ-fibres** – large myelinated. Fibres do not convect nociceptive stimuli, they mediate tactile stimuli
- Afferent fibres enter dorsal spinal roots. In this region exist excitatory and inhibitory interneurons. Inhibitory interneurons gate the passage of information into thalamus and cortex.

Painful stimuli

-chemical

-endogenous inflammation mediators (bradykinin, prostaglandins, serotonin, histamin, K+, H+, Il-1)

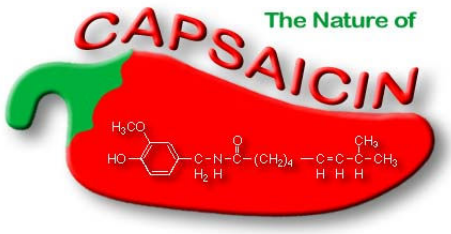
-exogenous substances (capsaicin, formalin = formaldehyde)

-low/ high temperatures

-temperature above 42°C is damaging

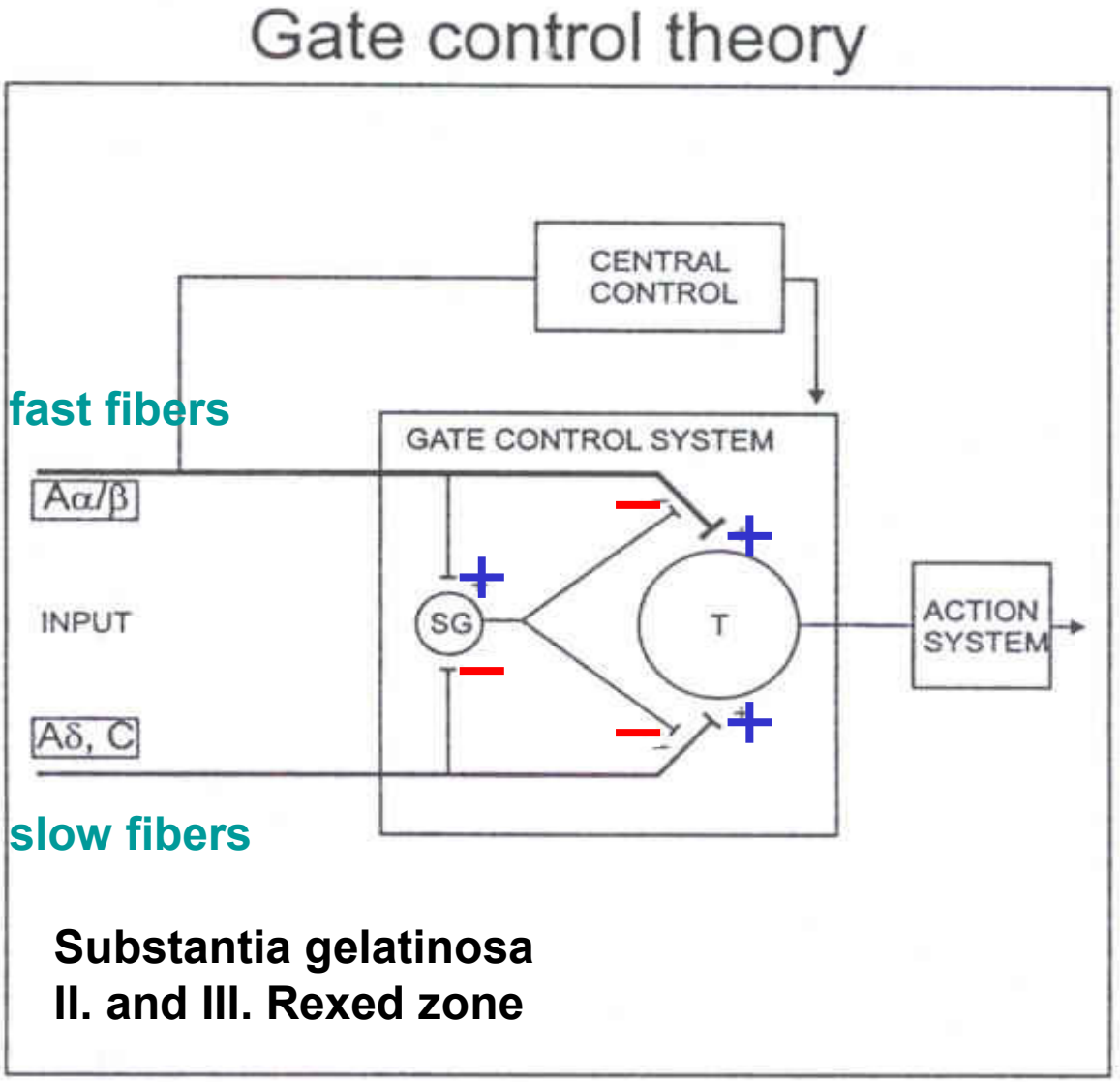
-mechanical

During painful stimuli…



- are activated tetrodotoxin resistant (TTX-R) channels
- ATP is relased from damaged cells and acts as pain mediator. ATP receptors are purin receptors (P_2X)
- vaniloid receptors (VR_1) are receptors for capsaicin, also activated above 42°C, pH < 6.5
- activated acid sensing ion channels (ASIC), when pH < 6.5
- Up-regulation of post-synaptic receptors of excitation neuro-transmitters - glutamate (NMDA) and substance P (NK_1)

Pain gating control – spinal cord



Opioid system and others

- nigro-striatal and meso-limbic, dopaminergic
  - motor systems and reward pathways
- hypothalamo-hypophyseous
  - central hormone modulation
- ascendent and descendent pathways
  - modulation
  - ascendent – spinal cord, talamus
  - descendent – peri-aquaeductal grey, nuclei raphe

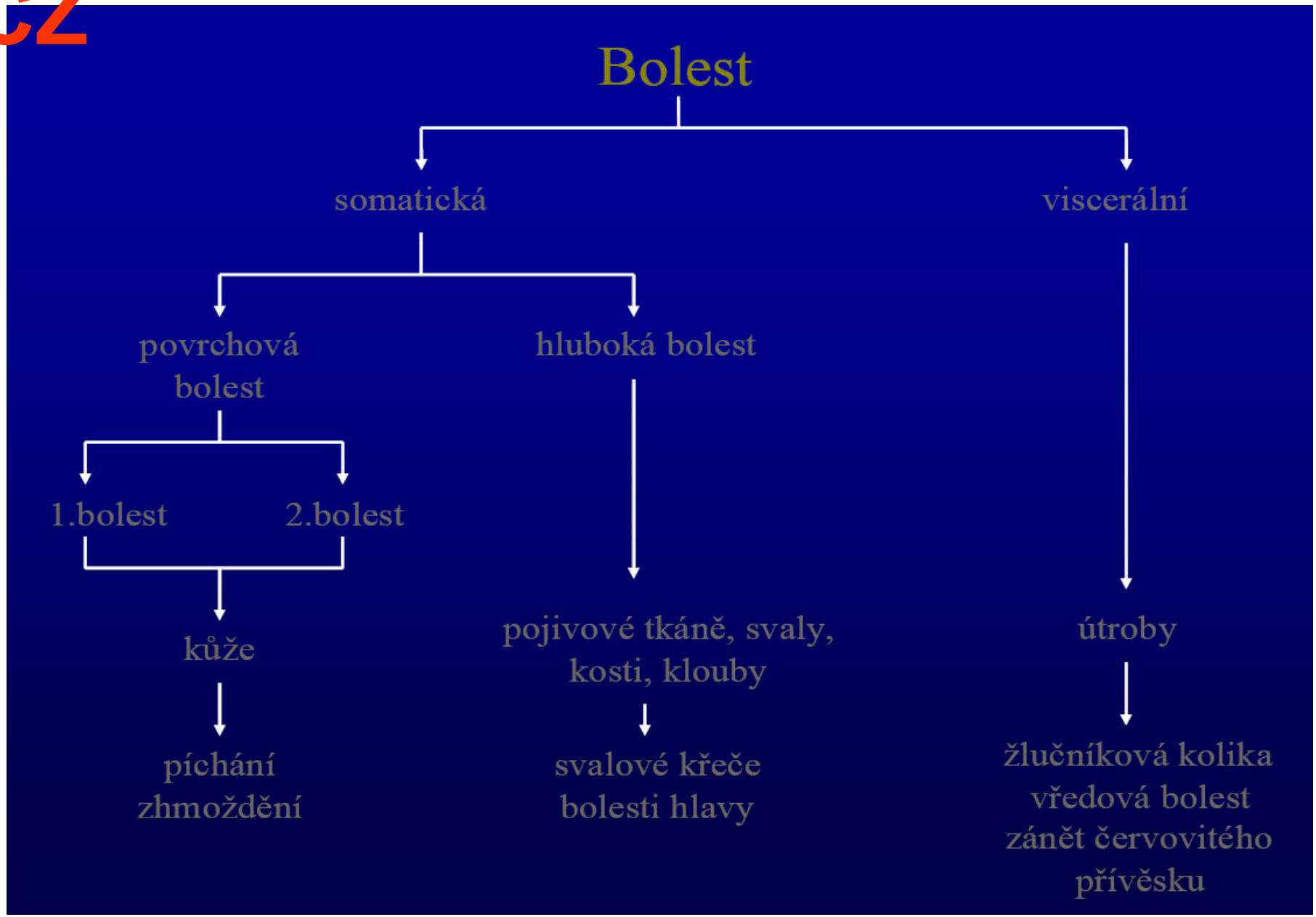
Endogenous opioids

- β-endorphine (31 AA) - μ
- Endomorphine (4 AA) - μ
- Leu-enkefalin (5 AA) - δ
- Met-enkefalin (5 AA) - δ
- Dynorphine(A:AA 1-8, B:AA1-17) - κ
- nociceptin/ orphanin
- nocistatin
- pre-synaptic receptors
  - Inhibiting neuro-transmitter release
  - ⇓ Ca^{2+}
- post-synaptic receptors
  - ⇑ K^{+} conductance – hyperpolarization

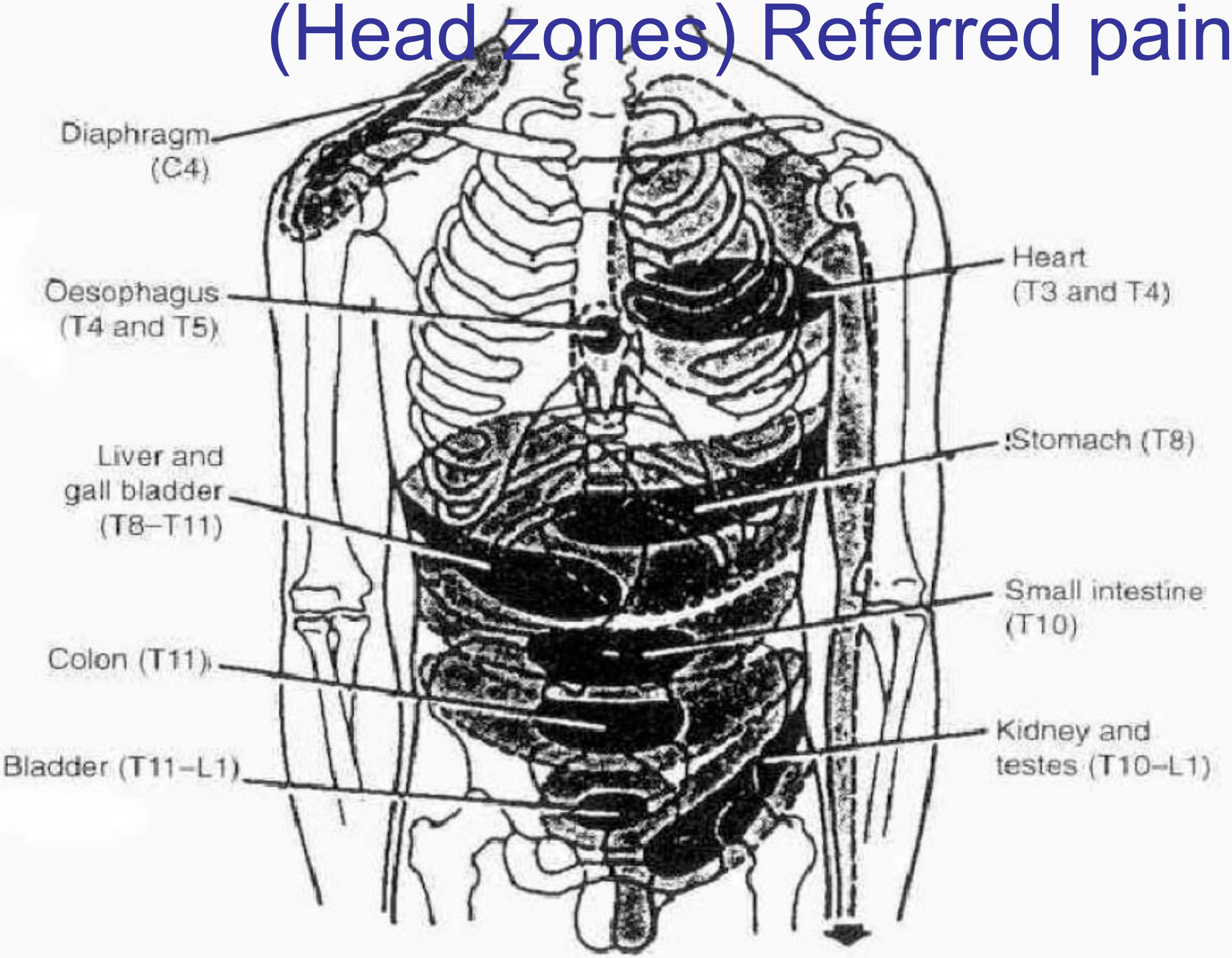
Endogenous cannabinoids

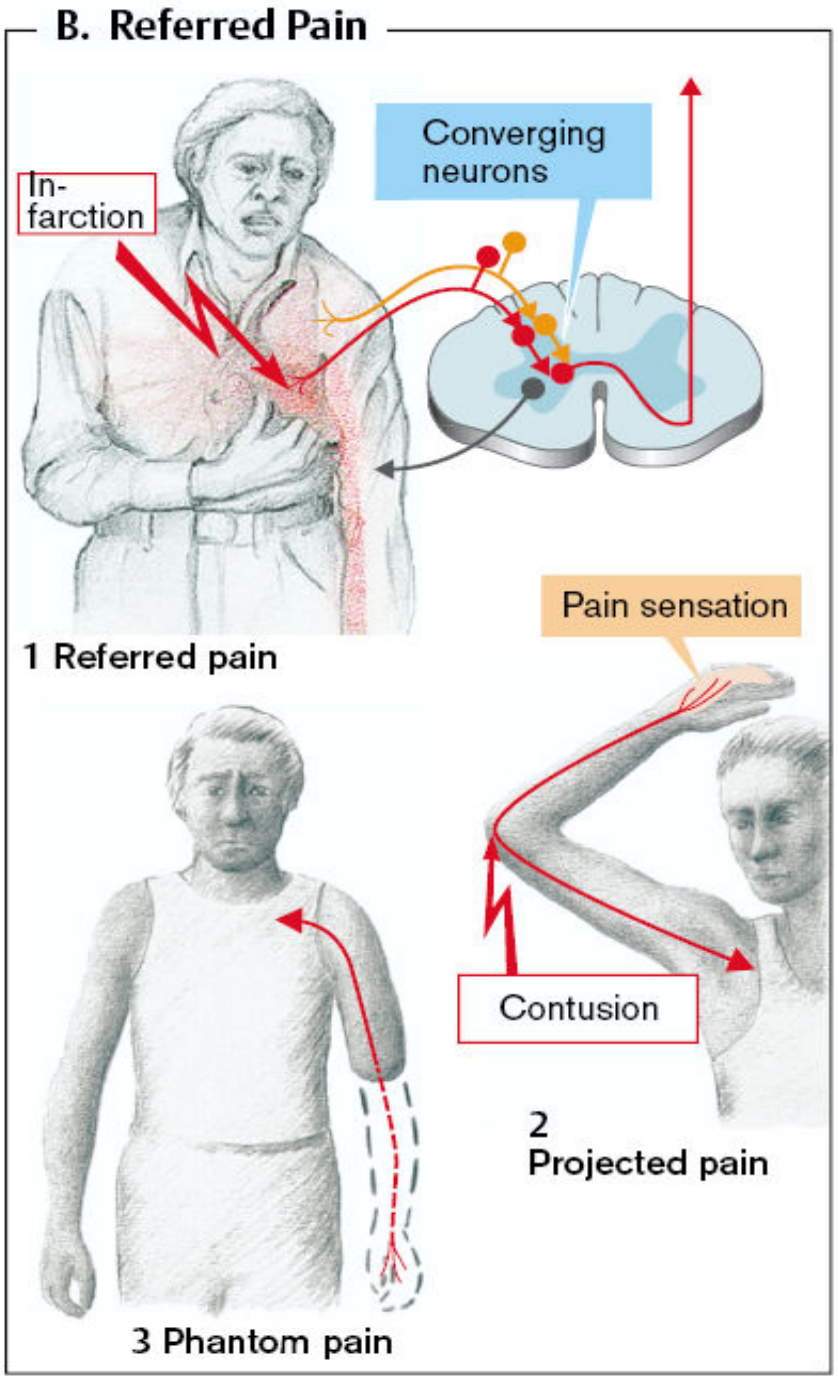
- amids and esthers of fatty acids
- anandamid
- palmitoyl-etanolamid (PEA)
- receptors CB1 a CB2
- CB1 in PAG and RVM, sensory neuron
- CB2 in structures of immune system
- FAAH – hydrolasis of FA amids
- In the inner ear and auditory pathway as well

Types of pain, phenomenology(2) CZ



(Head zones) Referred pain

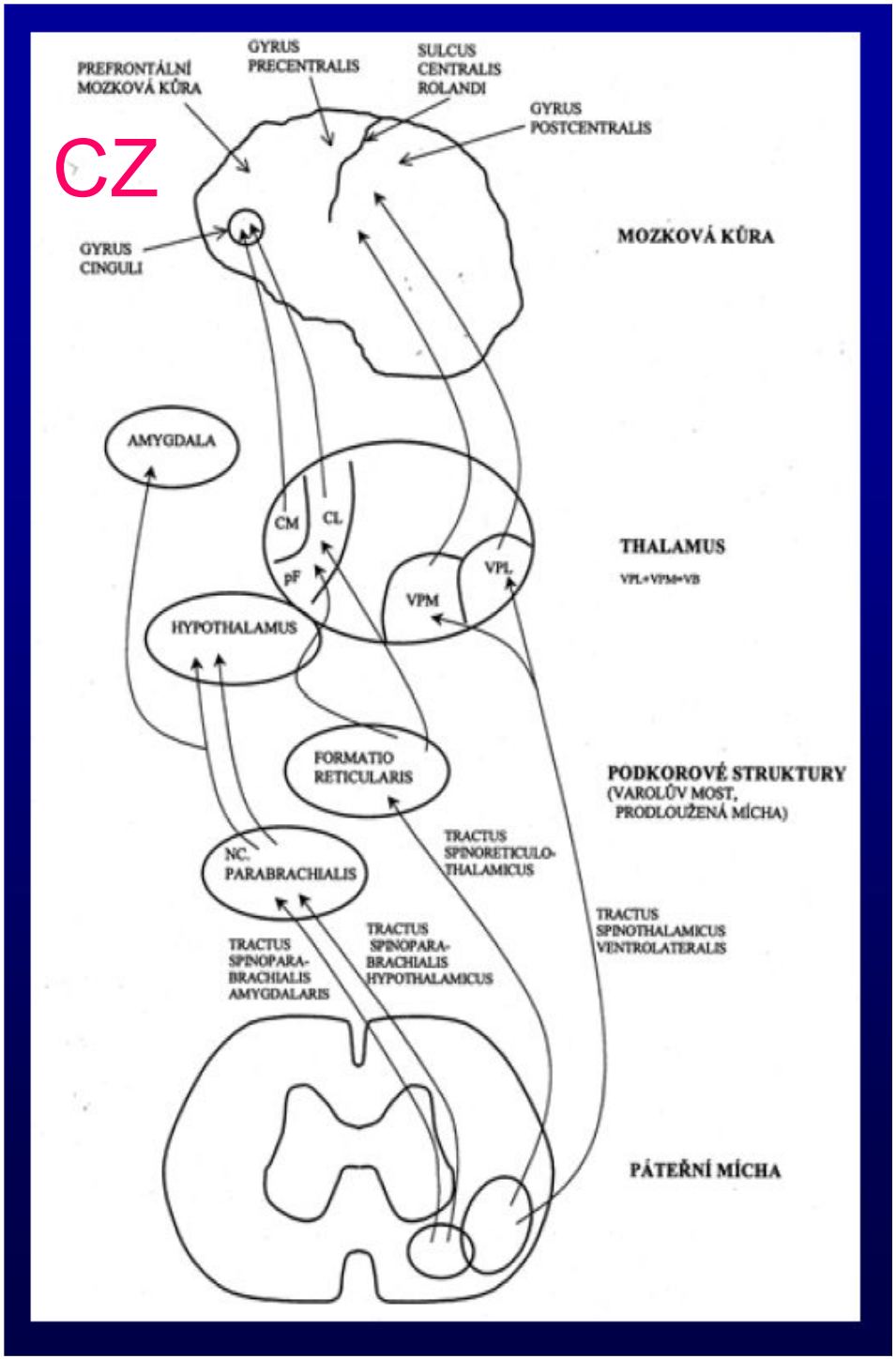




Referred and pathologic pain

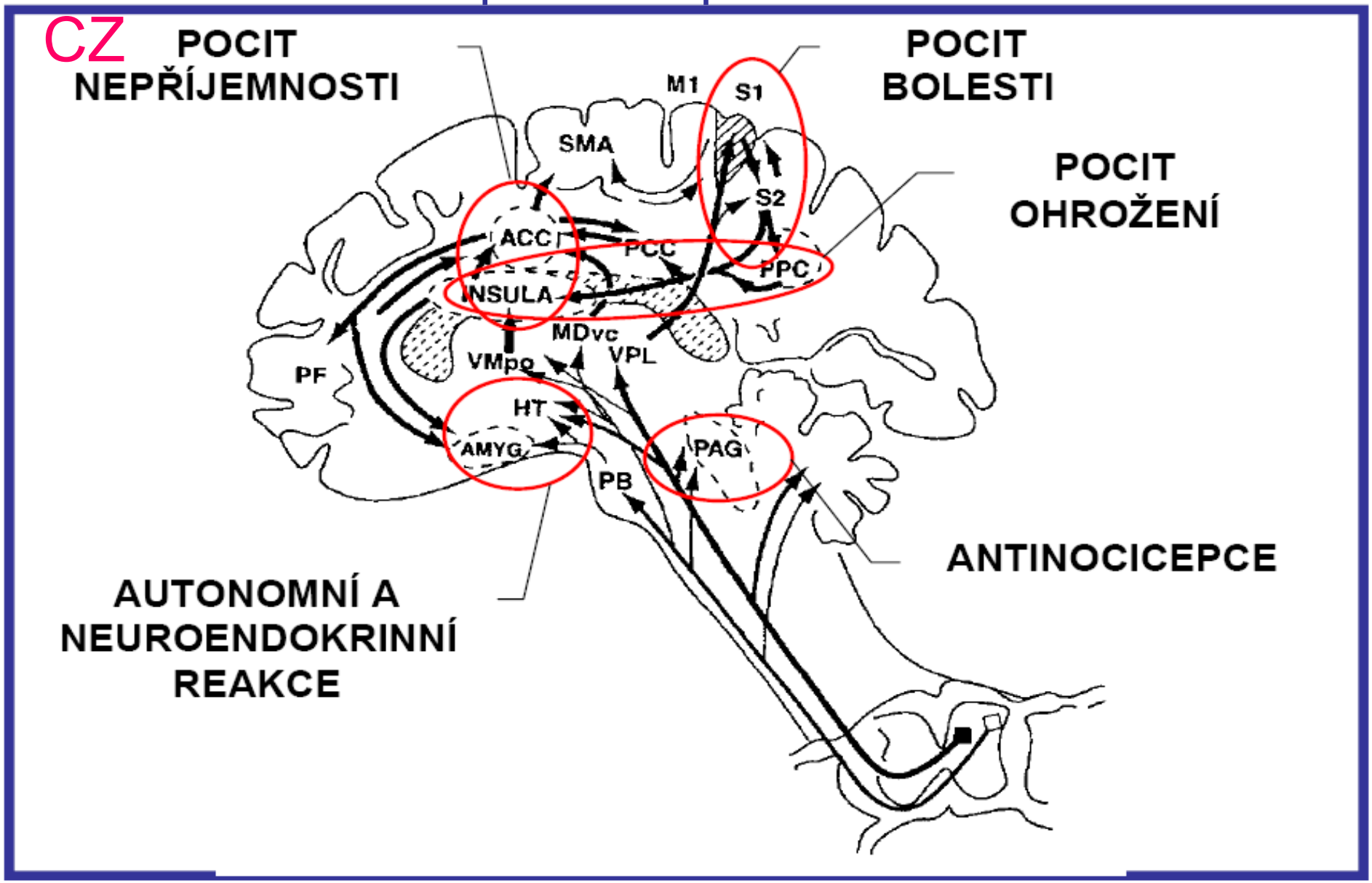
Other pathologic painful sensations:

…,
headache,
n. trigeminus,
Migraine,…

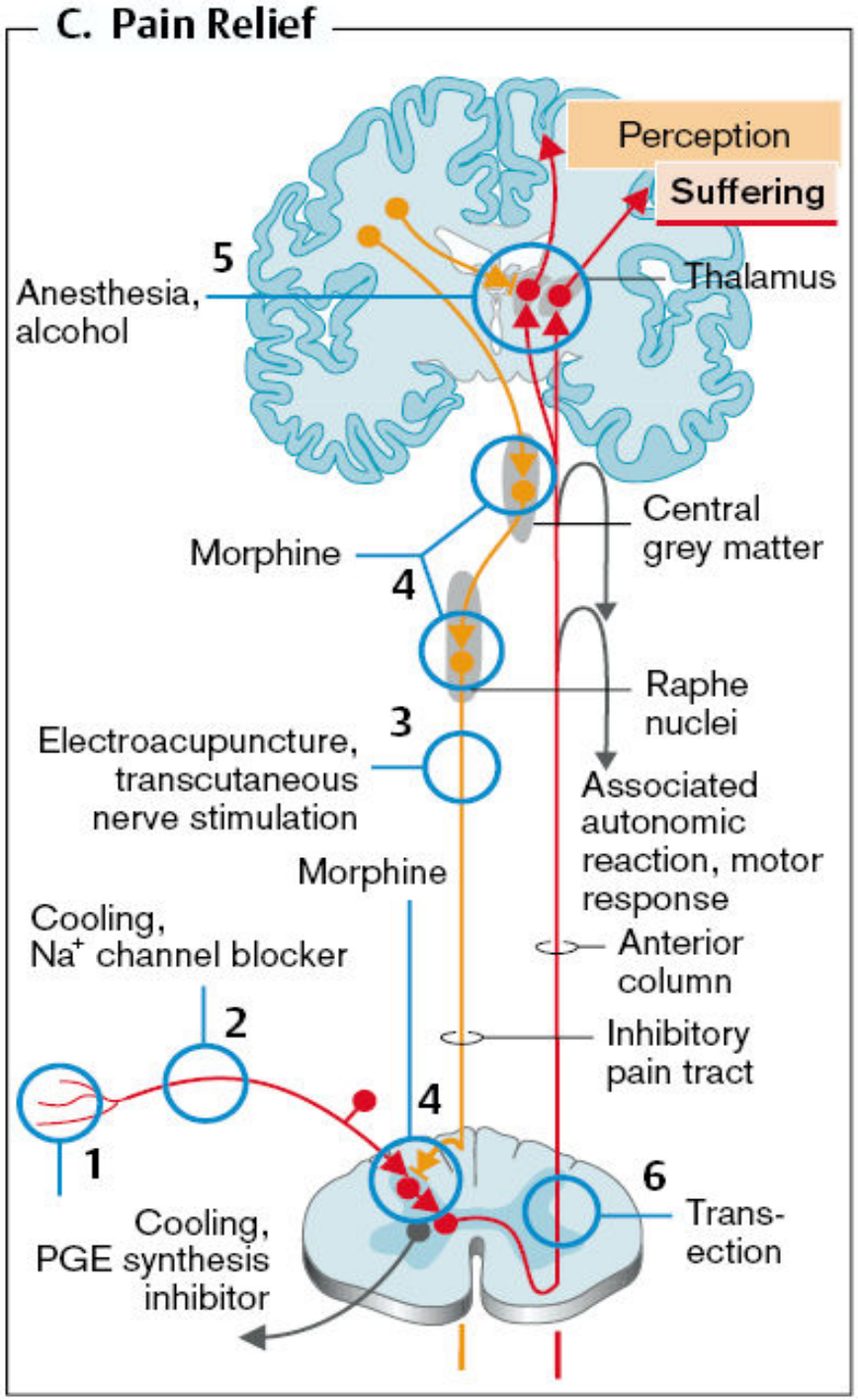


Localization of CNS pain pathways

Localization of sensory, affective and cognitive pain components



Pain Relief

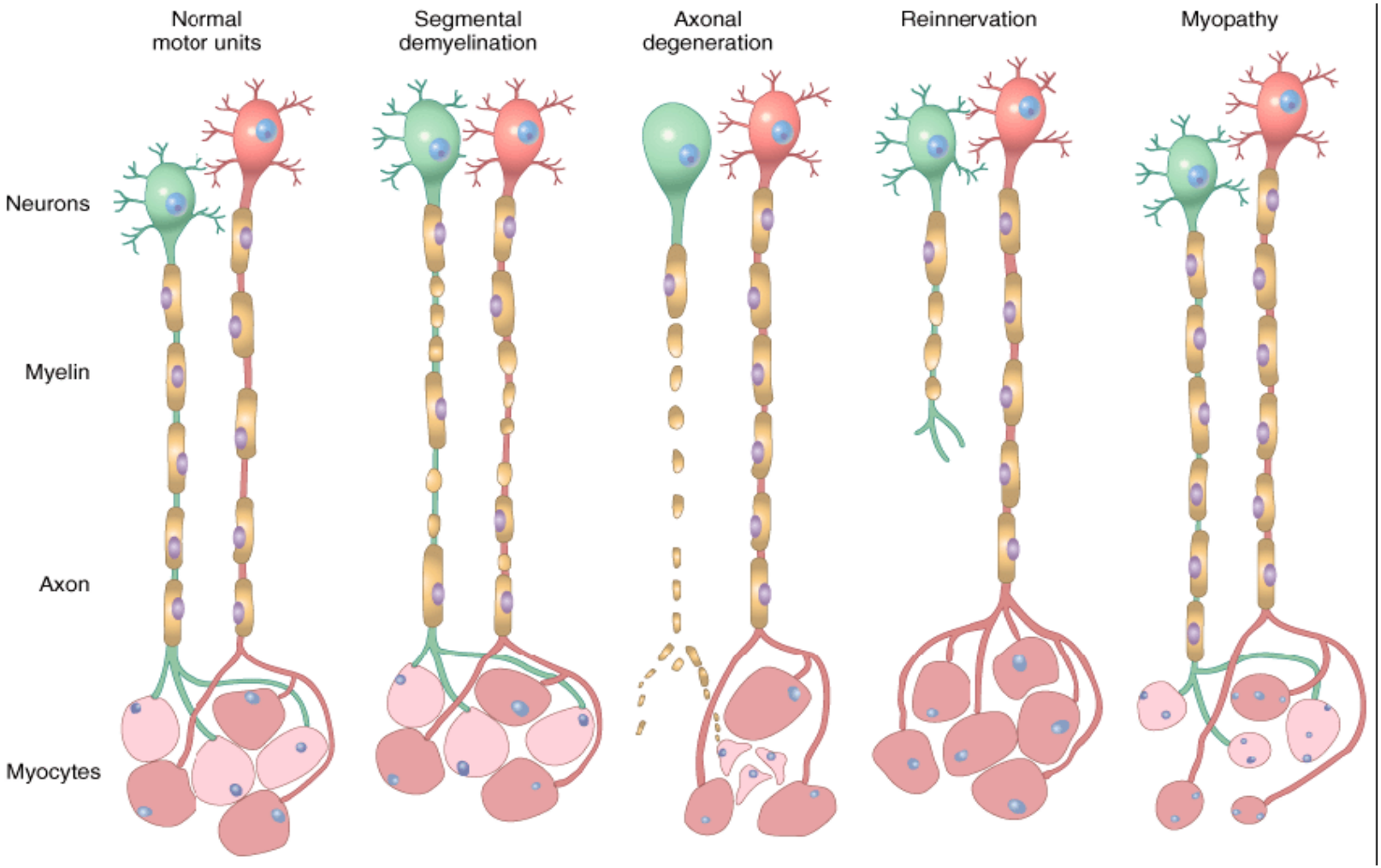

C. Pain Relief
Perception
Suffering
Thalamus
5
Anesthesia, alcohol
Central grey matter
Morphine
4
Raphe nuclei
3
Electroacupuncture, transcutaneous nerve stimulation
Associated autonomic reaction, motor response
Morphine
Cooling, Na+ channel blocker
Anterior column
2
Inhibitory pain tract
4
1
6
Trans-ection
Cooling, PGE synthesis inhibitor

Motor disorders/
Movement disorders

Movement disorders

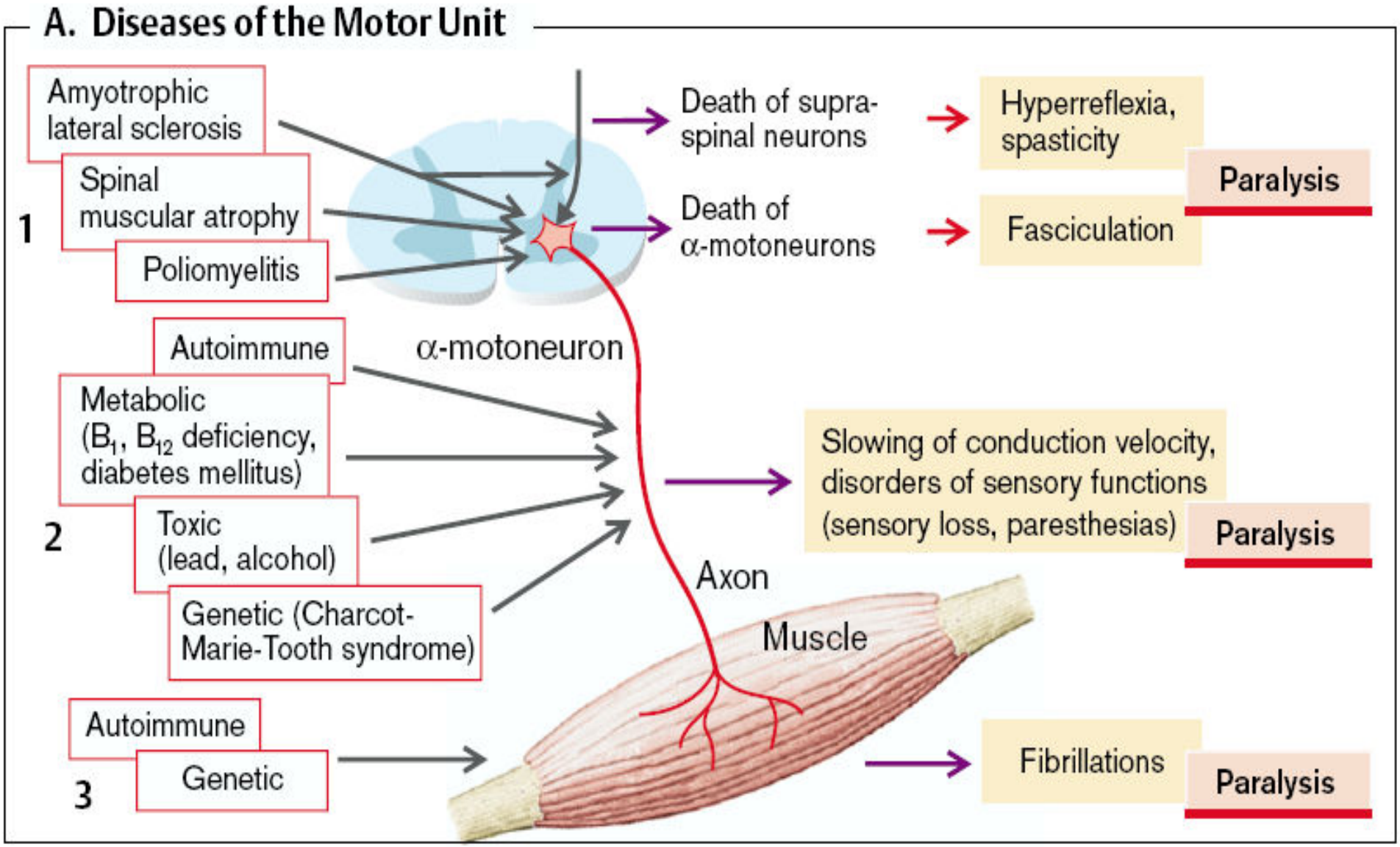
- Muscle disorders
- Lower motoneuron disorders
- Upper motoneuron disorders
- Basal ganglia disorders
- Cerebellum disorders
- Disorders of passive movement apparatus

Lower motoneuron - Neuromuscular unit disorders



norm neuropathy myopathy

Diseases of the motor unit-neuropathies



Neuropathies versus myopathies

Clinical findings	**Neuropathy**	**Myopathy**
Muscle weakness	**++**	**++**
Loss of reflexes	**+**	0
Fasciculations (twitchings)	**+**	0
Sensory deficit	**+**	0
Abnormal reflexes (Babinski)	**+**	0

Lower motoneuron disorders

- Peripheral nerve affected
  - Axonal degeneration; injury $\rightarrow$ Waller degeneration
  - Axonal demyelinization (Guillain Barre syndrome)

(Both motor and sensory disorder)

- α-motoneuron soma affected
  - Inflammation (example poliomyelitis)

Lower motoneuron disorders

- (phenomenology of sole motor disorders)
  - Motor unit (fasciculations)
  - atrophia of the whole motor unit
  - when denervated, first comes fibrillation, then atrophia

Upper motoneuron

Is it a

- Pyramidal pathway ?

or

- Extra-pyramidal system ?

Upper motoneuron, signs

- plegia, paralysis
- spasticity
- cogged wheel sign
- hyperreflexia
- clonus
- abnormal exteroceptive reflexes (Babinski)
- (no atrophy, no fasciculations)

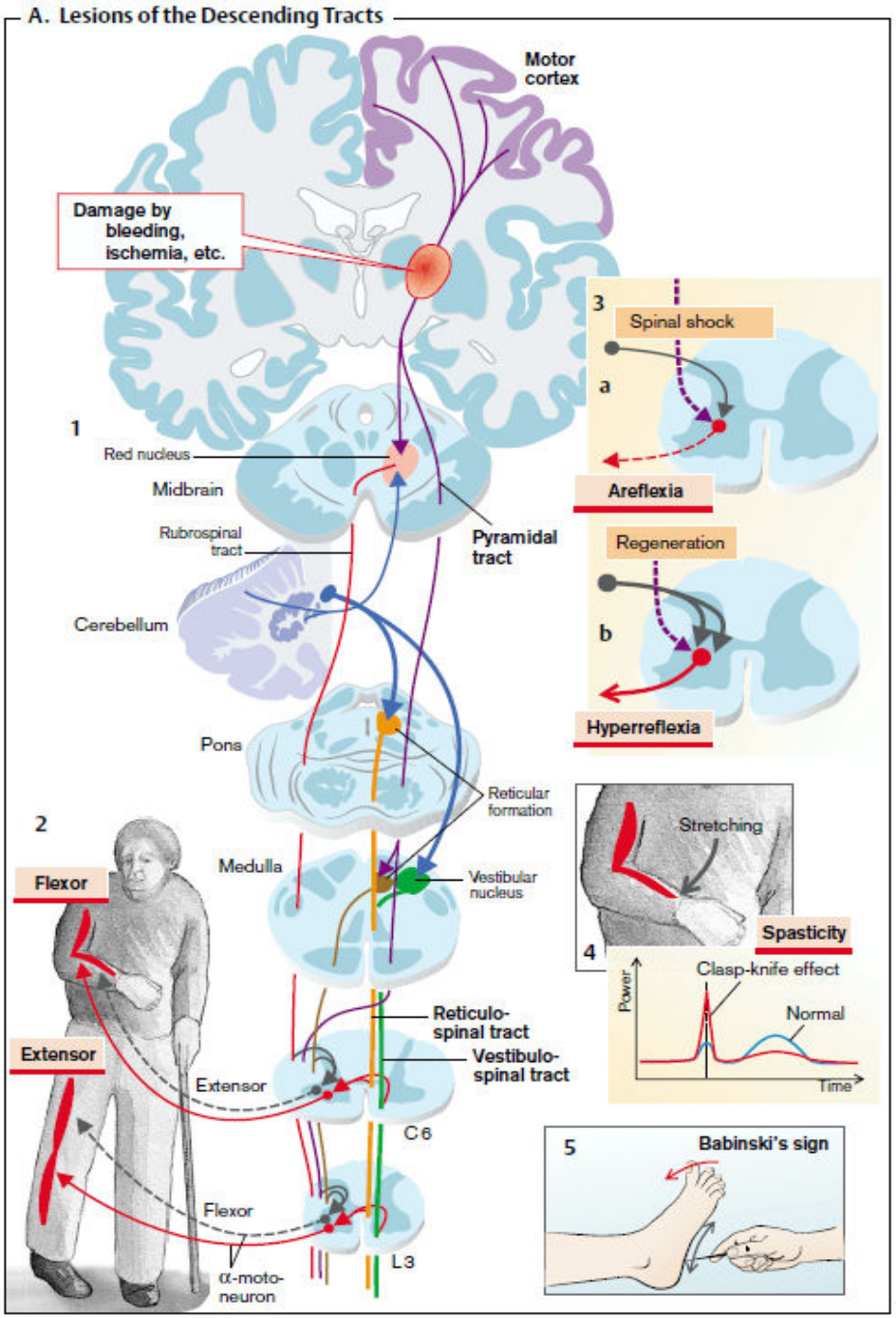
Upper motoneuron, point of view of general practice

"Upper motoneuron" means all descendent motor systems, not only tractus cortico-spinalis

Brain $\rightarrow$ lateral signs, hemiplegia

Spinal cord $\rightarrow$segmental signs, paraplegia, quadruplegia

Upper motoneuron disorders =descending tracts lesions

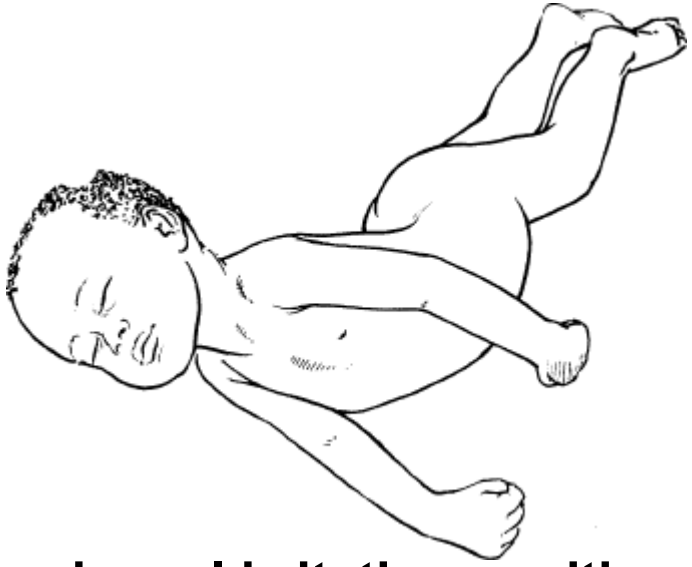


Spasticity

- Higher resistance towards passive movement, accented with higher velocity (scissor gait)
- Hyper-reflexivity
- Central spasticity (abnormal excitation)
- Spinal spasticity (interneurons)
  - Flexor reflexes
  - Extensor spasm (fragment of locomotion?)
  - Sensory neurons

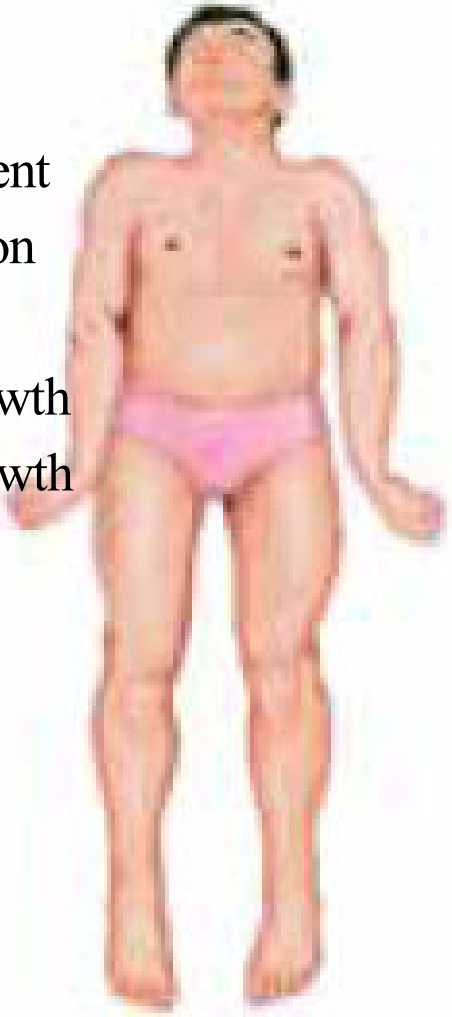
Spinal shock in man

Phase	Time	Physical exam finding	Underlying physiological event
1	0-1d	Areflexia/Hyporeflexia	Loss of descending facilitation
2	1-3d	Initial reflex return	Denervation supersensitivity
3	1-4w	Hyperreflexia (initial)	Axon-supported synapse growth
4	1-12m	Hyperreflexia, Spasticity	Soma-supported synapse growth



meningeal irritation position

In both meningeal irritation and spinal shock extensor systems take over flexor systems



Decerebration

spinal shock position

Central Nervous System (CNS) trauma. Spinal Cord Injury (SCI).

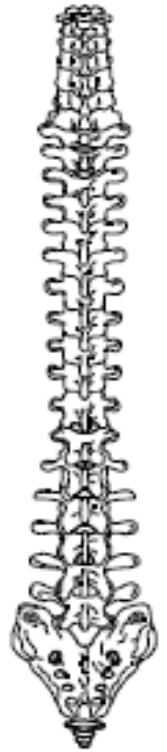
Comparison of CNS to PNS (peripheral nervous system/ peripheral nerve) injury

Progression of CNS injury (Spinal cord as a model)

- local swelling at the site of injury which pinches off blood perfusion → ischemia
- Excessive release of glutamate and excitotoxicity of neurons and oligodendrocytes at the site of injury
- Infiltration by immune cells (microglia, neutrophiles)
- Free radical toxicity
- Apoptosis/ necrosis

Pathophysiology

- **Common Sites**
  - ☺ **C5-6 and T12 ---- L1**
- **higher the injury, the greater the motor/ sensory loss: refer to syllabi/dermatomes**
- **neuro dysfunction depends on the level of the injury**
  - ☺ **T1 or above QUAD (tetraplegia)**
  - ☺ **T2 or below PARA**
  - ☺ **Above C4 Resp. Paralysis**



Pathophysiology (Extent of Injury)

Complete

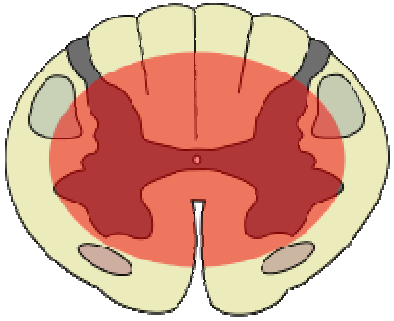
- Loss of voluntary movement/sensation below the injury
- reflex activity below level of lesion may return after spinal shock resolves
- worse prognosis for recovery--

Incomplete

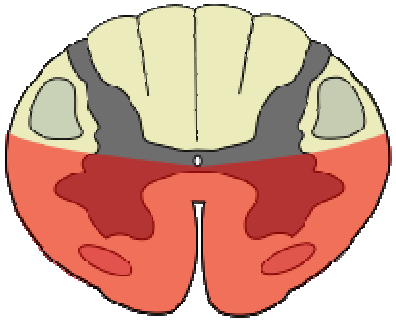
- (1) Varying degrees of motor/sensory loss below the level of injury & (2) central, lateral, posterior injury
  - Three types
    - Central Cord
    - Brown-Sequard
    - Anterior Cord

Incomplete cord injuries

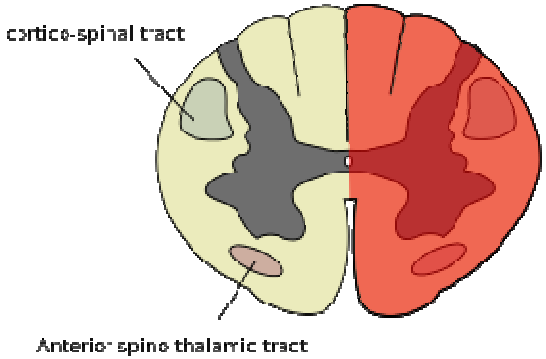
Central Cord Syndrome



Anterior Cord Syndrome



Brown-Séquard Syndrome



Types of incomplete spinal cord injury

Central cord syndrome

Characterized by:

disproportionately greater motor impairment in upper compared to lower extremities, and variable degree of sensory loss below the level of injury in combination with bladder dysfunction and urinary retention.

Incomplete SCI ANTERIOR

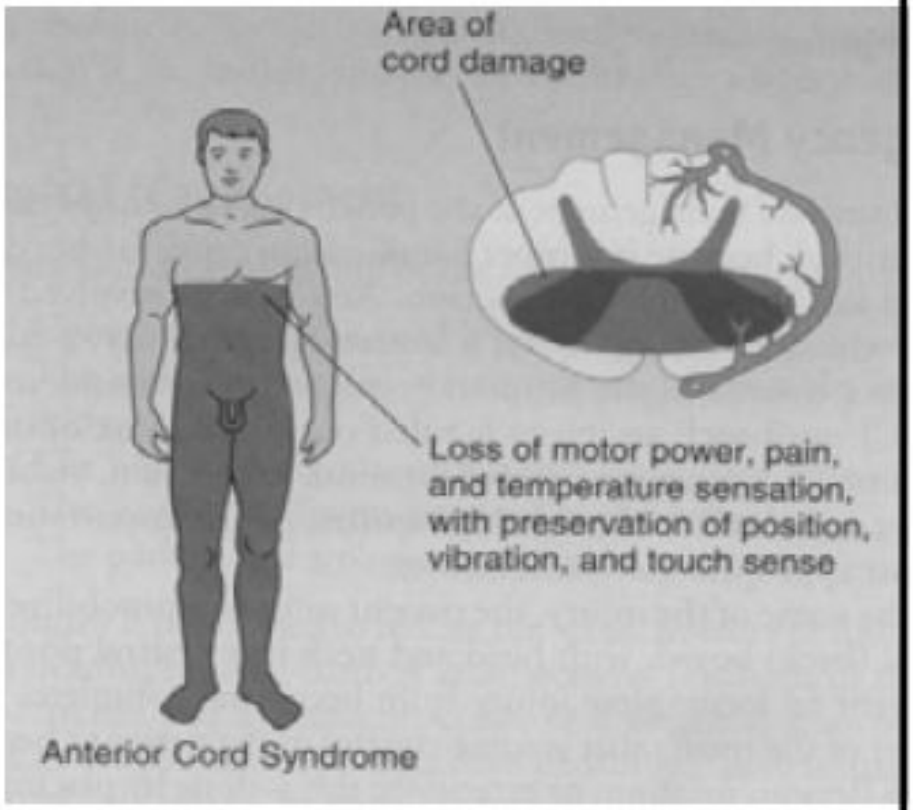
loss of motor, pain/temp

mixed sensory loss

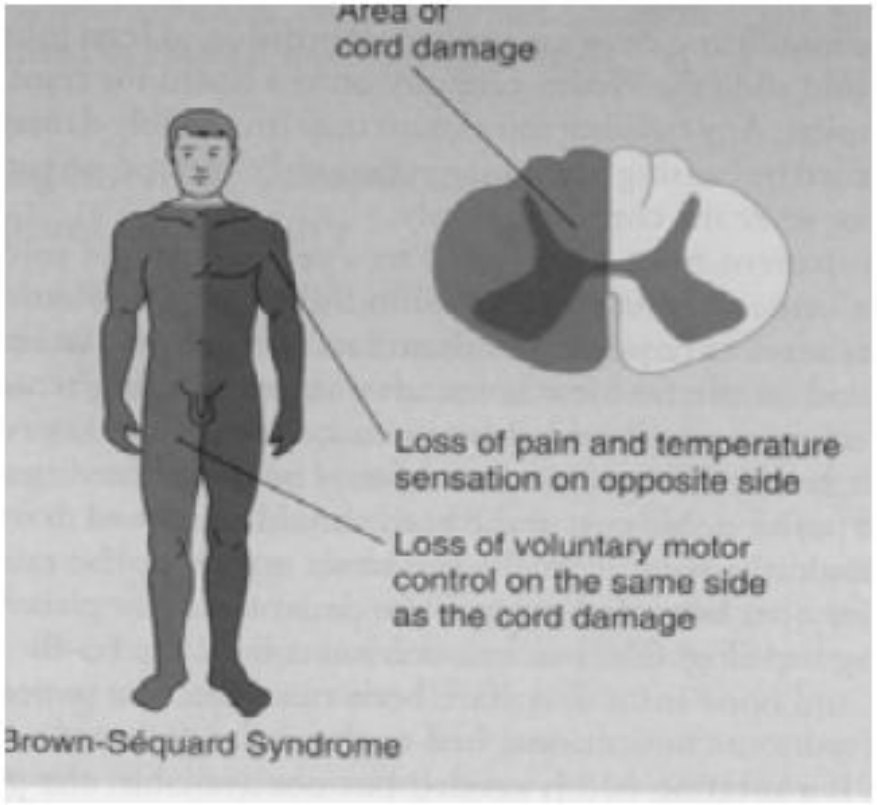
touch, proprioception, vibration remains intact

Cause: _____

_____



Incomplete SCI BROWN-SEQUARD
(cord hemi-section)



On same side as injury--loss of motor, touch, pressure, vibration BUT, pain/temp intact

On opposite side of injury--loss of pain/temp BUT, motor, touch, sensory vibration intact

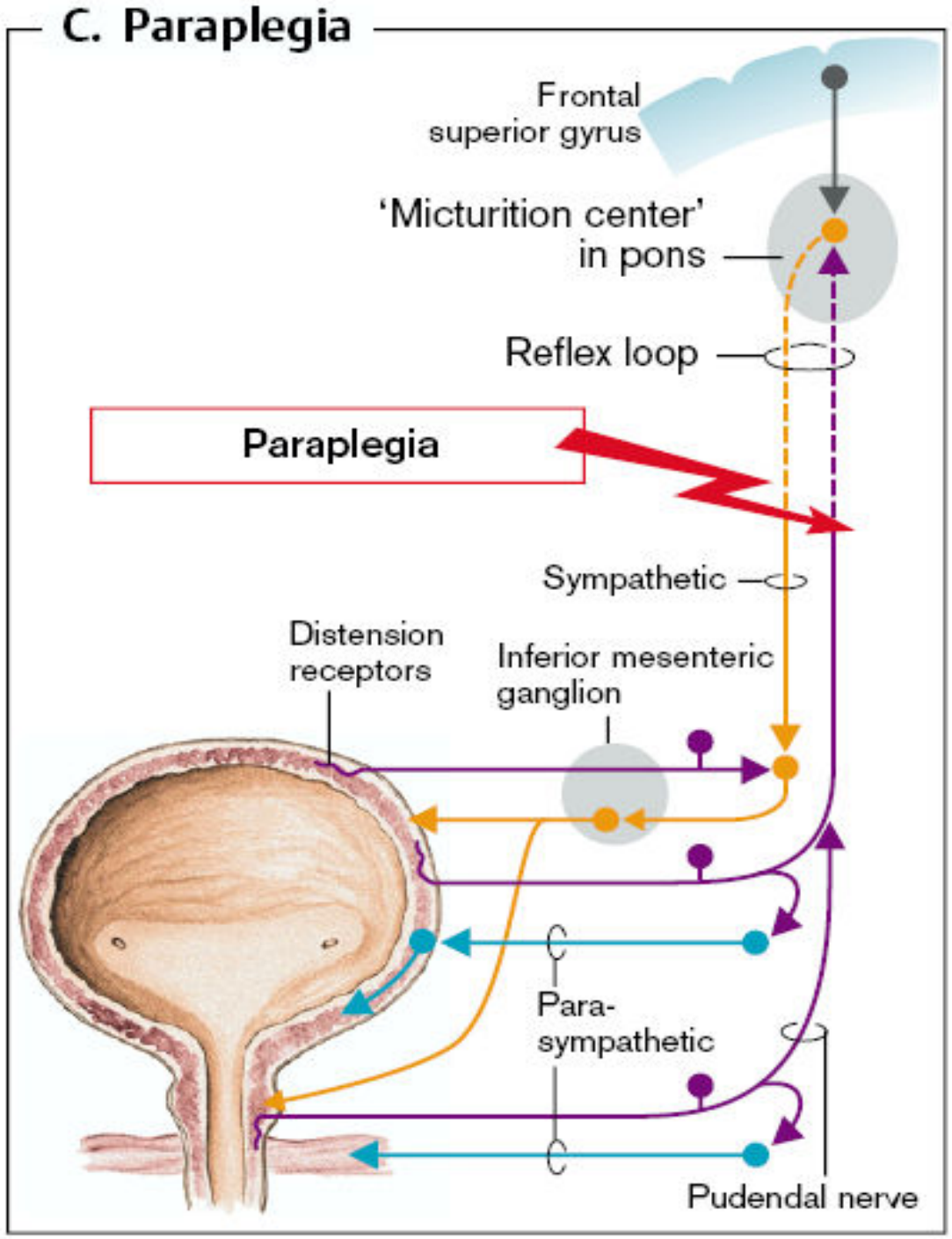
Cause: _____

_____

Incomplete SCI

conus medullaris/cauda equina

- Compression of lumbar-sacral area
  - **Conus T11-L1**
  - **Cauda L2-sacral**
- Better prognosis because injury in "horse tail" area
- Loss of motor is variable
- Sensory unimpaired
- Flaccid bowel and bladder
- Impaired sexual function



Autonomous urinary bladder