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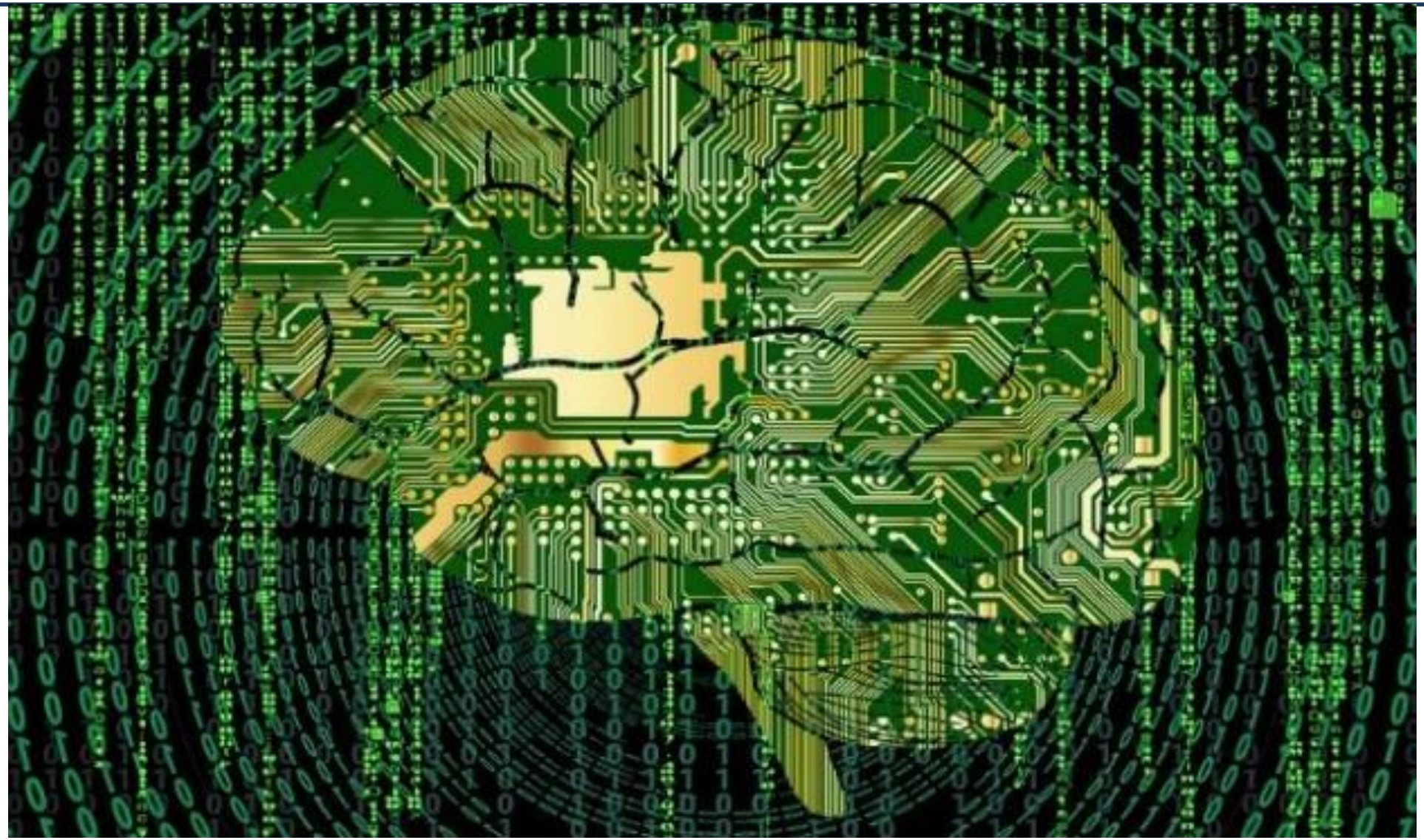
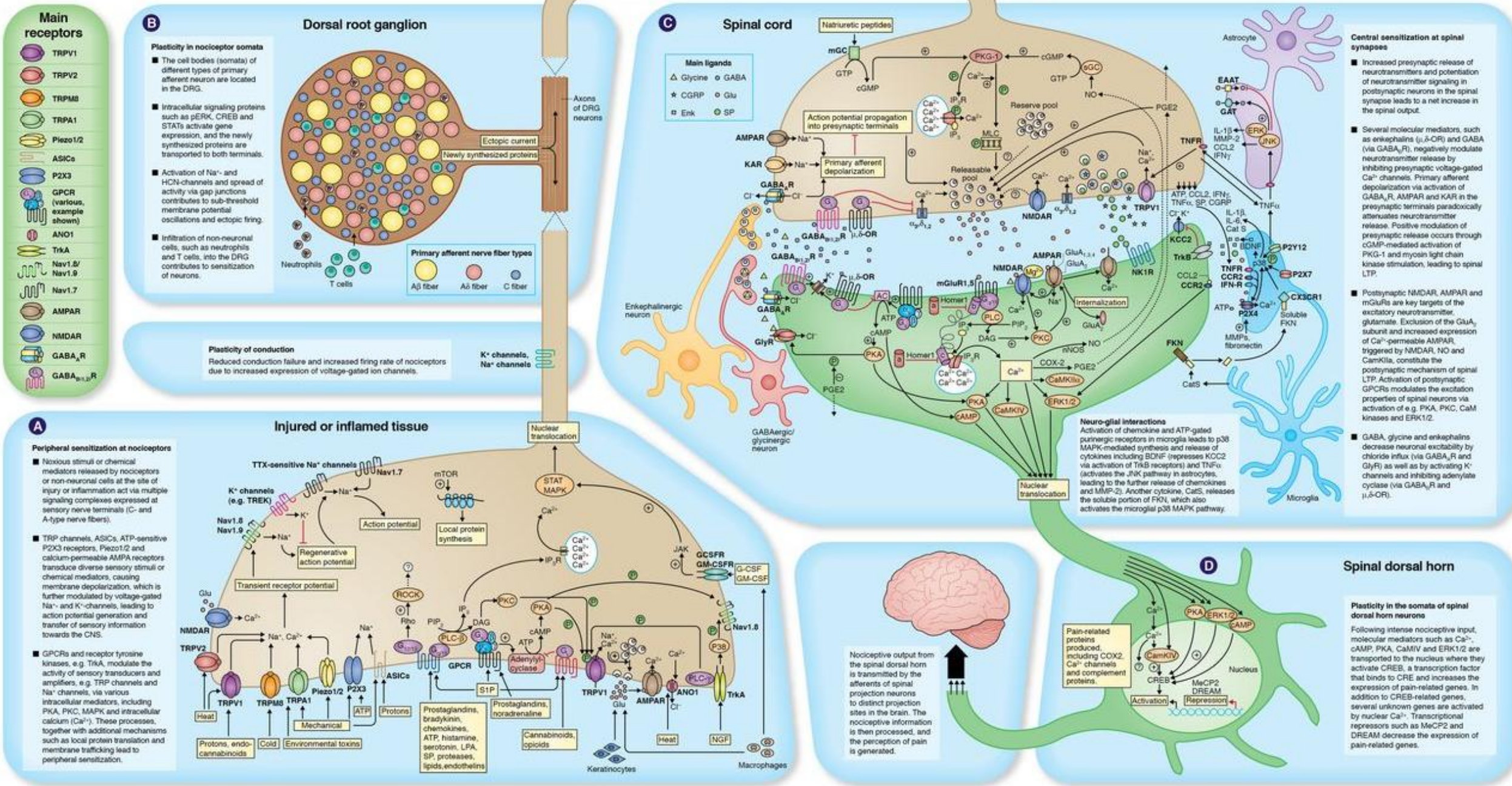
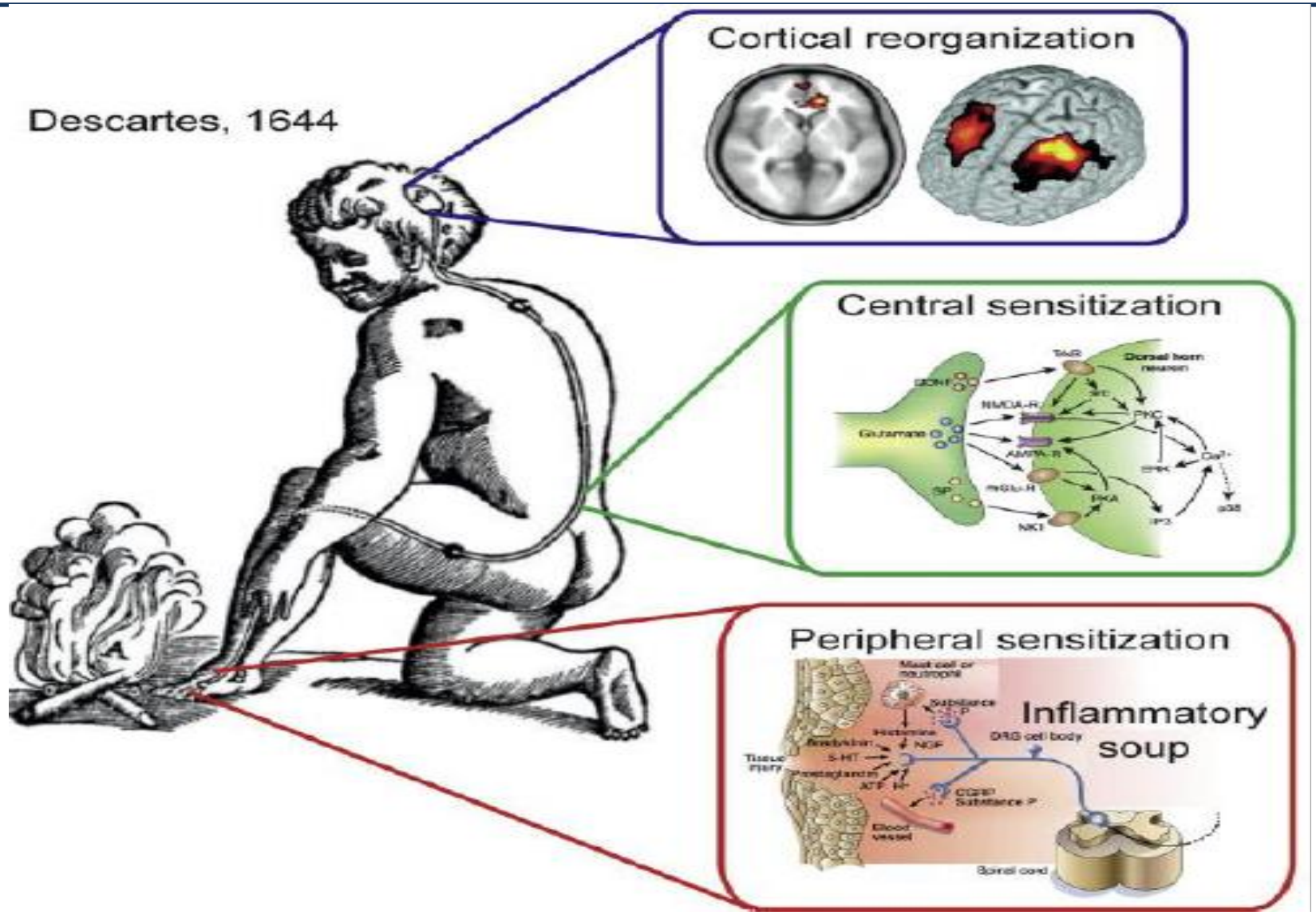
BOL – etiologija, patogeneza, patofiziologija II deo

ASS DR PREDRAG SAVIC

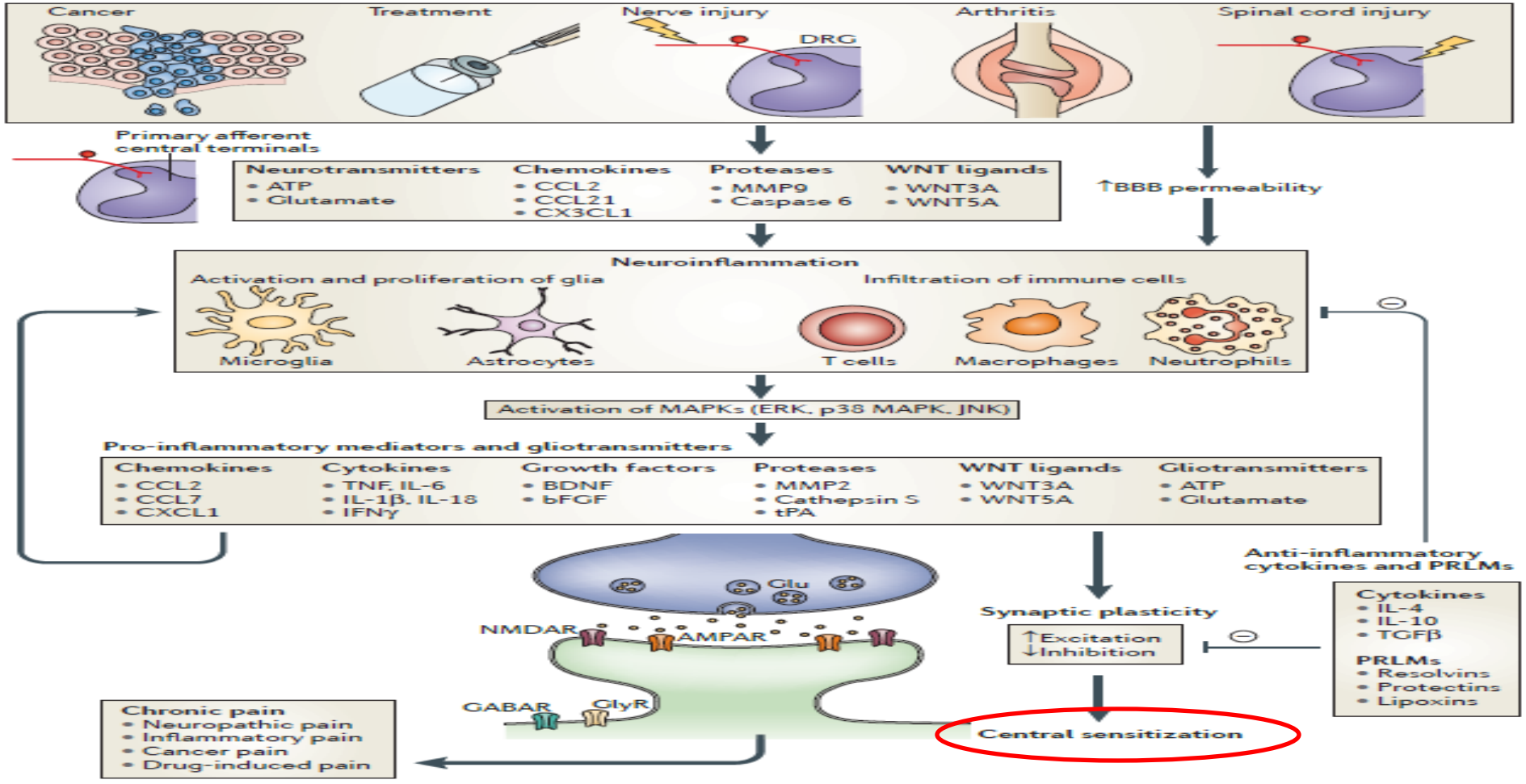

Everything Wrong With
The Matrix



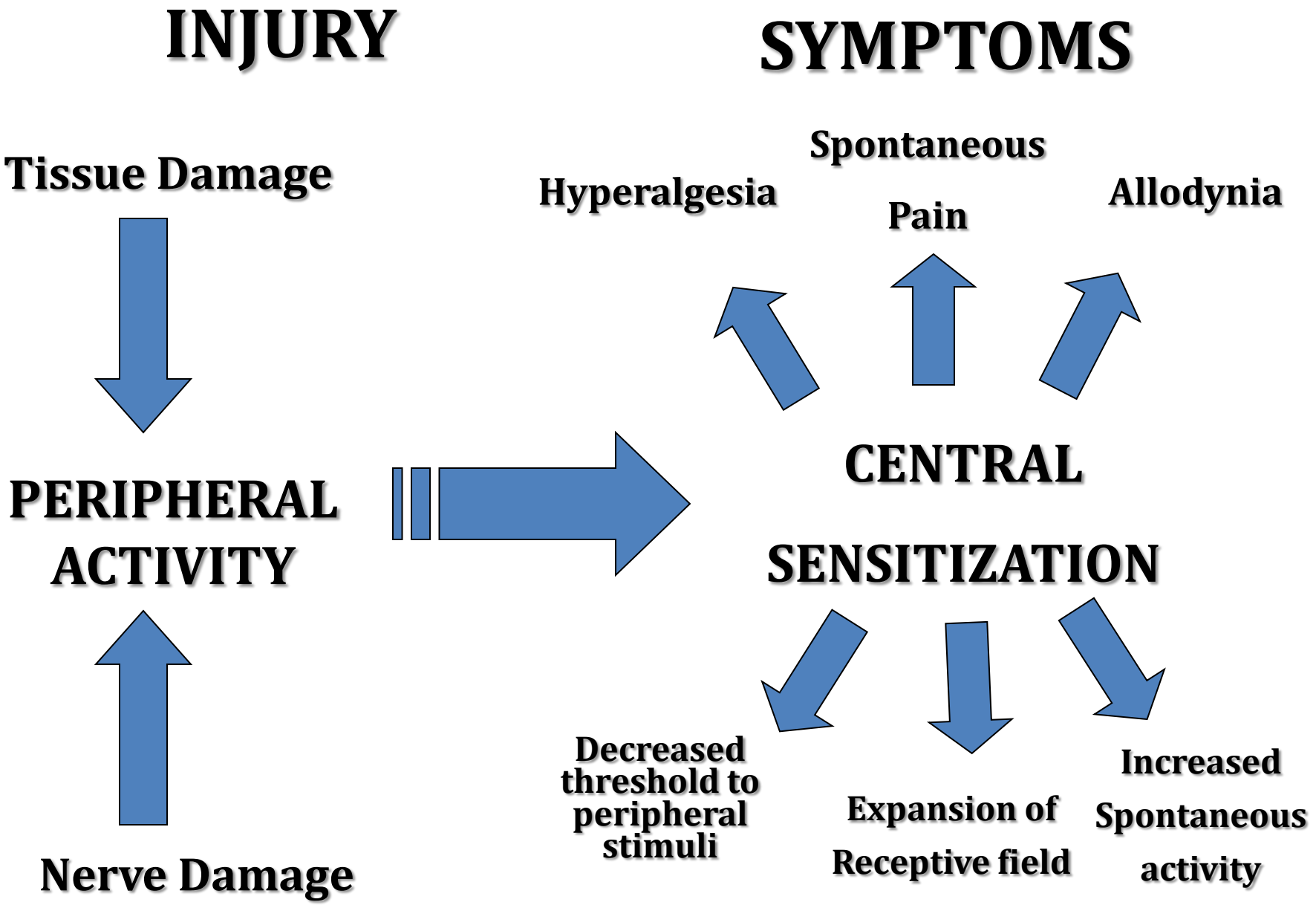

Main receptors
TRPV1
TRPV2
TRPM8
TRPA1
Piezo1/2
ASICs
P2X3
GPCR (various, example shown)
ANO1
TrkA
Nav1.8/ Nav1.9
Nav1.7
AMPAR
NMDAR
GABA$_A$R
GABA$_{B1,2}$R
B
Dorsal root ganglion
Plasticity in nociceptor somata
The cell bodies (somata) of different types of primary afferent neuron are located in the DRG.
Intracellular signaling proteins such as pERK, CREB and STATs activate gene expression, and the newly synthesized proteins are transported to both terminals.
Activation of Na+- and HCN-channels and spread of activity via gap junctions contributes to sub-threshold membrane potential oscillations and ectopic firing.
Infiltration of non-neuronal cells, such as neutrophils and T cells, into the DRG contributes to sensitization of neurons.
Ectopic current
Newly synthesized proteins
Axons of DRG neurons
Neutrophils
T cells
Primary afferent nerve fiber types
Aβ fiber
Aδ fiber
C fiber
Plasticity of conduction
Reduced conduction failure and increased firing rate of nociceptors due to increased expression of voltage-gated ion channels.
K+ channels, Na+ channels
C
Spinal cord
Main ligands
Glycine
GABA
CGRP
Glu
Enk
SP
Natriuretic peptides
mGC
GTP
cGMP
PKG-1
cGMP
sGC
GTP
NO
PGE2
Action potential propagation into presynaptic terminals
Reserve pool
Releasable pool
Primary afferent depolarization
AMPAR
KAR
GABA$_A$R
GABA$_{B1,2}$R
μ,δ-OR
NMDAR
TRPV1
TNFR
Astrocyte
EAAT
GAT
ERK
JNK
IL-1β
MMP-2
CCL2
IFNγ
ATP, CCL2, IFNγ, TNFα, SP, CGRP
IL-1β, IL-6, Cat S
TNFα
KCC2
TrkB
BDNF
P2Y12
p38
TNFR
CCR2
IFN-R
P2X7
CX3CR1
Soluble FKN
ATP
P2X4
MMPs, fibronectin
Enkephalinergic neuron
GABAergic/ glycinergic neuron
Homer1
mGluR1,5
PLC
PIP$_2$
DAG
PKC
AC
ATP
cAMP
PKA
Internalization
GluA$_2$
NK1R
nNOS
COX-2
CaMKIIα
CaMKIV
ERK1/2
FKN
CatS
Microglia
Nuclear translocation
Central sensitization at spinal synapses
Increased presynaptic release of neurotransmitters and potentiation of neurotransmitter signaling in postsynaptic neurons in the spinal synapse leads to a net increase in the spinal output.
Several molecular mediators, such as enkephalins (μ,δ-OR) and GABA (via GABA$_A$R), negatively modulate neurotransmitter release by inhibiting presynaptic voltage-gated Ca2+ channels. Primary afferent depolarization via activation of GABA$_A$R, AMPAR and KAR in the presynaptic terminals paradoxically attenuates neurotransmitter release. Positive modulation of presynaptic release occurs through cGMP-mediated activation of PKG-1 and mycosin light chain kinase stimulation, leading to spinal LTP.
Postsynaptic NMDAR, AMPAR and mGluRs are key targets of the excitatory neurotransmitter, glutamate. Exclusion of the GluA$_2$ subunit and increased expression of Ca2+-permeable AMPAR, triggered by NMDAR, NO and CamKIIa, constitute the postsynaptic mechanism of spinal LTP. Activation of postsynaptic GPCRs modulates the excitation properties of spinal neurons via activation of e.g. PKA, PKC, CaM kinases and ERK1/2.
GABA, glycine and enkephalins decrease neuronal excitability by chloride influx (via GABA$_A$R and GlyR) as well as by activating K+ channels and inhibiting adenylate cyclase (via GABA$_B$R and μ,δ-OR).
Neuro-glial interactions
Activation of chemokine and ATP-gated purinergic receptors in microglia leads to p38 MAPK-mediated synthesis and release of cytokines including BDNF (represses KCC2 via activation of TrkB receptors) and TNFα (activates the JNK pathway in astrocytes, leading to the further release of chemokines and MMP-2). Another cytokine, CatS, releases the soluble portion of FKN, which also activates the microglial p38 MAPK pathway.
A
Injured or inflamed tissue
Peripheral sensitization at nociceptors
Noxious stimuli or chemical mediators released by nociceptors or non-neuronal cells at the site of injury or inflammation act via multiple signaling complexes expressed at sensory nerve terminals (C- and A-type nerve fibers).
TRP channels, ASICs, ATP-sensitive P2X3 receptors, Piezo1/2 and calcium-permeable AMPA receptors transduce diverse sensory stimuli or chemical mediators, causing membrane depolarization, which is further modulated by voltage-gated Na+- and K+-channels, leading to action potential generation and transfer of sensory information towards the CNS.
GPCRs and receptor tyrosine kinases, e.g. TrkA, modulate the activity of sensory transducers and amplifiers, e.g. TRP channels and Na+ channels, via various intracellular mediators, including PKA, PKC, MAPK and intracellular calcium (Ca2+). These processes, together with additional mechanisms such as local protein translation and membrane trafficking lead to peripheral sensitization.
TTX-sensitive Na+ channels
Nav1.7
K+ channels (e.g. TREK)
Nav1.8
Nav1.9
Action potential
Regenerative action potential
Transient receptor potential
mTOR
Local protein synthesis
Nuclear translocation
STAT
MAPK
JAK
GCSFR
GM-CSFR
G-CSF
GM-CSF
Glu
NMDAR
TRPV2
TRPV1
TRPM8
TRPA1
Piezo1/2
P2X3
ASICs
Heat
Protons, endo-cannabinoids
Cold
Mechanical
Environmental toxins
ATP
Protons
ROCK
Rho
PIP$_2$
PLC-β
DAG
IP$_3$
PKC
PKA
cAMP
ATP
Adenylyl-cyclase
GPCR
S1P
Prostaglandins, bradykinin, chemokines, ATP, histamine, serotonin, LPA, SP, proteases, lipids,endothelins
Prostaglandins, noradrenaline
Cannabinoids, opioids
Nav1.8
P38
TrkA
NGF
Keratinocytes
Macrophages
Nociceptive output from the spinal dorsal horn is transmitted by the afferents of spinal projection neurons to distinct projection sites in the brain. The nociceptive information is then processed, and the perception of pain is generated.
D
Spinal dorsal horn
Pain-related proteins produced, including COX2, Ca2+ channels and complement proteins.
PKA
ERK1/2
cAMP
CaMKIV
CREB
Nucleus
MeCP2
DREAM
Activation
Repression
Plasticity in the somata of spinal dorsal horn neurons
Following intense nociceptive input, molecular mediators such as Ca2+, cAMP, PKA, CaMIV and ERK1/2 are transported to the nucleus where they activate CREB, a transcription factor that binds to CRE and increases the expression of pain-related genes. In addition to CREB-related genes, several unknown genes are activated by nuclear Ca2+. Transcriptional repressors such as MeCP2 and DREAM decrease the expression of pain-related genes.


Descartes, 1644
Cortical reorganization
Central sensitization
Peripheral sensitization
Inflammatory soup

NEUROINFLAMMATION IN THE SPINAL CORD DRIVES CHRONIC PAIN VIA NEURON–GLIAL INTERACTIONS AND CENTRAL SENSITIZATION

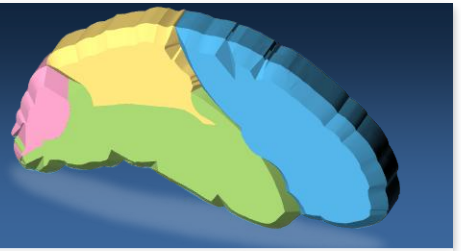


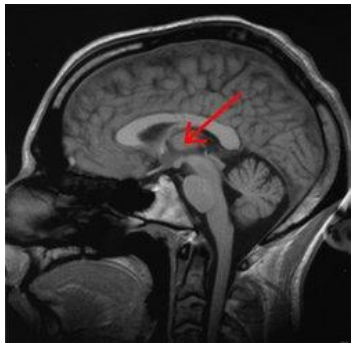
Ru-Rong J., Zhen-Zhong X., Yong-Jing G. Nature reviews , Drug discovery, 2018.


INJURY
SYMPTOMS
Tissue Damage
Spontaneous Pain
Hyperalgesia
Allodynia
PERIPHERAL ACTIVITY
CENTRAL SENSITIZATION
Nerve Damage
Decreased threshold to peripheral stimuli
Expansion of Receptive field
Increased Spontaneous activity

NOCICEPTIVNI BOL

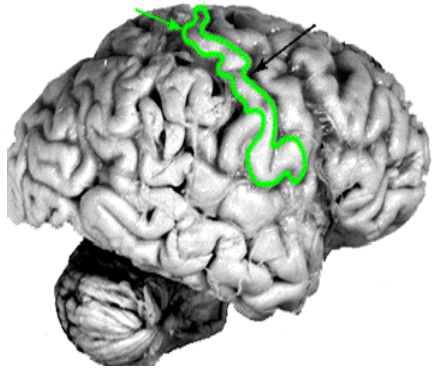
TRANSMISIJA





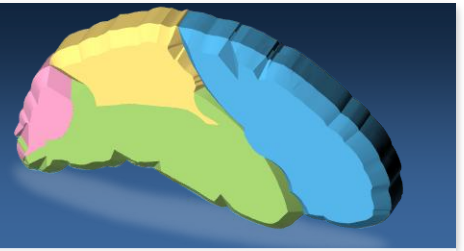
- vlakna senzornog neurona III reda polaze iz talamusa u sastavu talamokortikalnog snopa završavaju se u **primarnom somatosenzornom polju** (postcentralna vijuga i zadnja trećina paracentralnog režnja)

- deo vlakana se završava u **sekundarnom somatosenzornom** polju (operkularni deo parijetalnog režnja)

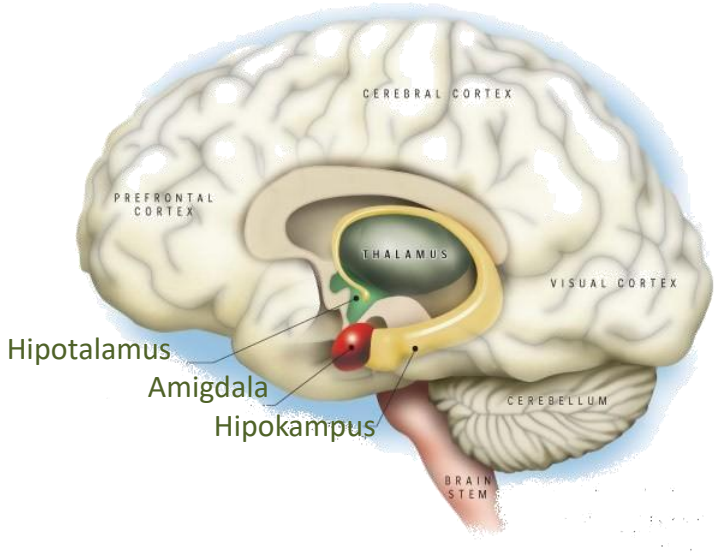


NOCICEPTIVNI BOL

PERCEPCIJA



- svesna spoznaja bola
- dešava se samo ako bolni impulsi stignu do **talamokortikalnog nivoa**
- precizna uloga talamusa i kortikalnih senzornih područja nije u potpunosti razjašnjena



The brain first perceives the sensation of pain

- The thalamus, sensitive cortex :

  perceiving
  describing
  localizing
  } of pain

- Parts of thalamus, brainstem and reticular formation:
  - identify dull longer-lasting, and diffuse pain

- The reticular formation and limbic system:
  - control the emotional and affective response to pain

Because the cortex, thalamus and brainstem are interconnected with the hypothalamus and autonomic nervous system, perception of pain is associated with an autonomic response

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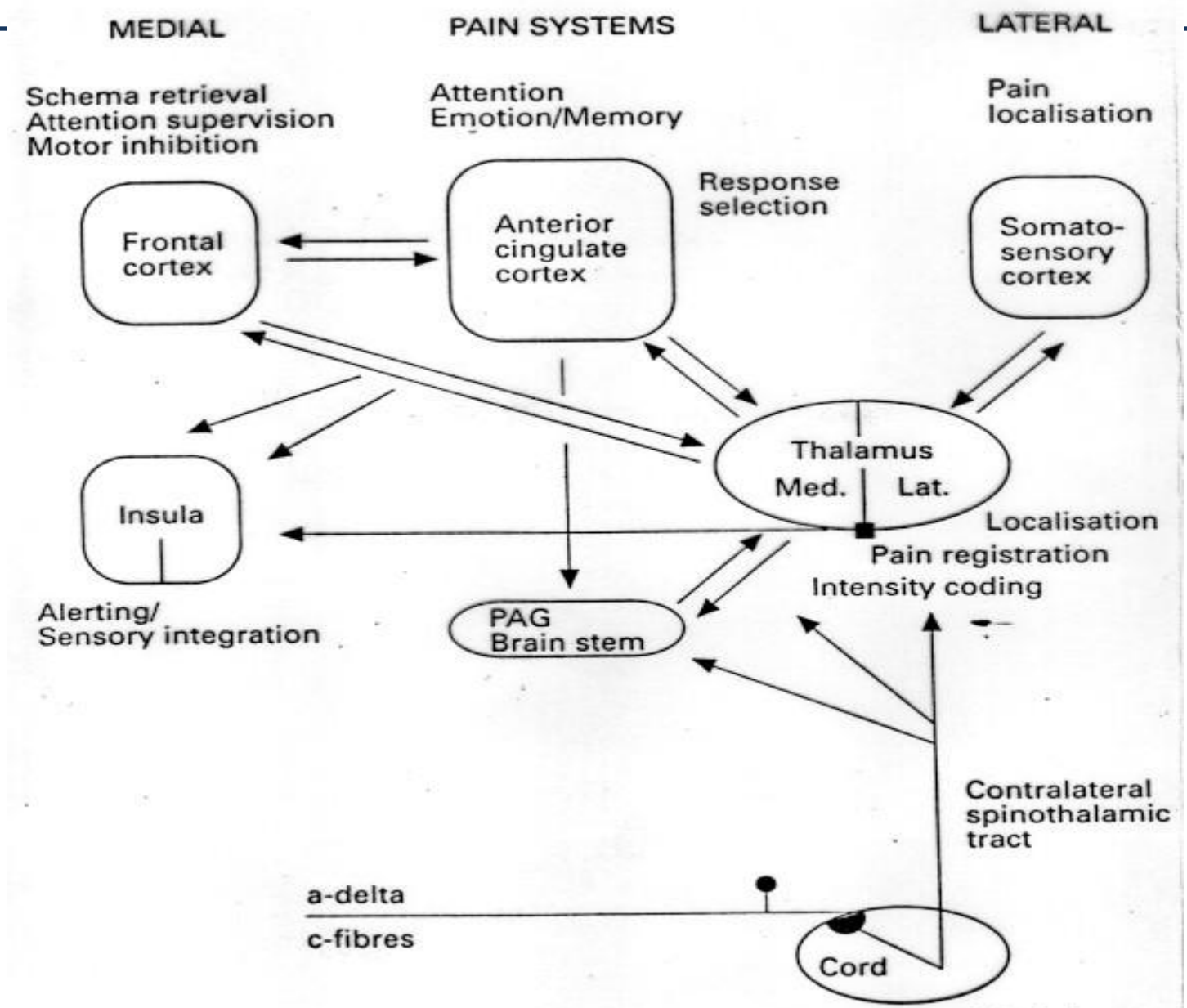

Figure 1 Schematic diagram of some of the main anatomical components of the 'pain matrix', and their possible functional significance. PAG = Periaqueductal grey matter.

Efferent analgesic system

Its role: - inhibition of afferent pain signals

Mechanisms:

- pain afferents on their way up to CNS send branches to periaqueductal gray (PAG) - gray matter surrounding the cerebral aqueduct in the midbrain, and stimulates the neurons there→ → activation of efferent (descendent) anti-nociceptive pathways

- from there the impulses are transmitted through the spinal cord to the dorsal horn

- there thay inhibit or block transmission of nociceptive signals at the level of dorsal horn

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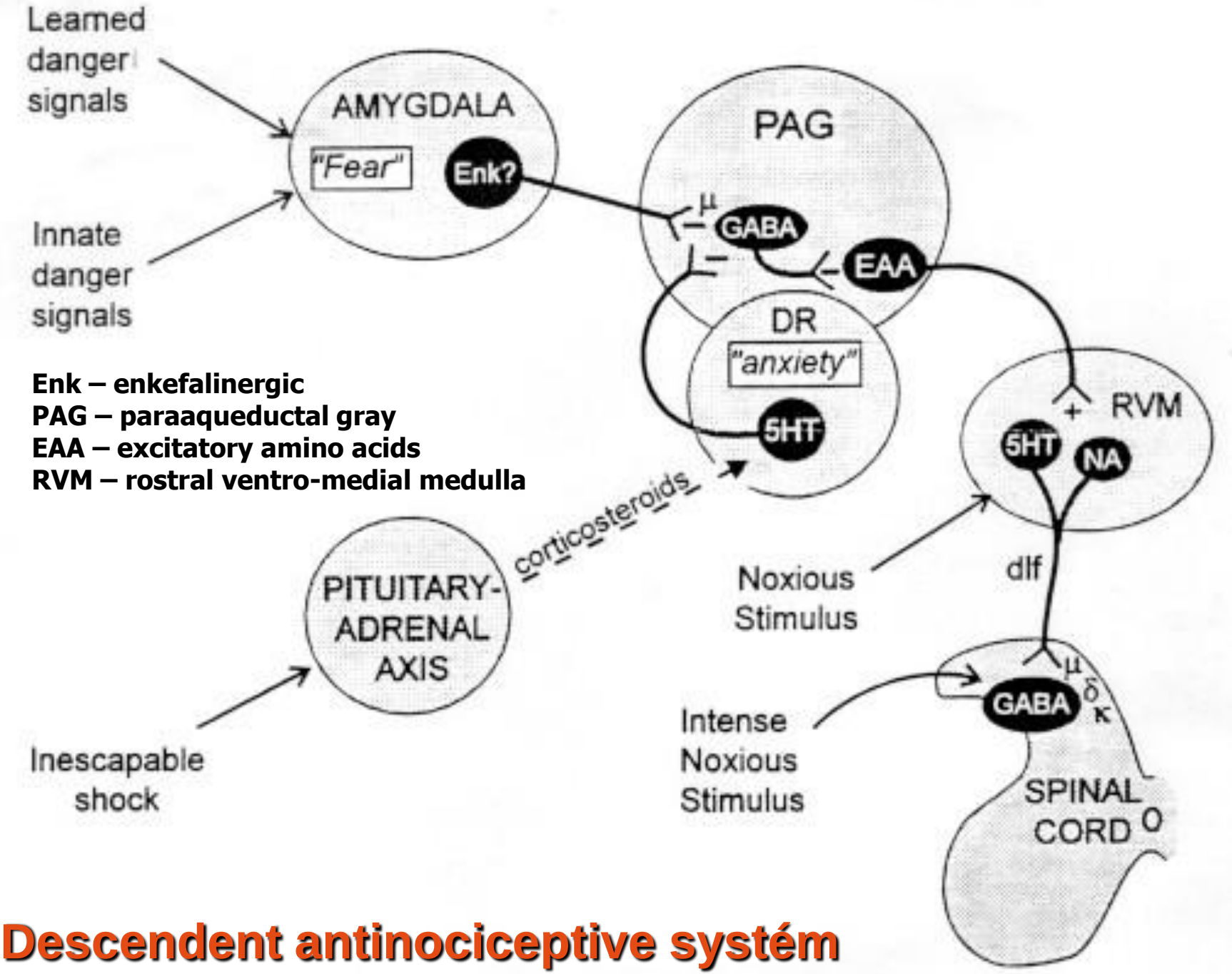
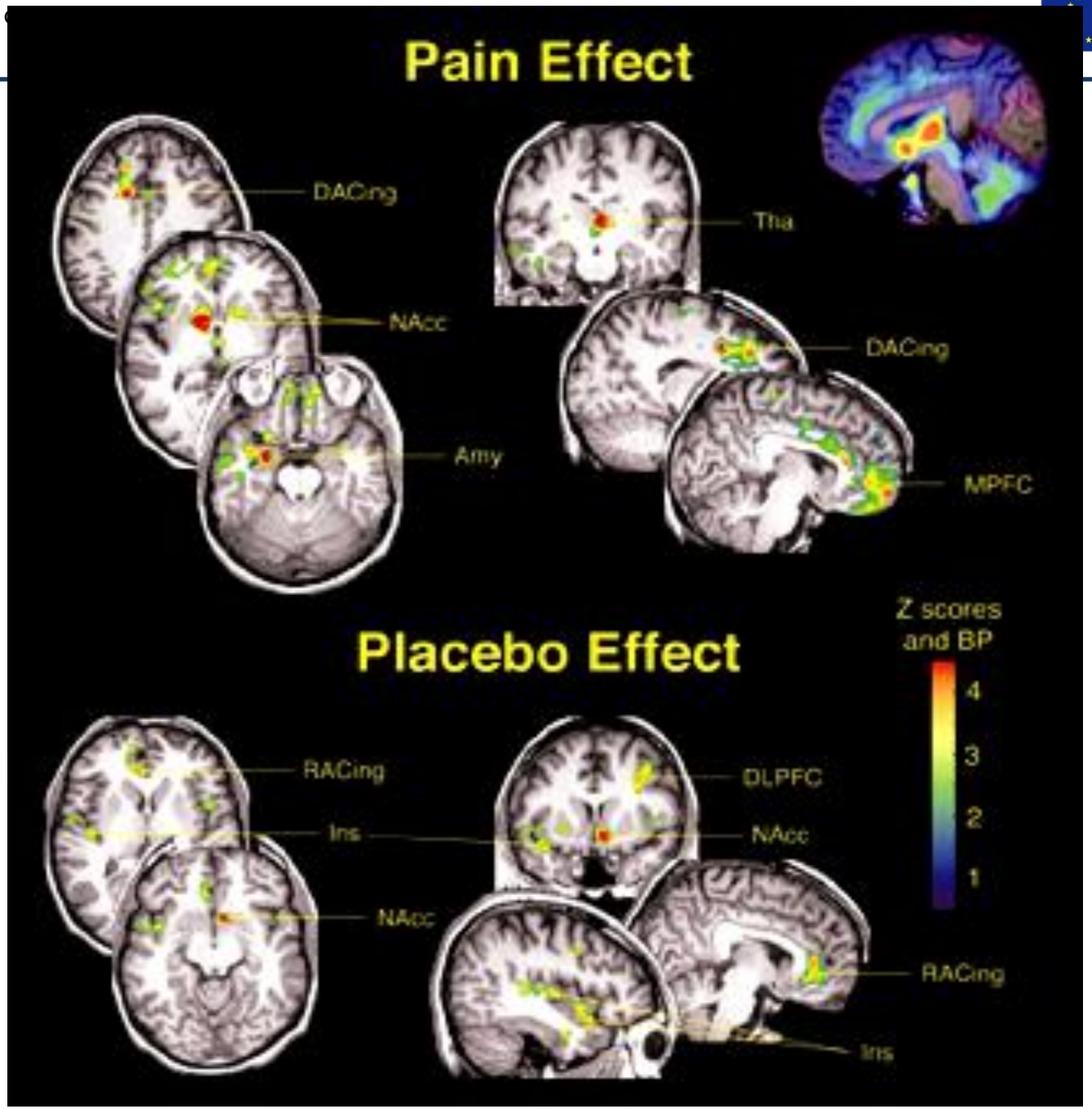


Enk – enkefalinergic
PAG – paraaqueductal gray
EAA – excitatory amino acids
RVM – rostral ventro-medial medulla

Descendent antinociceptive systém

Antinociceptive placebo effect
(Zubieta J-Ket al.,2005)



Neuropathic pain (NP)

- It occurs as a result of injury to or dysfunction of the nervous system itself, peripheral or central. The nerve injury may be induced by pathology in surrounding tissue.

Characteristics of NP – it may mimic quality of somatic pain
- it may have characteristic of „disesthetic“ pain (e.g. uncomfortable, unfamiliar sensation such as burning, shock-like, tingling
- may be associated with reffered pain, allodynia, hyperalgesia, hyperpathia

- **Hyperpathia** – exaggerated pain responses following a stimulus often with aftersensations and intense emotional reaction

What causes neuropathic pain?

Neuropathic pain often seems to have no obvious cause, but, some common causes of neuropathic pain include:

- Hereditary disorders
- Traumatic nerve damage
- Metabolic disorders,
- Toxic nerve damage
- Nerve ischemia,
- Infection of nerve tissue
- Nerve compression,
- Immune mediated nerve tissue damage

Example of some diseases leading to NP development

Alcoholism, Amputation, Back, and Leg, and Hip problems, Chemotherapy, Diabetes mellitus, Facial nerve problems, HIV syndrome, Multiple sclerosis, Shingles (Herpes zoster), Spine surgery

What are the symptoms of neuropathic pain?

a) Stimulus indipendent pain

b) Stimulus evoked pain

Neuropathic pain – subtypes (according a primary location of sustaining mechanism)

a) **Predominating peripheral generator:**

e.g. compression or entrapment neuropathies, plexopathies, radiculopathies, polyneuropathies

b) **Predominating central generator:**

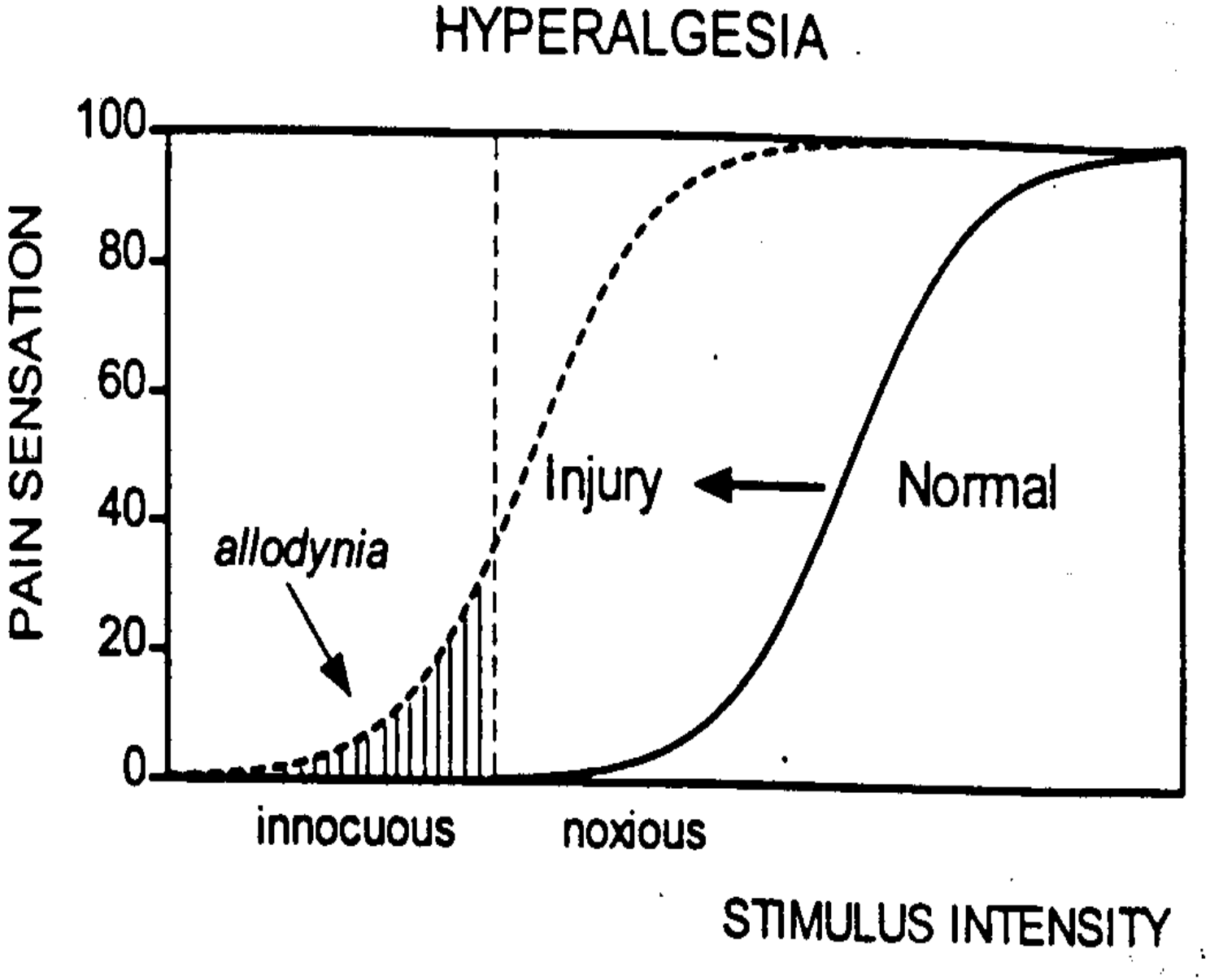
e.g. spinal cord injury,post-stroke pain

- **Deaferentation pain** - **form of neuropathic pain: a term implying that sensory deficit in the painful area is a prominent feature (anesthesia dolorosa)**
- **Phantom pain- pain localizei into non-existing organ (tissue)**

- **Hypersensitivity –** increased sensitivity of the system involved in the pain processing
- **Hyperalgesia –** increased the pain sensitivity to noxious stimuli

- **Allodynia** - phenomenon characterised by painful sensations provoked by non-noxious stimuli, (e.g. touch), transmitted by fast- conducting nerve fibres

Mechanism: changes of the response characteristics of second - order spinal neurons, so that normally inactive or weak synaptic contact mediating non-noxius stimuli acquire the capability to activate a neuron that normally responds only to impulses signaling pain


HYPERALGESIA
PAIN SENSATION
100
80
60
40
20
0
allodynia
Injury
Normal
innocuous
noxious
STIMULUS INTENSITY

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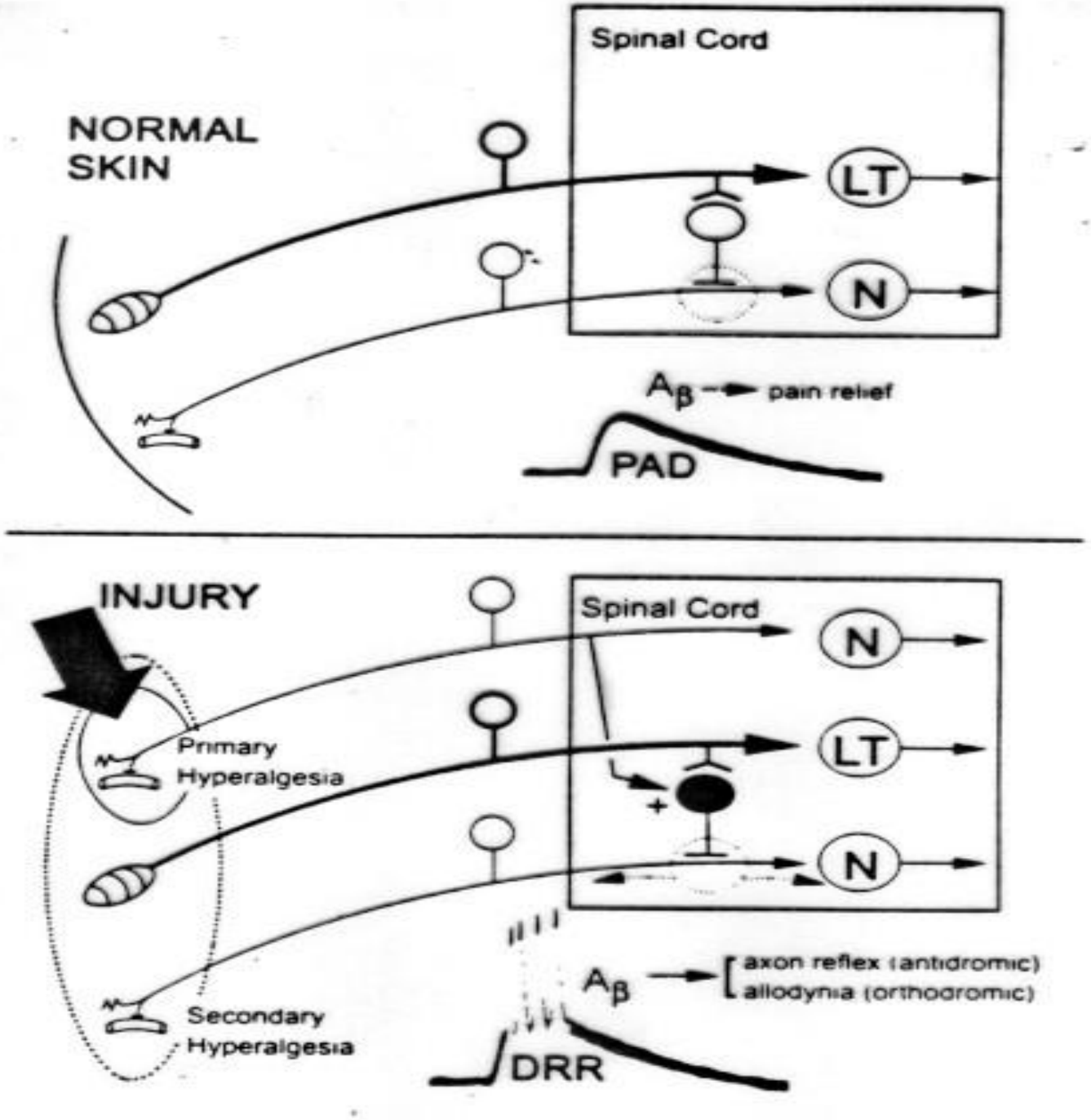


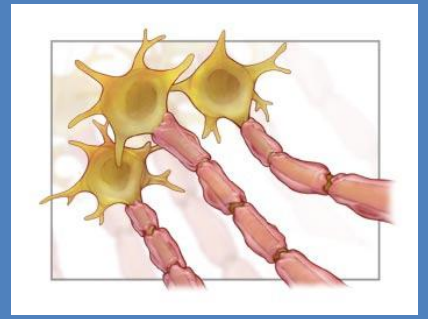
Pathomechanisms involved in genesis of neuropathic pain

1) Neurophysiologic and neuroanatomic changes that may occur in peripherally generated neuropathic pain

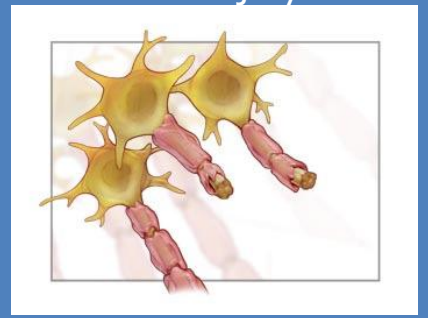
a) Abnormal nerve morphology
- – grow multiple nerve sprouts,
- – some of these sprouts may form neuromas

- Nerve sprouts and neuromas can generate spontaneuos activity
- Areas of spontaneuos activity (↑sensitivity) are associated with a change in Na^+ receptors concentration
  - – at sites of demyelination
  - – are more sensitive to physical stimuli (manifested as tenderness)

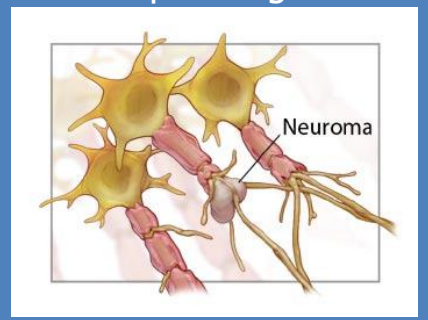
Neural axon



Neural axon injury

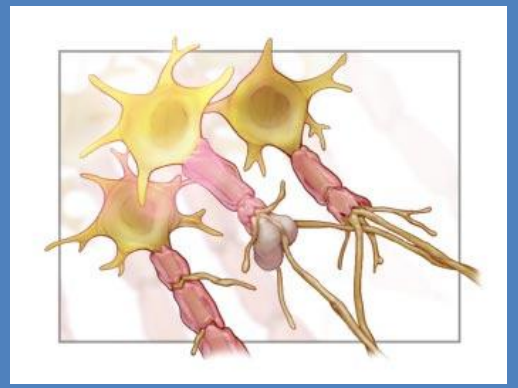


Neural axon sprouting and neuroma

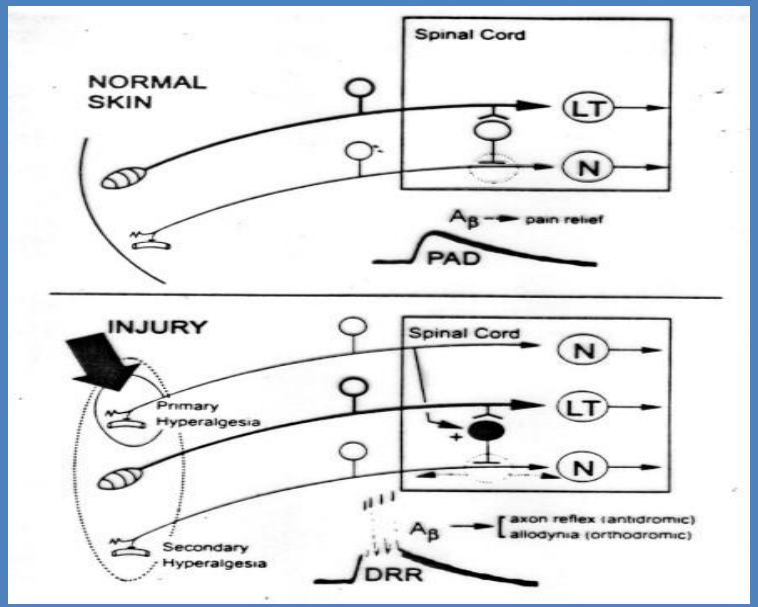


b) Development atypical connections between nerve sprouts or demyelinated axons in the region of nerve damage

– permitting „cross–talk" between somatic or sympathetic efferents and nociceptors



c) **Anterograde and retrograde transport of coumpounds → → stimulation of nerve cell body to production of specific genes**



Common clinical forms of neuropathic pain

Peripheral neuralgias after trauma or surgery

- lumbosacral and cervical rhizotomy,
- peripheral neuralgia

- Most peripheral neuralgias are the result of trauma or surgery. Such a conditions does not necessary occur as a result of damaging a major nerve trunk but may be caused by an incision involving only small nerve branches (incisional pain)

Mechanism: the pain is due to neuroma formation in the scar tissue (?)

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Deaferentation pain following spinal cord injury

- Incidence of severe pain due to spinal cord and cauda equina lesions ranges from 35 to 92 % of patients

This pain is ascribed to 3 causes:

1. mechanically induced pain (fracture bones, myofascial pain)

2. radicular pain (compression of nerve root)

3. central pain (deaferentation mechanism)

Psychogenic pain – mechanism

- Dysfunction of central mechanisms responsible for processing of sensoric afferent informations

  - releasing of mediators decreasing pain threshold
  - prolonged muscle contraction due to psychogenic stress
  - incresed activity of SNS → decreasing pain threhold
  - inhibition of activity of descending antinociceptive system

Clinical Manifestation of Pain

Acute Pain

We can distinguish two types of acute pain:

1. Somatic
2. Visceral
   – referred

Somatic pain is superficial coming from the skin or close to the surface of the body.

Visceral pain refers to pain in internal organs, the abdomen, or chest.

Referred pain is pain that is present in an area removed or distant from its point of origin. The area of referred pain is supplied by the nerves from the same spinal segment as the actual site of pain

Different types of chronic somatic pain

I. Nervous system intact

1. nociceptive pain
2. nociceptive - neurogenic pain
   (nerve trunk pain)

II. Permanent functional and/or morphological abnormalities of the nervous system (preganglionic, spinal - supraspinal)

1. neurogenic pain
2. neuropathic pain
3. deafferentation pain

The most common chronic pain

1. **Persistent low back pain**
   - **result of poor muscle tone, inactivity, muscle strain, sudden vigorous exercise**
2. Chronic pain associated with cancer
3. Neuralgias
4. Myofascial pain syndromes
5. Hemiagnosia
6. Phantom limb pain

Neuralgias - results from damages of peripheral nerves

a) **Causalgia** - severe burning pain appearing 1 to 2 weeks after the nerve injury associated with discoloration and changes in the texture of the skin in the affected area.

b) **Reflex sympathetic dystrophies** - occur after peripheral nerve injury and is characterised by **continuous severe burning pain.** Vasomotor changes are present (vasodilatation→ vasoconstriction → cool cyanotic and edematous extremities).

Myofascial pain syndromes – second most common cause of chronic pain.

These conditions include: **myositis, fibrositis, myalgia, muscle strain, injury to the muscle and fascia**

The pain is a result of **muscle spasm, tenderness and stiffness**

Hemiagnosia

– is a loss of ability to identify the sorce of pain on one side (the affected side) of the body. Application of painful stimuli to the affected side thus produces anxiety, moaning, agitation and distress but no attempt to withdrawal from or push aside the offending stimulus. Emotional and autonomic responses to the pain my be intensified.

- Hemiagnosia is associated with stroke that produces paralysis and hypersensitivity to painful stimuli in the affected side

Phantom limb pain – is pain that an individual feels in amputated limb

Pathophysiology of muscle pain

- **Muscle pain** - a part of **somatic deep pain**,

  (MP) - it is common in rheumathology and sports medicine

  - is rather diffuse and difficult to locate

- MP is not a prominent feature of the serious progressive diseases affecting muscle, e.g. the muscular dystrophies, denervation, or metabolic myopathies, **but it is a feature of rhabdomyolysis**

- Muscles are relatively insensitive to pain when elicited by needle prick or knife cut, **but overlying fascia is very sensitive to pain.**

Events, processes which may lead to muscular pain are:

- **metabolic events:**
  - metabolic depletion (↓ ATP → muscular contracture)
  - accumulation of unwanted metabolities (K^+, bradykinin)

Pathophysiology of visceral pain

- **Visceral pain:**

Types - angina pectoris, myocardial infarction, acute pancreatitis, cephalic pain, prostatic pain, nephrlolythiatic pain

- **Receptors:** unmyelinated C - fibres

- For human pathophysiology the kinds of stimuli apt to induce pain in the viscera are important.

It is well-known that the stimuli likely to induce cutaneous pain are not algogenic in the viscera. This explains why in the past the viscera were considered to be insensitive to pain

Adequate stimuli of inducing visceral pain:

1. abnormal distention and contraction of the hollow viscera muscle walls
2. rapid stretching of the capsule of such solid visceral organs as are the liver, spleen, pancreas...
3. abrupt anoxemia of visceral muscles
4. formation and accumulation of pain - producing substances
5. direct action of chemical stimuli (oesophagus, stomach)
6. traction or compression of ligaments and vessels
7. inflammatory processes
8. necrosis of some structures (myocardium, pancreas)

Characteristic feature of true visceral pain

a) it is dull, deep, not well defined, and differently described by the patients

b) sometimes it is difficult to locate this type of pain because it tends to irradiate

c) it is often accompanied by a sense of malaise

d) it induces strong autonomic reflex phenomena

- diffuse sweating, vasomotor responses, changes of arterial pressure and heart rate, and an intense psychic alarm reaction -"angor animi" – e.g. in angina pectoris)

e) when organ capsules or other structures, e.g. myocardium are involved, however, the pain is usually well localized and described as sharp , stubbing, or thobbing

- There are many visceral sensation that are unpleasant but below the level of pain, e.g. feeling of disagreeable fullness or acidity of the stomach or undefined and unpleasant thoracic or abdominal sensation. These visceral sensation may precede the onset of visceral pain

Refered visceral pain (transferred pain)

Refered pain = when an algogenic process affecting a viscus recurs frequently or becomes more intense and prolonged, the location becomes more exact and the painfull sensation is progressively felt in more superficial struftures

- **Refered pain may be accompanied by allodynia and cutaneous and muscular hyperalgesia**

Mechanisms involved in refered pain creation:

a) convergence of impulses from viscera and from the skin in the CNS:

- Sensory impulses from the viscera create an irritable focus in the segment at which they enter the spinal cord. Afferent impulses from the skin entering the same segment are thereby facilitated, giving rise to true cutaneous pain.

b) senzitization of neurons in dorsal horn

- **Painful visceral afferent impulses activate anterior horn motor cells to produce rigidity of the muscle (viscero-motor reflexes)**

- **A similar activation of anterolateral autonomic cells induces pyloerection, vasoconstriction, and other sympathetic phenomena**

These mechanisms, which in modern terms can be defined as positive sympathetic and motor feedback loops, are fundamental in reffered pain

- **It is clear that painful stimulation of visceral structures evokes a visceromuscular reflex, so that some muscles contract and become a new source of pain**

- It has been observed that the **local anesthetic block of the sympathetic ganglia** led to the disappearance, or at least to a marked **decrease, of reffered pain, allodynia, hyperalgesia.**

- In some conditions, **reffered somatic** pain is long-lasting, increases progressively, and is accompanied by **dystrophy of somatic structures.**

Possible mechanisms:

- onset of self-maintaining **vicious circle** impulses:

peripheral tissue → afferent fibers → central nervous system → somatic and sympathetic efferent fibres → peripheral tissue

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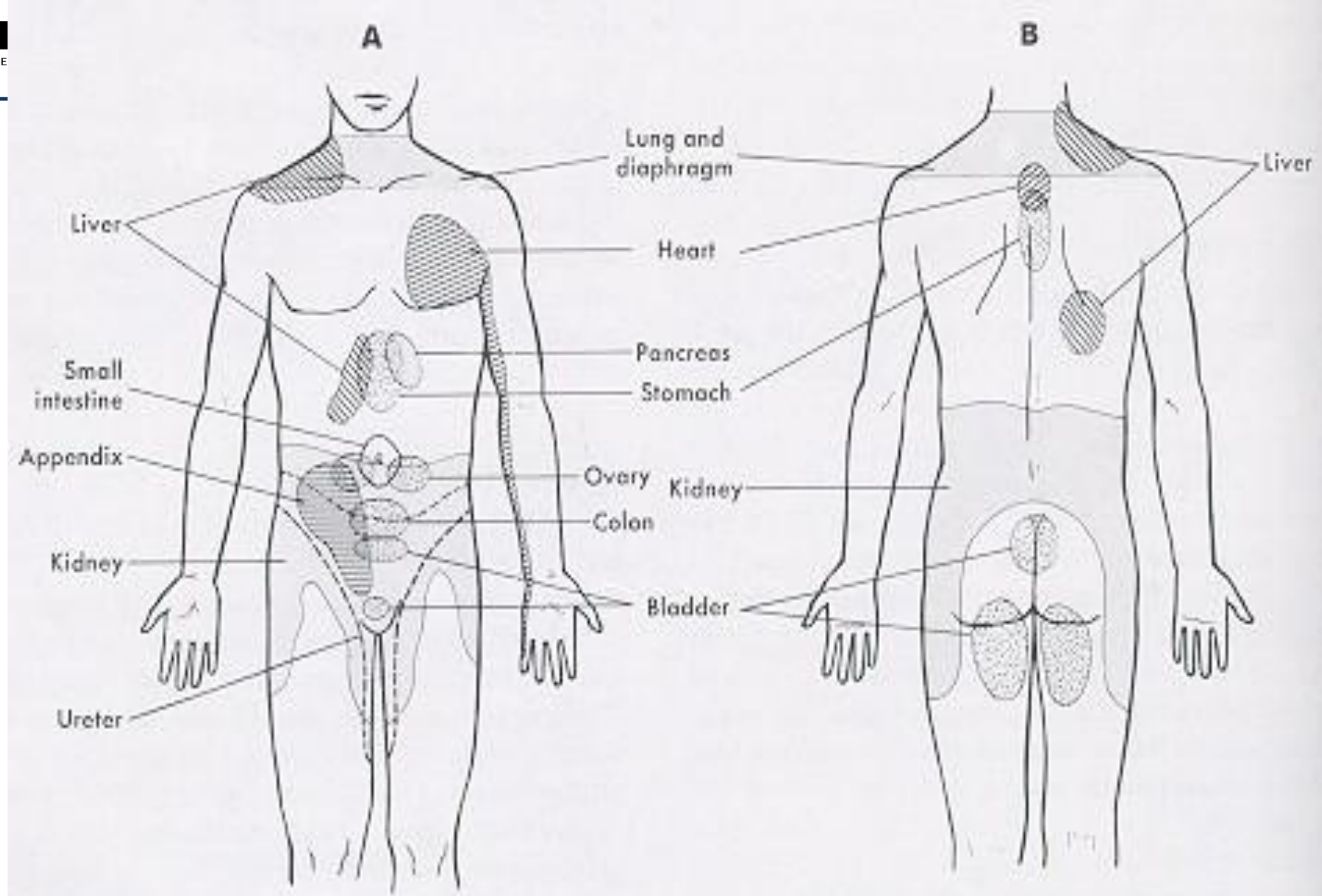

FIG. 13-6. Sites of referred pain. A, Front. B, Back. (From Phipps, Long, & Woods, 1987.)

- **Intricate conditions** - in some types of pain, e.g. chest pain, is difficult to distinguish the true cause of pain because such kind of pain may be related to cervical osteoarthrosis, esophageal hernia, cholecystitis, MI, other pathologic processes. It is diffcult to ascertain whether this pain is due to a simple addition of impulses from different sources in the CNS or to somatovisceral and viscerosomatic reflexes mechanisms.

- It has been demonstrated that the mnemonic process is facilitated if the experience to be retained is repeated many times or is accompanied by pleasant or unpleasant emotions.

Pain is, at least in part, a learned experience - e.g. during the first renal colic, true somatic pain followed visceral pain after a variable interval. In subsequent episodes of renal colic pain, somatic pain developed promptly and was not preceded by true visceral pain.

This is probably due to the activation of mnemonic traces.

Silent myocardial ischemia (SMI)

- Chest pain is only a late and inconstant marker of episodes of transient MI in vasospastic angina (30 %), in stable angina (50 %)

- Mechanisms of SMI

a) Lack of the pain is, in part, related to the duration and severity of MI. Episodes shorter than 3 min, and those accompanied by a modest impairment of left ventricle (↑ in end-diastolic pressure inferior to 6 mm Hg) are always painless.

Longer and more severe episodes are acccompanied by chest pain in some instances but not in others.

b) Pacients with predominantly SMI appear to have a generalized defective perception of pain (↑threshold and tolerance).

Mechanism: ↑ level of circulating β-endorphin (?)

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Disturbances in pain perception and nociception

Most of the disturbances are **congenital**

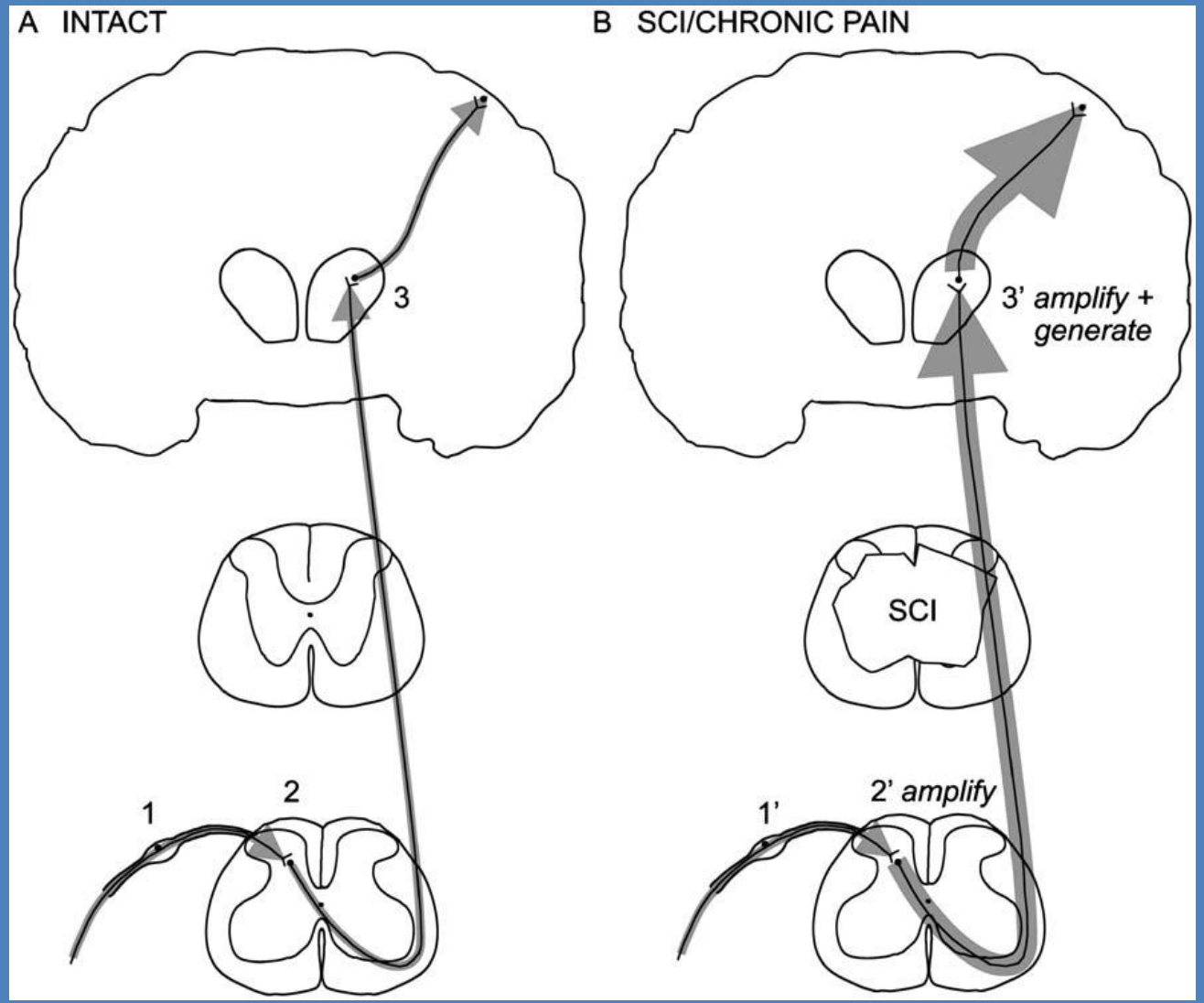
a) **Congenital analgesia** - nociceptive stimuli are **not processed and/or integrated at a level of brain.** Patient does not feel a pain

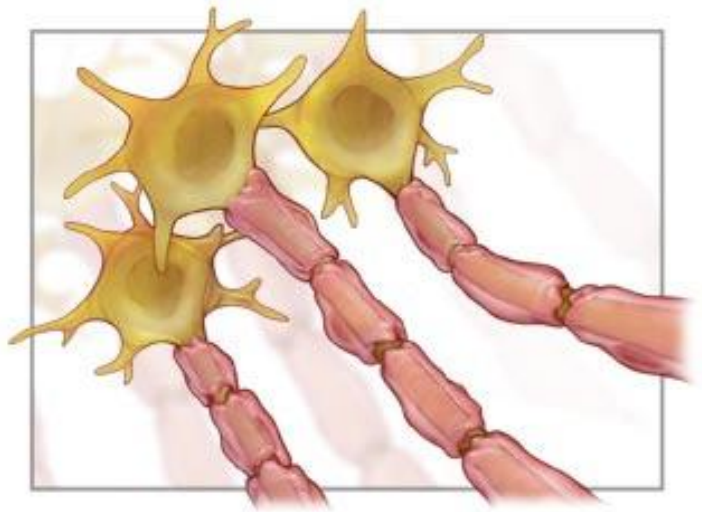
b) **Congenital sensoric neuropathy** - nociceptive stimuli are **not transmitted** by peripheral nerves or by spinal afferent tracts.

Acquired disturbances in pain perception and nociception

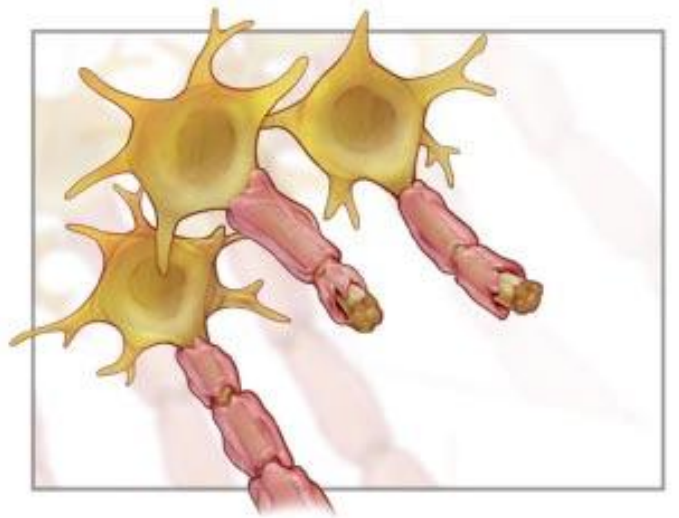
They may occur at **syringomyely, disturbances of parietal lobe of brain, in patients suffering from neuropathy (e.g. chronic diabetes mellitus)**

Development of neuropathic chronic pain after spinal cord injury

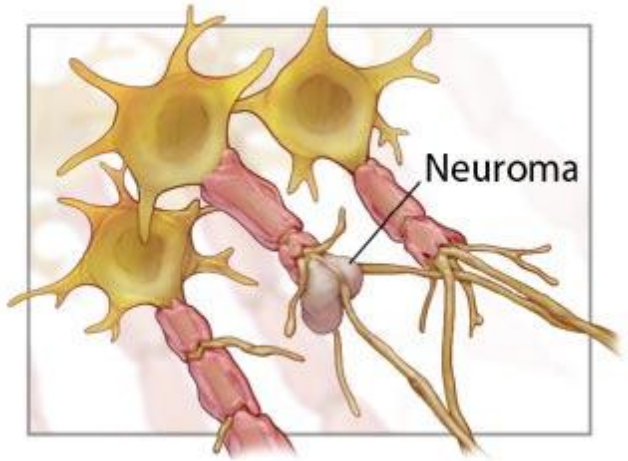


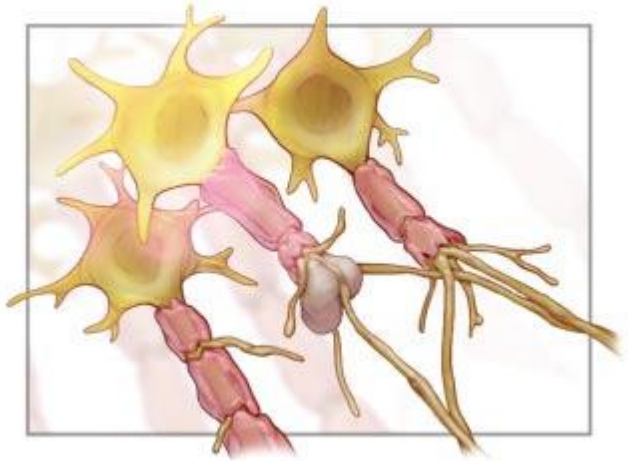


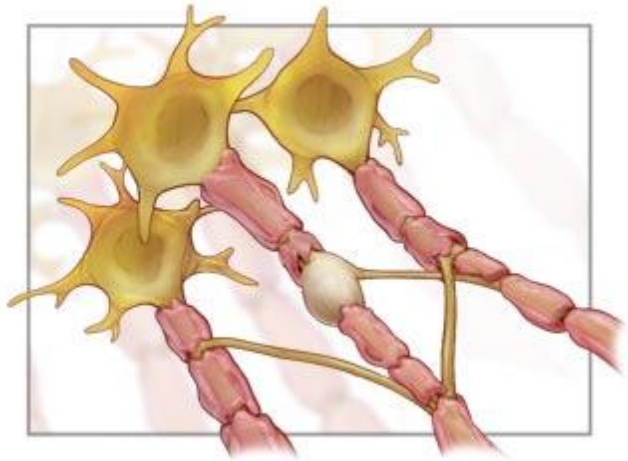
Neural axon

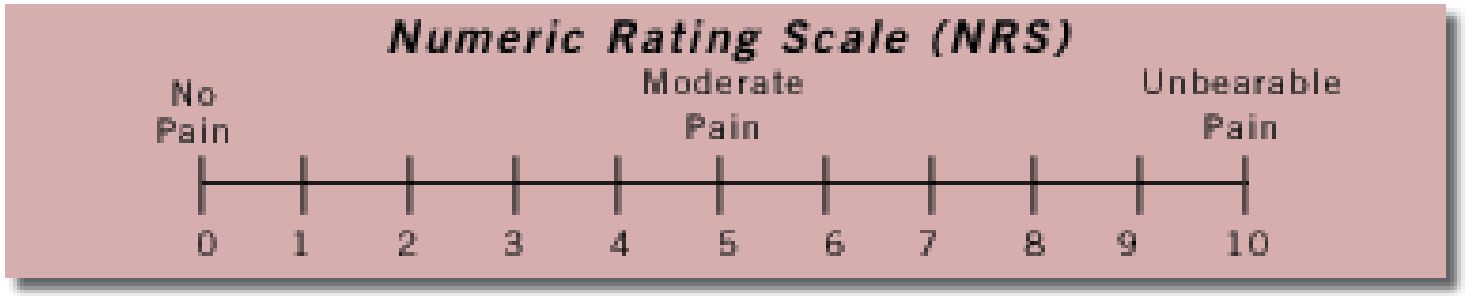


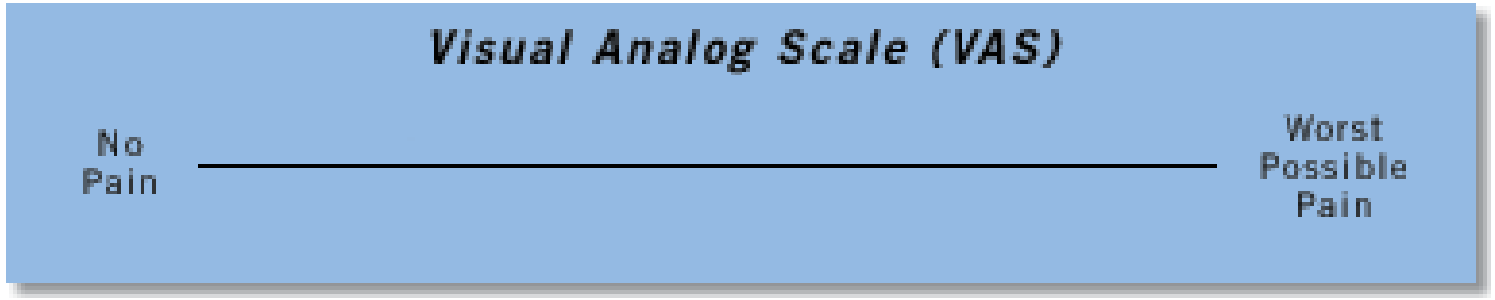
Neural axon injury


Neuroma






Numeric Rating Scale (NRS)
No Pain
Moderate Pain
Unbearable Pain
0 1 2 3 4 5 6 7 8 9 10


Visual Analog Scale (VAS)
No Pain
Worst Possible Pain

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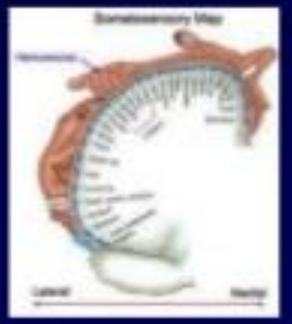
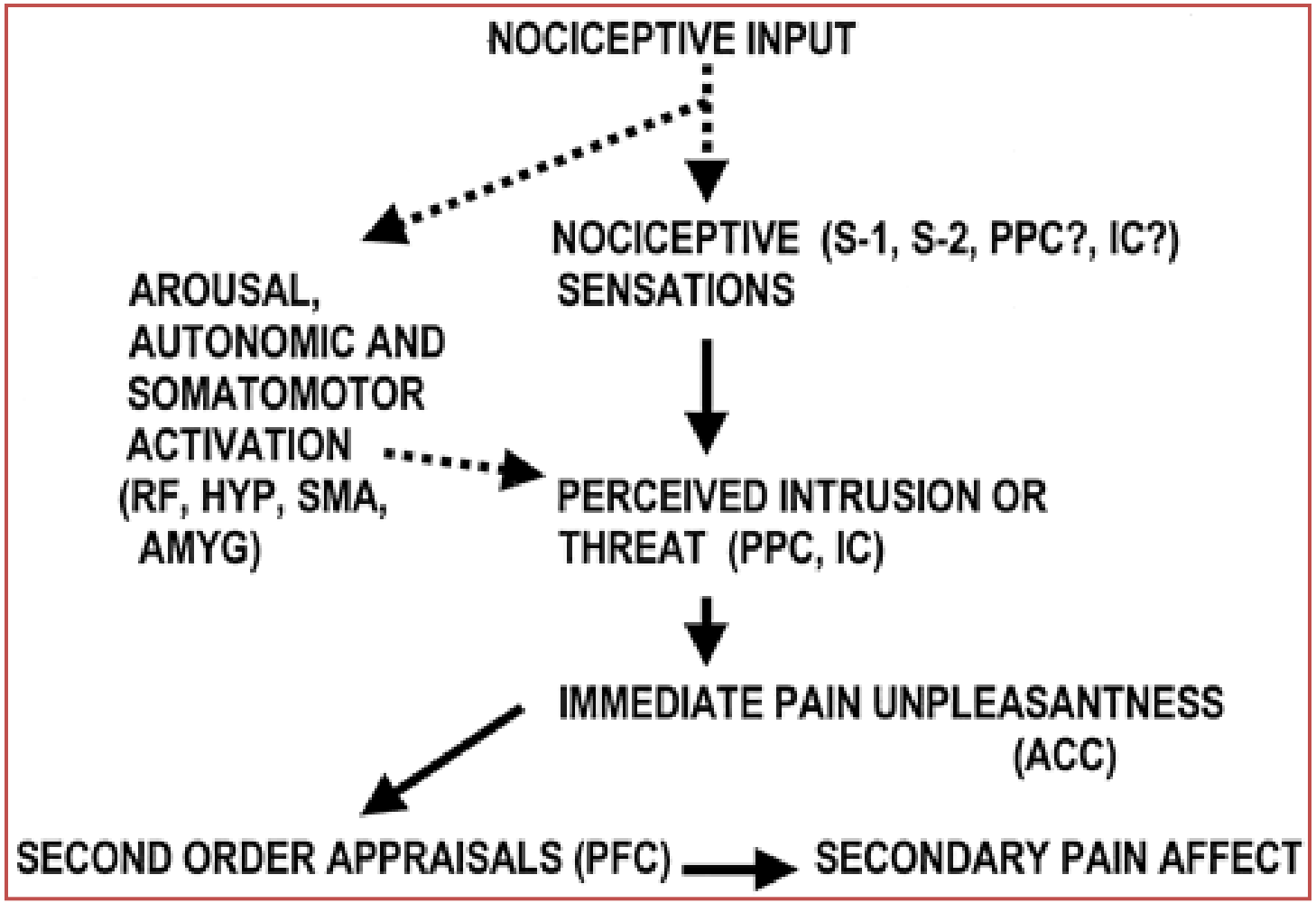
Pain perception

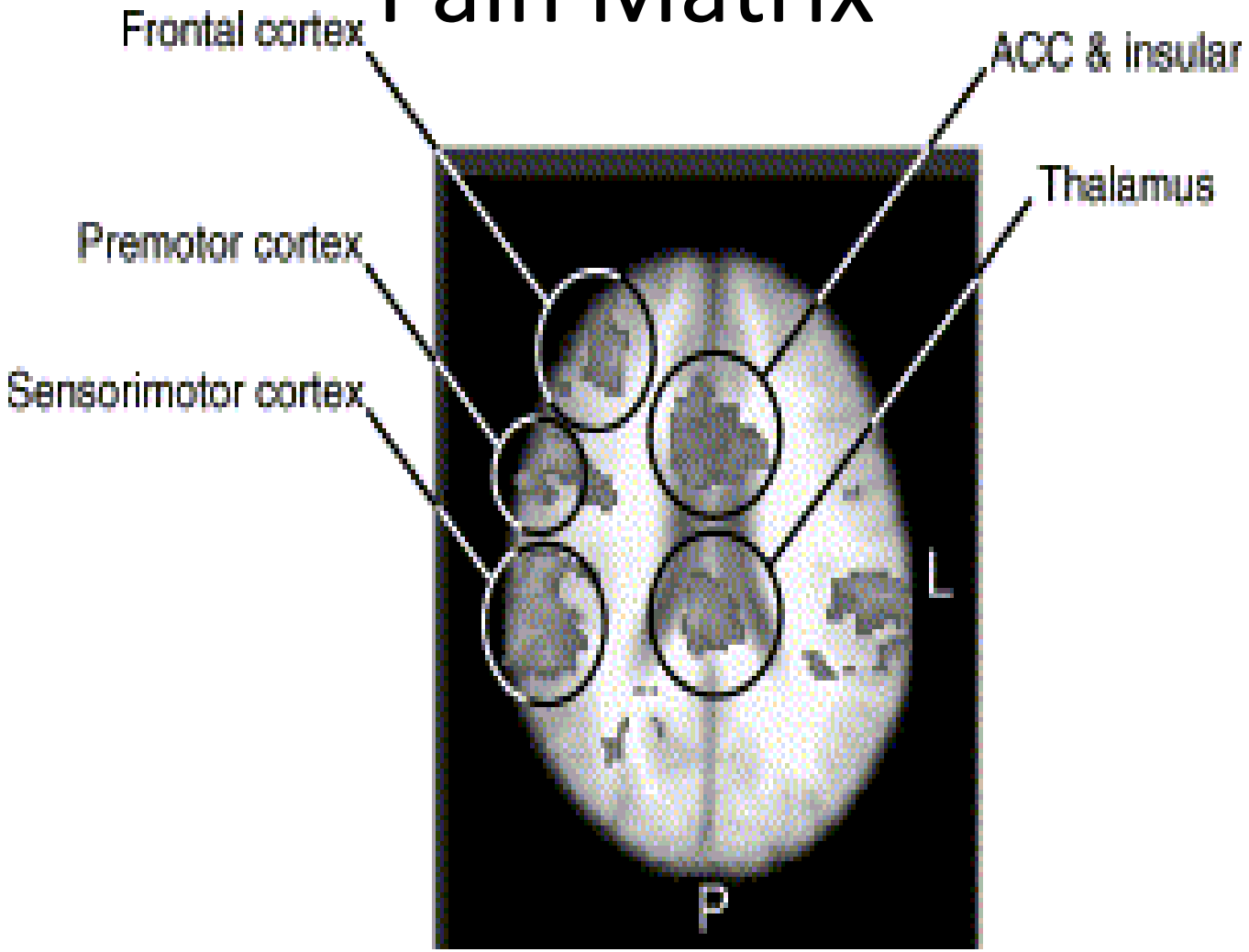
- This occurs at different levels
  - **thalamus is an important centre of pain perception**
    - **lesions of thalamus produces severe type of pain known as 'thalamic pain'**
  - **Sensory cortex is necessary for the localisation of pain**
  - **Other areas are also important**
    - **reticular formation, limbic areas, hypothalamus and other subcortical areas**





Price DD. *Science*. 2000;288:1769-1772.

"Pain Matrix"



Moseley GL. *Man Ther.* 2003;8(3):130-140.

"Pain Matrix"

- Anterior cingulate cortex (ACC)
- Insular cortex (IC)
- Thalamus
- Sensorimotor cortex (SSI, SSII)
- Cerebellum

Moseley GL. *Man Ther.* 2003;8(3):130-140.

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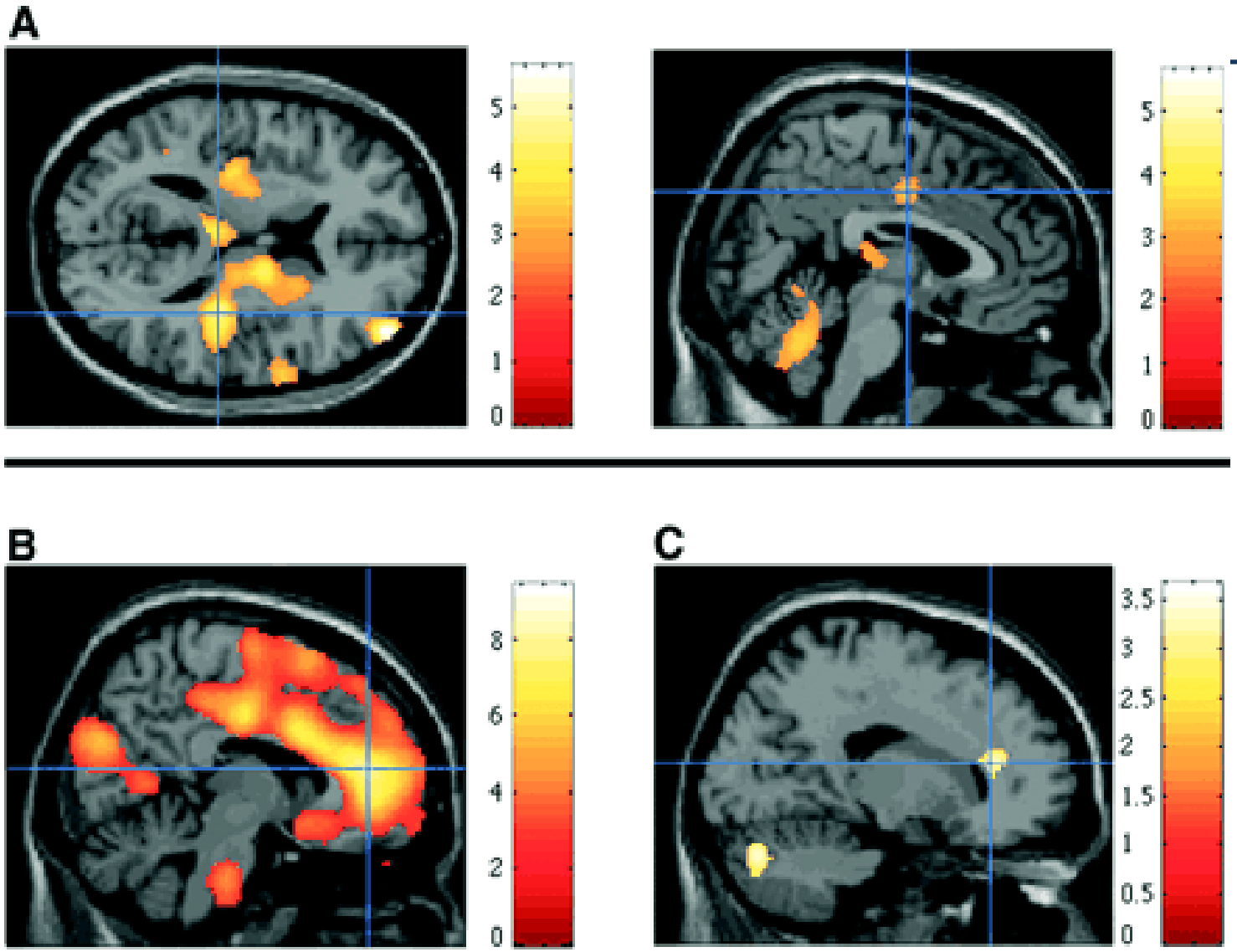

Petrovic P, et al. *Science* 2002;295:1737-1740.

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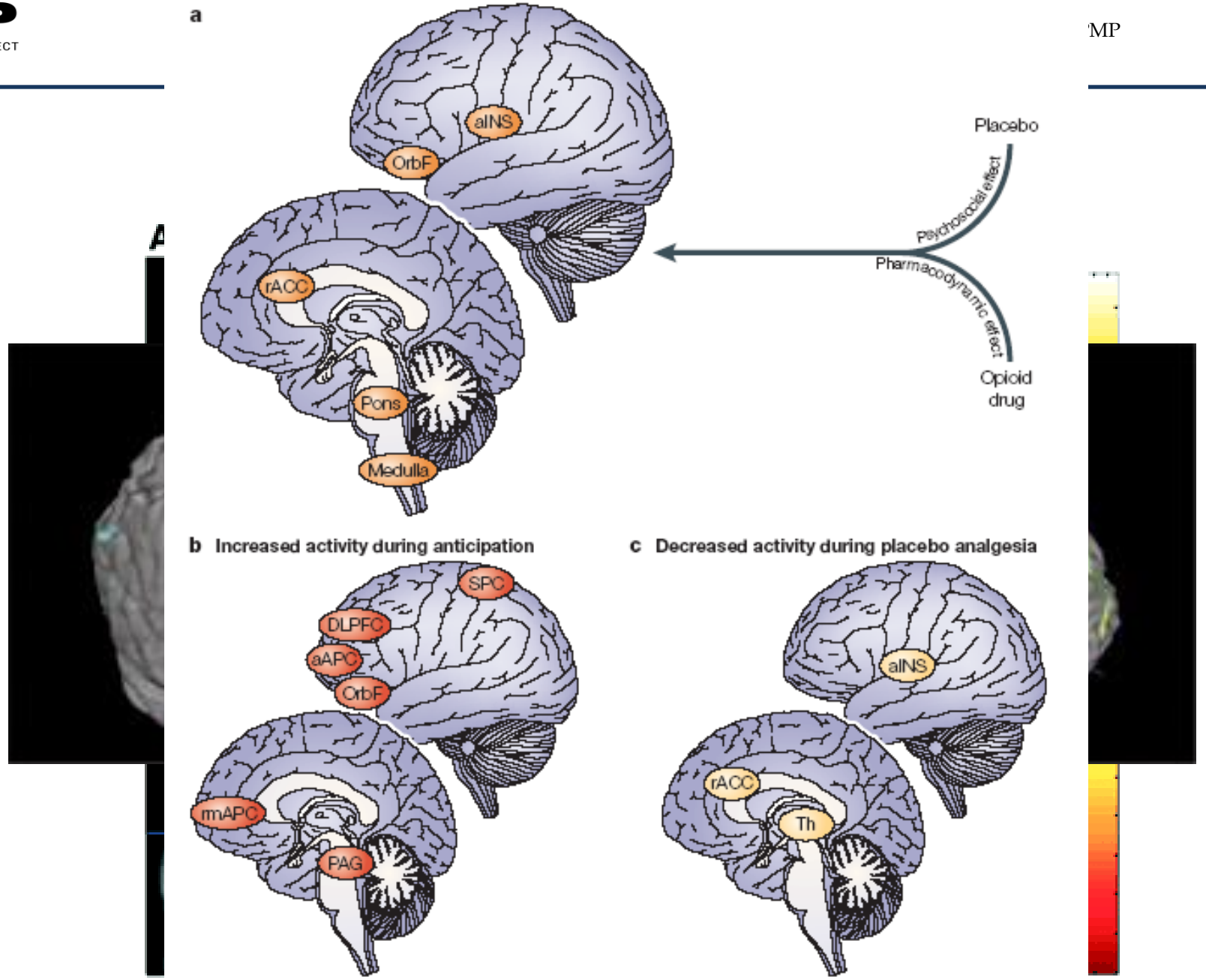

Petrovic P, et al. *Science*. 2002;295:1737-1740.

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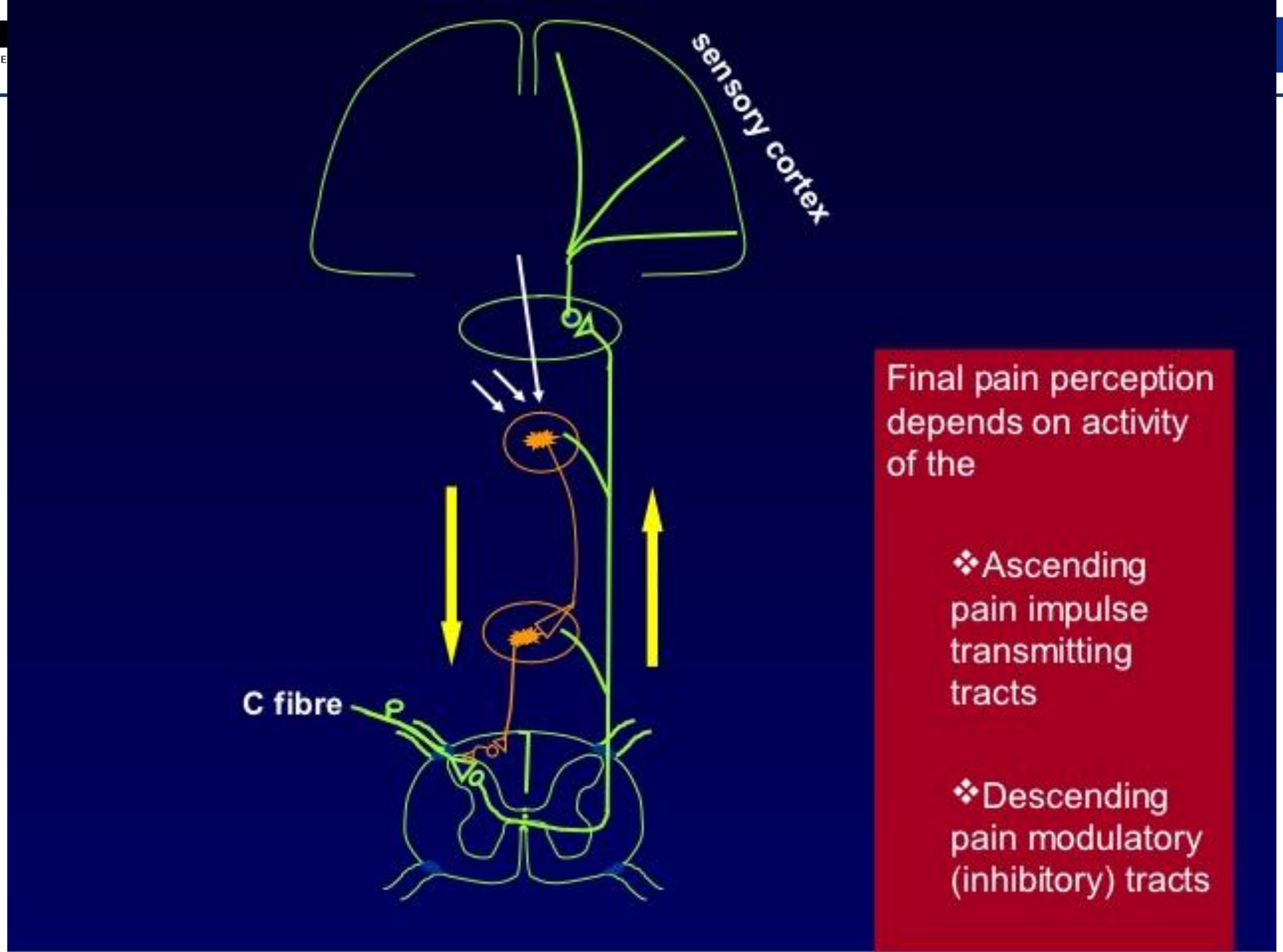
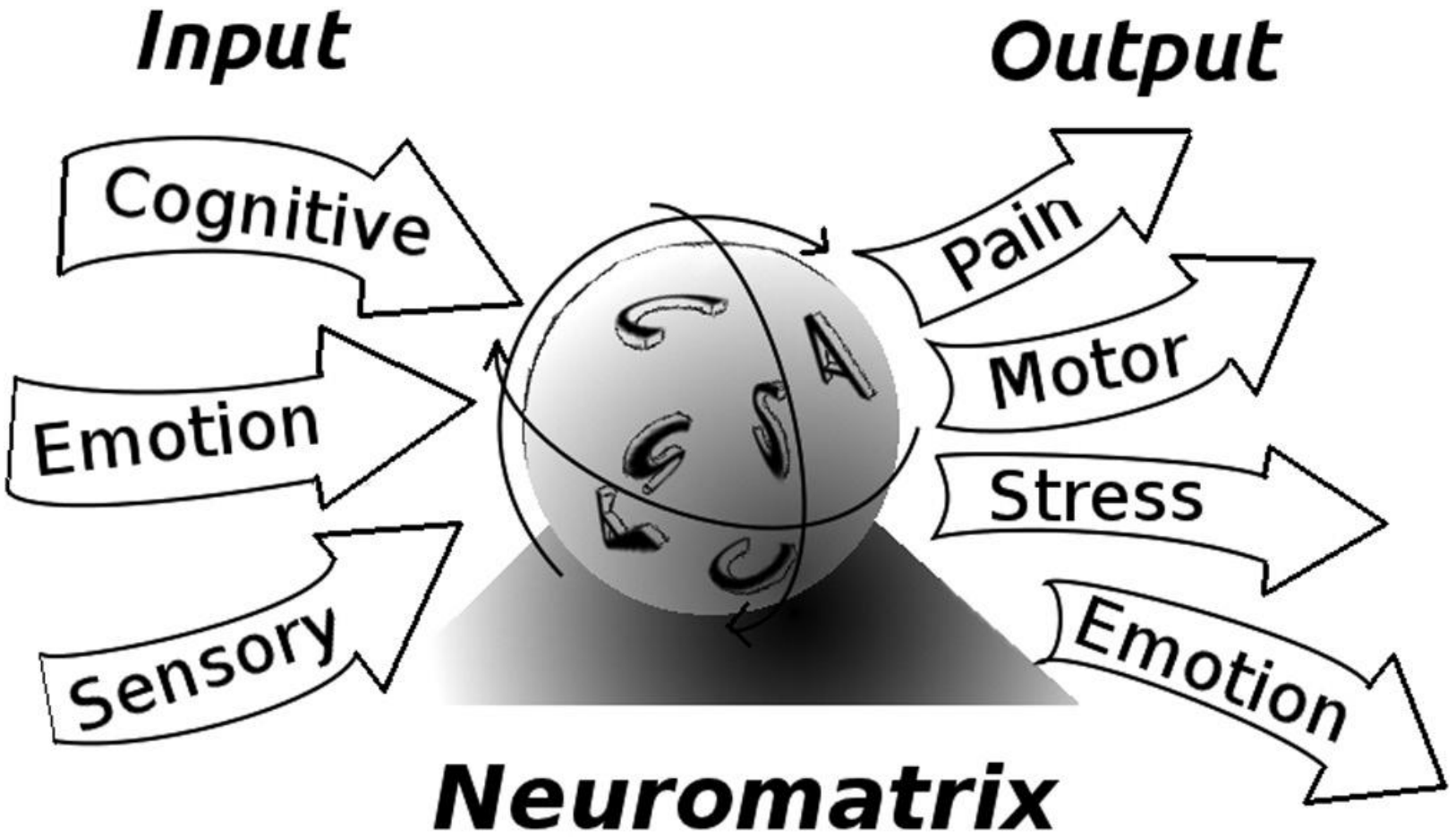


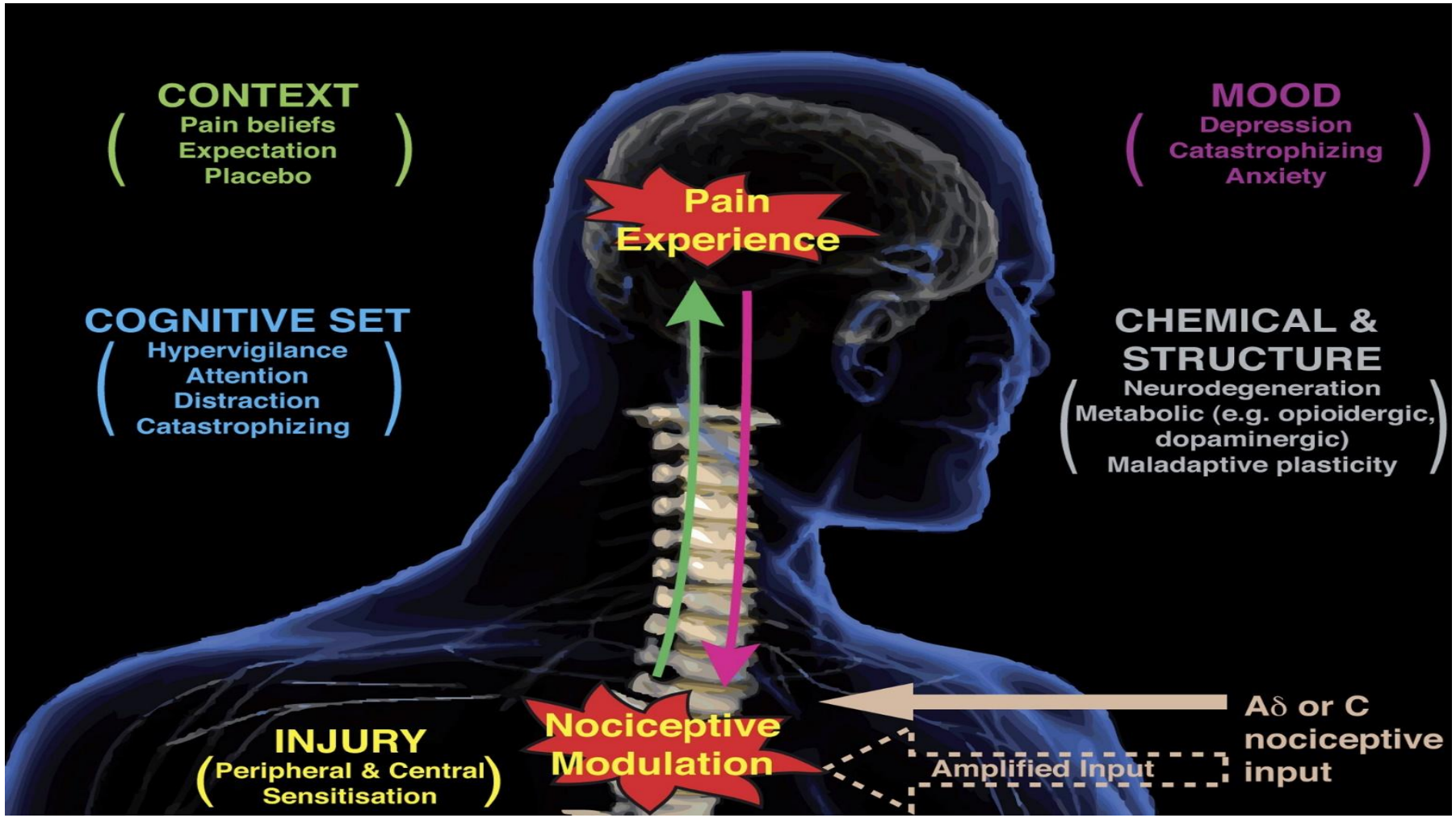
Final pain perception depends on activity of the

- Ascending pain impulse transmitting tracts
- Descending pain modulatory (inhibitory) tracts

Perception of pain



NOCICEPTIONS LEADS TO PAIN. HOW MUCH PAIN IS EXPERIENCED DEPENDS ON:



MULTI DIMENZIONALNI KONCEPT BOLA

ence. (IASP Taxonomy 2012) The individual experience and manifestation of pain is influenced by a complex series of interactions involving sensory, pathophysiological, affective, socio-cultural, behavioural and cognitive elements (Fig. 1; Dalal and Bruera 2012).

Brien TO, EJP 2017; 21: 3-19.

I tako smo danas ovde !

- Lečenje bola je podcenjeno
- Bol je 5^{ti} vitalni znak
- „Bol“ je pitanje ljudskih prava

Kako dalje?

Prvi korak - edukacija:

- Edukacija zdravstvenih radnika,
- Pacijenata,
- Podizanje svesti opšte populacije (društva) o značaju problema bola i njegovom obimu, kroz kampanje borbe protiv bola.

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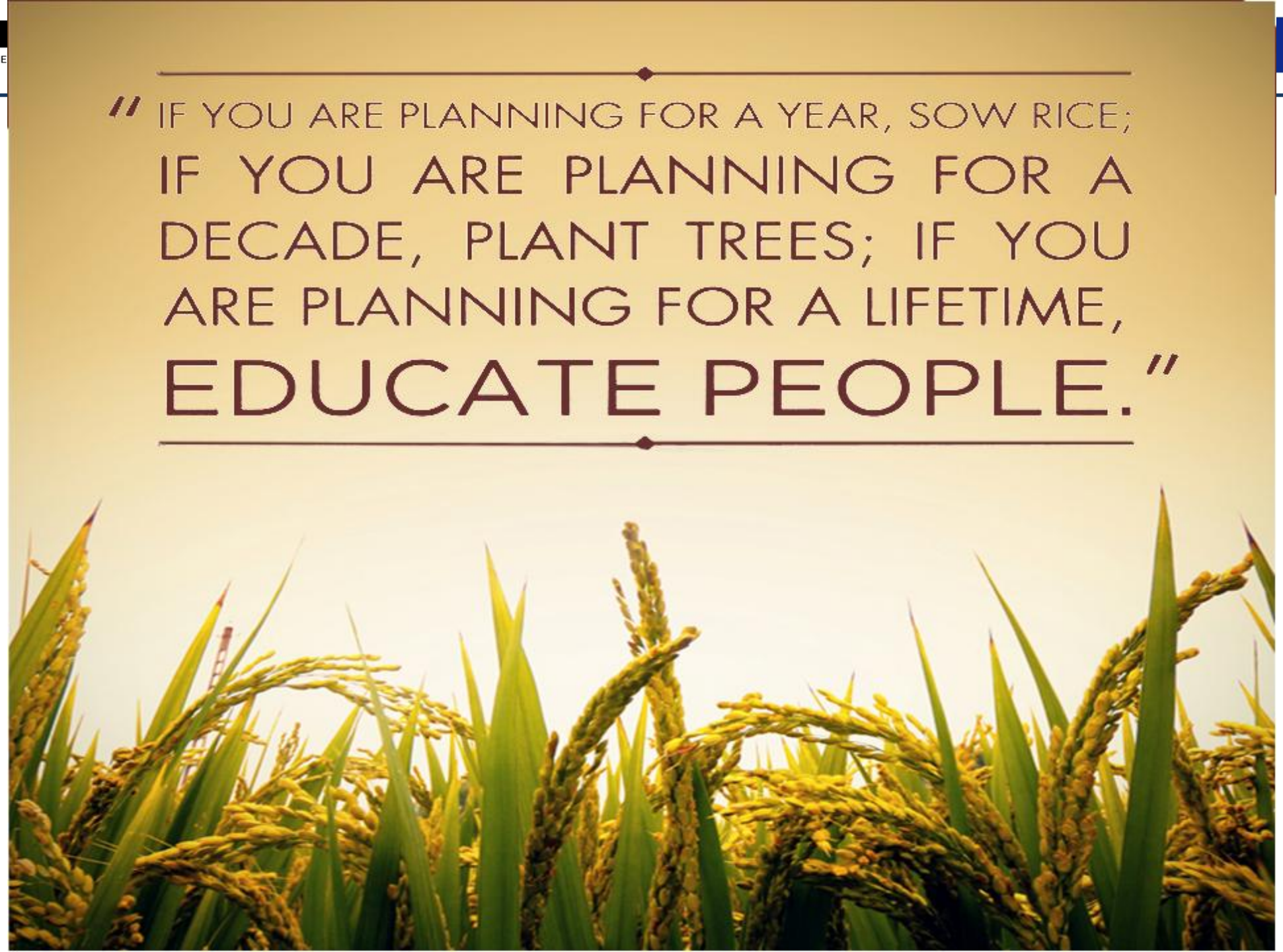

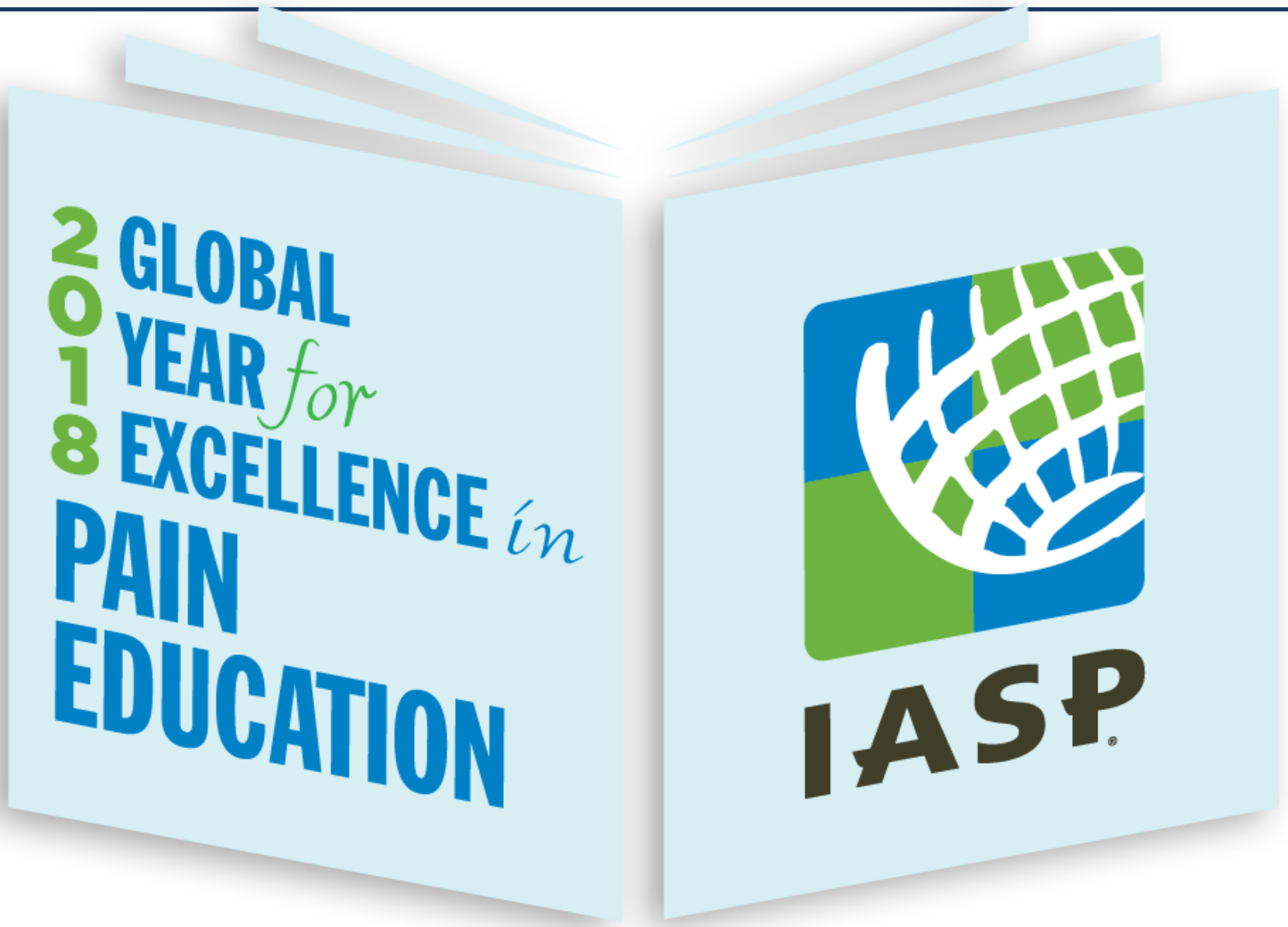
2018 GLOBAL YEAR for EXCELLENCE in PAIN EDUCATION
IASP


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Project number: 585927-EPP-1-2017-1-RS-EPPKA2-CBHE-JP (2017 - 3109 / 001 - 001)
WELCOME ADDRESS

HVALA NA PAŽNJI !!!

ODLIKE HRONIČNOG BOLNOG SINDROMA

- UPORAN bol u trajanju dužem od 6 MESECI
- Značajna PROMENA ponašanja
- Značajna RESTRIKCIJA dnevnih aktivnostri
- PRETERANA upotreba lekova ili česte posete lekaru
- Bez jasnog odnosa sa organskim poremećajem
- Različiti pokušaji lečenja (lekovi... , operacije)