痛与镇痛
(Pain and analgesia)

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Somatic sensation (躯体感觉):

Touch: Mechanoreceptors of skin (触觉感受器)

Temperature: Thermoreceptors （温度感受器）

Pain: Nociceptors （痛感受器）

痛与镇痛
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Pain teaches us to avoid harmful situations. It elicits withdrawal reflexes from noxious stimuli. It exhorts us to rest an injured part of our body. Pain is vital. In any case, life without pain is not a blessing.

痛与镇痛
(Pain and analgesia)

Pain is initiated as activation of peripheral sensory fibers by injury or an insult to tissue but is perceived as a sensation through central responses.

痛与镇痛
(Pain and analgesia)

1. Pain
   - Peripheral events in the initiation of pain
   - Central events in the transmission of pain

2. Analgesia
   - Melzack and Wall's gate theory of pain
   - Descending inhibitory pathway
   - Endogenous opiate

1. Pain

Peripheral events in the initiation of pain

Tissue damage and chemical mediators

Sensory receptors-Nociceptors

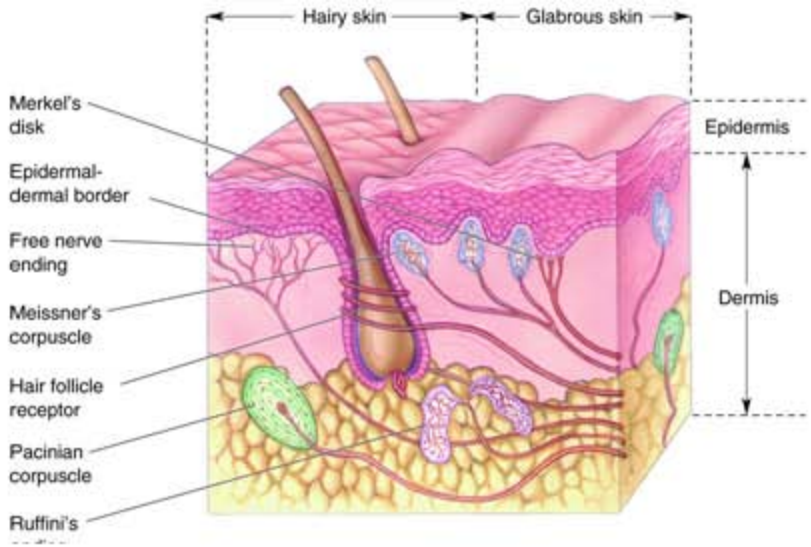
Primary afferent fibers mediating painful inputs:

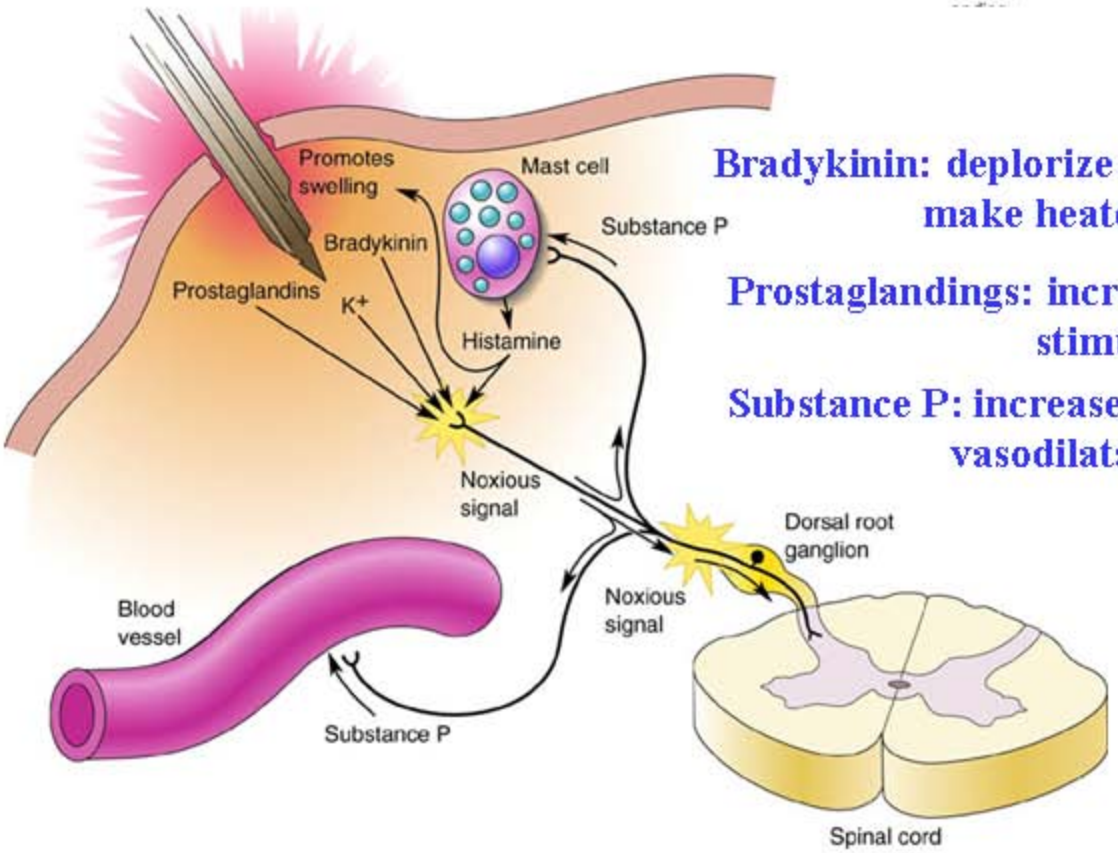
Aβ-, Aδ- and C-fibers

Pain and Nociception

- Pain is the feeling or perception of irritating, sore stinging, aching, throbbing, miserable, or unbearable sensations arising from a part of the body.

- Nociception is the sensory process that provides the signals that trigger pain.





Bradykinin: deplorize nociceptors, make heated-activated ion channels more sensitive.

Prostaglandings: increase the sensitive nociceptors to stimuli.

Substance P: increase the sensitive nociceptors to stimuli vasodilatation, histamine release,

1. Pain

Peripheral events in the initiation of pain

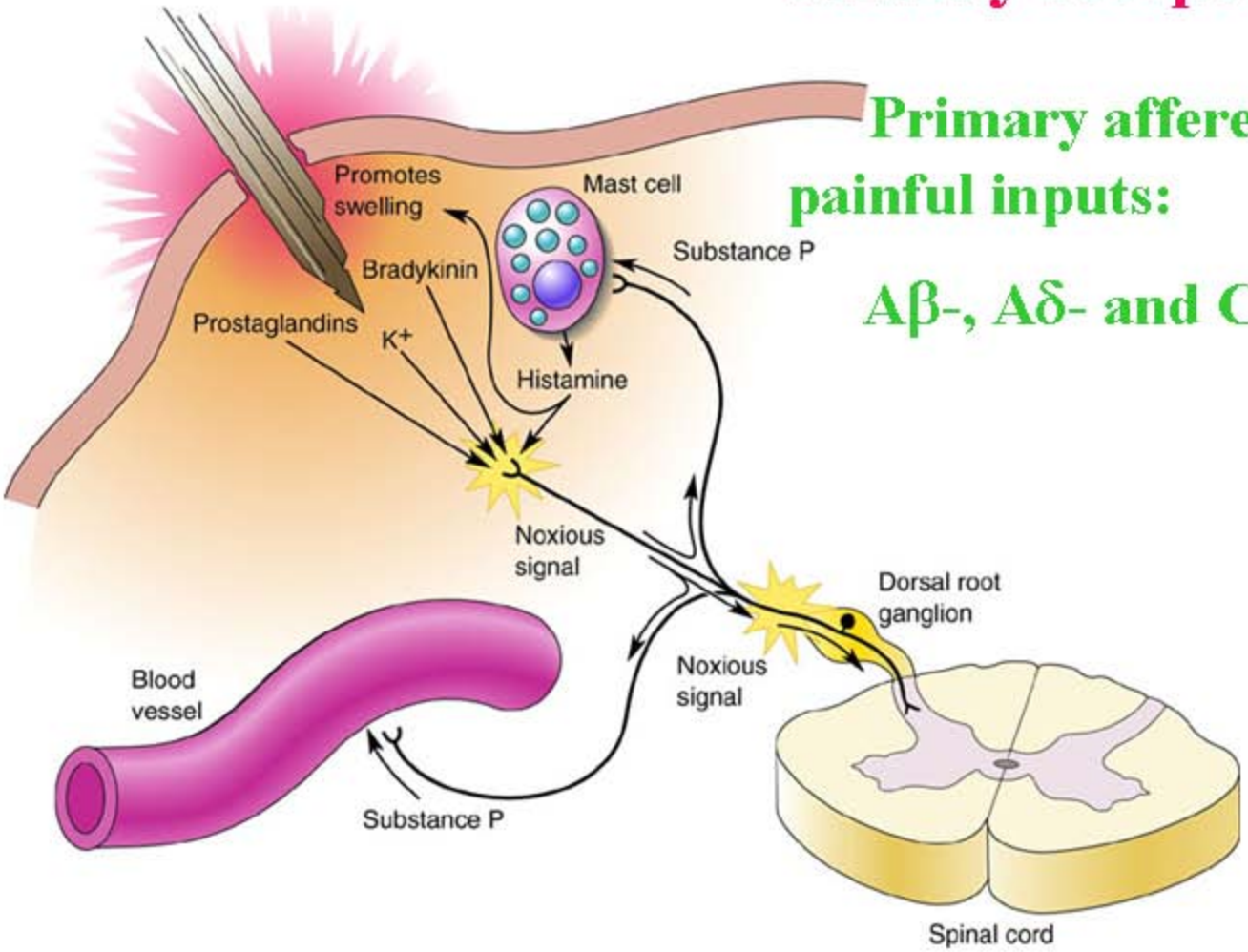
Tissue damage and chemical mediators

Sensory receptors-Nociceptors

Primary afferent fibers mediating painful inputs:

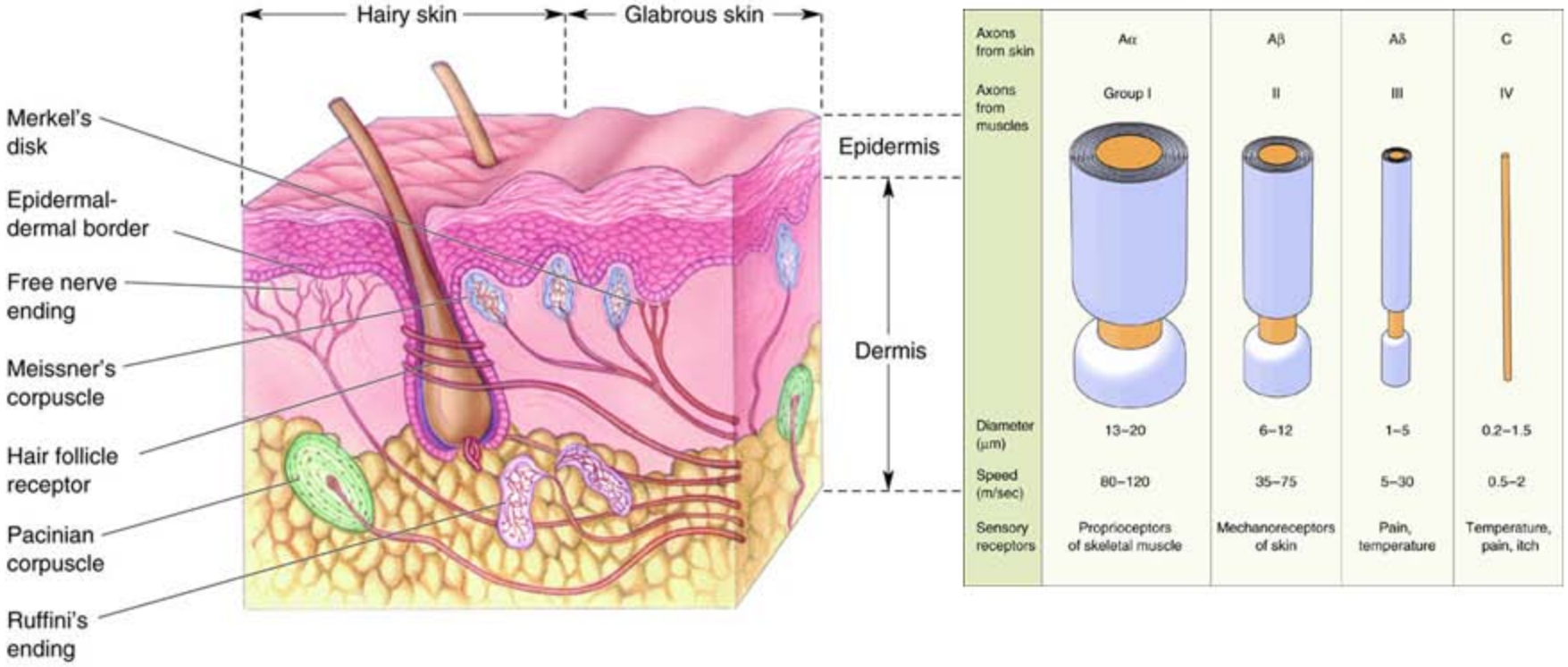
Aβ-, Aδ- and C-fibers

Sensory receptors-Nociceptors

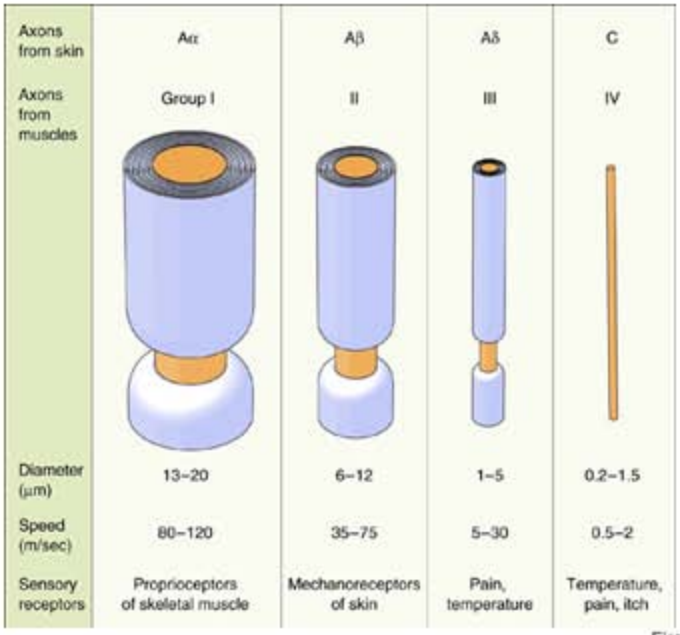


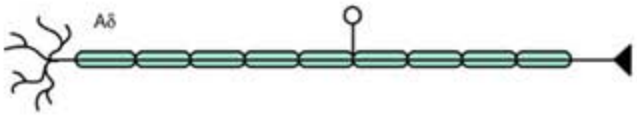
Primary afferent fibers mediating painful inputs:

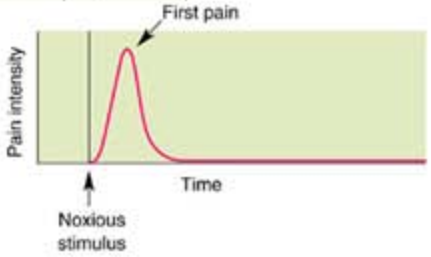
Aβ-, Aδ- and C-fibers

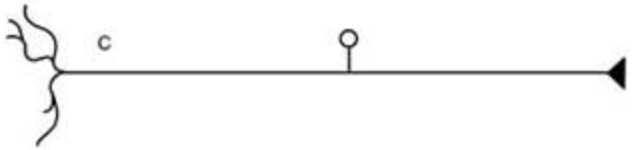


1. The pain pathways has only free nerve endings;
2. The touch pathway is swift and uses thick myelinated A β fiber;
   the pain pathway is slow and uses thin, lightly myelinated Aδ fibers and unmyelinated C fibers;
3. They differ with respect to their connections in the spinal cord.









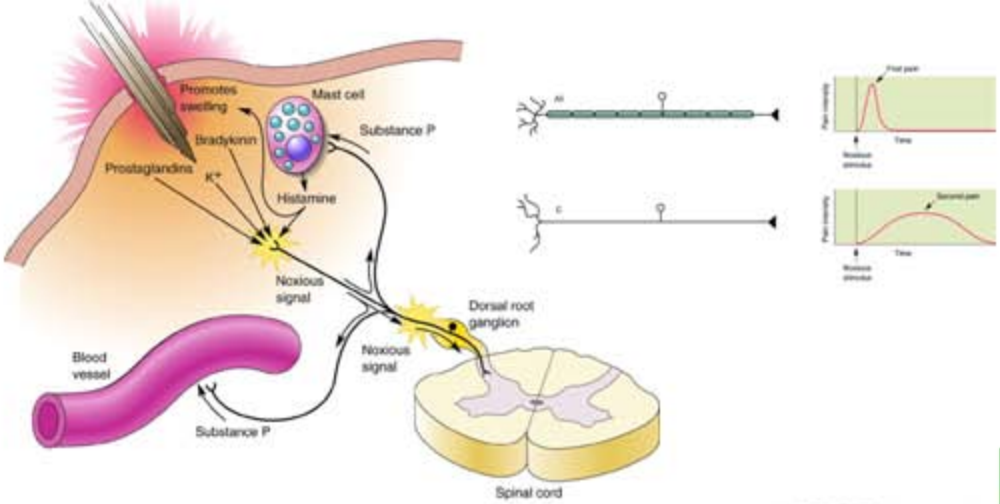
Activation of skin nociceptors produces two distinct perceptions of pain: A fast sharp first pain followed by a duller, longer-lasting second pain. First pain is caused by the activation of Aδ fibers; second pain , C fibers.

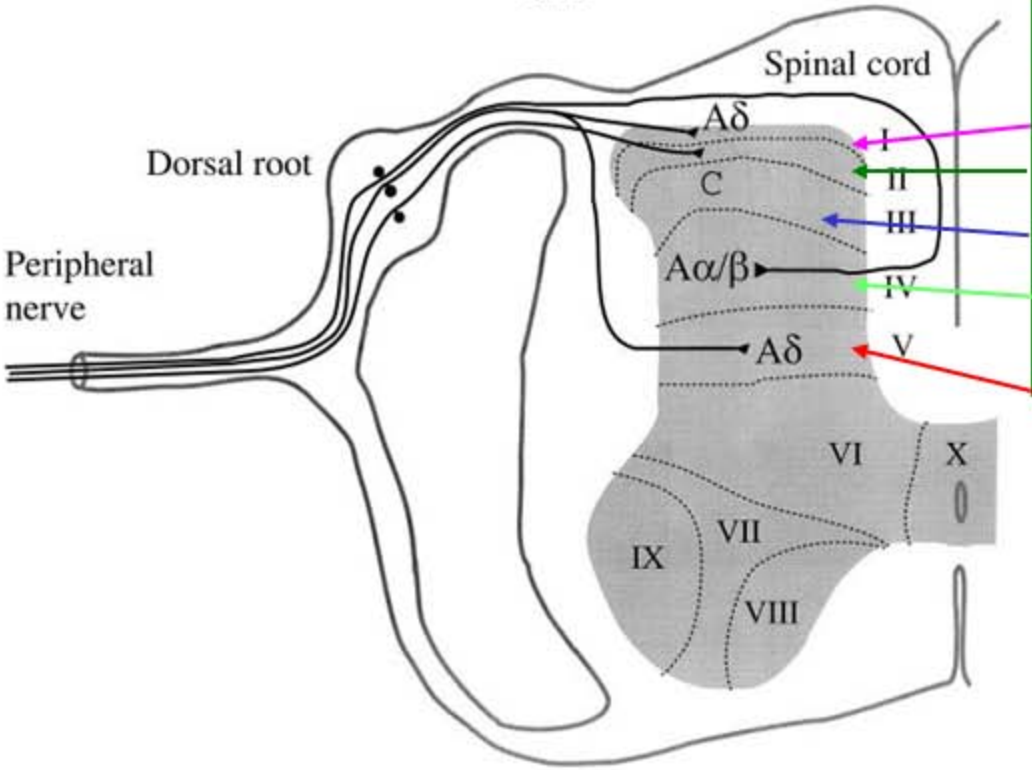
1. Pain

Central events in the transmission of pain

Ascending pain pathways:

- Sensory transmission in the spinal cord
- Pathways;
- Neurotransmitters





Laminae II:

Laminae III

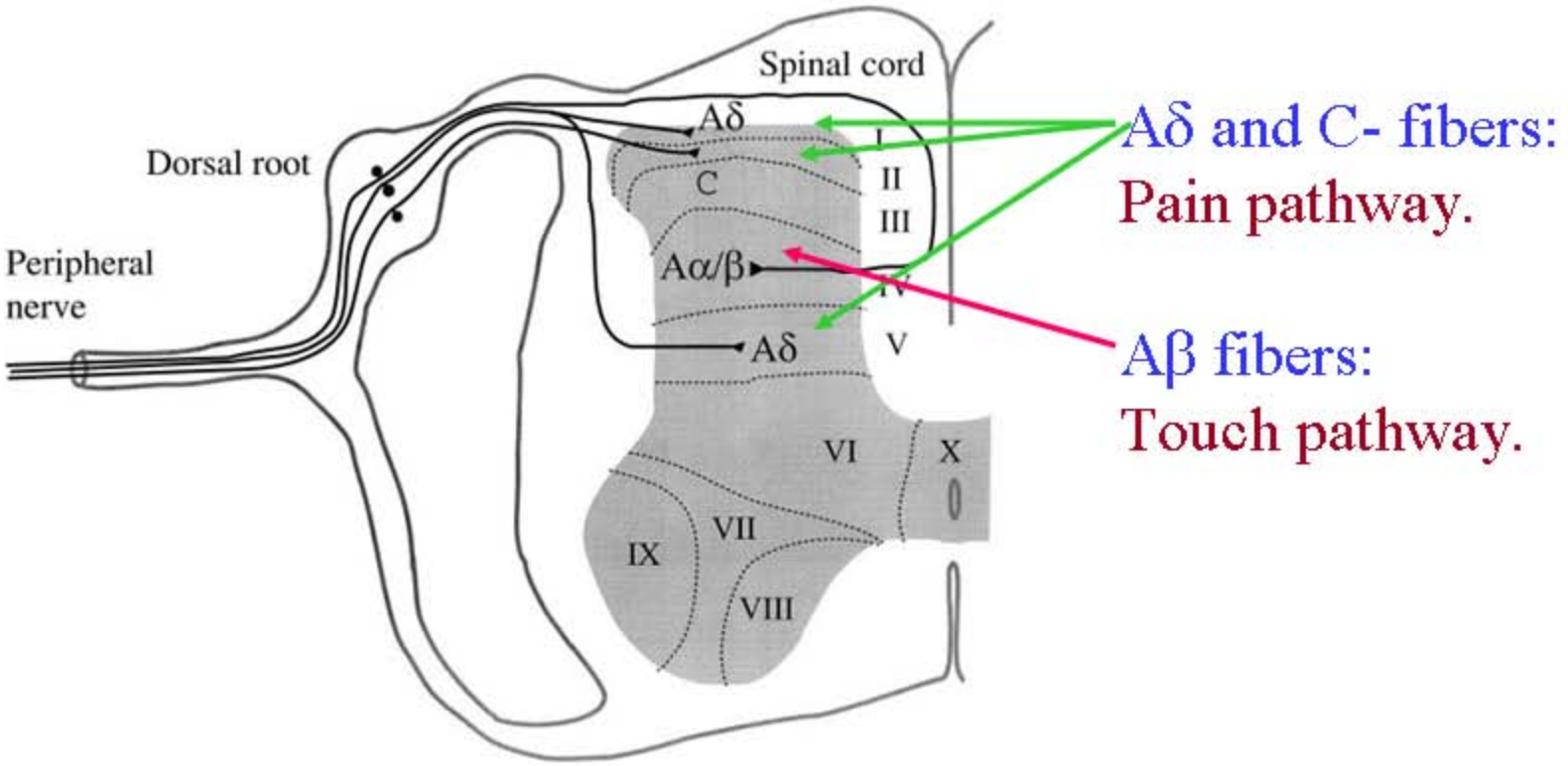
Laminae IV

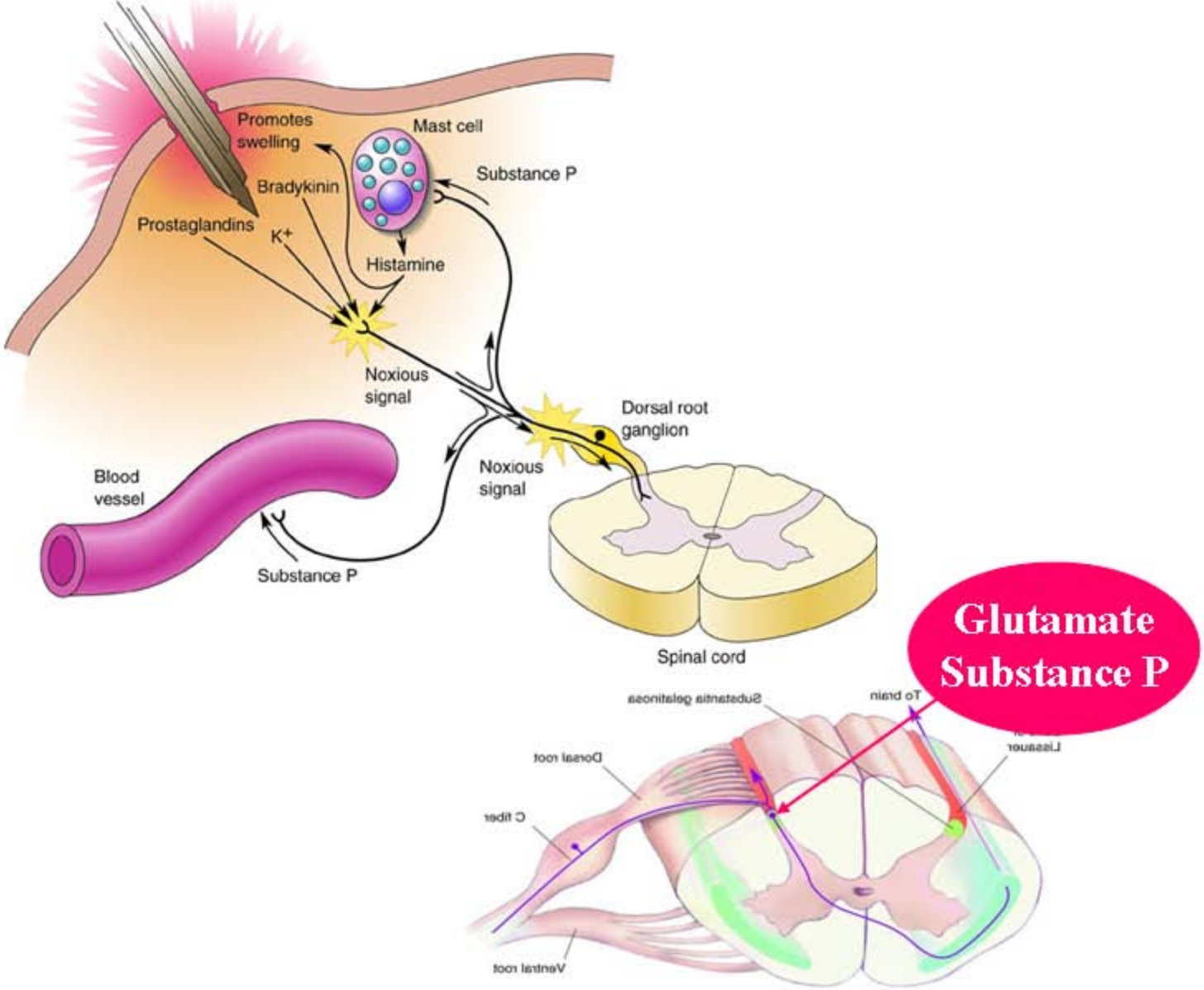
Laminae V

Three types Projection cells:
- Spinocervical tract (SCT)
- Postsynaptic dorsal collumn(PSDC)
- Spinothalamic tract (STT)

Inter neurons

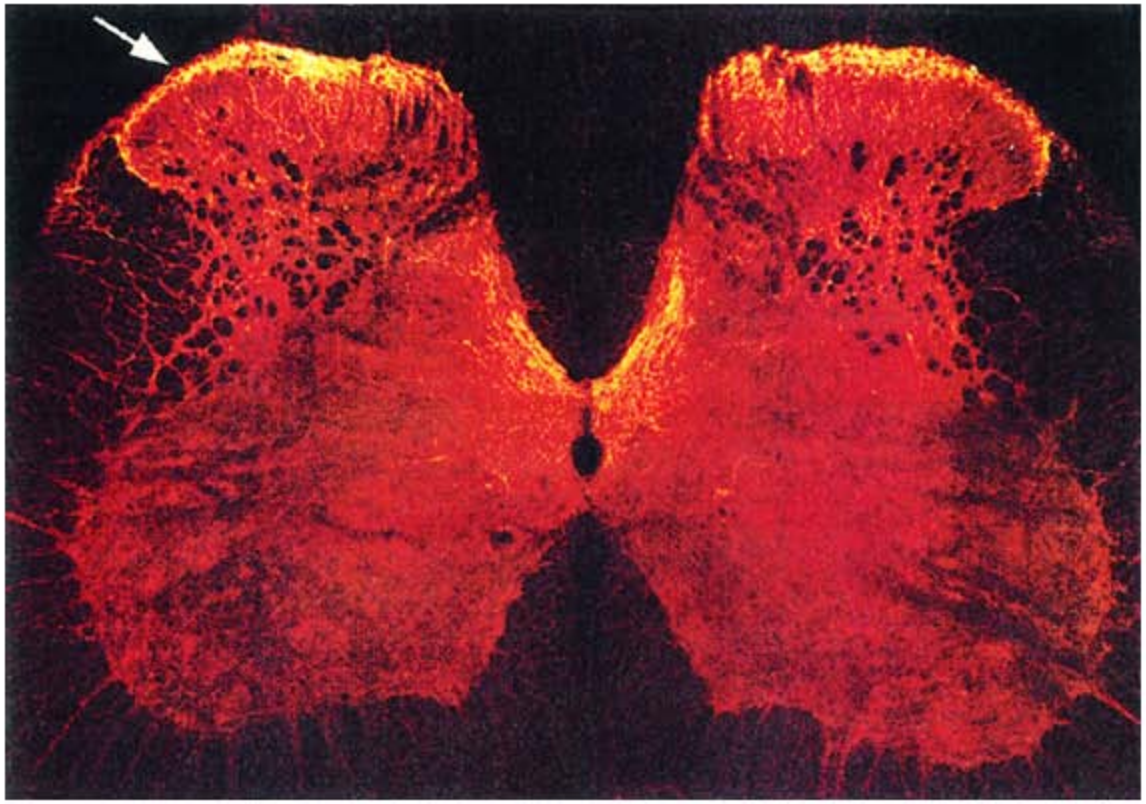
Receive Aδ and C-fiber inputs:
- Low- & high-threshold mechanical stimuli
- Nociceptive inputs from the viscerae

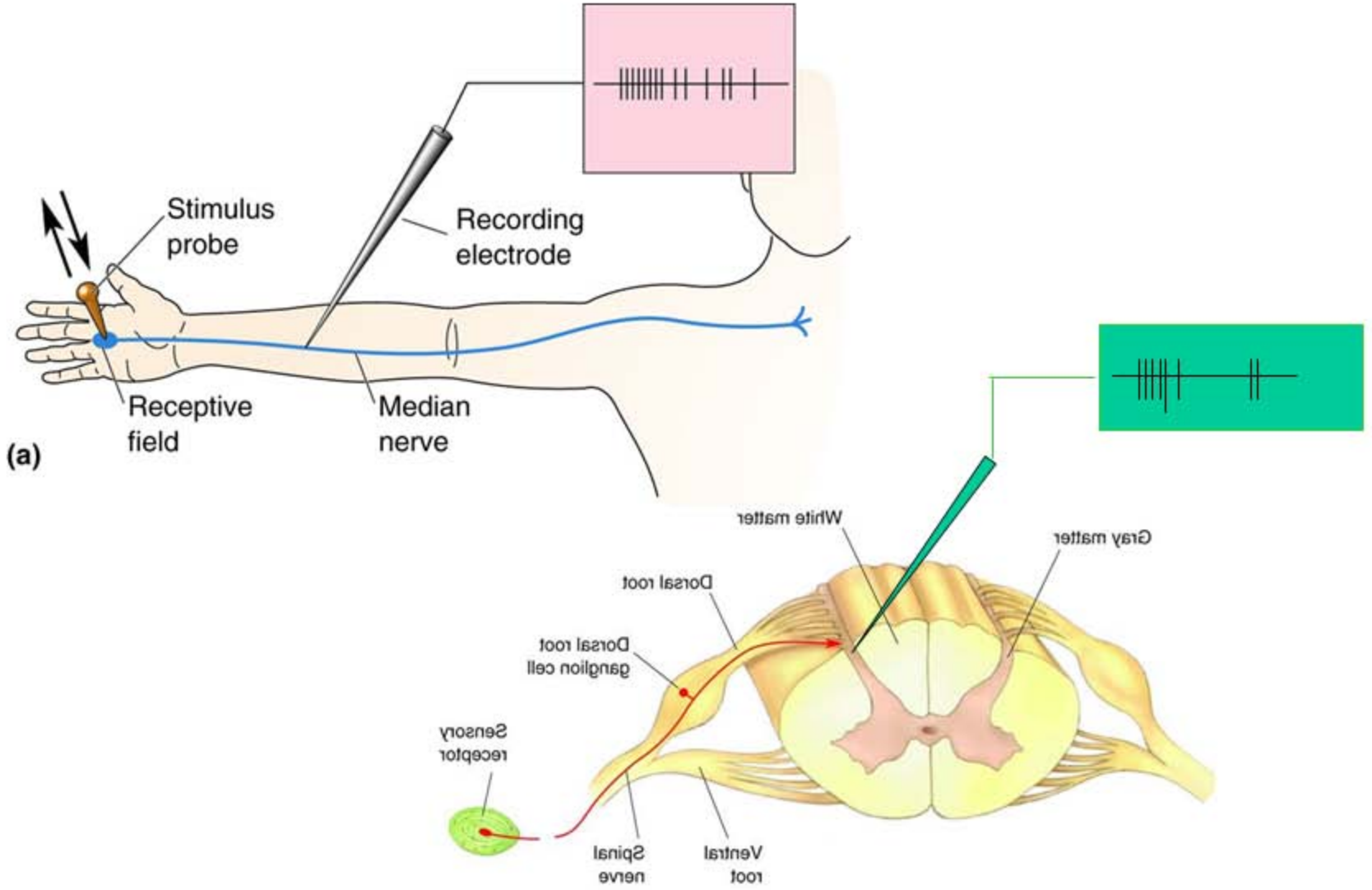

Spinal cord
Aδ
Dorsal root
C
I
II
III
Aα/β
Peripheral
nerve
Aδ
V
VI
X
VII
IX
VIII
Aδ and C- fibers:
Pain pathway.
Aβ fibers:
Touch pathway.



The neurotransmitter of the pain afferents is believed to be glutamate(Aδ, Aβ, and C fibers), substance P (C-fibers).

Substance P in the SG




Stimulus probe
Recording electrode
Receptive field
Median nerve
(a)
White matter
Gray matter
Dorsal root
Dorsal root ganglion cell
Sensory receptor
Spinal nerve
Ventral root

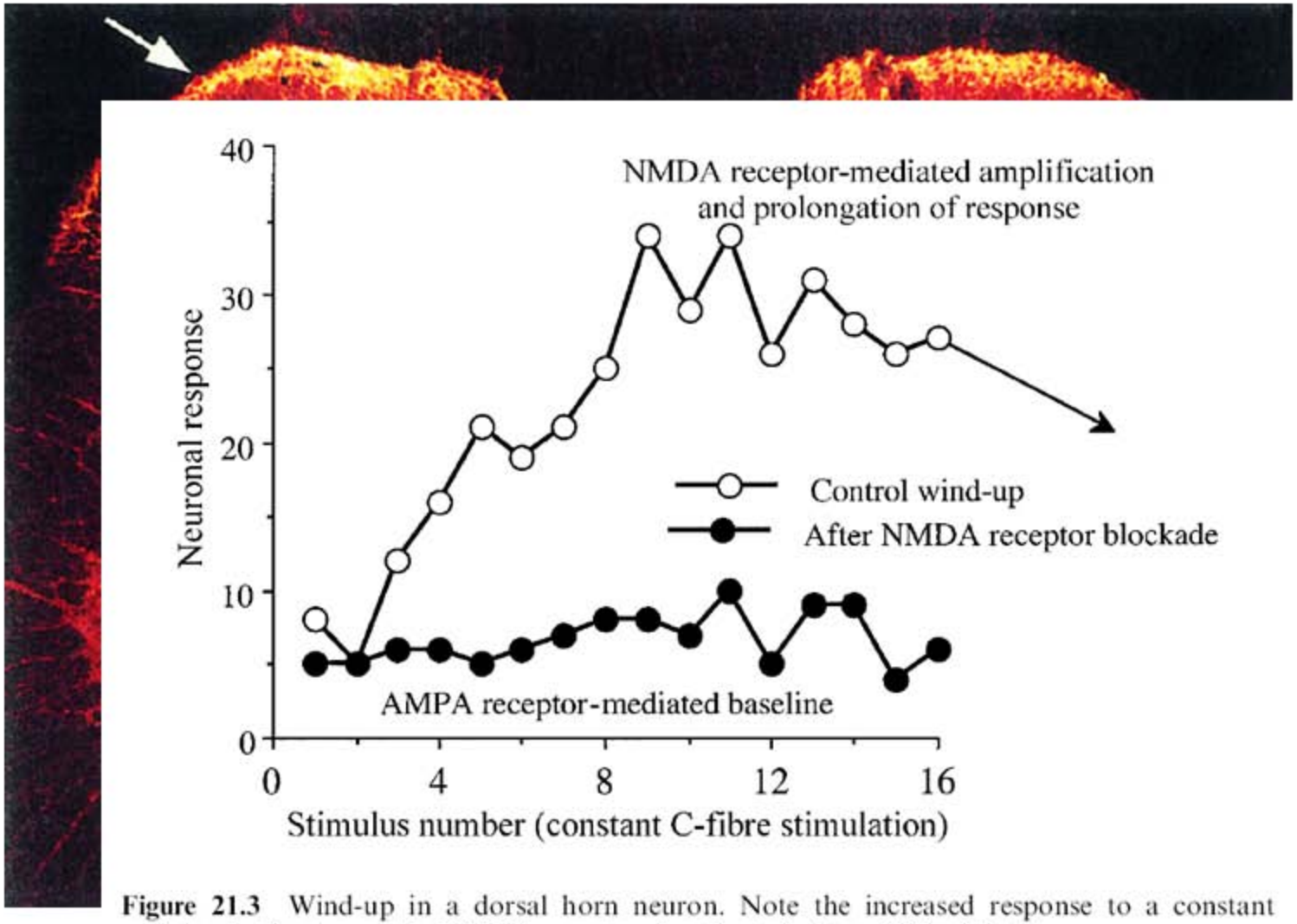
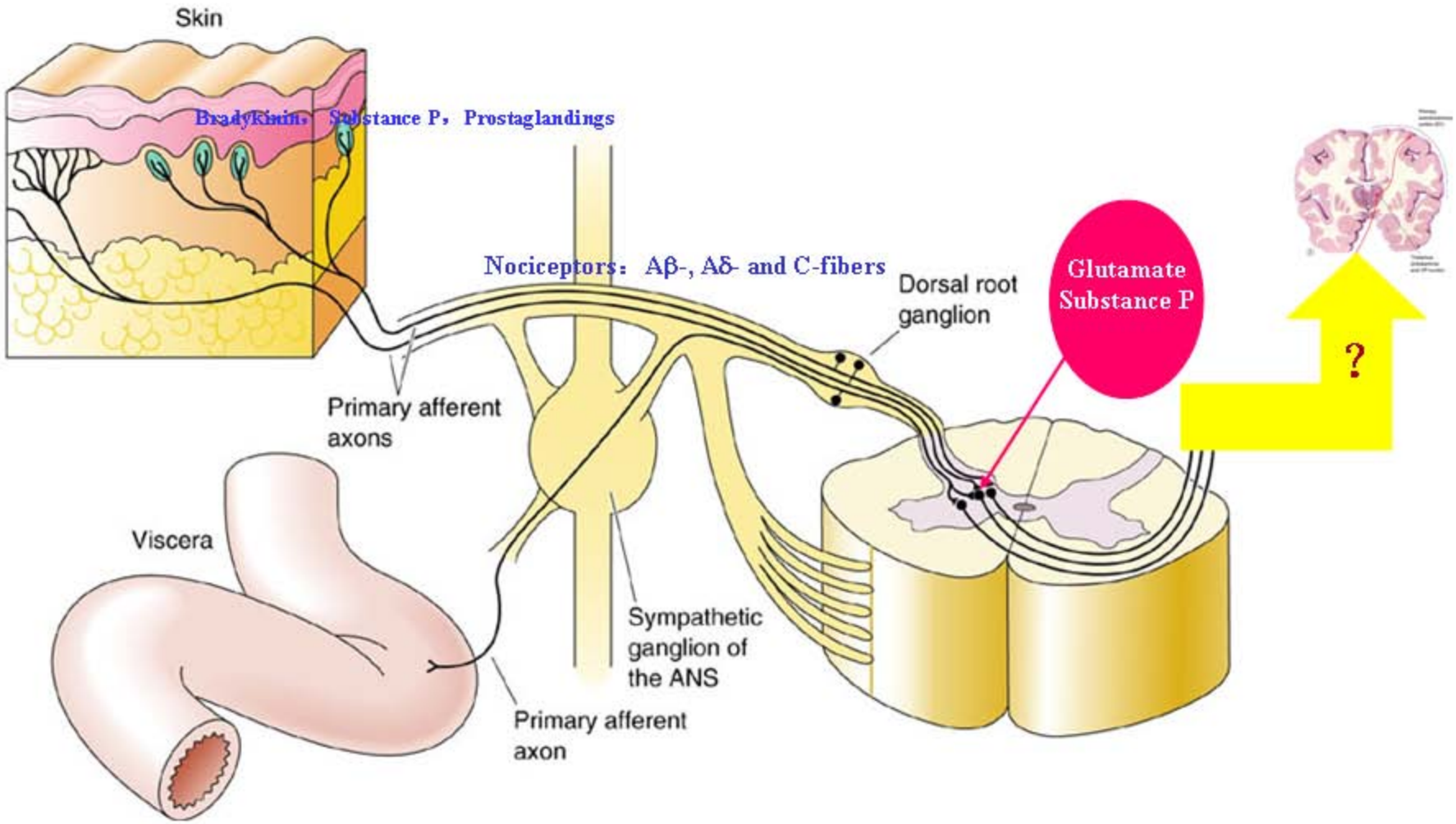


Figure 21.3 Wind-up in a dorsal horn neuron. Note the increased response to a constant peripheral stimulus as the NMDA receptor is activated. (Unpublished data)


Skin
Bradykinin, Substance P, Prostaglandings
Nociceptors: Aβ-, Aδ- and C-fibers
Dorsal root ganglion
Glutamate
Substance P
?
Primary afferent axons
Viscera
Sympathetic ganglion of the ANS
Primary afferent axon

1. Pain

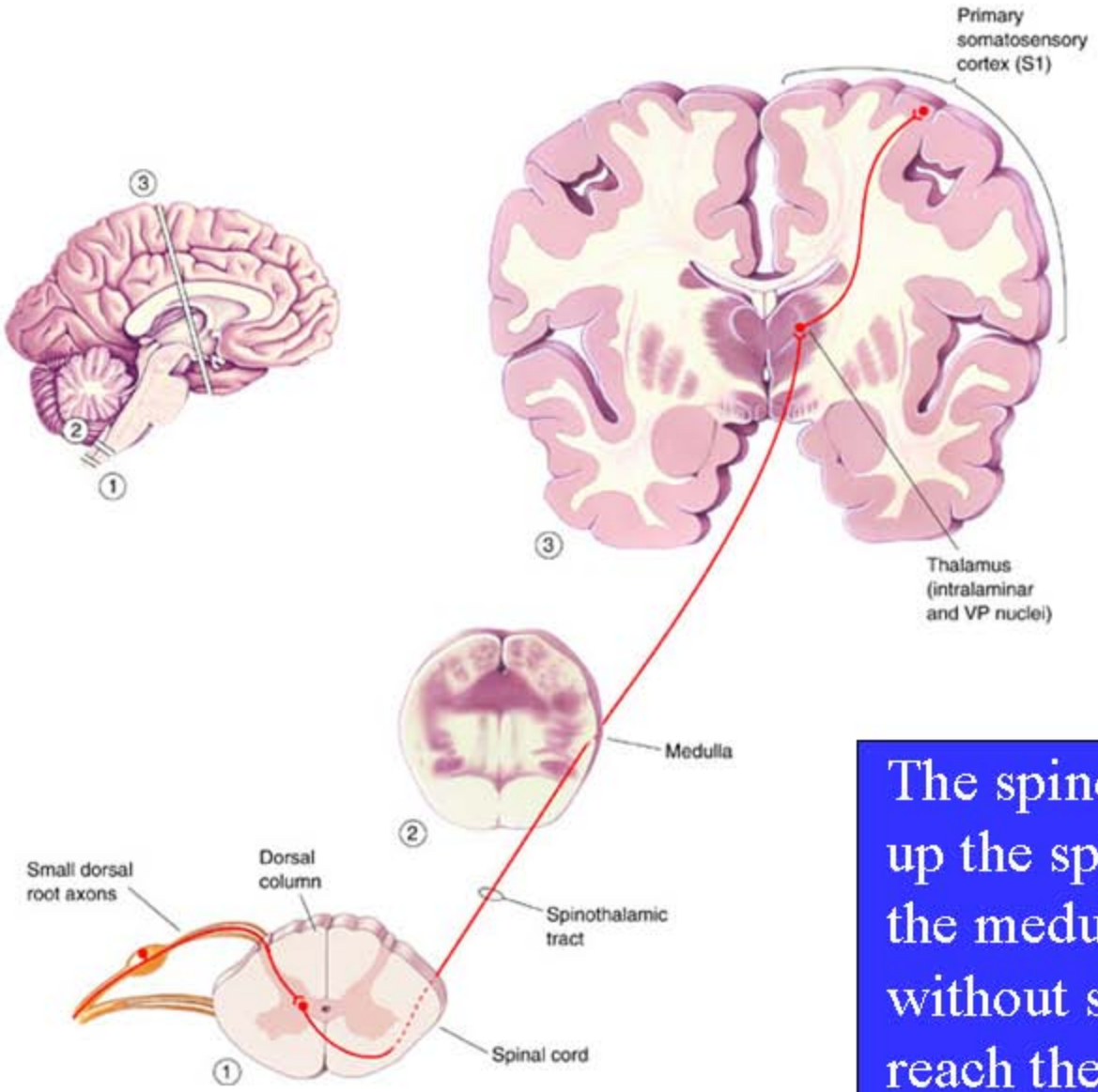
Central events in the transmission of pain

Ascending pain pathways:

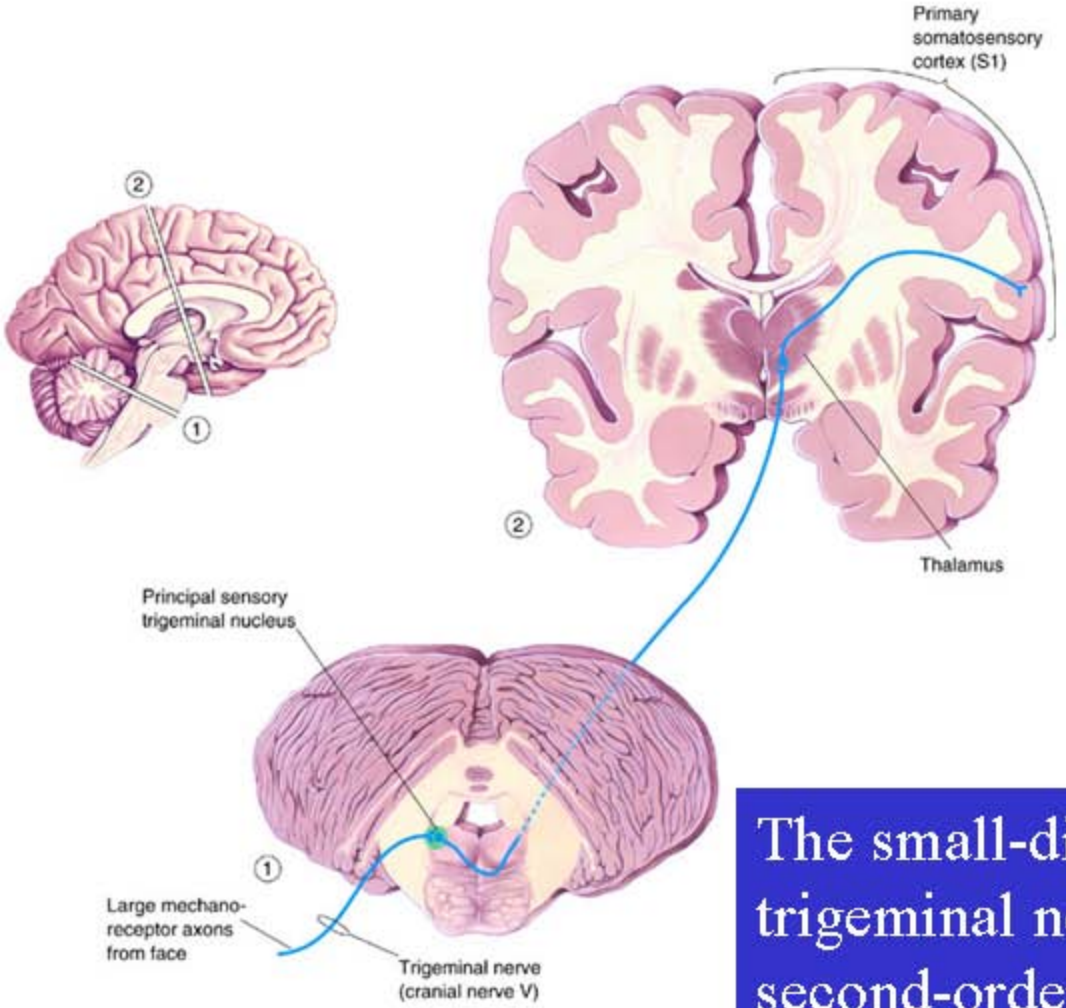
- Sensory transmission in the spinal cord
- Pathways;
- Neurotransmitters

Asending pain pathways:

- The spinothalamic pain pathway
- The trigeminal pain pathway
- The thalamus and cortex

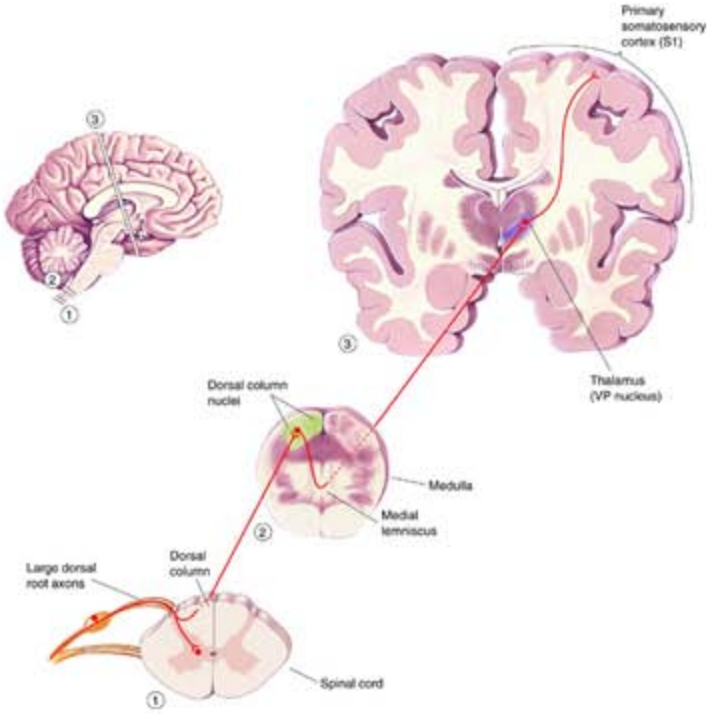


The spinothalamic fibers project up the spinal cord and through the medulla, pons, and midbrain without synapsing until they reach the thalamus.



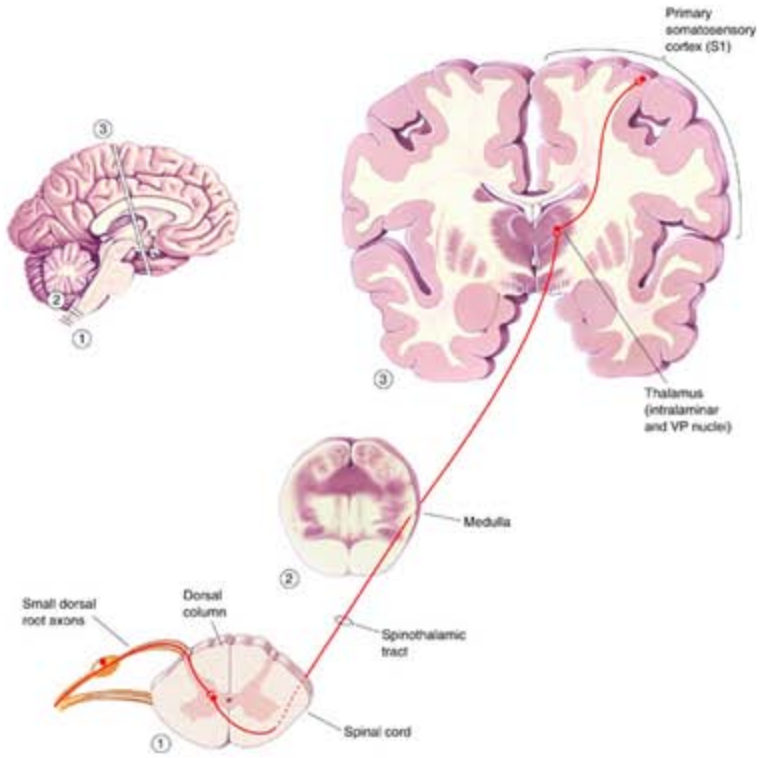
The small-diameter fibers in the trigeminal nerve synapse first on second-order sensory neurons in the spinal trigeminal nucleus of the brain stem. The axons of these cells cross and ascend to the thalamus in the trigeminal lemniscuses.

The dorsal column-medial lemniscal pathway
背柱内侧丘系通路

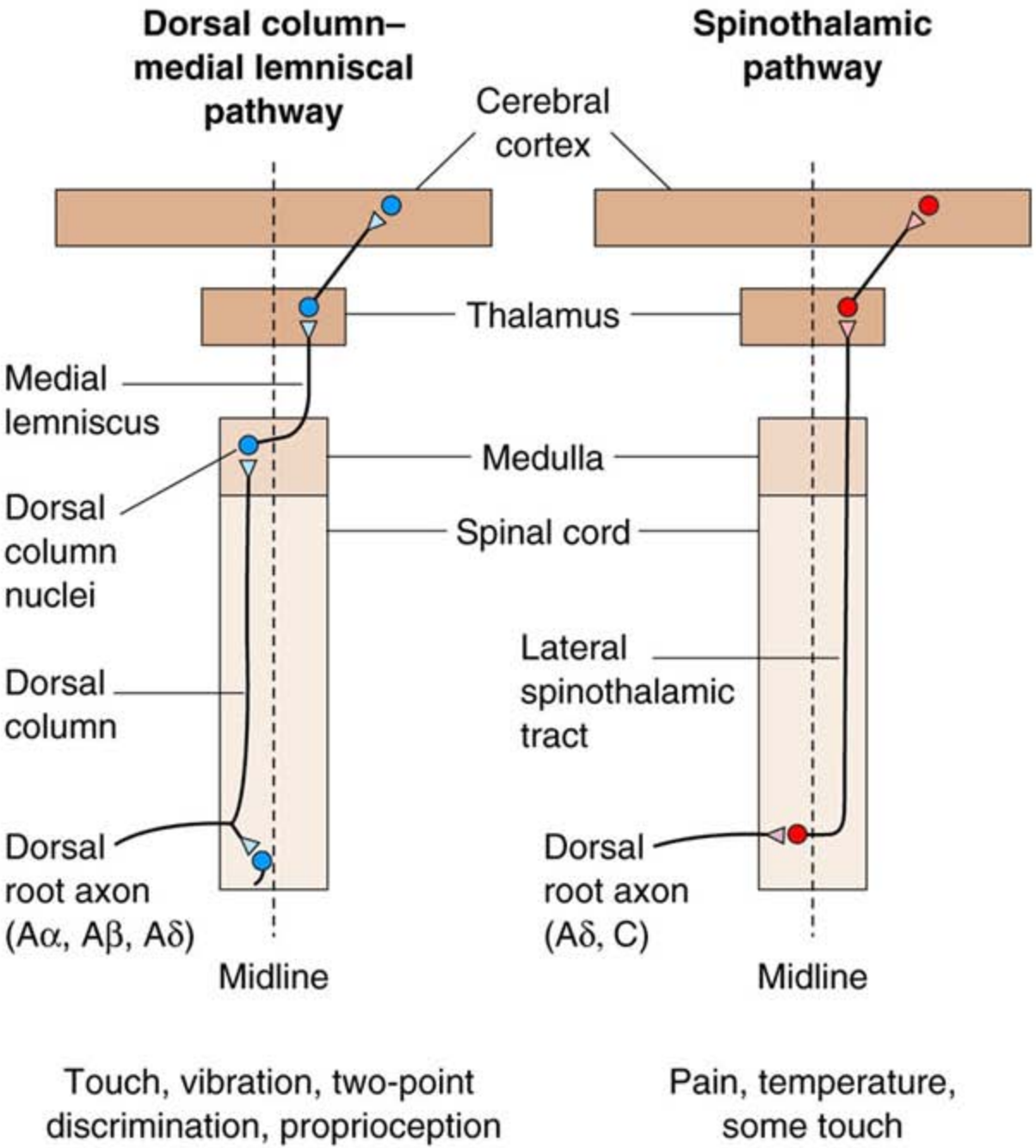


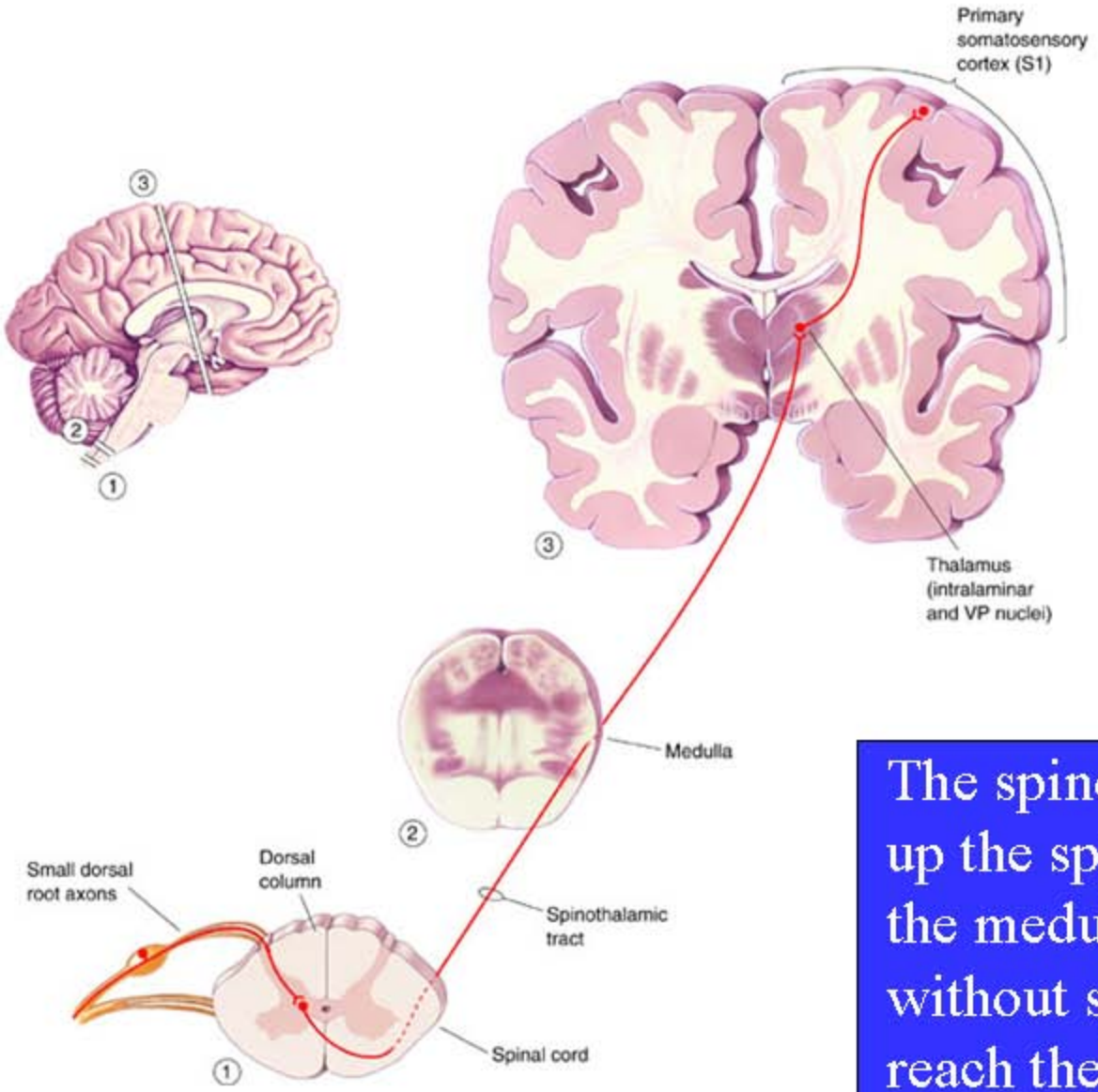
触压觉

The spinothalamic pathway
脊丘束通路



痛觉


Dorsal column–
medial lemniscal
pathway
Spinothalamic
pathway
Cerebral
cortex
Thalamus
Medial
lemniscus
Medulla
Dorsal
column
nuclei
Spinal cord
Lateral
spinothalamic
tract
Dorsal
column
Dorsal
root axon
(Aα, Aβ, Aδ)
Dorsal
root axon
(Aδ, C)
Midline
Midline
Touch, vibration, two-point
discrimination, proprioception
Pain, temperature,
some touch



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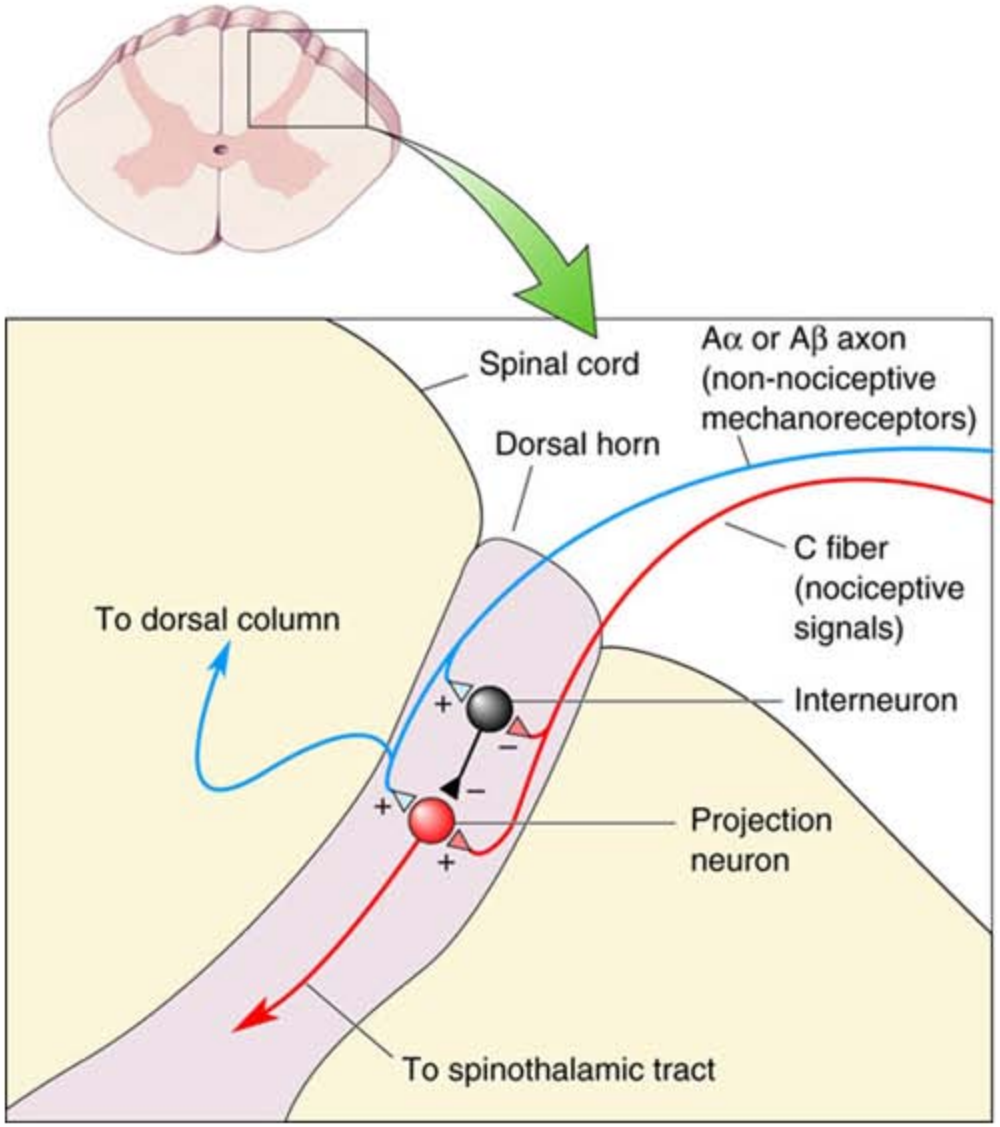


Melzack and Wall's gate theory of pain

2. Analgesia

Central inhibitory system:

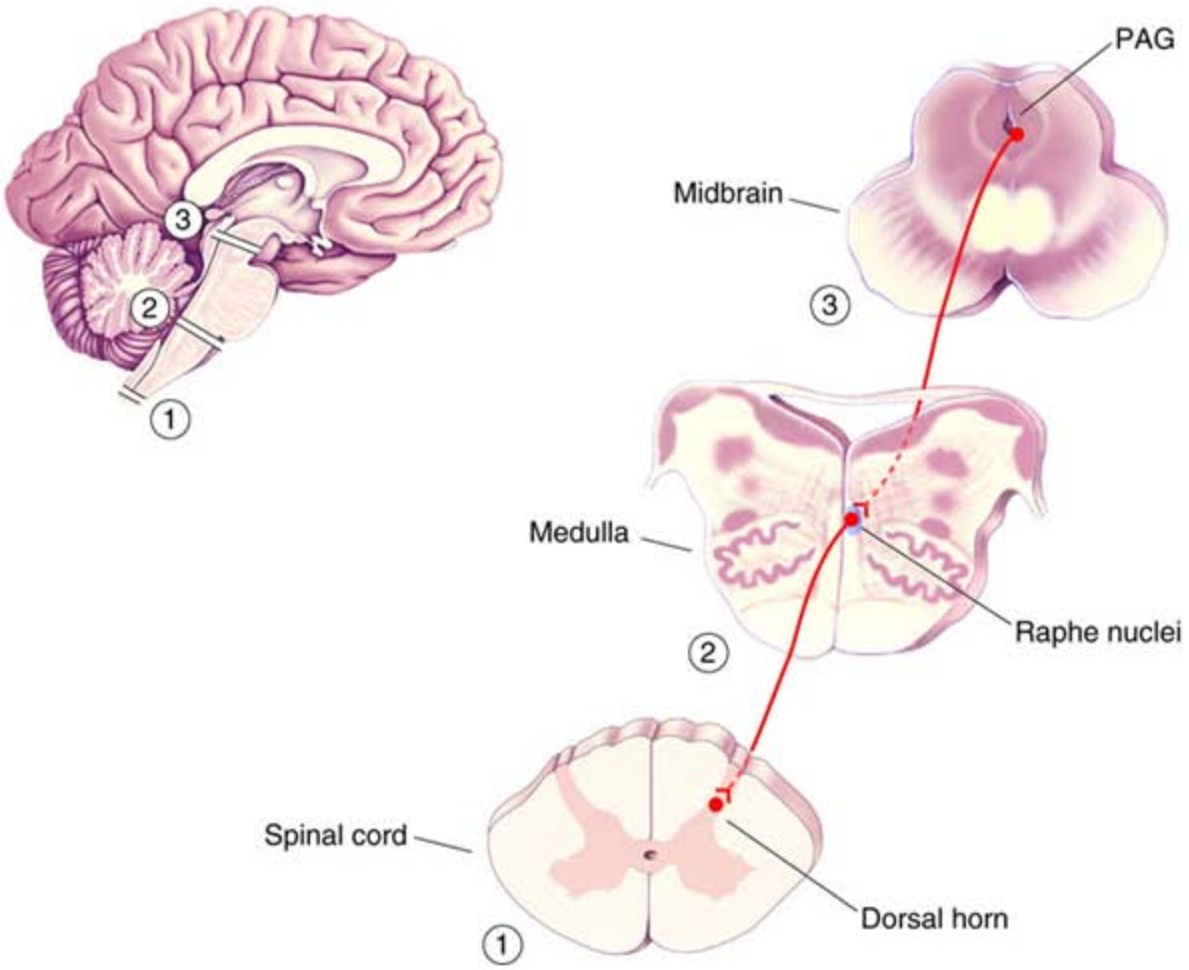
Descending pathways

Neurotransmitters

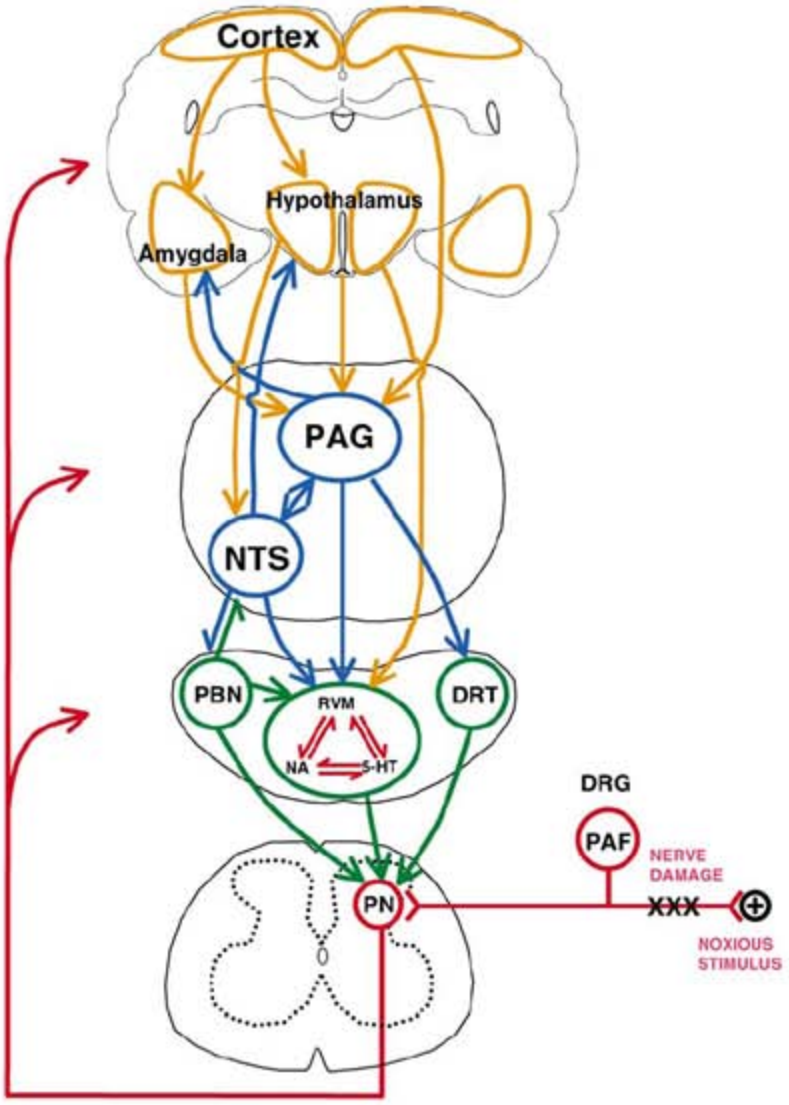
Opiates: Opiate receptor

Spinal opiate analgesia

Supraspinal opiate analgesia



Descending pain-control pathways.


Cortex
Hypothalamus
Amygdala
PAG
NTS
PBN
RVM
DRT
NA
5-HT
DRG
PAF
NERVE
DAMAGE
PN
XXX
NOXIOUS
STIMULUS

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Central events in the transmission of pain

Asending pain pathways:

Sensory transmission in the spinal cord---

Neurotransmitters and Morphology; Pathways;

Central inhibitory system: Descending pathways

Opiates: Opiate receptor

Spinal opiate analesia

Supraspinal opiate analgesia

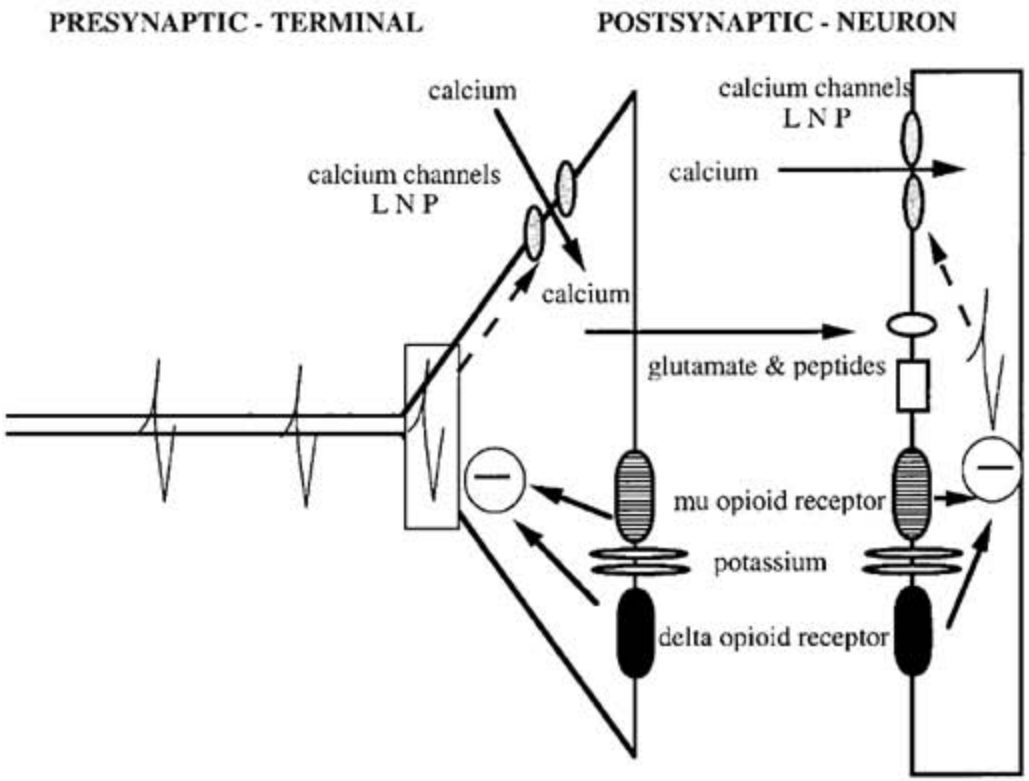

Figure 21.5 Mechanisms of opioid analgesia at the spinal level. Action potentials in nociceptive afferent fibres invade the terminal and by opening calcium channels (L, N and P-type) cause the release of glutamate and peptides that further transmit pain subsequent to activation of their postsynaptic receptors. Presynaptic opioid receptor activation (mu- and delta-mediated effects have been most clearly shown) opens potassium channels which hyperpolarise the terminal, so reducing transmitter release and inhibiting the postsynaptic neuron

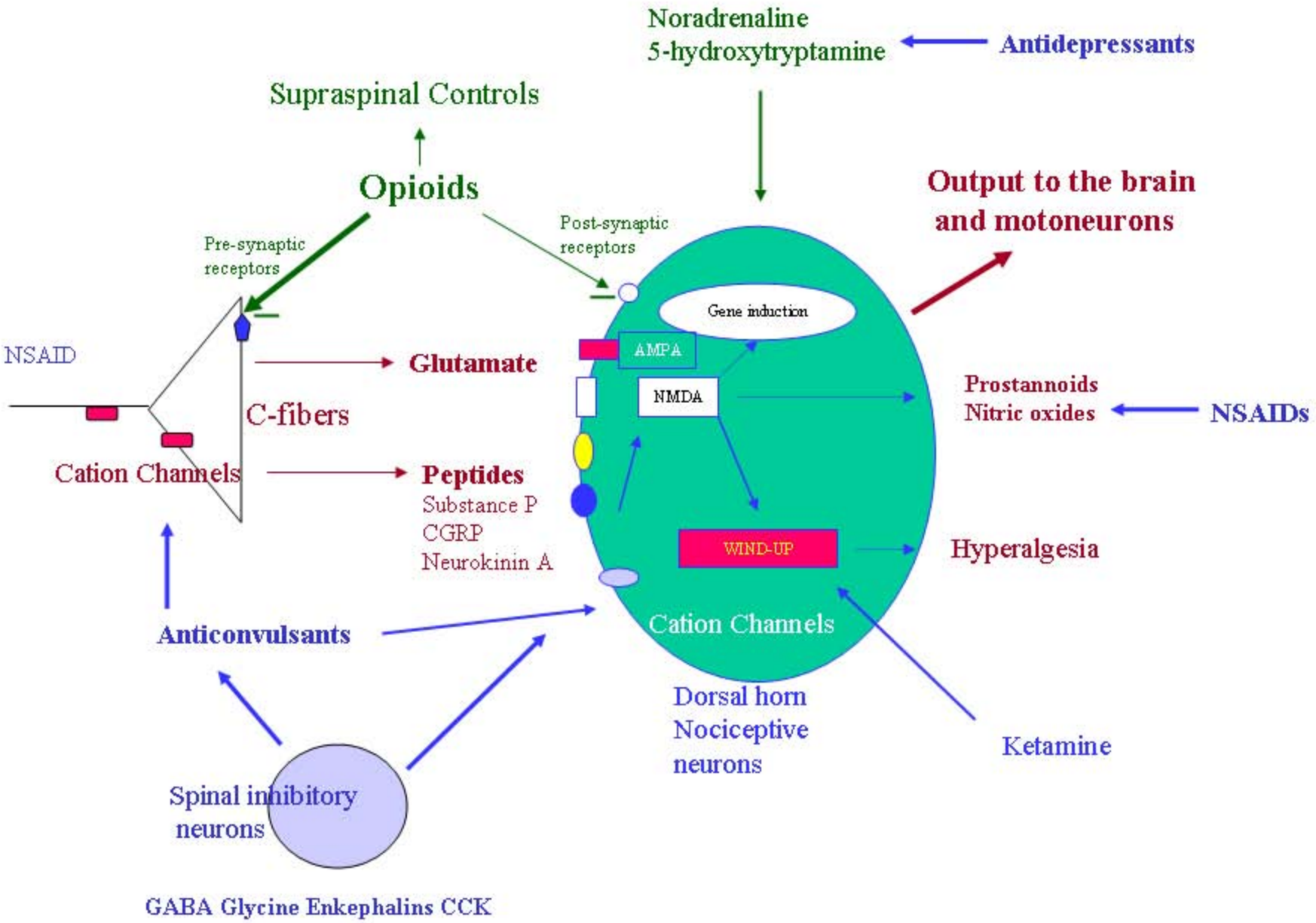
Noradrenaline
5-hydroxytryptamine
Antidepressants
Supraspinal Controls
Opioids
Output to the brain and motoneurons
Pre-synaptic receptors
Post-synaptic receptors
Gene induction
AMPA
NMDA
NSAID
Glutamate
C-fibers
Prostannoids
Nitric oxides
NSAIDs
Cation Channels
Peptides
Substance P
CGRP
Neurokinin A
WIND-UP
Hyperalgesia
Anticonvulsants
Cation Channels
Dorsal horn Nociceptive neurons
Ketamine
Spinal inhibitory neurons
GABA Glycine Enkephalins CCK

Table 21.2 The four opioid receptors with transmitters and drugs acting on the various receptors together with the effector mechanisms and the effects of receptor activation for each receptor

Receptor	Mu	Delta	Kappa	ORL-1
Endogenous opioid	β-endorphin Endomorphins	Enkephalins	Dynorphins	Nociceptin
Synthetic agonist	Morphine Codeine Fentanyl Pethidine	DSTBULET DPDPE	U50488H Pentazocine Oxycodone?	–
Antagonists	Naloxone Beta FNA	Naloxone Naltrindole	Naloxone Not BNI	Not naloxone
Effector mechanism	G-protein opens K^+ channel	G-protein opens K^+ channel	G-protein closes Ca^{2+} channel	G-protein opens K^+ channel
Effects	Hyperpolarisation of neurons, inhibition of neurotransmitter release			
	Analgesia Relief of anxiety Euphoria Nausea Constipation Cough suppression Dependence	Similar to mu but less marked	Analgesia Aversion Diuresis	Analgesia Hyperalgesia