260-2017-11-03-pain

Rick Gilmore

2017-11-02 11:11:42

Prelude I (5:56)

Bob Dylan - Like a Rolling Stone

Prelude II (4:56)

The Police - King of Pain (rare music video)

Today's Topics

- Wrap up on somatosensation
- Pain
- Blog #2 deadline today

Size/speed trade-off

TABLE 8.2 *Fibers That Link Receptors to the CNS*

Sensory function(s)	Receptor type(s)	Axon type	Diameter (μm)	Conduction speed (m/s)
Proprioception (see Chapter 11)	Muscle spindle	 Aα	13–20	80–120
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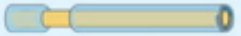
Pain, temperature	Free nerve endings; VRL1	 Aδ	1–5	5–30
Temperature, pain, itch	Free nerve endings; VR1, CMR1	C	0.02–1.5	0.5–2

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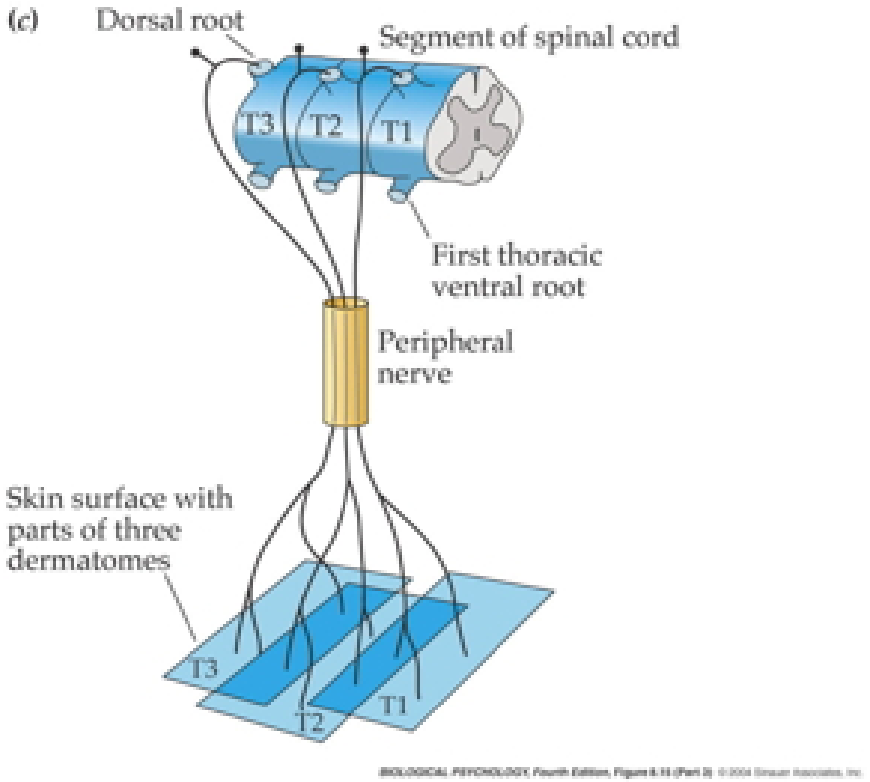
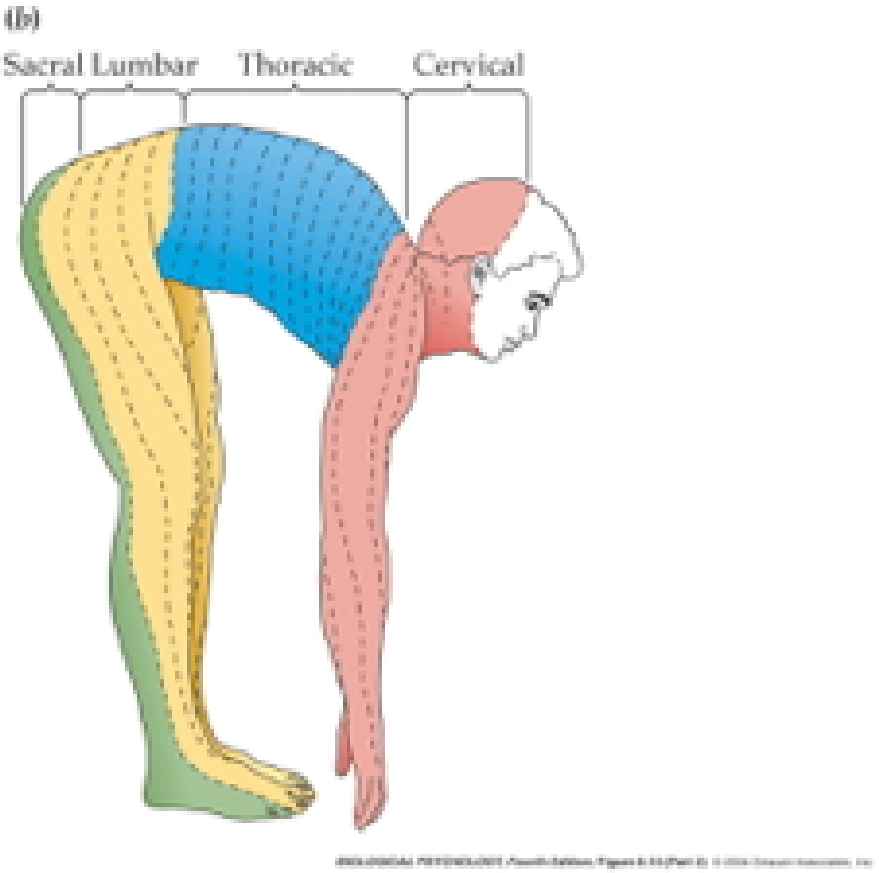
From skin to brain

- Cutaneous receptors
- Dorsal root ganglion
- Ventral posterior lateral thalamus
- Primary somatosensory cortex (S1)
    - Parietal lobe

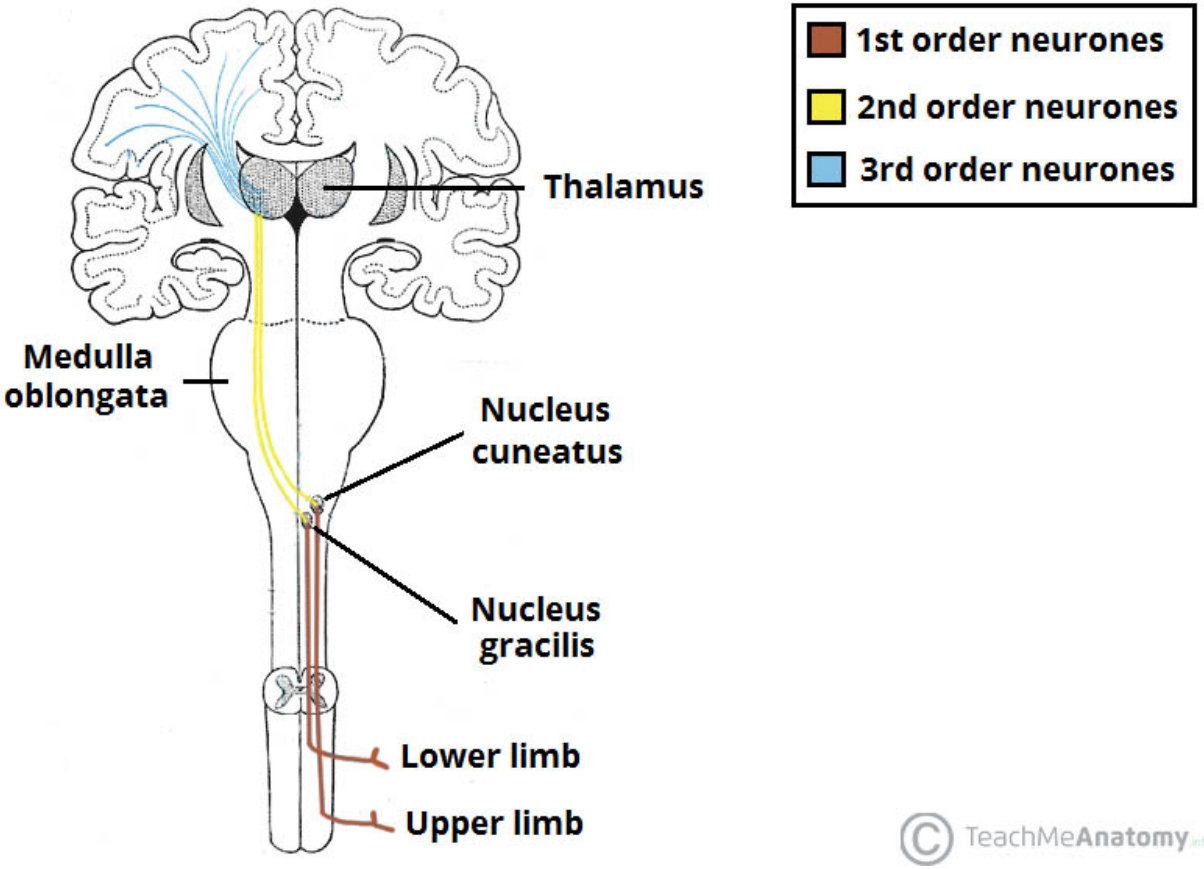
Dermatomes

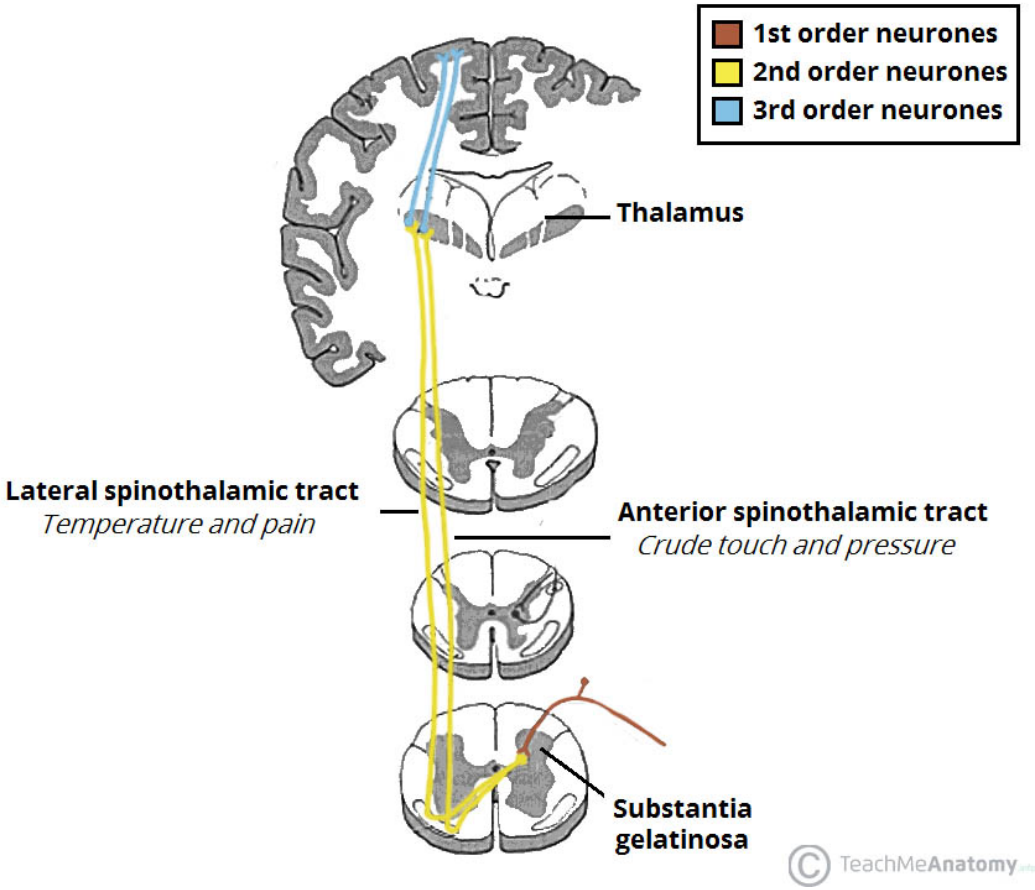

(c)
Dorsal root
Segment of spinal cord
T3
T2
T1
First thoracic ventral root
Peripheral nerve
Skin surface with parts of three dermatomes
T3
T2
T1

Dermatomes



Functional segregation

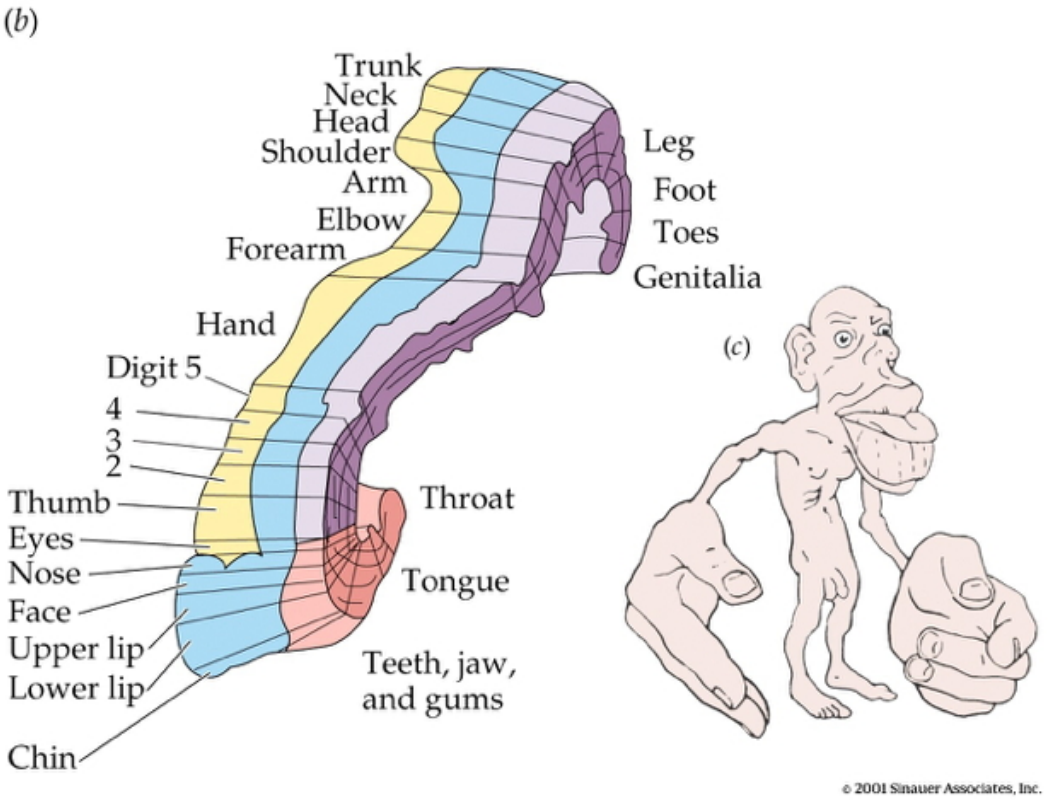



1st order neurones
2nd order neurones
3rd order neurones
Thalamus
Lateral spinothalamic tract
Temperature and pain
Anterior spinothalamic tract
Crude touch and pressure
Substantia gelatinosa
© TeachMeAnatomy

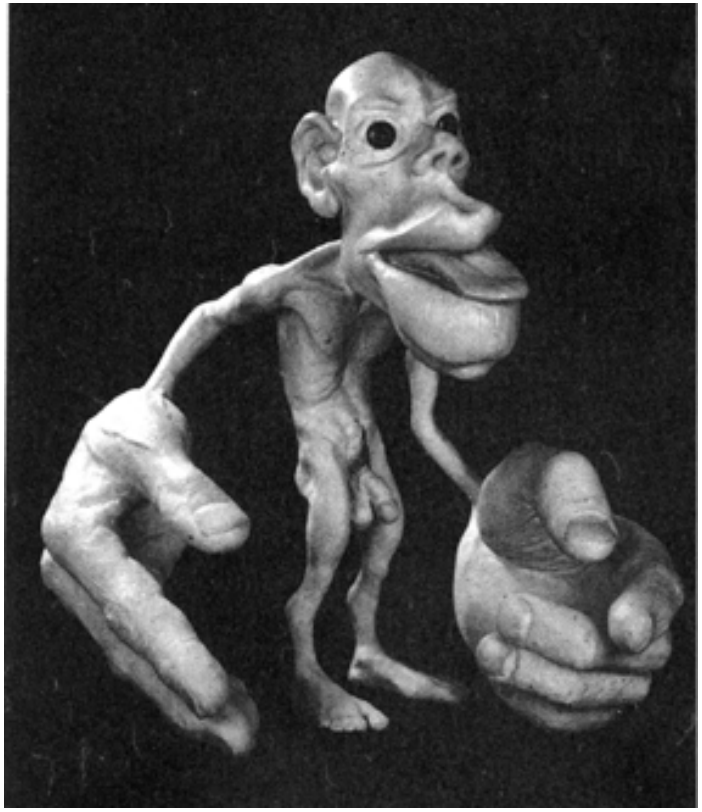
Functional segregation

- Dorsal column/medial leminiscal pathway
    - Touch, proprioception
- Spinothalamic tract
    - Pain, temperature

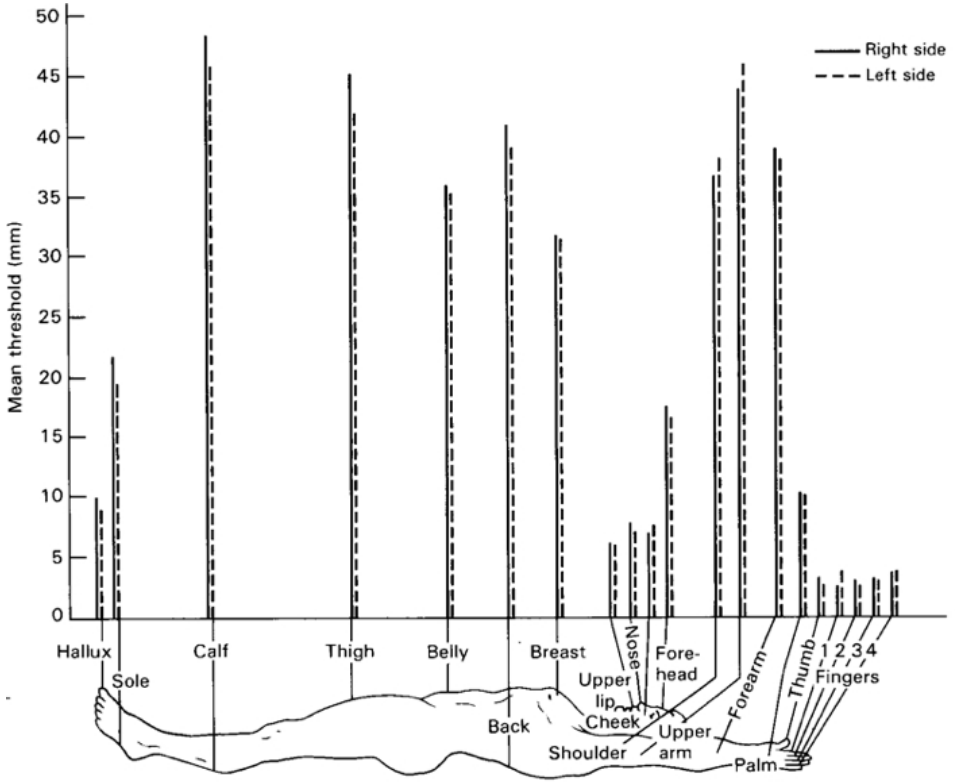
Somatatopic maps



Non-uniform mapping of skin surface



Non-uniform mapping of skin surface



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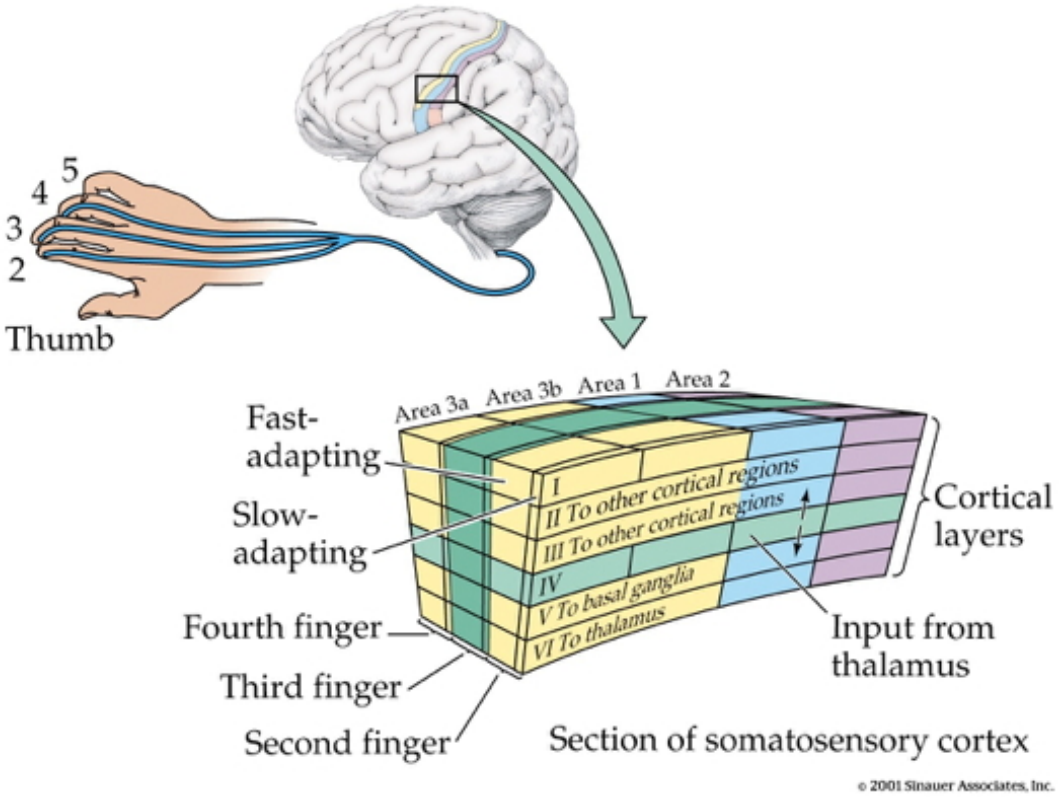
Columnar organization/functional segregation



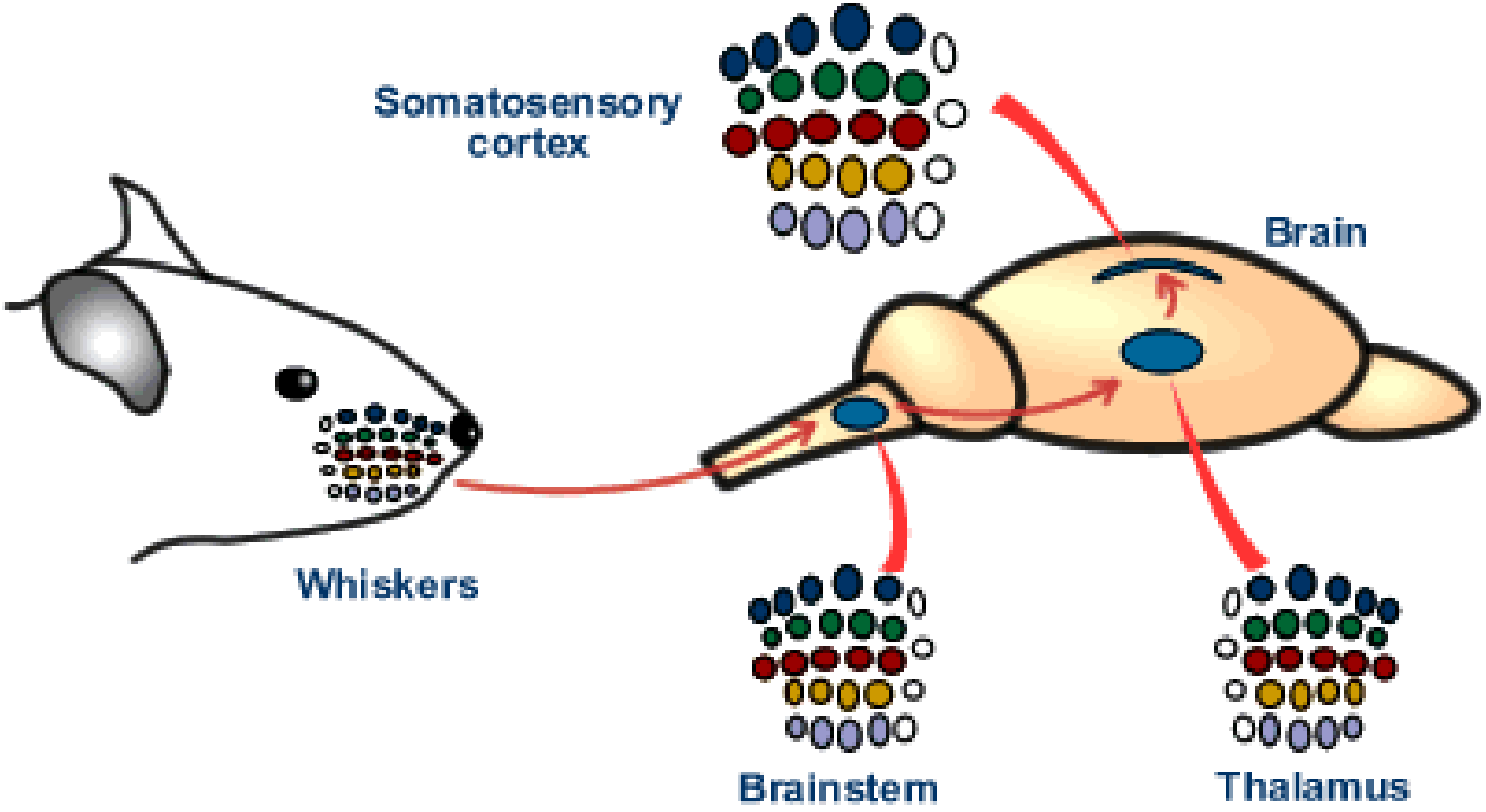
Phantom Limbs

Phantom Limb Video

What/where

- Perceiving Where
  - Somatotopic maps – where on skin
  - Kinesthesia – configuration of limbs
- Perceiving What
  - Patterns of smoothness, roughness, shape, temperature

Somatosensation in other animals



The neuroscience of pain

- *Nociceptors* (Latin *nocere* to harm or hurt) detect harmful or potentially harmful stimuli of varied types:
    - chemical
    - mechanical
    - thermal

Nociception

- External
  - Skin, cornea (eye), mucosa
- Internal
  - Muscles, joints, bladder, gut

Interoception

- Receptors for
  - metabolism (acidic pH, hypoxia, …)
  - cell rupture (ATP and glutamate)
  - cutaneous parasite penetration (histamine)
  - mast cell (white blood cell) activation (serotonin, bradykinin, …)
  - immune and hormonal activity (cytokines and somatostatin)

Fast ($A\delta$) and slow (C) transmission to CNS

TABLE 8.2 *Fibers That Link Receptors to the CNS*

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Temperature, pain, itch	Free nerve endings; VR1, CMR1	C	0.02–1.5	0.5–2

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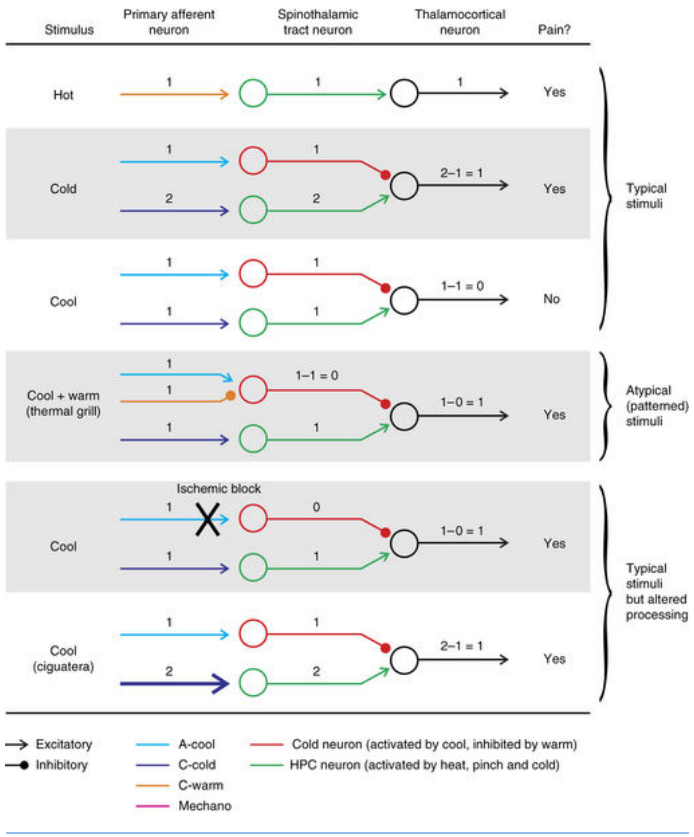
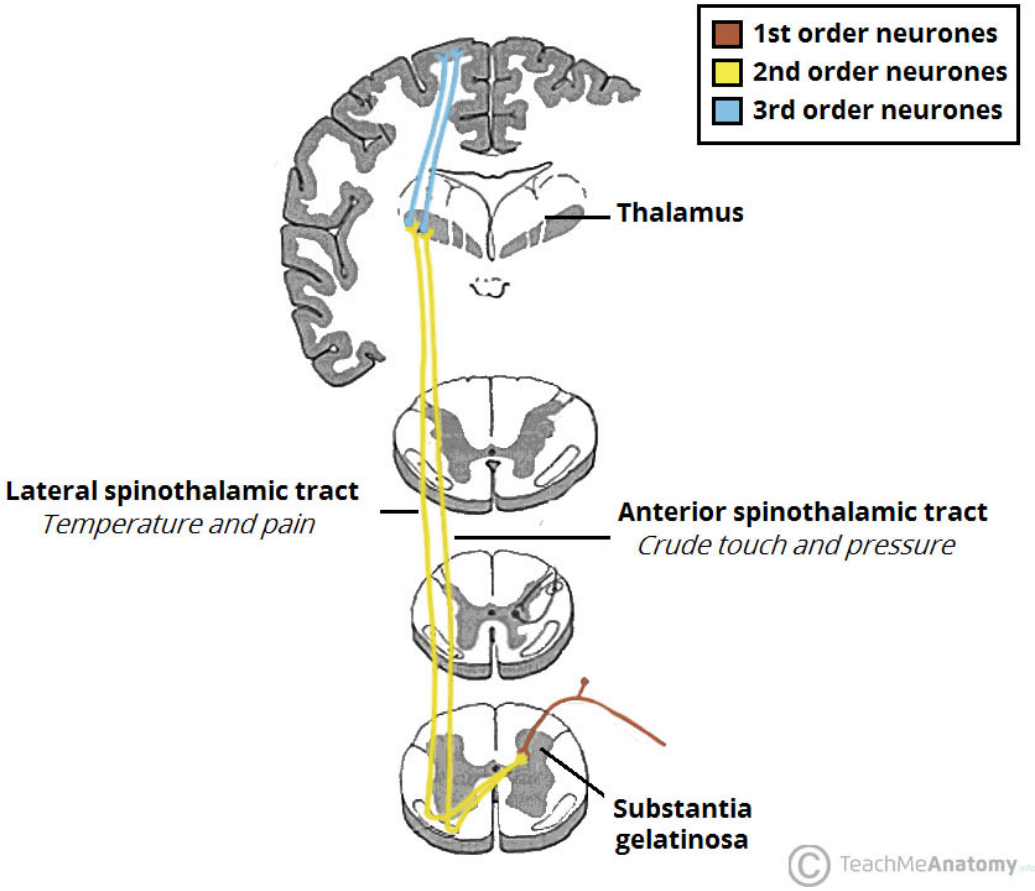
Thermal grill illusion

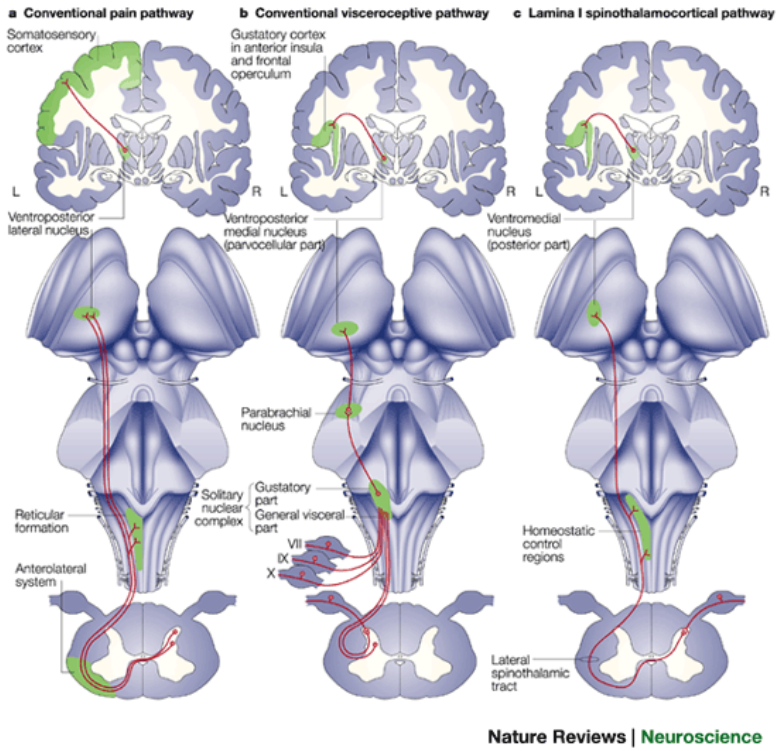
Dune pain box - thermal grill illusion

'Cross-talk' between nociceptor channels



Projection to brain via anterolateral system




a Conventional pain pathway
b Conventional viscerоceptive pathway
c Lamina I spinothalamocortical pathway
Somatosensory cortex
Gustatory cortex in anterior insula and frontal operculum
L
R
Ventroposterior lateral nucleus
Ventroposterior medial nucleus (parvocellular part)
Ventromedial nucleus (posterior part)
Parabrachial nucleus
Solitary nuclear complex
Gustatory part
General visceral part
Reticular formation
VII
IX
X
Anterolateral system
Homeostatic control regions
Lateral spinothalamic tract
Nature Reviews | Neuroscience

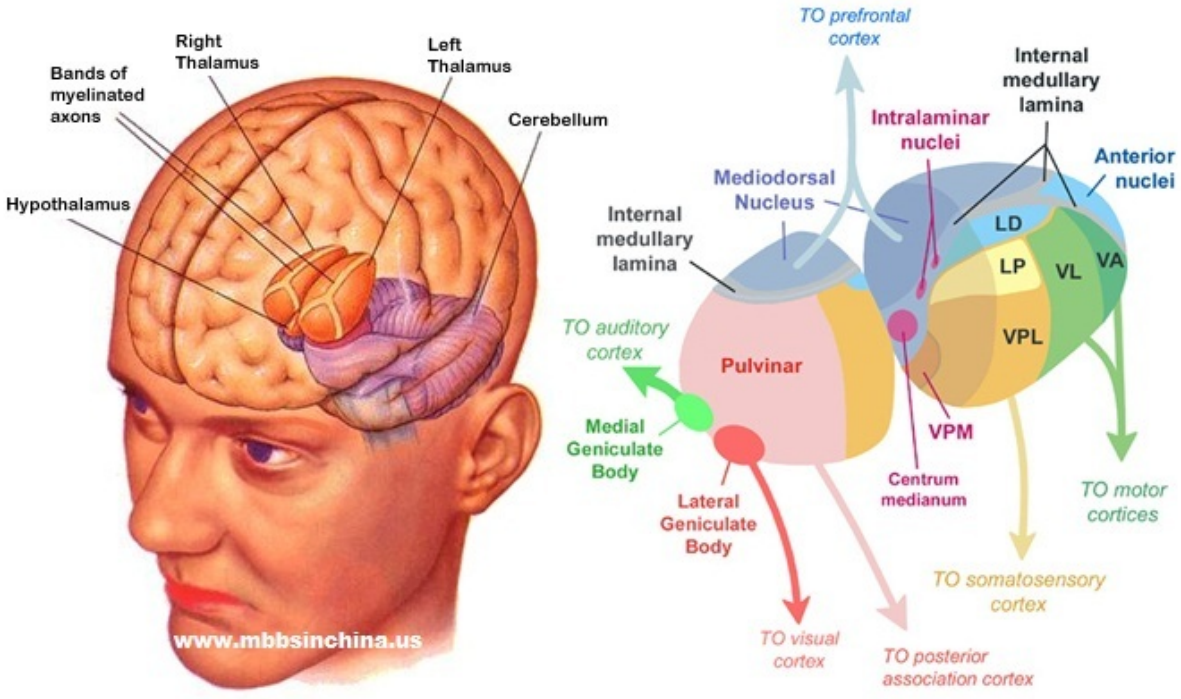
(Craig 2002)

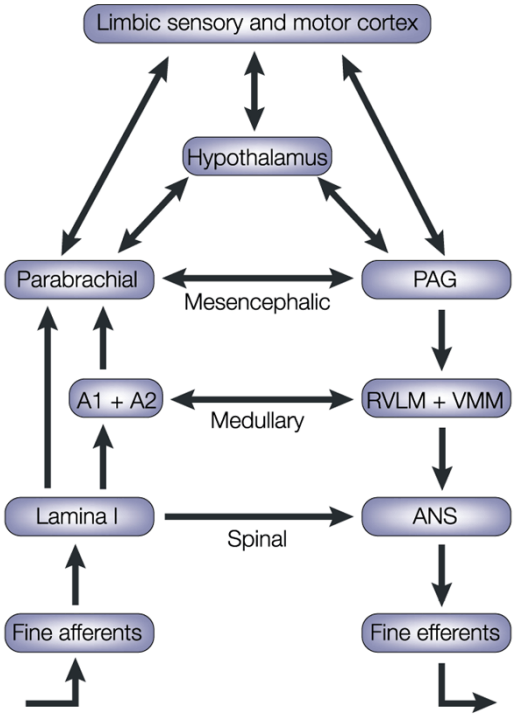
Key CNS nodes in network

- Periaqueductal grey (PAG)
- Insular cortex (insula)
- Hypothalamus
- Amygdala

Key CNS nodes in network

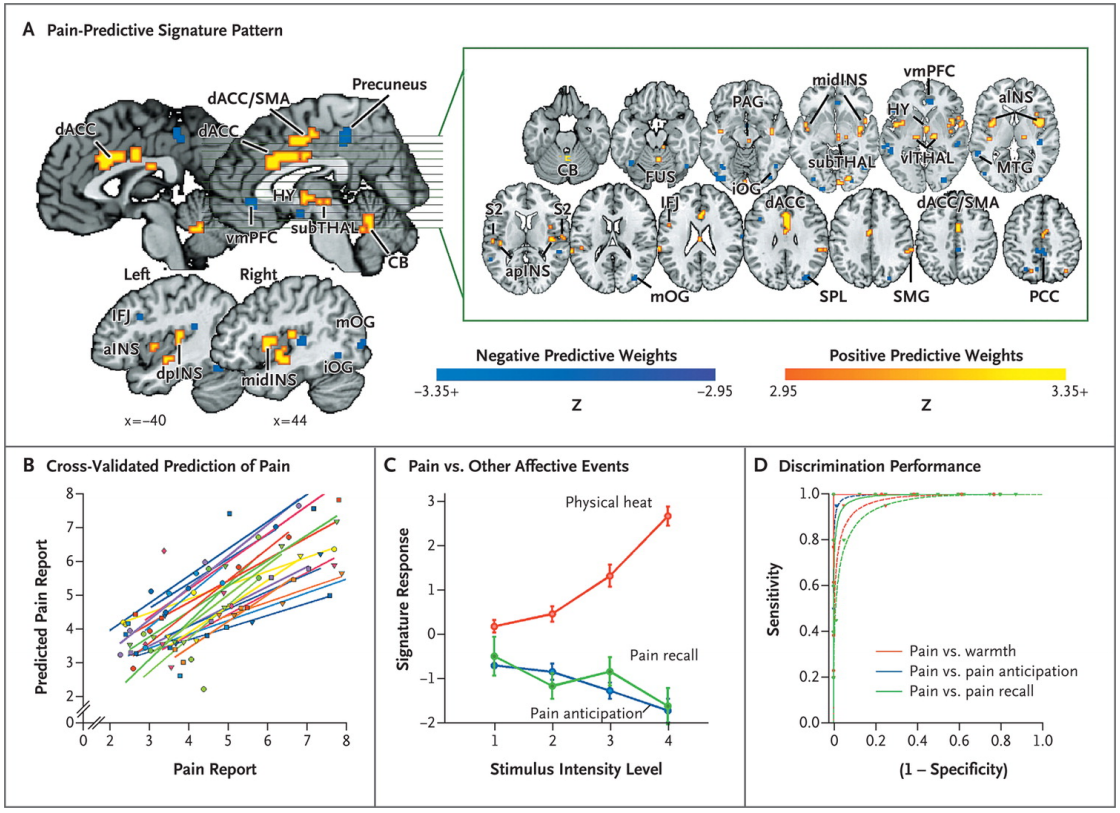
- Thalamus
  - Ventroposterior lateral nucleus
  - Ventroposterior medial nucleus
  - Ventromedial nucleus


Right Thalamus
Left Thalamus
Bands of myelinated axons
Cerebellum
Hypothalamus
www.mbbsinchina.us
TO prefrontal cortex
Internal medullary lamina
Intralaminar nuclei
Anterior nuclei
Mediodorsal Nucleus
Internal medullary lamina
LD
LP
VL
VA
VPL
TO auditory cortex
Pulvinar
Medial Geniculate Body
VPM
Centrum medianum
Lateral Geniculate Body
TO motor cortices
TO somatosensory cortex
TO visual cortex
TO posterior association cortex


Limbic sensory and motor cortex
Hypothalamus
Parabrachial
Mesencephalic
PAG
A1 + A2
Medullary
RVLM + VMM
Lamina I
Spinal
ANS
Fine afferents
Fine efferents
Nature Reviews | Neuroscience

(Craig 2002)

Pain in the brain



(Wager et al. 2013)

Pain in the brain

"…we used machine-learning analyses to identify a pattern of fMRI activity across brain regions — a neurologic signature — that was associated with heat-induced pain. The pattern included the thalamus, the posterior and anterior insulae, the secondary somatosensory cortex, the anterior cingulate cortex, the periaqueductal gray matter, and other areas…"

(Wager et al. 2013)

Pain relief

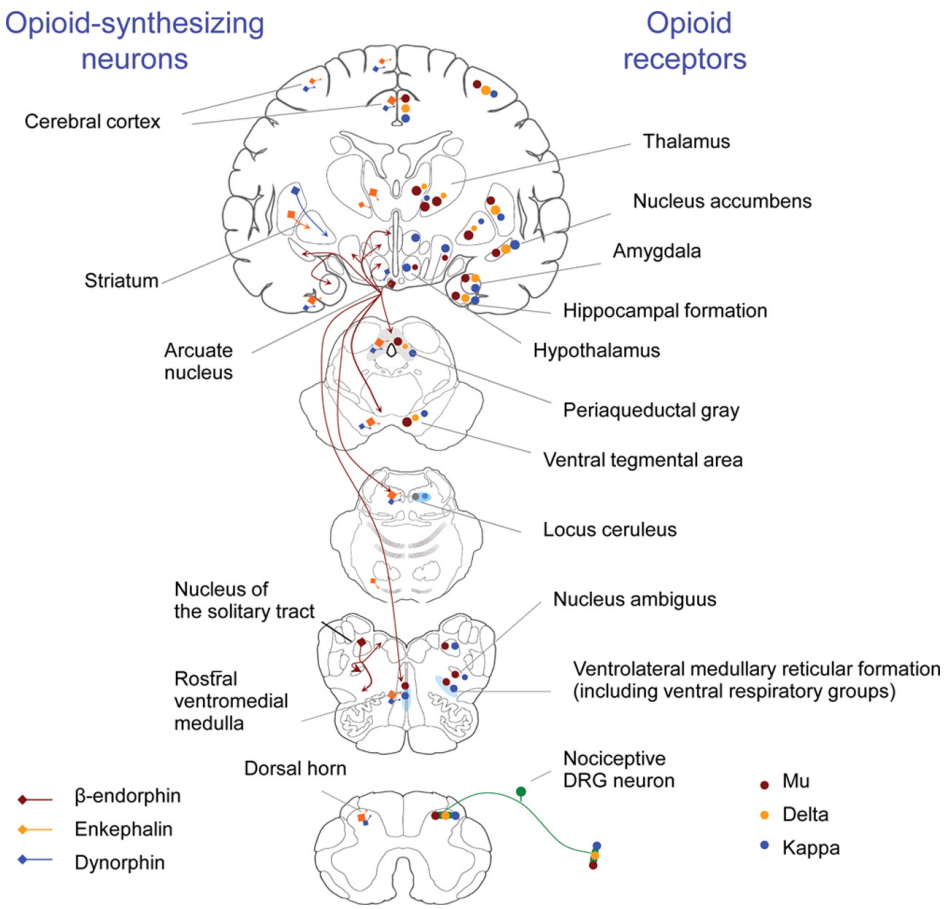
- *Prostaglandins*
  - hormone-like effects, but released in many places
  - trigger vasodilation and inflammation

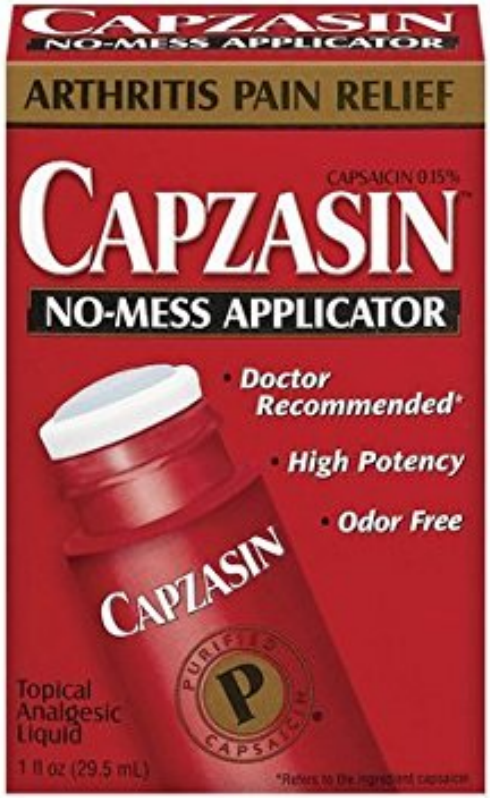
Pain relief

- *Paracetymol (acetaminophen)*
  - Mechanism not fully understood
  - inhibits synthesis of prostaglandins via cyclooxygenase (COX) enzyme
  - may modulate endocannabinoid system
- *Nonsteroidal anti-inflamatory drugs (NSAIDs)*: aspirin, ibuprofen
  - Also inhibit prostaglandins via COX

Pain relief

- *Opioids*
  - Activate endogenous opioid systems
  - multiple receptor types (δ, κ, μ,…)
  - peripheral sensory neurons, amygdala, hypothalamus, PAG, spinal cord, cortex, medulla, pons,…
  - brainstem opioid neurons provide *descending* inhibition of nociceptors


Opioid-synthesizing neurons
Opioid receptors
Cerebral cortex
Thalamus
Nucleus accumbens
Amygdala
Striatum
Hippocampal formation
Arcuate nucleus
Hypothalamus
Periaqueductal gray
Ventral tegmental area
Locus ceruleus
Nucleus of the solitary tract
Nucleus ambiguus
Rostral ventromedial medulla
Ventrolateral medullary reticular formation (including ventral respiratory groups)
Dorsal horn
Nociceptive DRG neuron
β-endorphin
Enkephalin
Dynorphin
Mu
Delta
Kappa


CAPZASIN
NO-MESS APPLICATOR
ARTHRITIS PAIN RELIEF
CAPSAICIN 0.15%
CAPZASIN
NO-MESS APPLICATOR
• Doctor Recommended*
• High Potency
• Odor Free
CAPZASIN
PURIFIED
P
CAPSAICIN
Topical Analgesic Liquid
1 fl oz (29.5 mL)
*Refers to the ingredient capsaicin

Pain relief

- *Capsaicin*
  - Binds to TRPV1 receptor in thermo/nociceptors
  - Alters how peripheral neuron responds to mechanical stimulation
  - (Borbiro, Badheka, and Rohacs 2015)

Pain relief

- Why rubbing can help

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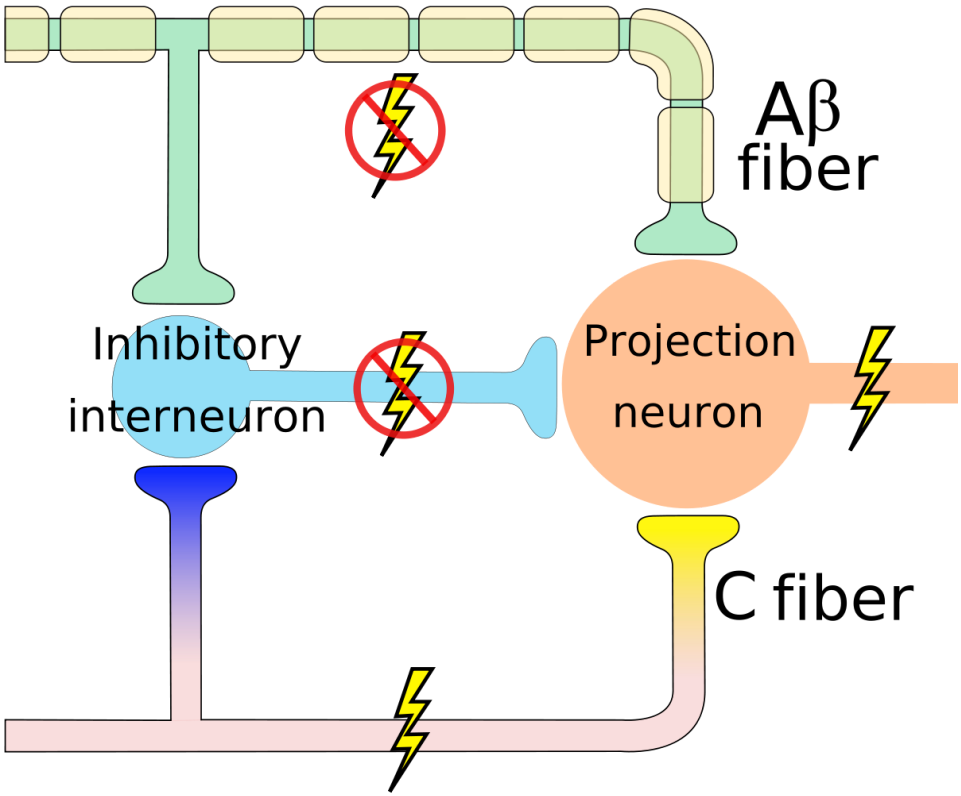
Gate control theory (Melzack and Wall 1965)



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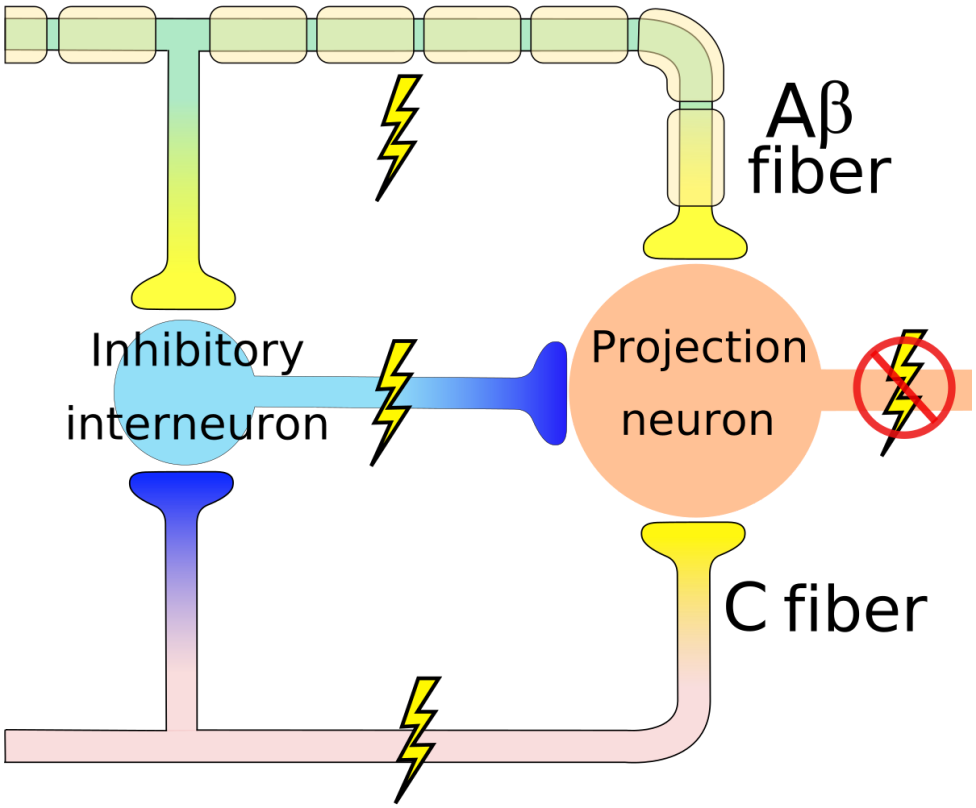
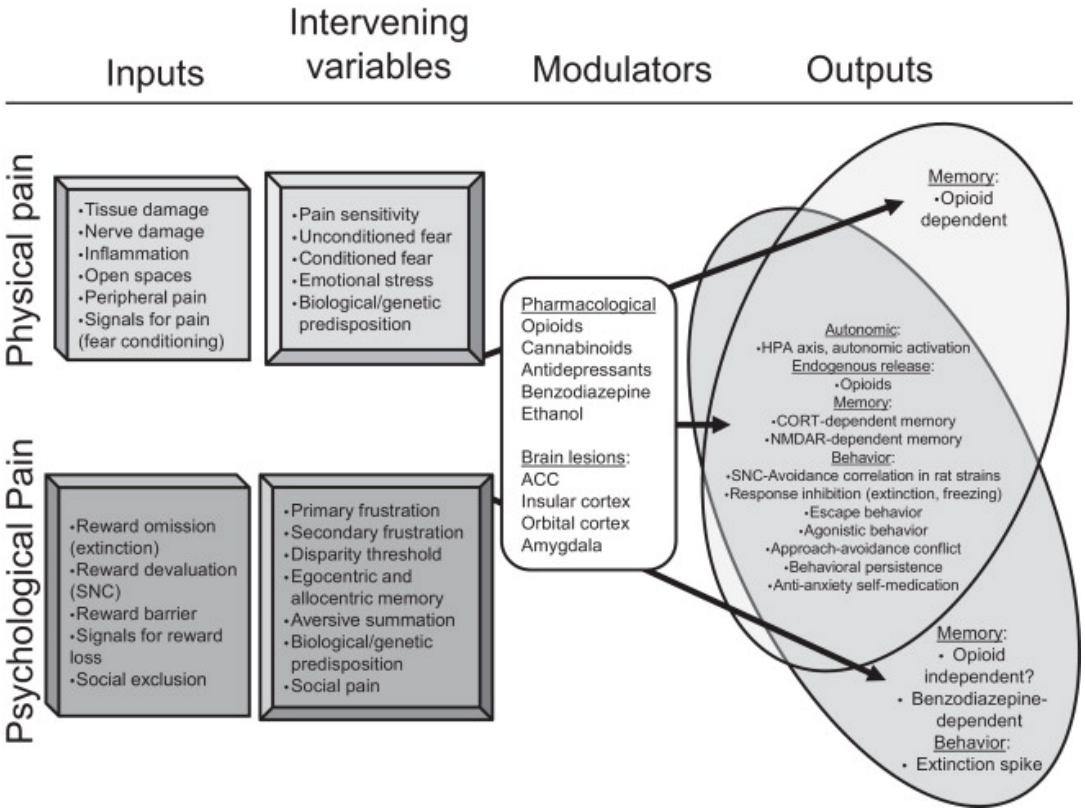


Psychological and physical dimensions



(Papini, Fuchs, and Torres 2015)

Main points

- Somatosensation
  - Exteroception via
    - Cutaneous receptors + proprioception
  - Interoception via
    - Widely distributed receptors
    - Specific and non-specific

Main points

- Pain
  - Multiple receptor channels
  - Highly interconnected CNS network
  - Multiple targets for modulation

Next time…

- Action

References

Borbiro, Istvan, Doreen Badheka, and Tibor Rohacs. 2015. “Activation of Trpv1 Channels Inhibits Mechanosensitive Piezo Channel Activity by Depleting Membrane Phosphoinositides.” *Sci. Signal.* 8 (363): ra15. doi:10.1126/scisignal.2005667.

Craig, A D. 2002. “How Do You Feel? Interoception: The Sense of the Physiological Condition of the Body.” *Nat. Rev. Neurosci.* 3 (8): 655–66. doi:10.1038/nrn894.

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Wager, Tor D, Lauren Y Atlas, Martin A Lindquist, Mathieu Roy, Choong-Wan Woo, and Ethan Kross. 2013. “An fMRI-based Neurologic Signature of Physical Pain.” *N. Engl. J. Med.* 368 (15): 1388–97. doi:10.1056/NEJMoa1204471.