Pain & Analgesia

What would you do?

- 9 month old cat
- admitted for spay
- fit and healthy
- analgesia?

analgesia

- αν - negative prefix
- αλγεσειν - to feel pain

pain

- Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.
  - International Association for the Study of Pain

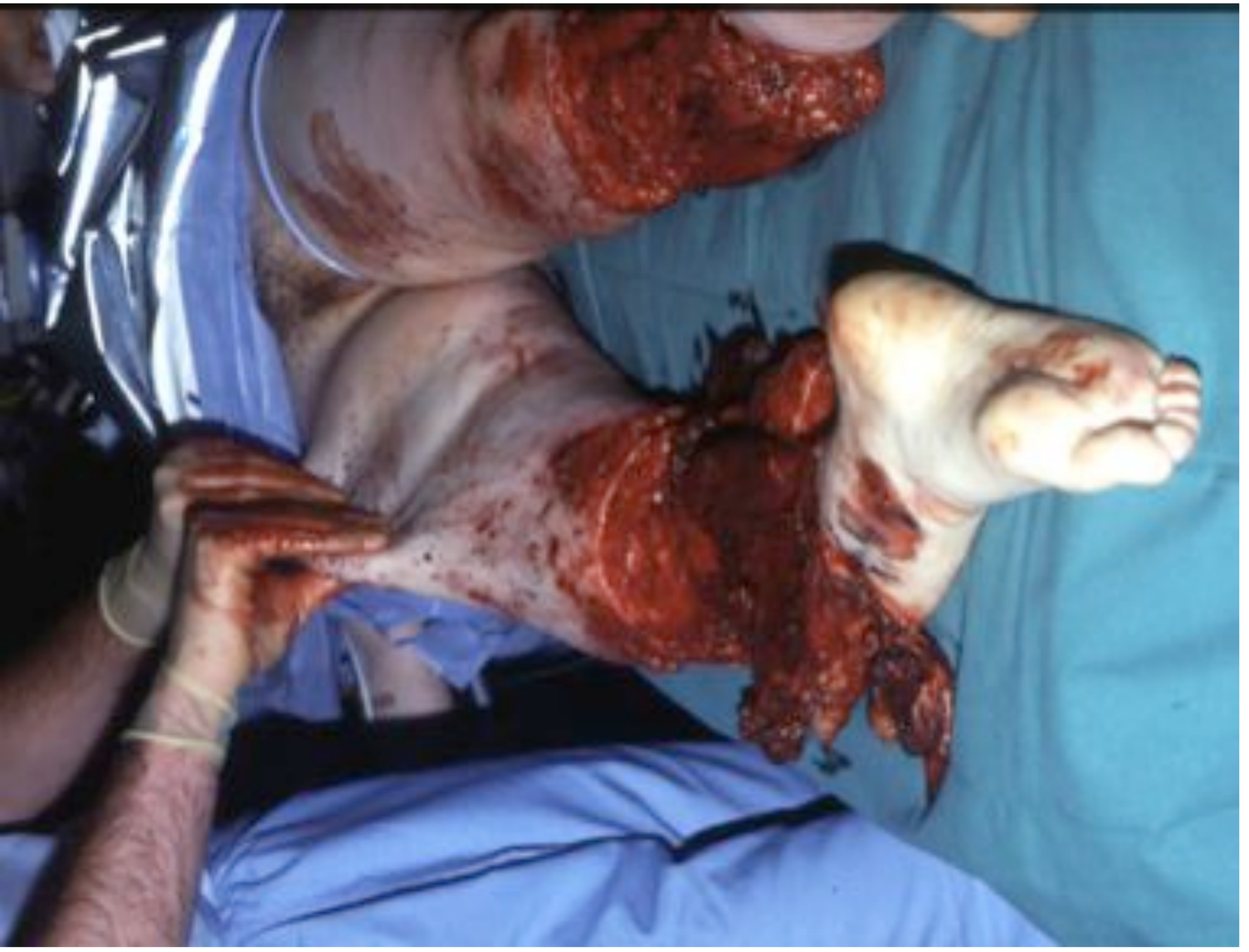
nociception

- transmission of pain signals to the cortex
- the sensory component of pain

definitions

- **hyperalgesia**
  - **sensation which would normally be slightly painful being very painful**
- **allodynia**
  - **sensation which would not normally be painful being painful**

Do animals feel pain?



Do animals feel pain?

- all mammals have similar
  - nervous structures
  - neurotransmitters
  - responses to noxious stimuli
  - responses to analgesic drugs

pain criteria

- peripheral nociceptors
- cortex or something similar
- opioid receptors in CNS
- response to analgesics
- aversive reaction to noxious stimuli
- aversion not overcome by reward
- response to noxious stimuli persists
- learning
- ie, all vertebrate animals!

invertebrates

	cephalopod	insect	earthworm
nociceptors	?	-	?
cortex	?	-	?
opioid R	+	+	+
analgesics	+	?	?
persistence	+	-	-
learning	+	+	-

assessing pain

- behaviour
- Not autonomic function
  - only measures stress
- response to analgesics
  - change in behaviour?
  - change in autonomic function?
  - reduction in hyperalgesia?

pain pathways

LOCAL ANAESTHETICS

H^+, heat capsaicin

XANTHINES?

H^+ Mg^{++}

endothelial cells

sympathetic varicosities

cells (esp.tumours)

Na channels

Na_V 1.8/9 channel

bradykinin receptor

VR_1

acid sensing channel

$P2_{X3}$

ATP

slow

excitation

adenosine

A_2

mGlu5

EP

stretch receptor

$P2_{Y1}$

ATP

Na channels

Glu

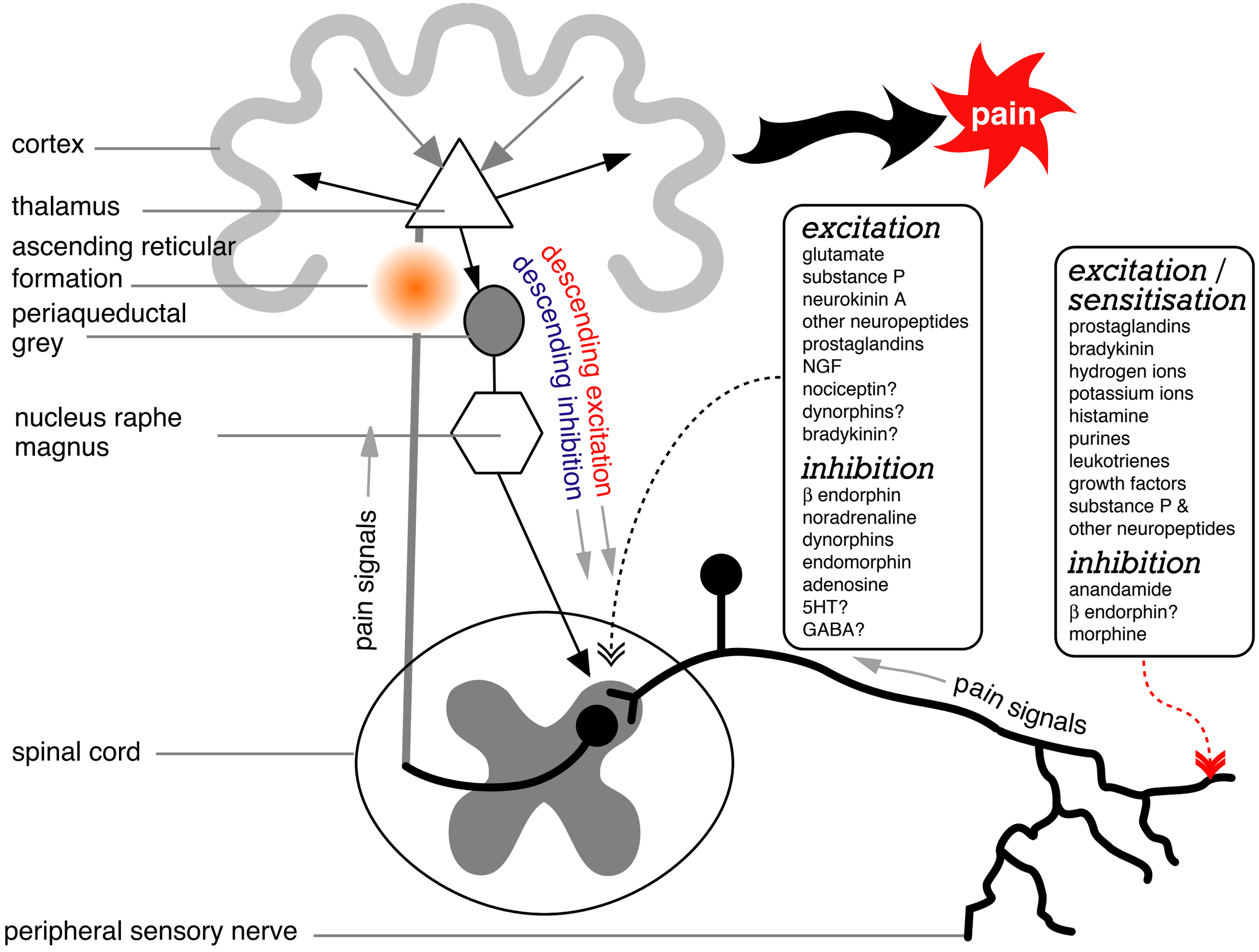
macrophage

PGE2

COX

arachidonic acid

NSAIDs


cortex
thalamus
ascending reticular formation
periaqueductal grey
nucleus raphe magnus
spinal cord
peripheral sensory nerve
pain
descending excitation
descending inhibition
pain signals
pain signals
excitation
glutamate
substance P
neurokinin A
other neuropeptides
prostaglandins
NGF
nociceptin?
dynorphins?
bradykinin?
inhibition
β endorphin
noradrenaline
dynorphins
endomorphin
adenosine
5HT?
GABA?
excitation / sensitisation
prostaglandins
bradykinin
hydrogen ions
potassium ions
histamine
purines
leukotrienes
growth factors
substance P &
other neuropeptides
inhibition
anandamide
β endorphin?
morphine

response to injury

- direct stimulation of nociceptors
- descending inhibition & release of inflammatory mediators
- sensitisation of nerve endings
- central sensitisation
- recovery of normal sensation

response to injury

- analgesia?
- acute pain
- chronic pain
- resolution

pain is plastic!

stimulus

AMPA receptors

NMDA receptors

second messengers

neurokinins

reflex withdrawal

immediate early genes

growth factors

immunomodulators

receptor numbers

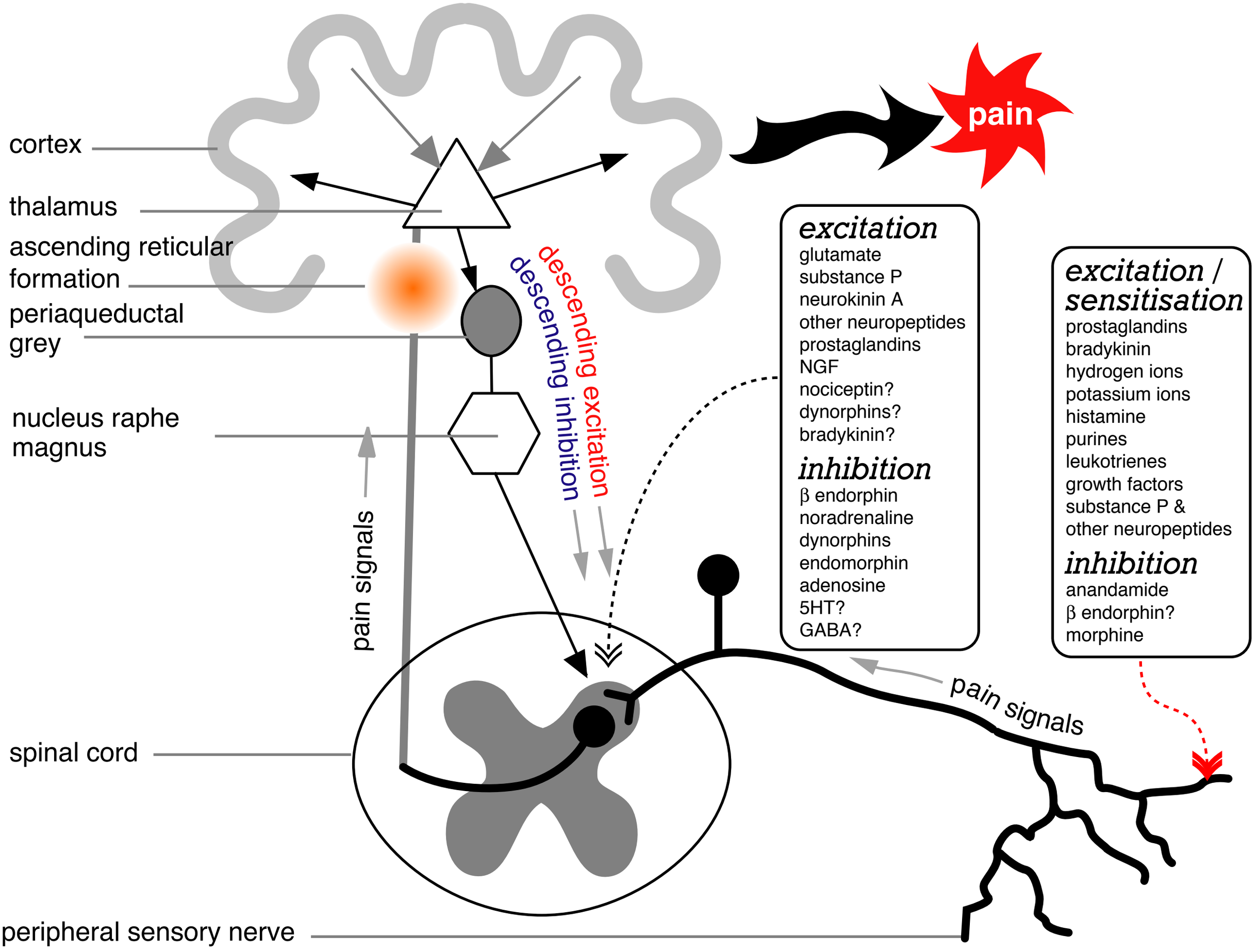
neuronal remodelling

return of normal sensation

1ms 10ms 100ms seconds minutes hours days weeks months

gate theory

- afferent pain signals are not just passed on up the spinal cord
- pain signals are depressed or amplified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morphine
pain signals
spinal cord
peripheral sensory nerve

gate theory

transmission	transmitter	receptor	analgesic
normal	glutamate	AMPA	local
enhanced	glutamate	NMDA	ketamine
	substanceP	NK1	capsaicin
reduced	encephalins	μ & κ	opioids
	endomorphin	μ	opioids
	noradrenaline	$\alpha 2$	$\alpha 2$ agonists

pain

- nociceptive
- neurogenic

pain

- acute
  - traumatic
  - post-operative
- chronic
  - arthritis
  - tumours

acute pain

- evolutionary advantage
  - promotes learning to avoid harm
- but
  - massive sympathetic stimulation

chronic pain

- immobility can promote healing

analgesia

- treat condition causing pain
- good nursing
- analgesic drugs
- anaesthesia
- euthanasia

analgesia??

- acupuncture
- TENS

pain intensity

pre-operative analgesia

- prevents wind up
  - analgesics more effective
  - longer post op analgesia
  - smoother anaesthetic

analgesic drugs

- opioids
- NSAIDs
- local anaesthetics
- α2 agonists

minor drugs

- NMDA blockers
- anticonvulsants
- capsaicin
- etc, etc

balanced analgesia

- combinations of drugs
- more later

clinical use

- mild pain
  - NSAIDs
- inflammatory pain
  - NSAIDs
- severe pain
  - opioids ± local
- surgical pain
  - opioids + local + NSAIDs depending on op

What would you do?

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pain & analgesia

- pain signals are carried from the periphery to the brain by a number of routes
- pain signals are modulated in the spinal cord
- most analgesics interfere with endogenous modulation systems
- pain changes over time - so must treatment
- give drugs before pain starts
- good nursing is very important!
- **If in doubt, give it morphine!**