Dolor crónico: por que unos sí y otros no

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La cronificación del Dolor

1. 30-35% neuropatía diabética ➔ dolorosa
2. 5-10% lesión traumática nervios ➔ CRPS-II
3. 5-8% lesiones menores periféricas ➔ CRPS-I
4. 10% herpes zóster ➔ neuralgia post-herpética
5. 5-15% cirugía mayor ➔ dolor neuropático crónico
6. 3-7% hernia inguinal ➔ dolor crónico
7. 4-8% amputaciones ➔ miembro fantasma doloroso
1. ……..

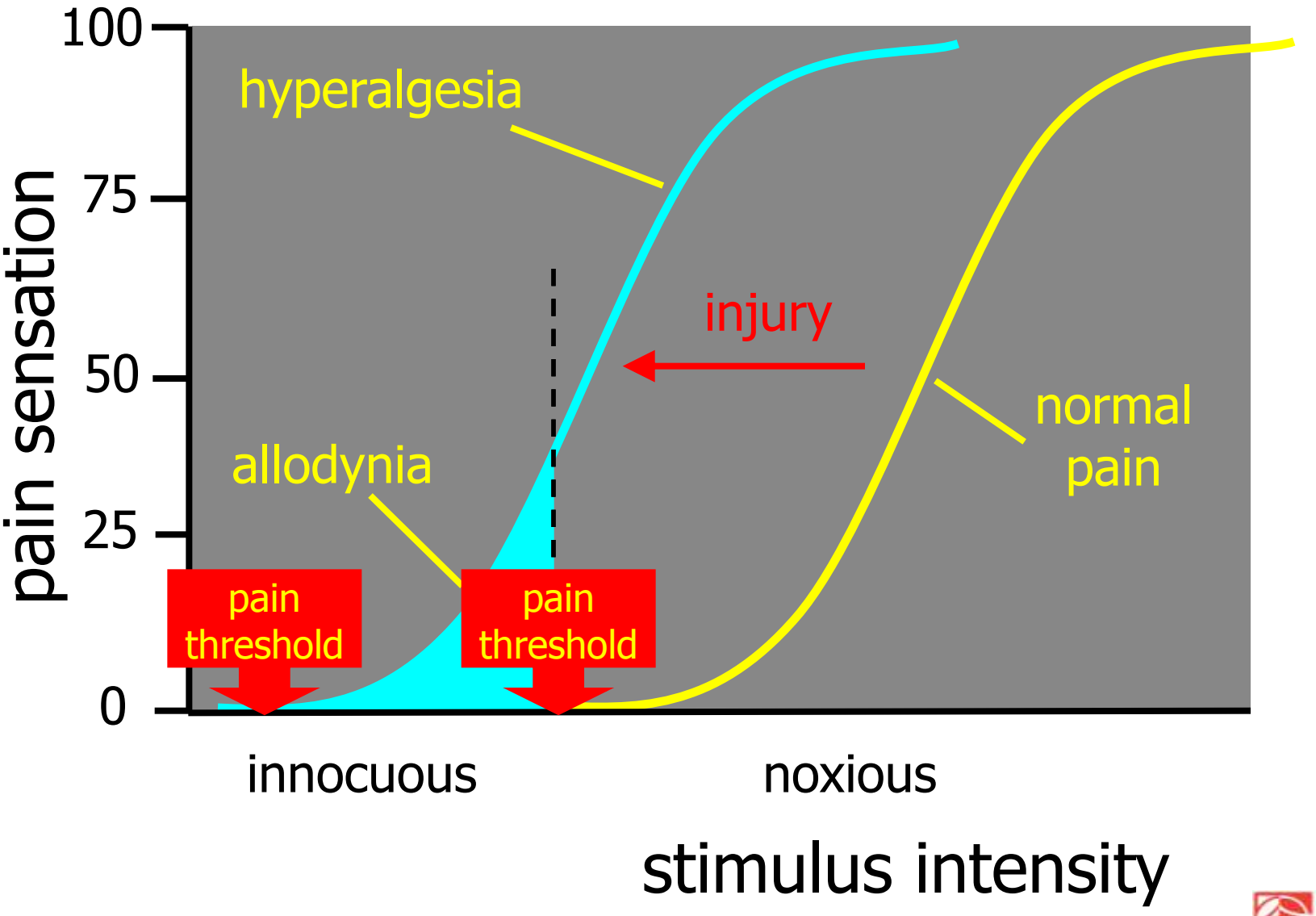
La cronificación del Dolor

Entre el 80 y el 95% del dolor agudo NO se cronifica

(solo un porcentaje pequeño de dolor agudo se cronifica)

?

The dynamics of pain sensation (Cervero & Laird, 1996)



La cronificación del Dolor

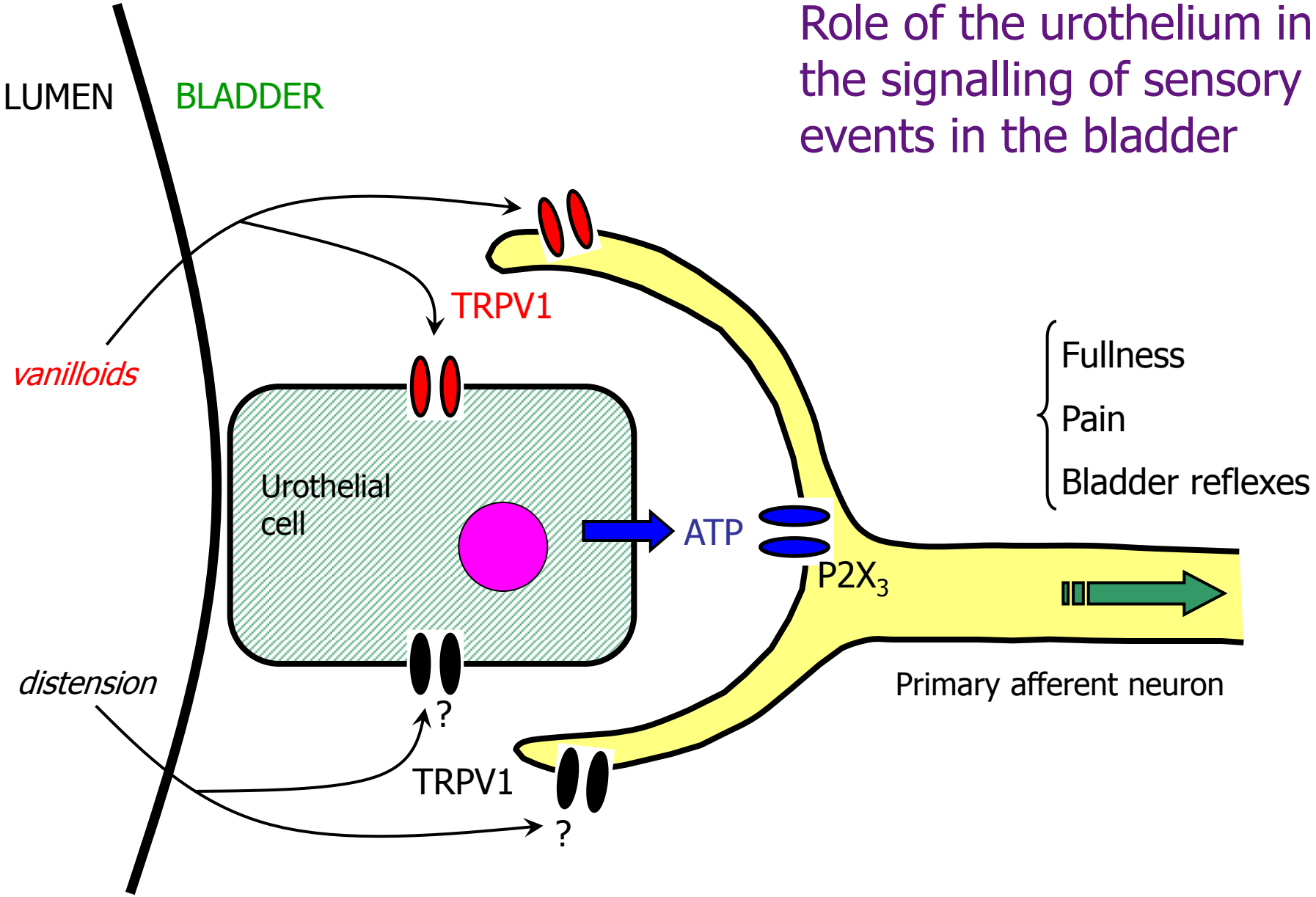
1. El inicio: sensibilización: reversible
2. El mantenimiento: des-inhibición: reversible
3. La cronificación: alteraciones estructurales: reversibles?
4. El futuro: alterationes genéticas?: reversibles?

La cronificación del Dolor

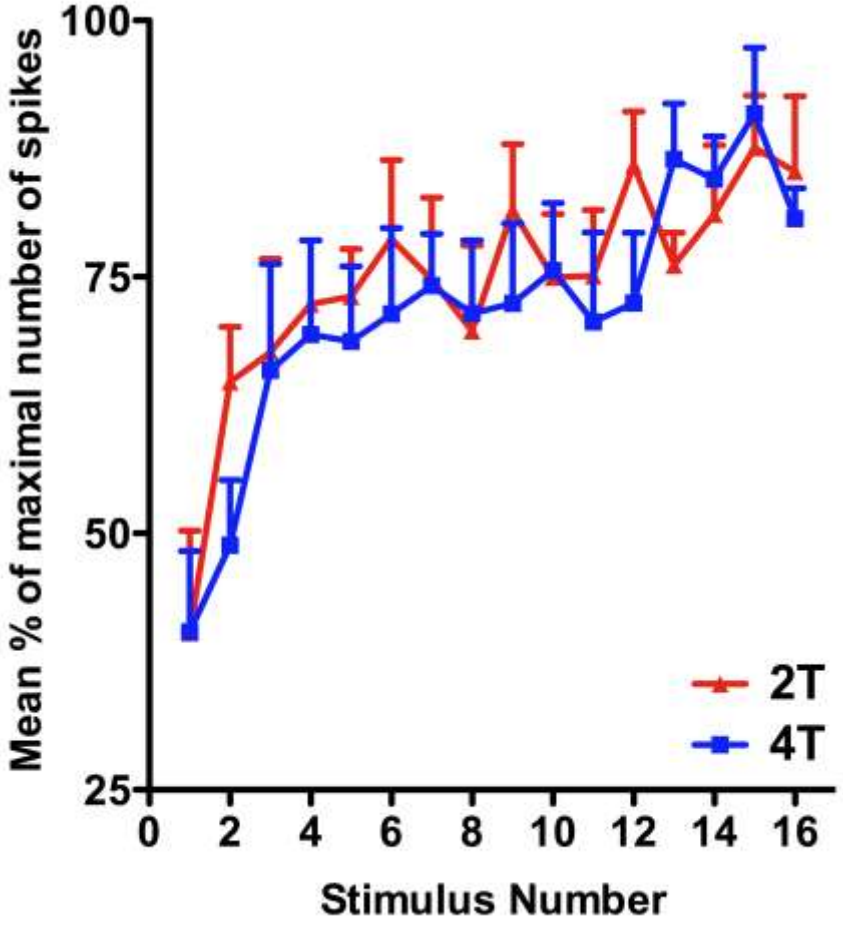
INICIO

Sensibilización periférica y central

Role of the urothelium in the signalling of sensory events in the bladder



Wind-up of Nociceptive Reflexes



(de Felipe et al, 1998)

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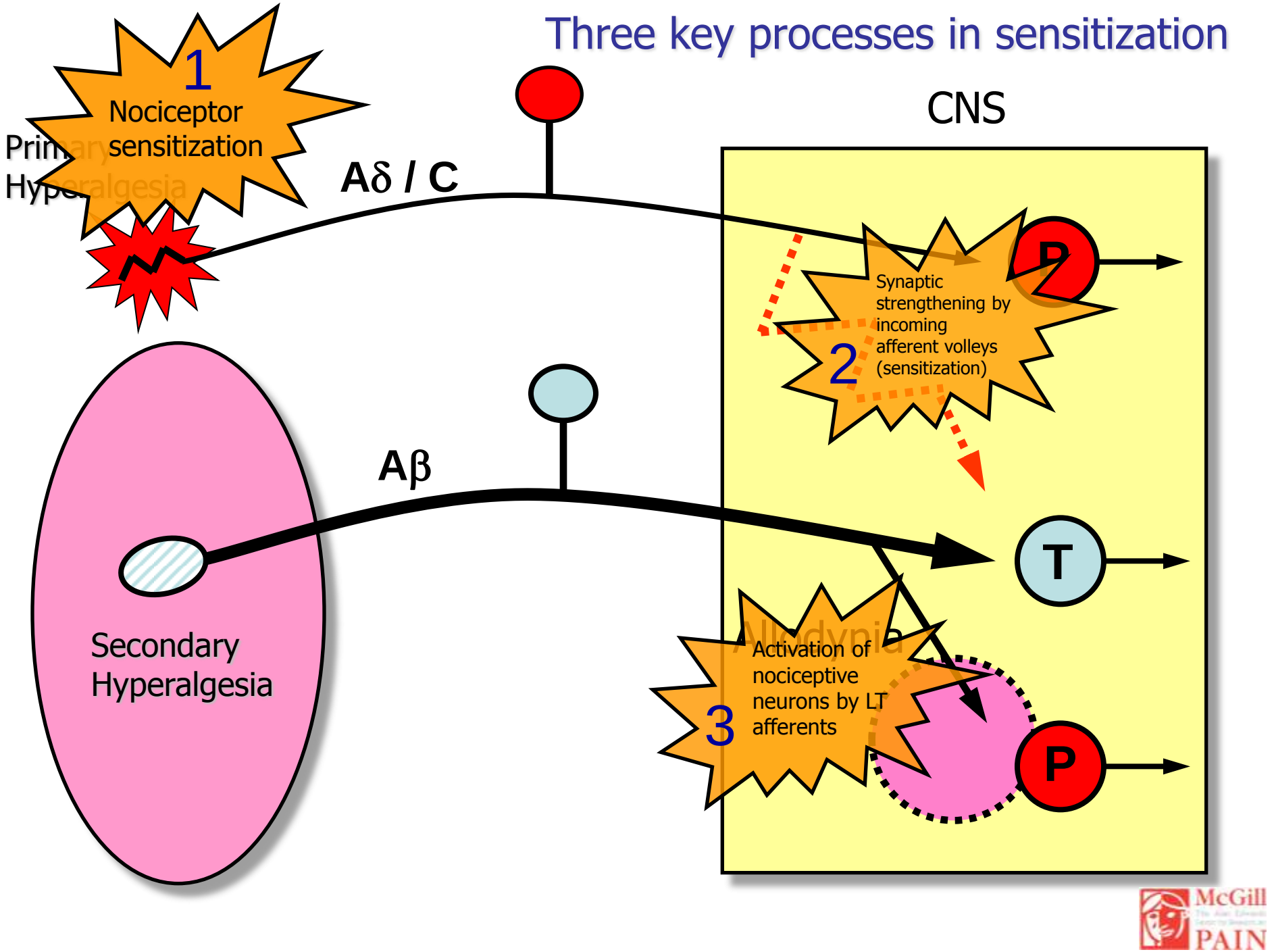
Three key processes in sensitization



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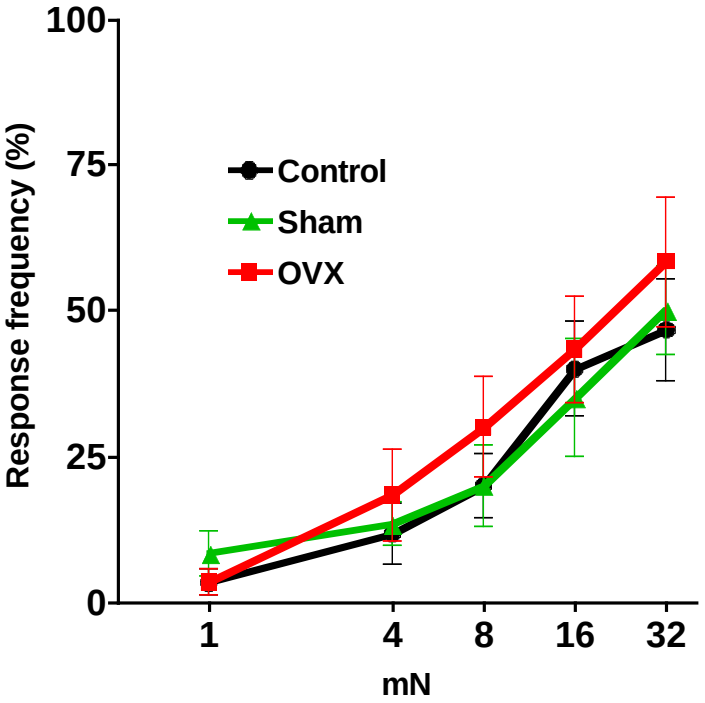
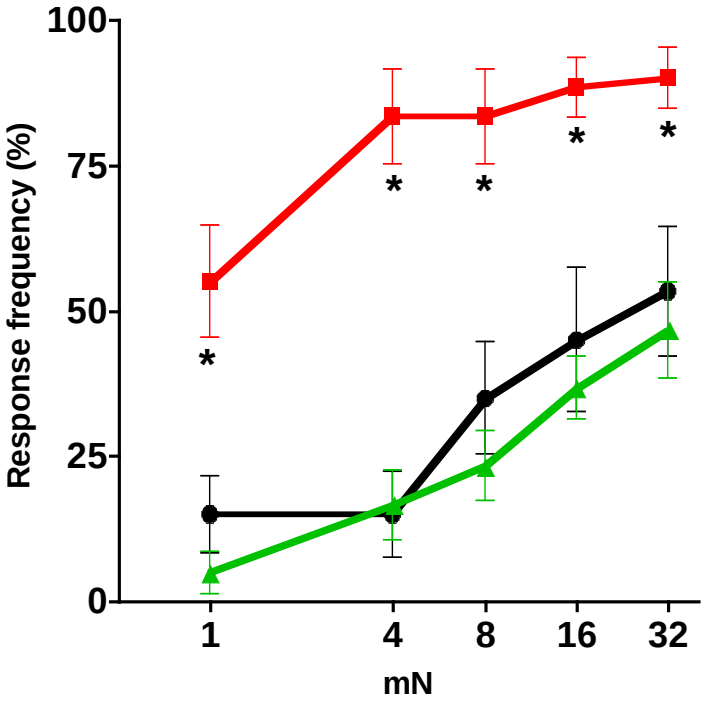
MANTENIMIENTO

Des-inhibición

OVX induces a long lasting abdominal mechanical hyperalgesic state



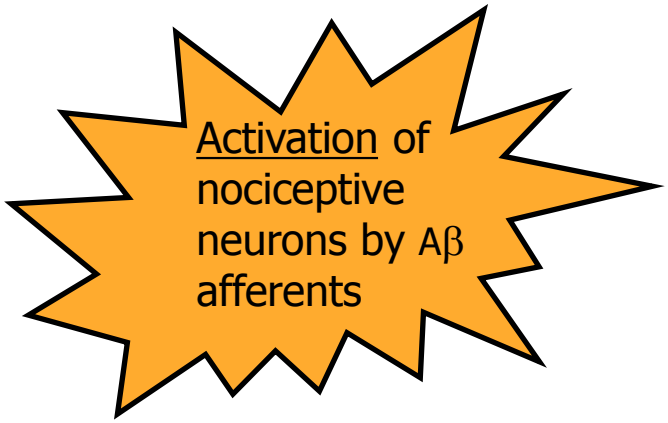
Week 1



Week 5

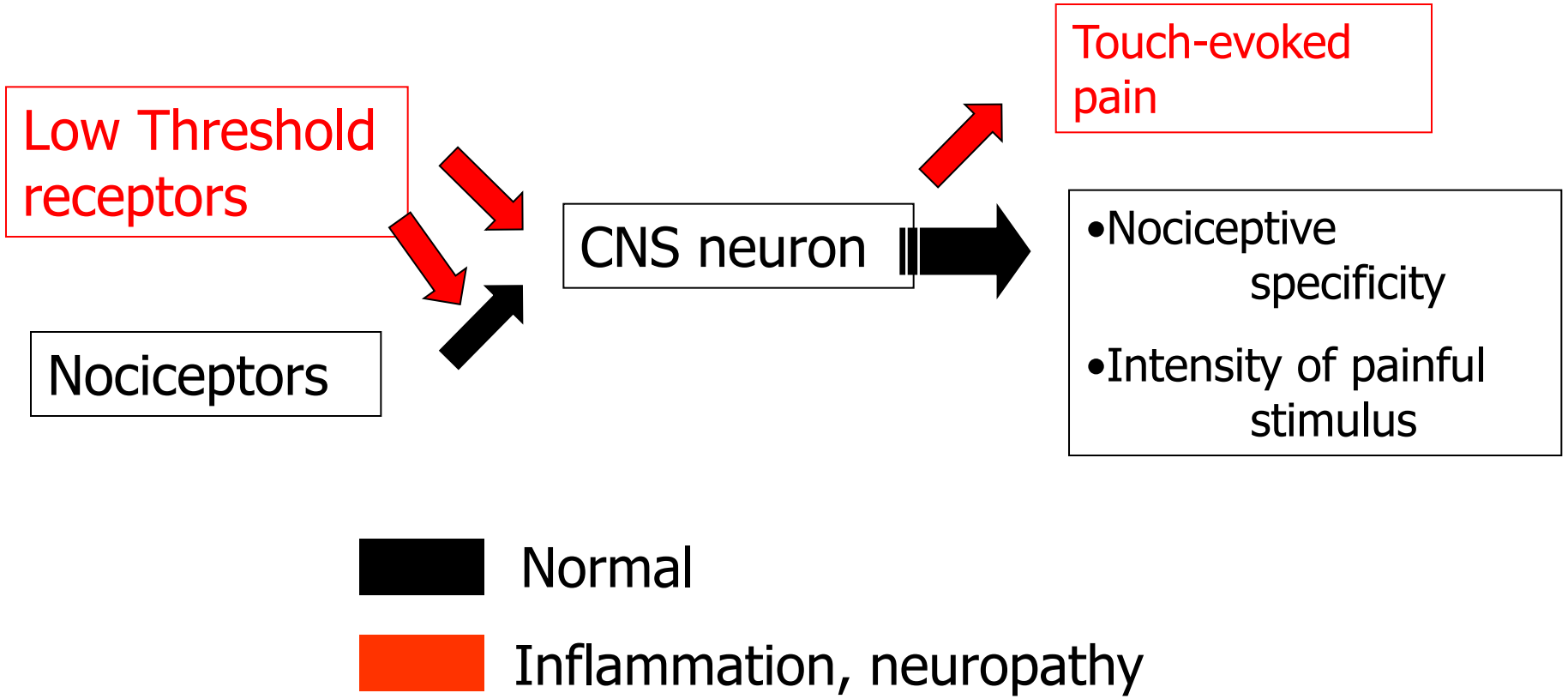
Hyperalgesic states:

inflammatory, neuropathic…

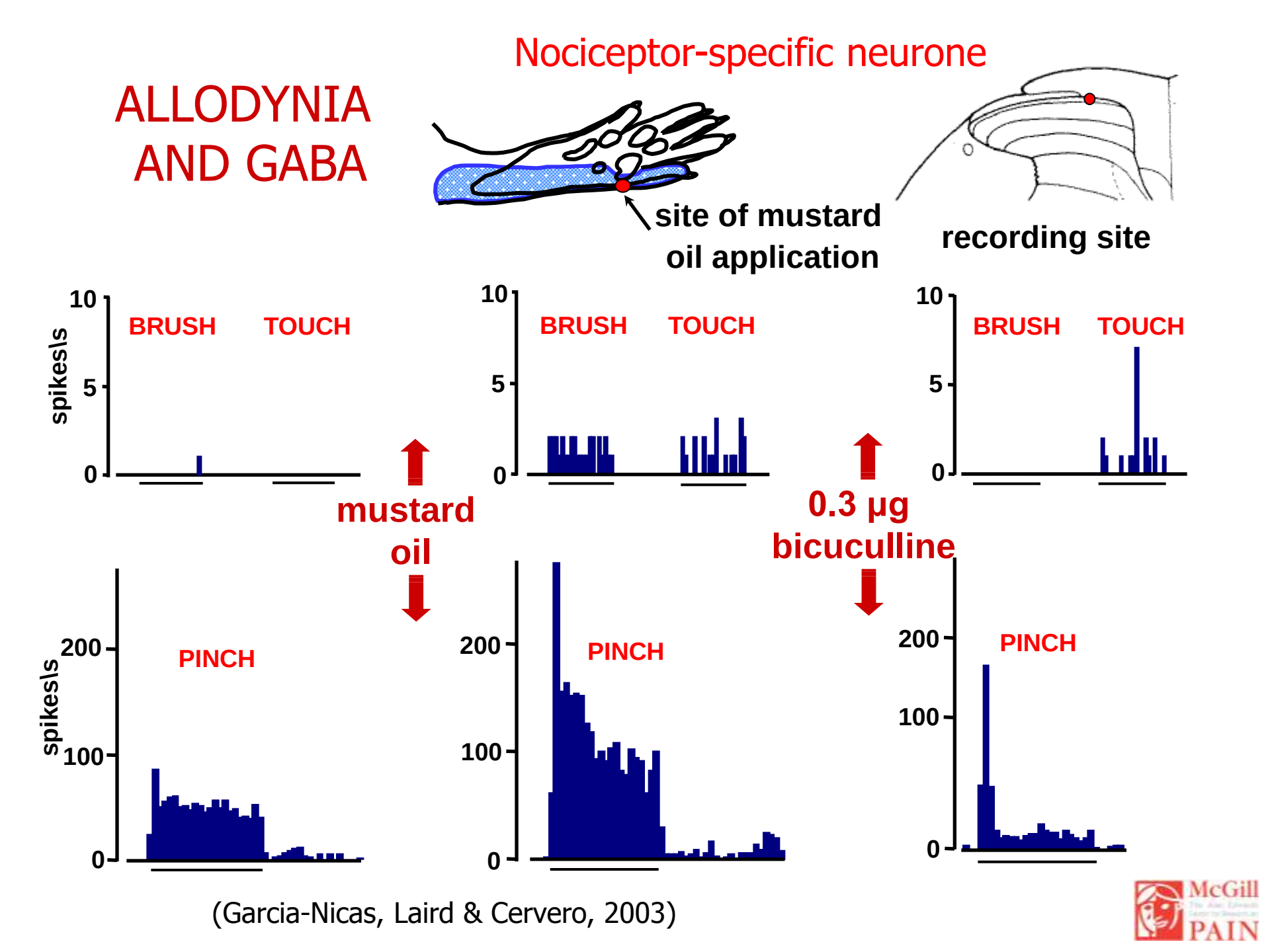


- Neuronal switch from pain inhibition to excitation
- Reversal of the postsynaptic actions of GABA
- Enhancement of the presynaptic actions of GABA

Des-inhibition of nociceptive neurons

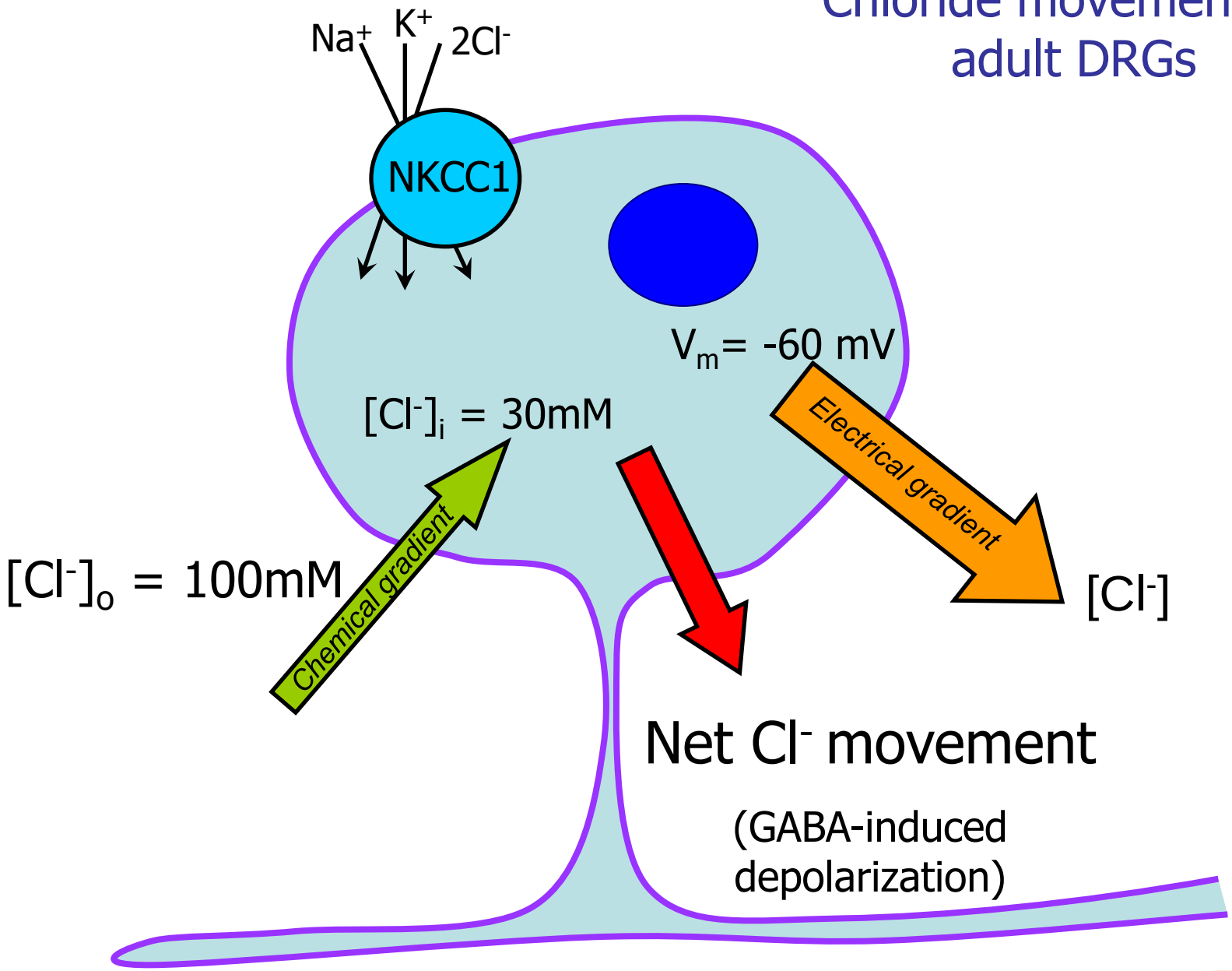


ALLODYNIA AND GABA

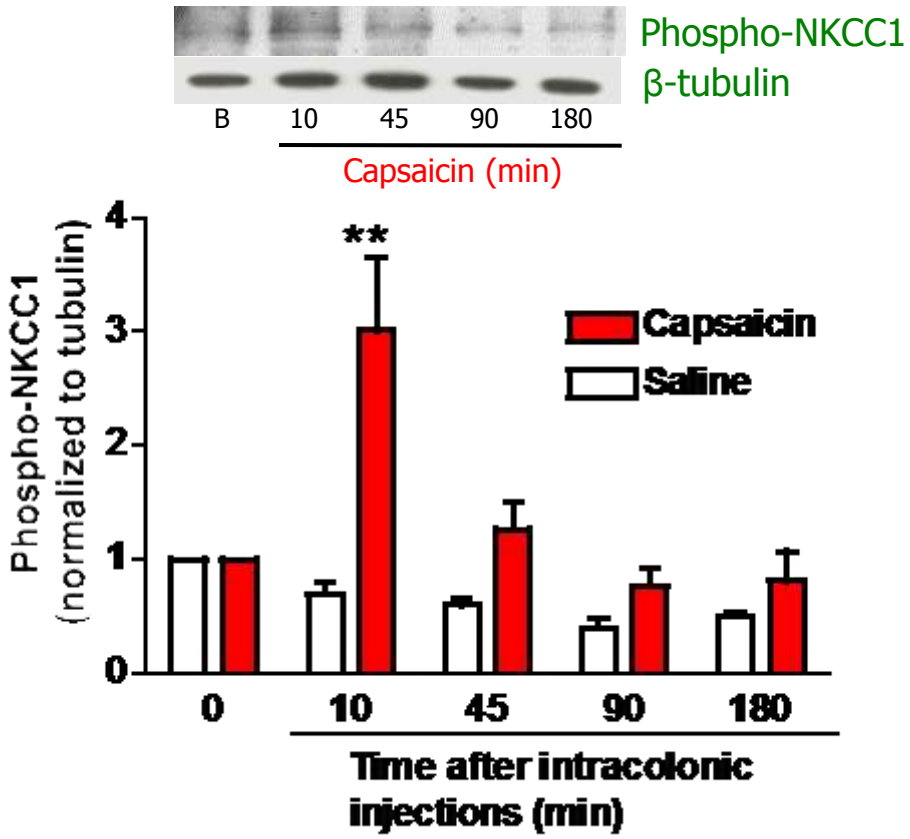


(Garcia-Nicas, Laird & Cervero, 2003)

Chloride movements in adult DRGs



Painful stimuli induce *in vivo* phosphorylation of mouse spinal cord NKCC1 co-transporter



Galan & Cervero, 2005

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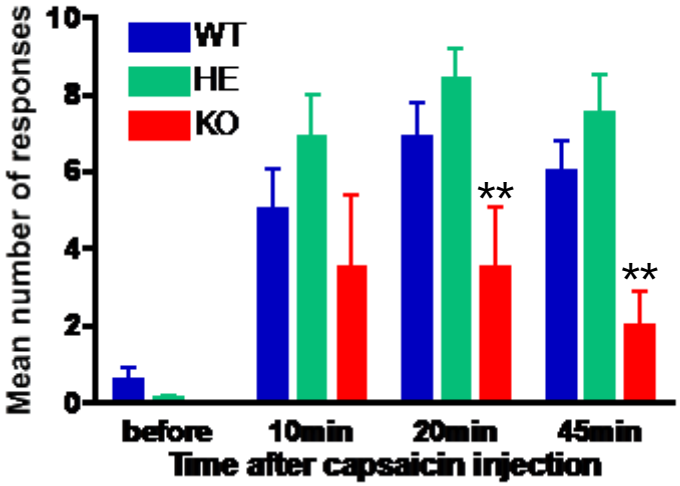
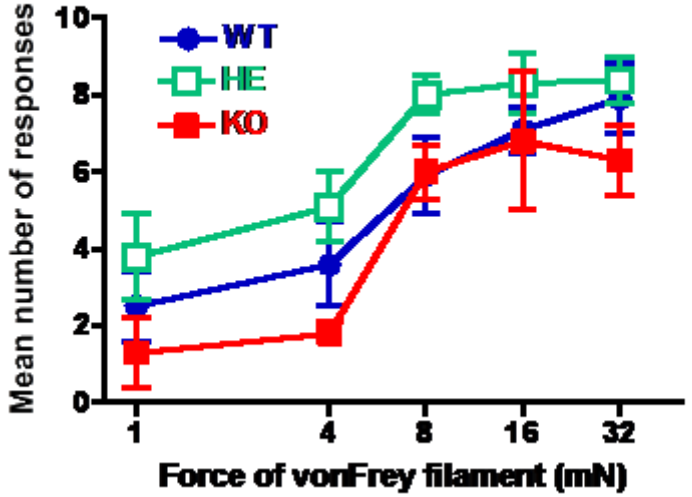
NKCC1 null mice:
Reduced tactile hyperalgesia

Touch-evoked



Punctate



Laird et al, 2004

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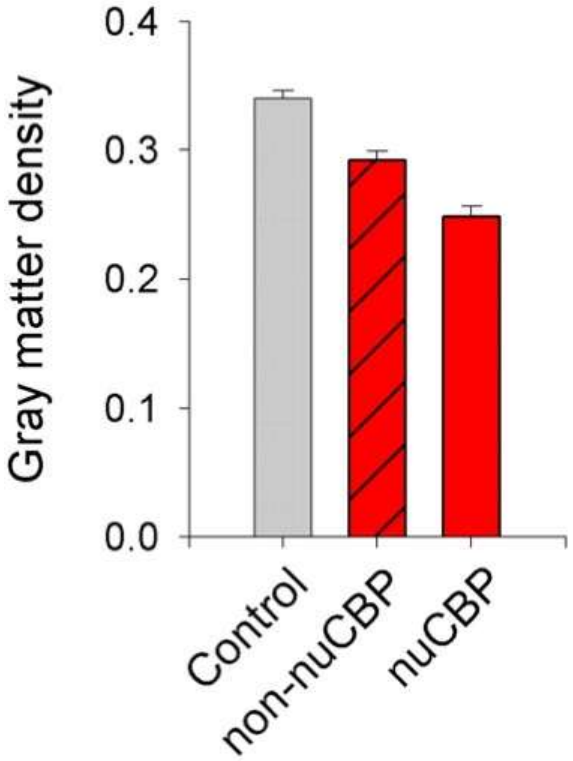
CRONIFICACION

Alteraciones estructurales del cerebro

Anatomical and functional brain changes in Chronic Back Pain patients

- Chronic pain patients have changes in brain grey matter that reflect changes in pain modulation
- Gray matter decreased first shown in back pain patients
- Chronic back pain is associated with decreased prefrontal and thalamic gray matter density (Apkarian et al 2004)



- Similar findings with multiple chronic pain conditions: chronic tension-type headache, fibromyalgia, IBS
- Chronic back pain patients are impaired on emotional decision-making task
- FM patients have impaired working memory

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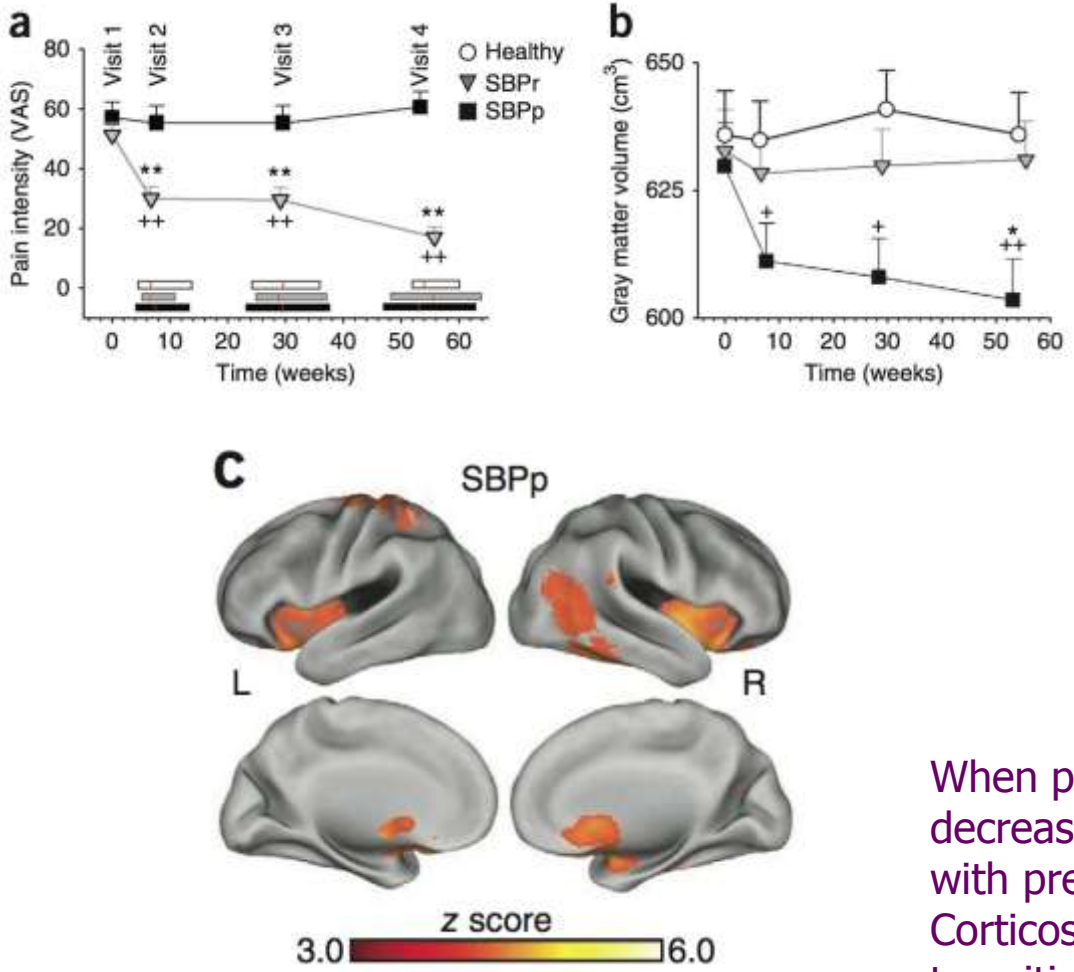
Corticostriatal functional connectivity predicts transition to chronic back pain



When pain persists brain gray matter density decreases. Connectivity of nucleus accumbens with prefrontal cortex predicts pain persistence. Corticostriatal circuitry is involved in the transition from acute to chronic pain.

Baliki et al. Nature Neurosci. 2012

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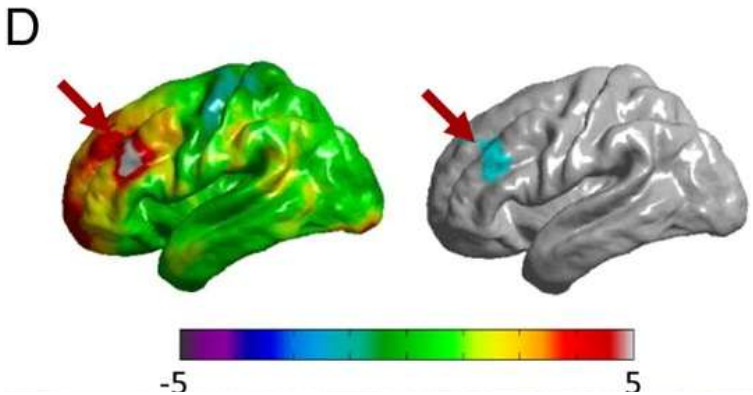
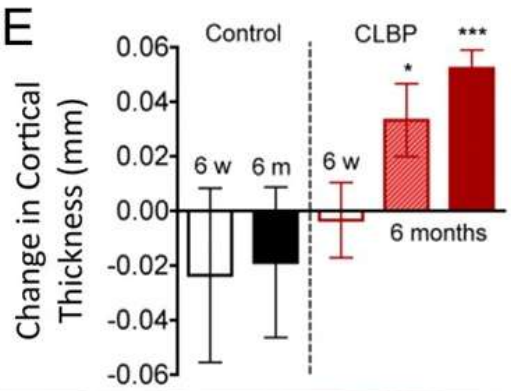
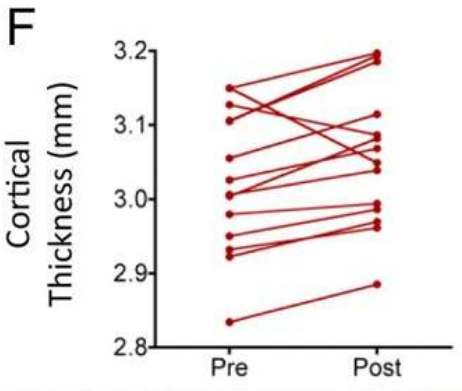
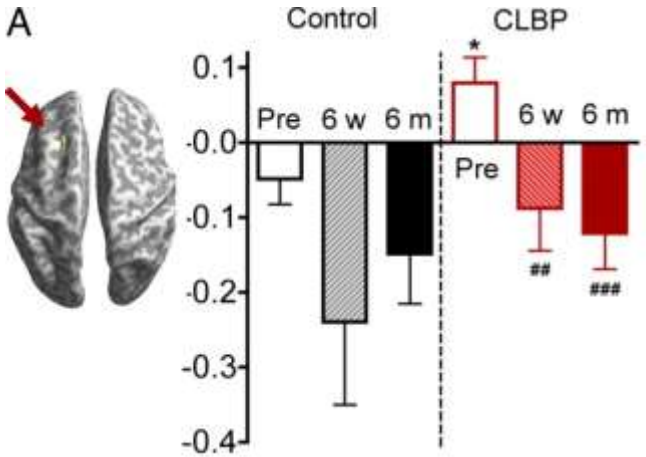
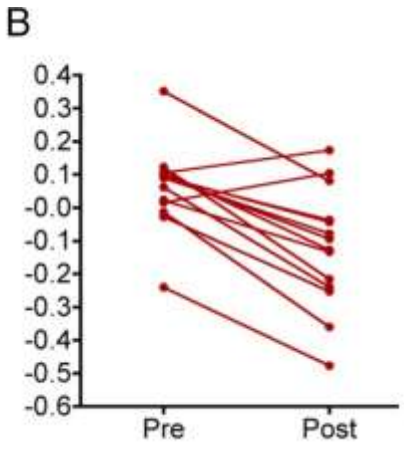
Can gray matter changes be reversed with treatment of pain?











Pain-related neuroanatomical and functional changes are reversible with effective treatment

Seminowicz et al. J. Neurosci. 2011;31:7540-7550

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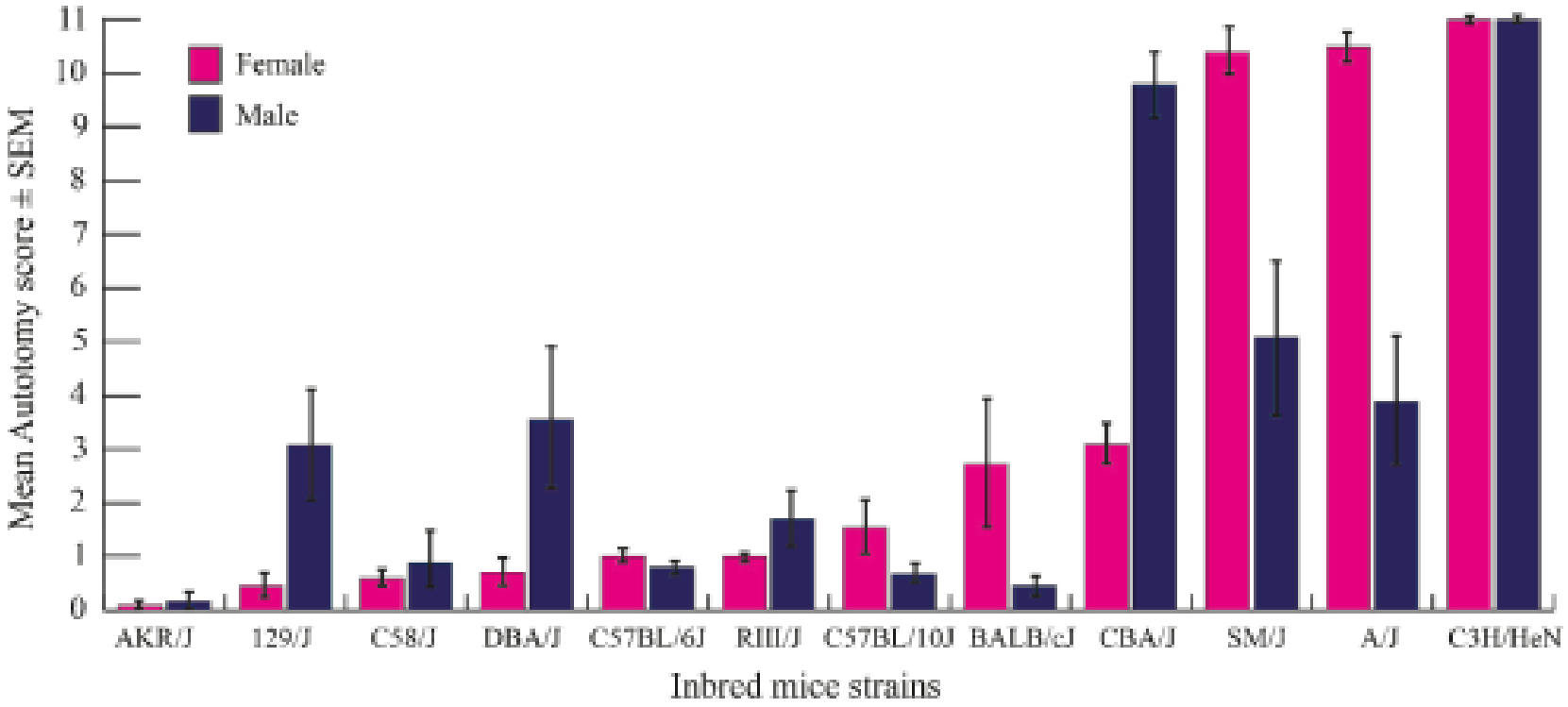
FUTURO

Alteraciones genéticas?

Variability of neuropathic pain among 12 inbred mouse strains



Mogil *et al*, *PAIN,* 1999

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1. Quantitative trait locus mapping

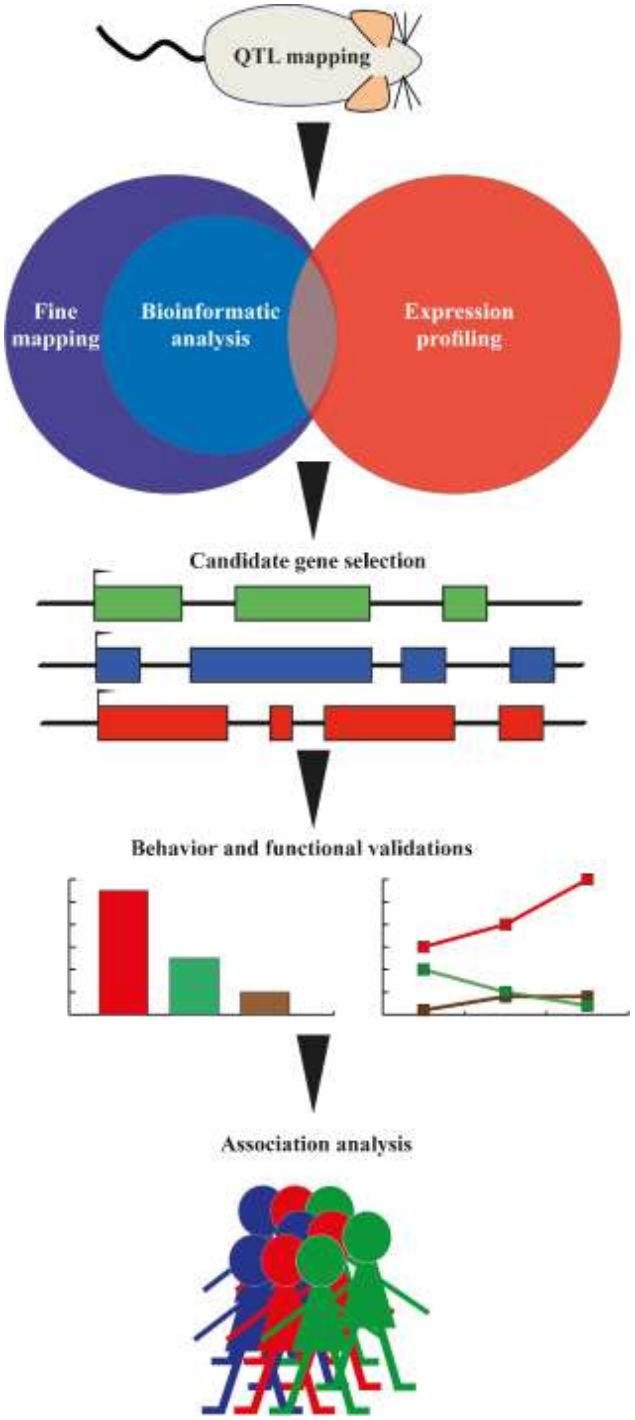
2. Fine-mapping strategies (recombinant progeny testing and recombinant inbred segregation test)

3. Sequence-based analysis and mRNA profiling

4. Selection of the most promising candidate gene

5. Role in pain confirmed by behavior and functional analyses in mutated mice

6. Association testing in human cohorts (breast cancer patients) establishing the connection of the gene to neuropathic pain susceptibility.



Nissenbaum, *Clinical Genetics,* 2012

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IASP

Trabajando juntos para aliviar el dolor en todo el mundo

www.IASP-pain.org