

MODULATING THE BODY'S NATURAL CANNABINOID SYSTEM – A PROMISING APPROACH FOR THE TREATMENT OF PAIN

Session 304

Dr. Niklas Schuelert

Modulating the Endocannabinoid System Can Reduce Pain Transmission
in Animal Models of Osteoarthritis Pain

Dr. Devi Sagar

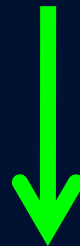
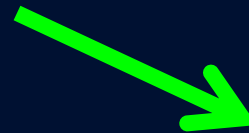
Endocannabinoid Modulation of Spinal Excitability in Osteoarthritic Pain

Dr. Mark Ware

Harnessing the Endocannabinoid System in Clinical Pain Management

Cannabinoids

Therapeutic effect



Bronchodilation
(asthma)

Epilepsy

Appetite
stimulation
(HIV)

Antiemetic
(anti-cancer treatment)

Analgesia
(arthritis, cancer and neuropathic pain)

Cannabinoids: 3 classes

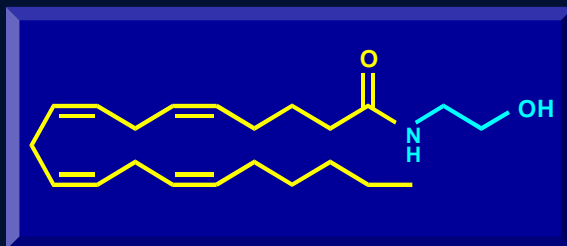
Phytocannabinoids

Δ 9-THC; cannabidiol; cannabitol; etc

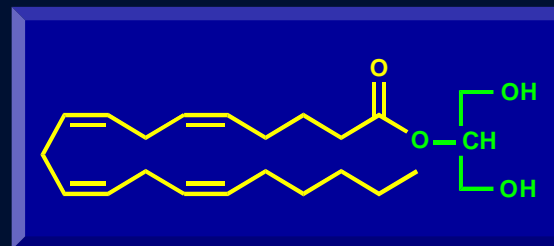
Synthetic cannabinoids:

ACEA; GW 405833; etc

Endocannabinoids:



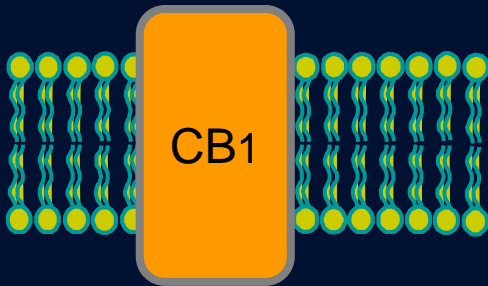
Anandamide (AEA)



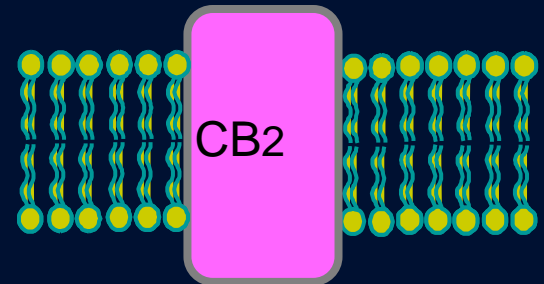
2-Arachidonoylglycerol
(2-AG)

Cannabinoid receptors

- Two CB receptor subtypes have been identified:

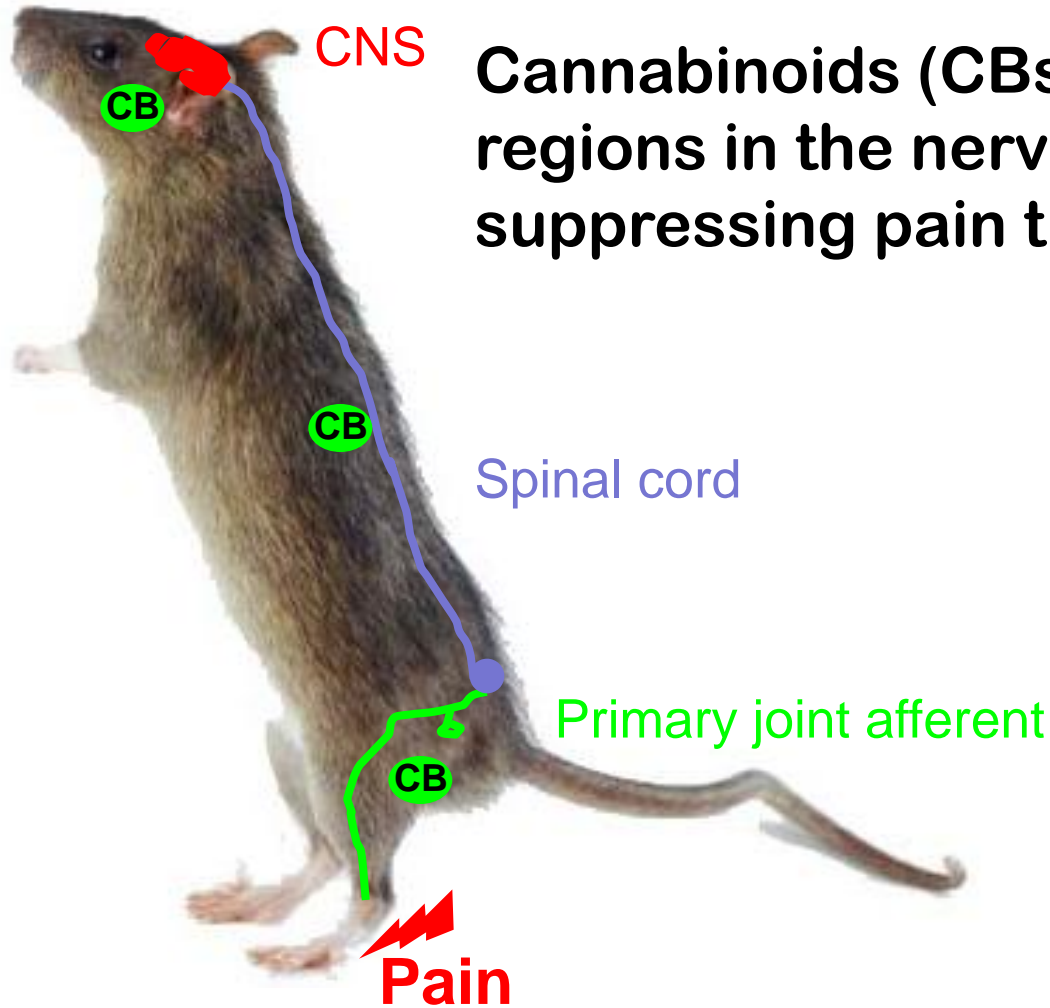


CNS, peripheral nerve terminals



Immune system

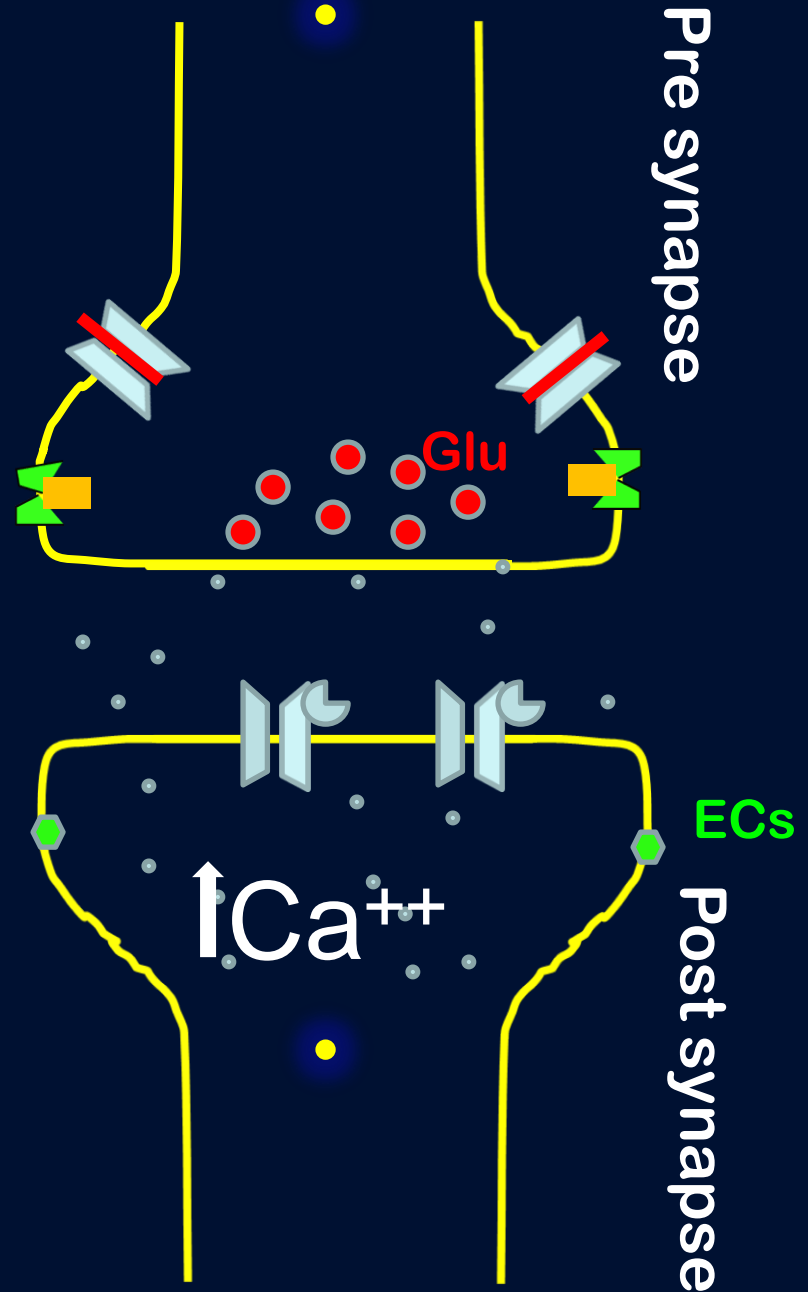
Pain Pathway



Cannabinoids (CBs) act on various regions in the nervous system, suppressing pain transmission

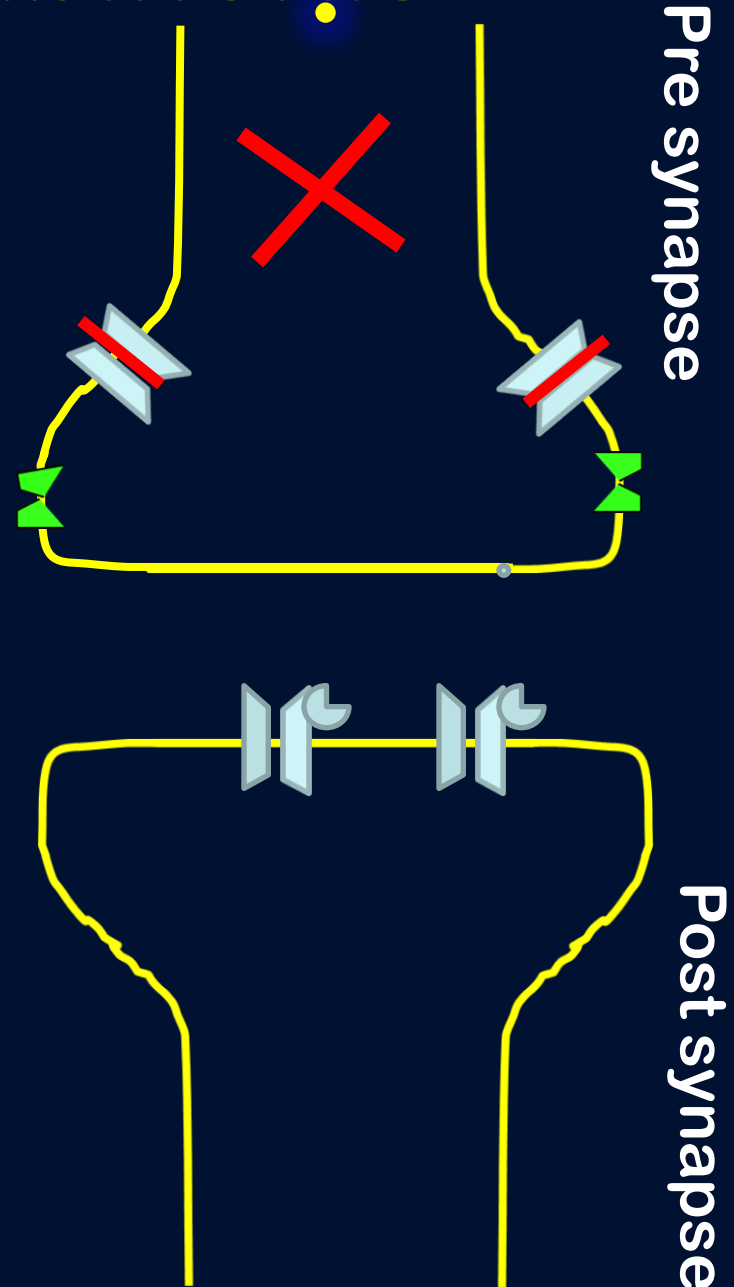
Endocannabinoids

- Endocannabinoids (ECs) are released on demand and act locally on the pre-synaptic neuron (retrograde signalling)
- Increased neuronal activity that occurs during noxious stimulation of the pain pathways is believed to drive the synthesis of ECs



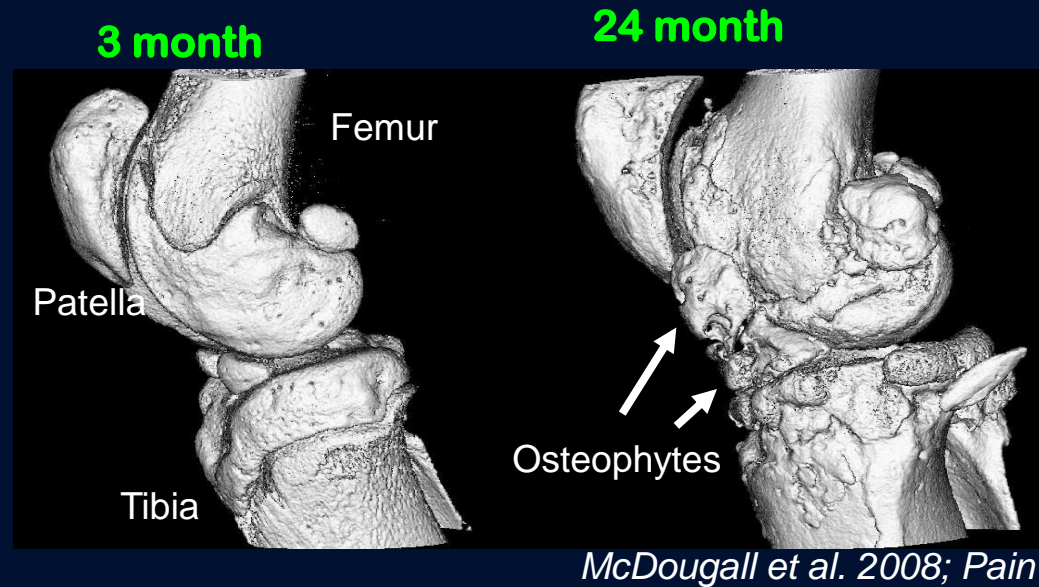
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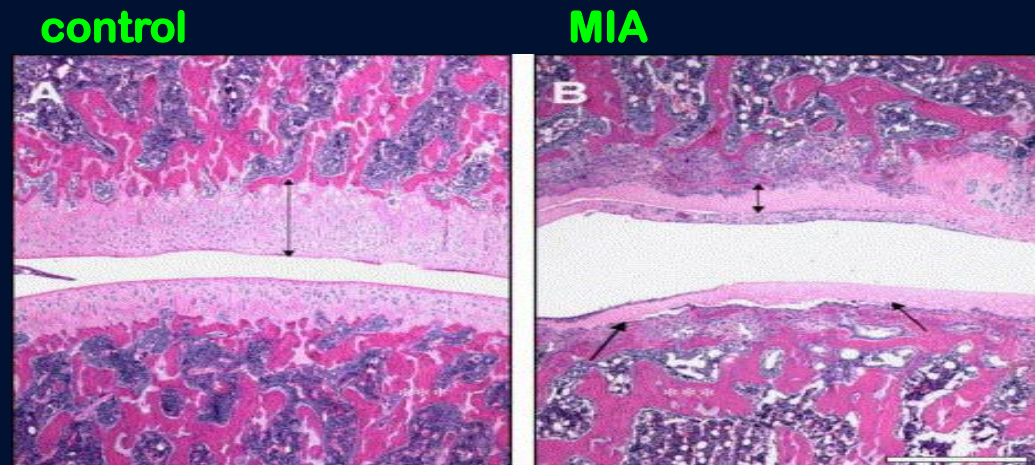


Rodent Models of Osteoarthritis

Spontaneous occurring osteoarthritis in the Dunkin Hartley guinea pig

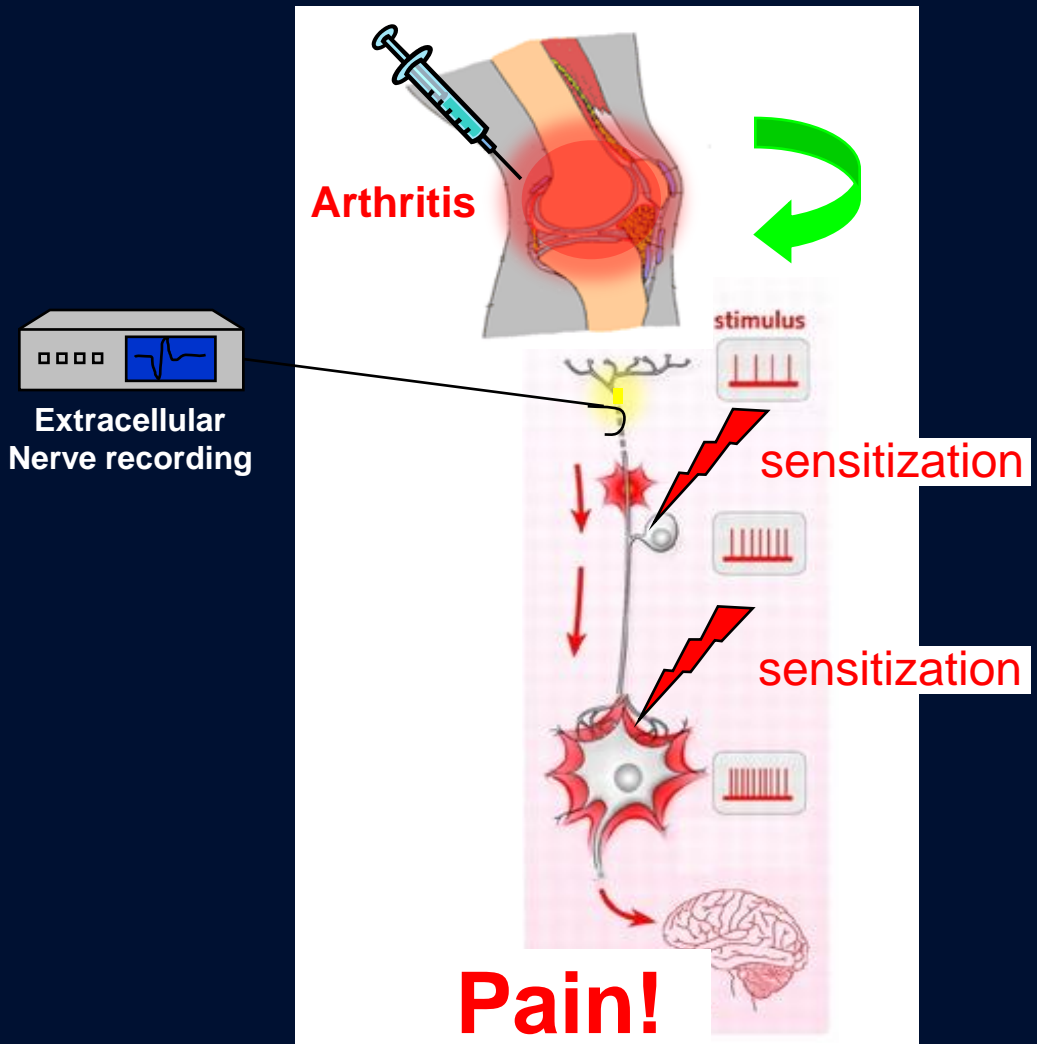


Chemically induced cartilage degeneration by intra-articular injection of Sodium monoiodoacetate (MIA)



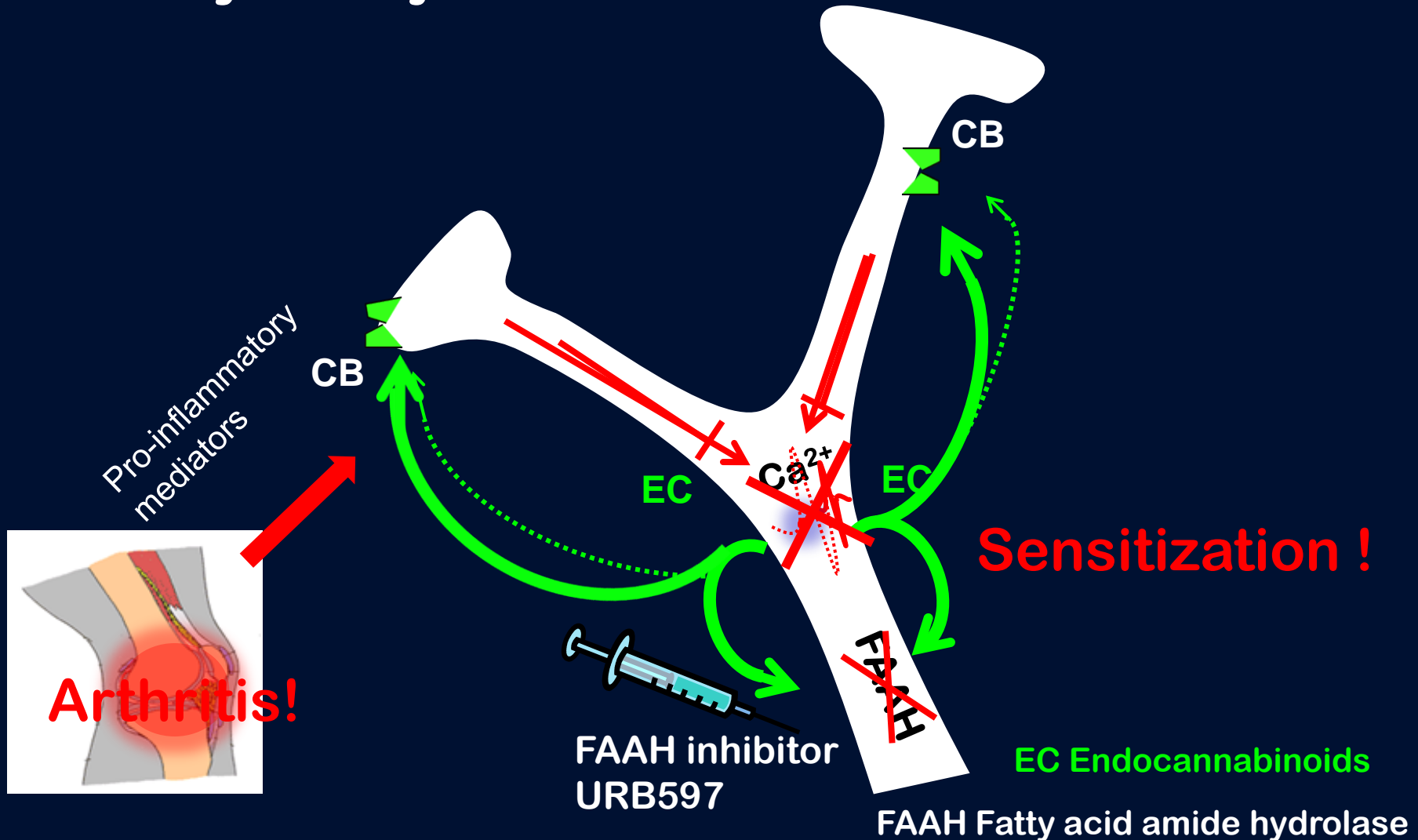
Osteoarthritis Sensitizes Nerves

Osteoarthritic joint

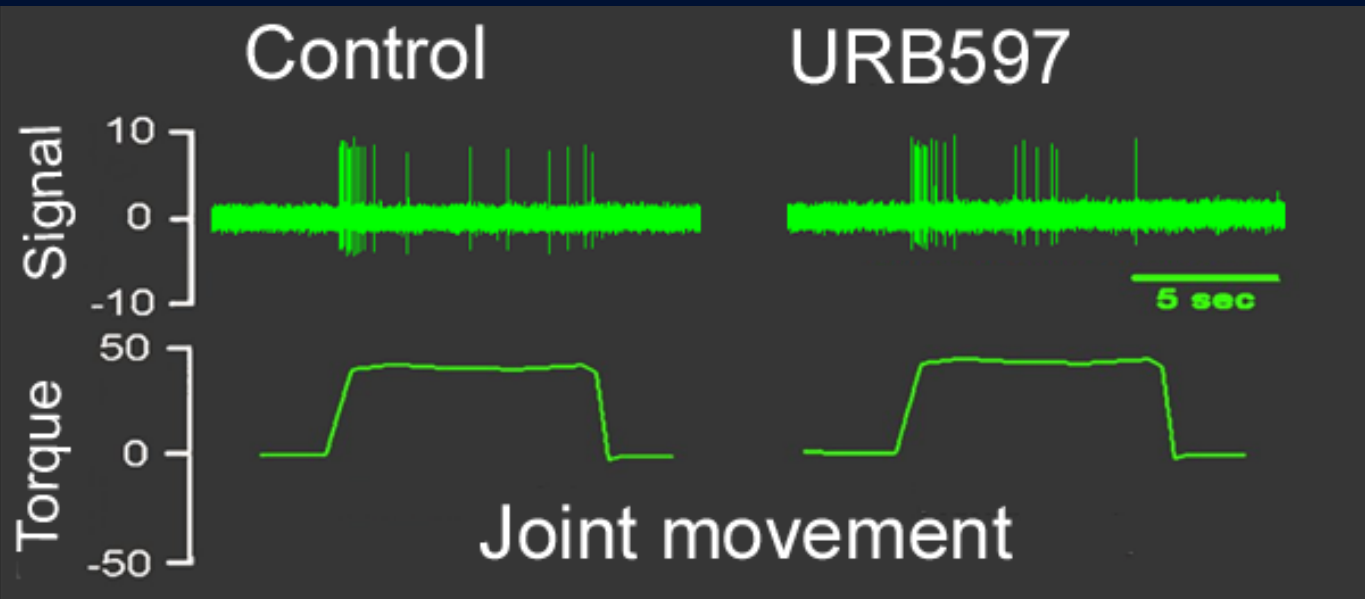


Endocannabinoids

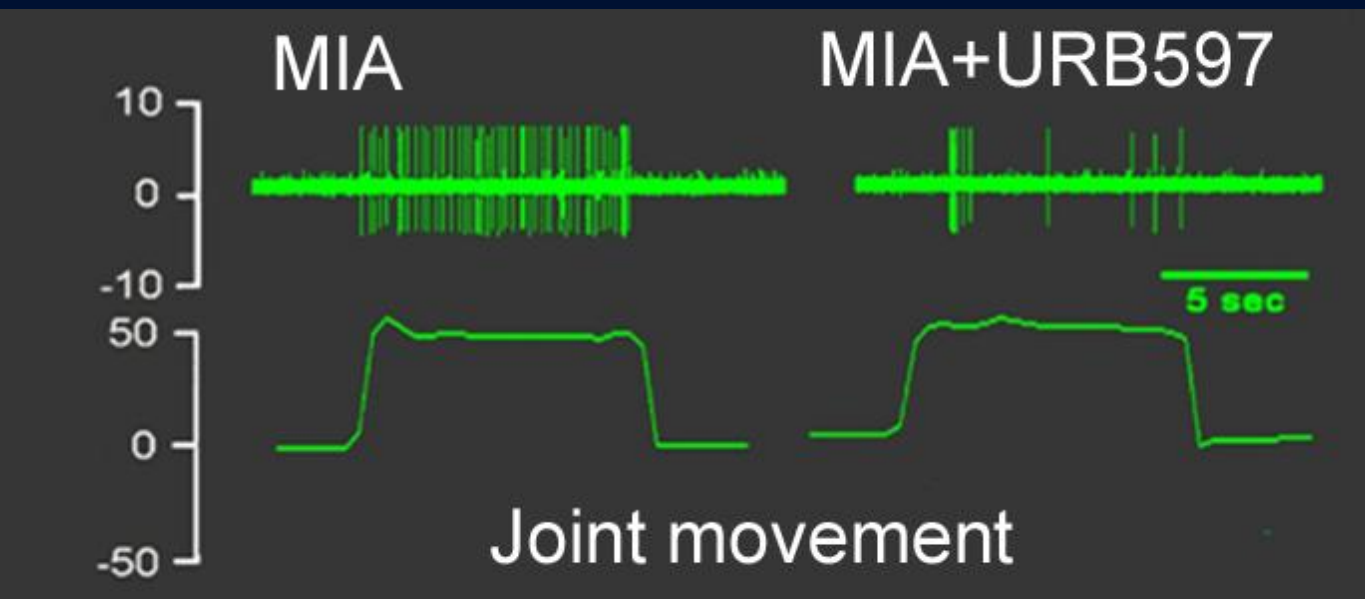
Primary knee joint afferent



Normal Joint

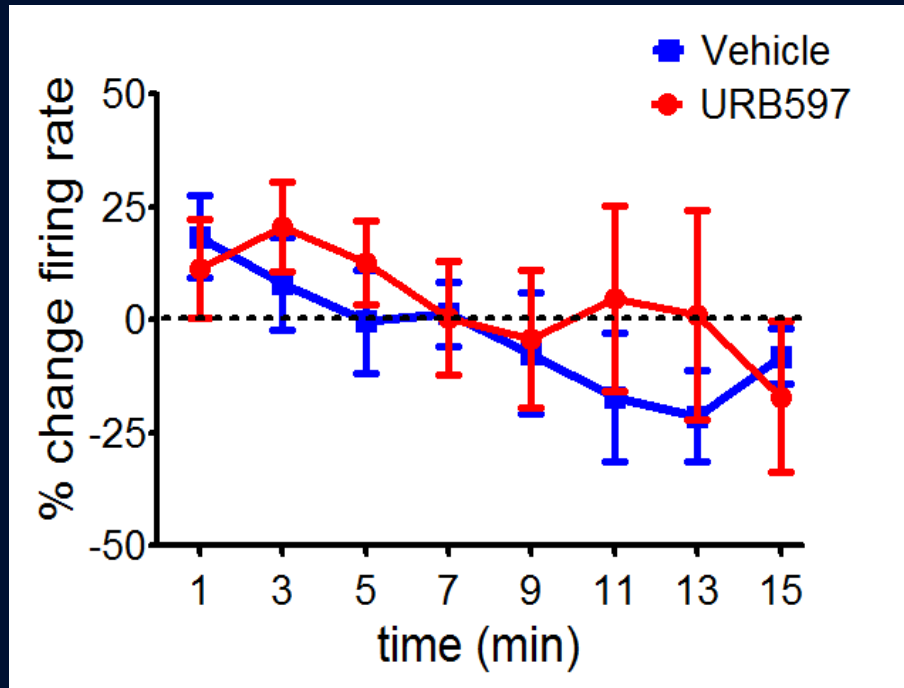


MIA Joint

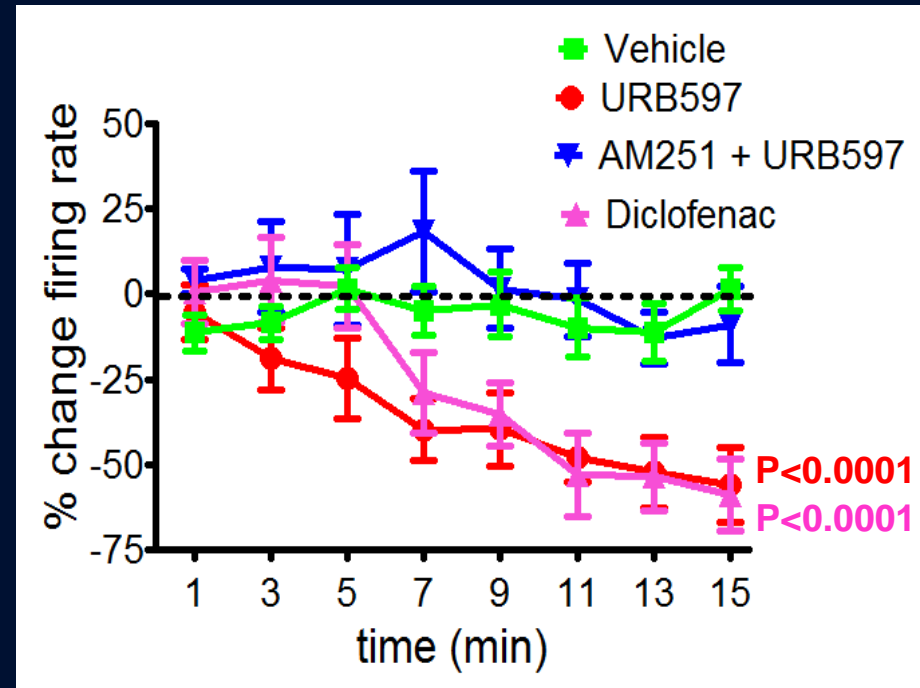


Joint afferent recordings rat

Control joint

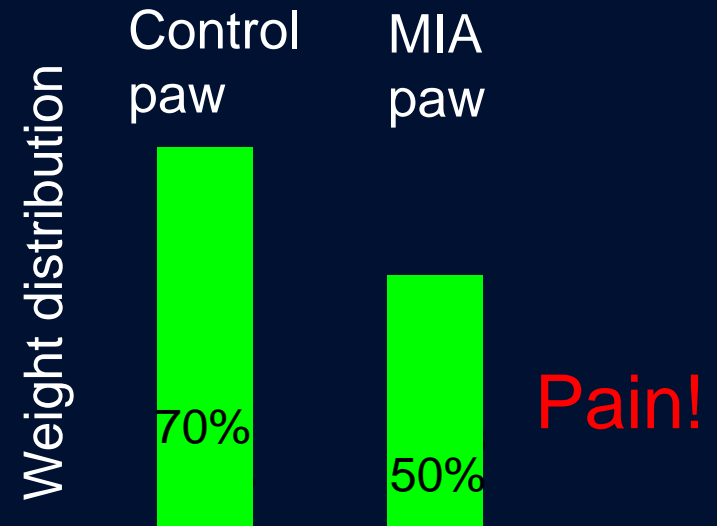
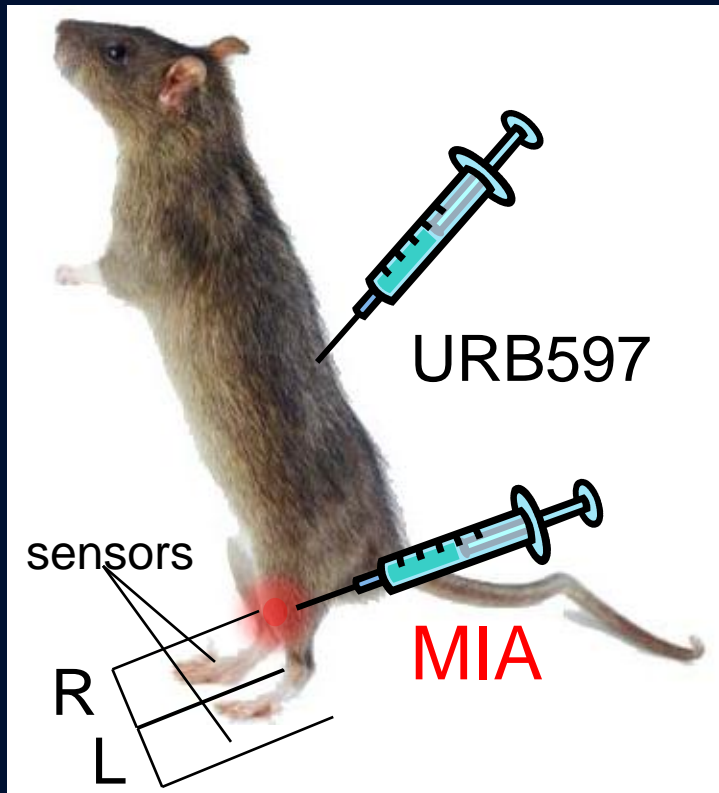


OA joint

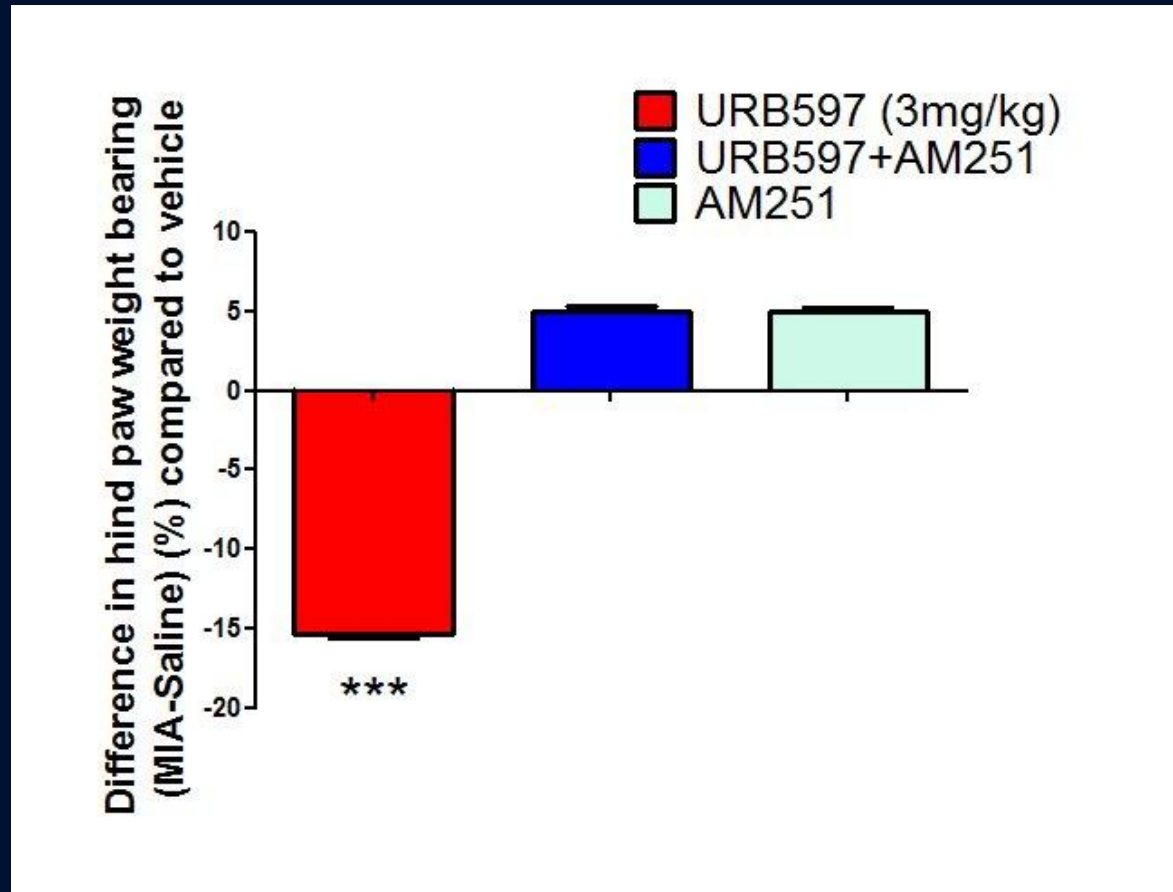


FAAH inhibitor URB597 reduces nociception in OA joints but does not impair physiological sensory function

Pain Behaviour MIA model



Pain Behaviour



URB597 reduces MIA induced pain behaviour
CB₁ antagonist AM251 abolishes analgesic effect

Conclusion

FAAH inhibitor
URB597

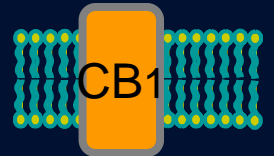
control

No effect Nociception

MIA

↓ Nociception
↓ Pain behaviour
= NSAID

Reduced side effects?

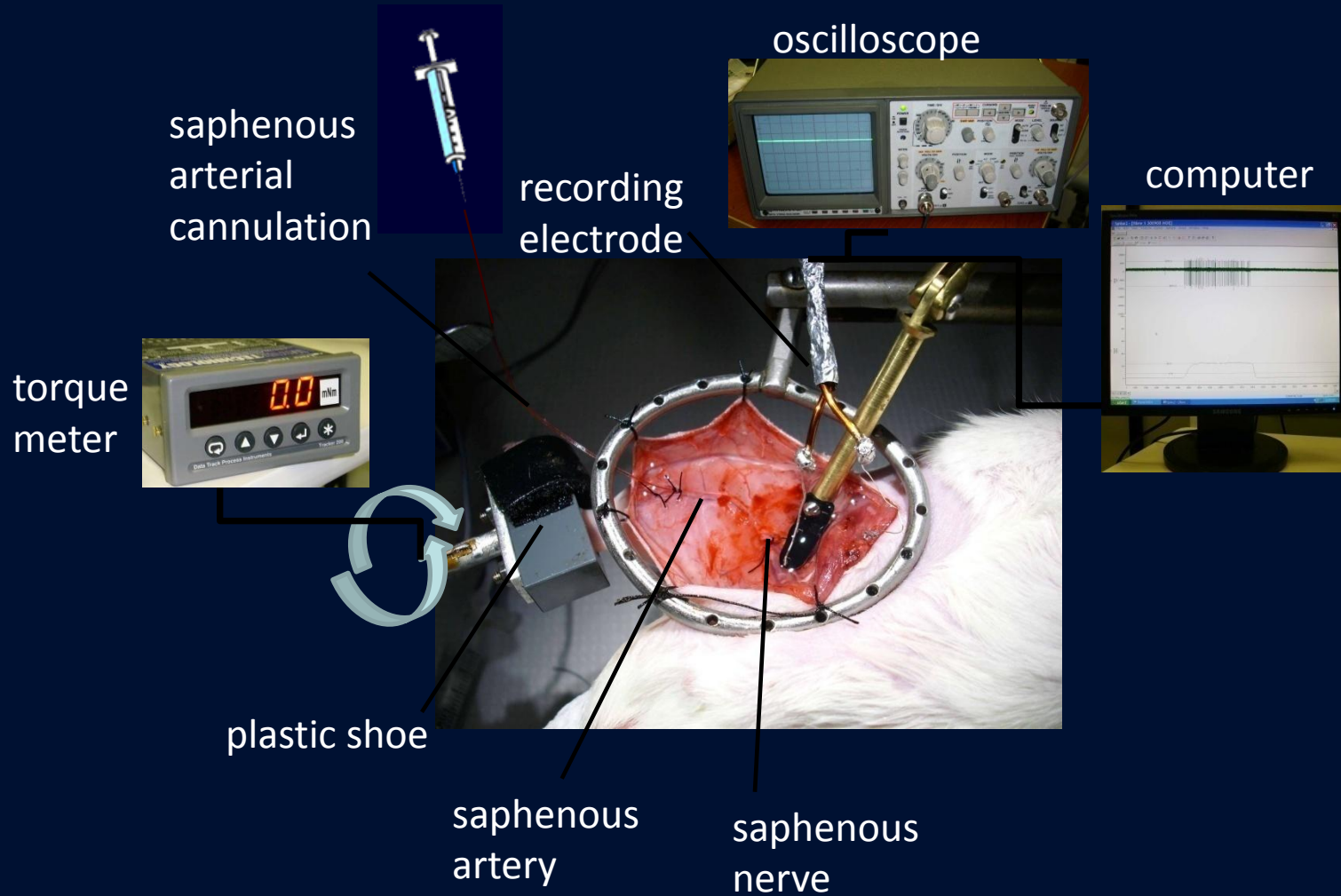


Acknowledgements

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- Dr. Mark Chambers (Eli Lilly, USA)
- Dr. Shu Zhan



E-phys Setup



In vivo electrophysiological recordings from joint primary afferents allows objective measurement of nociception