

# Electroactivity of biological systems

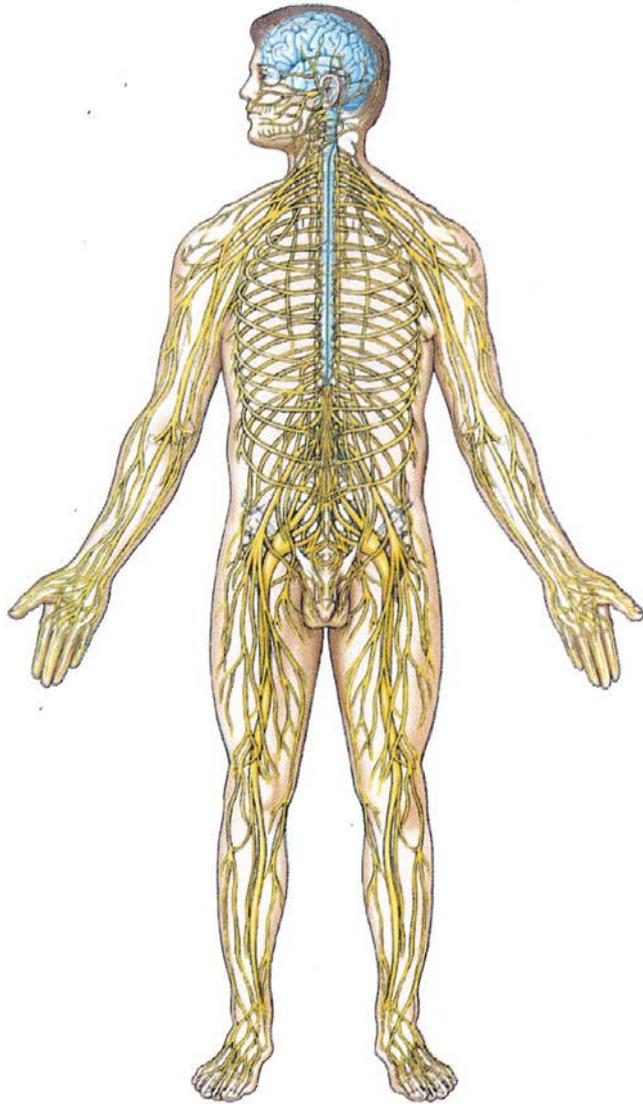
## *Spinal cellular and network activities modulate pain perception*

Pascal Darbon

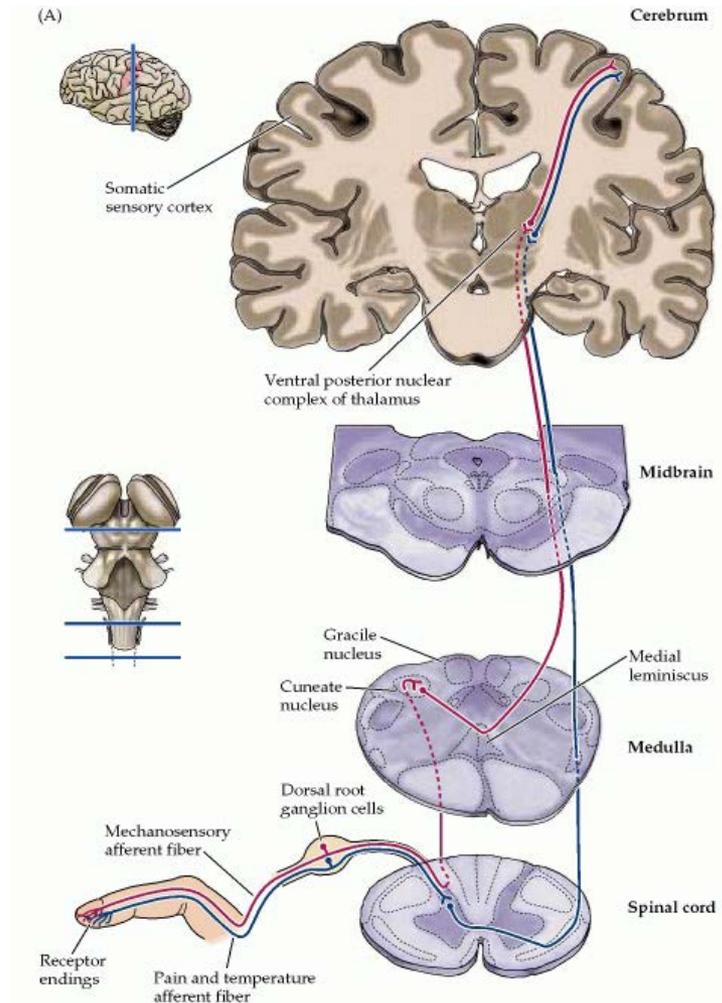
Institut des Neurosciences Cellulaires et Intégratives

CNRS – Université de Strasbourg

# Introduction: Collecting nociceptive information

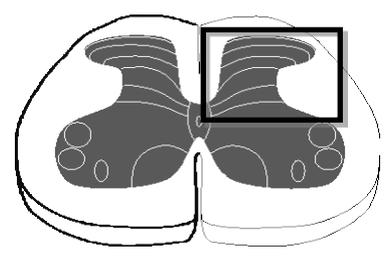


Peripheral Nervous System



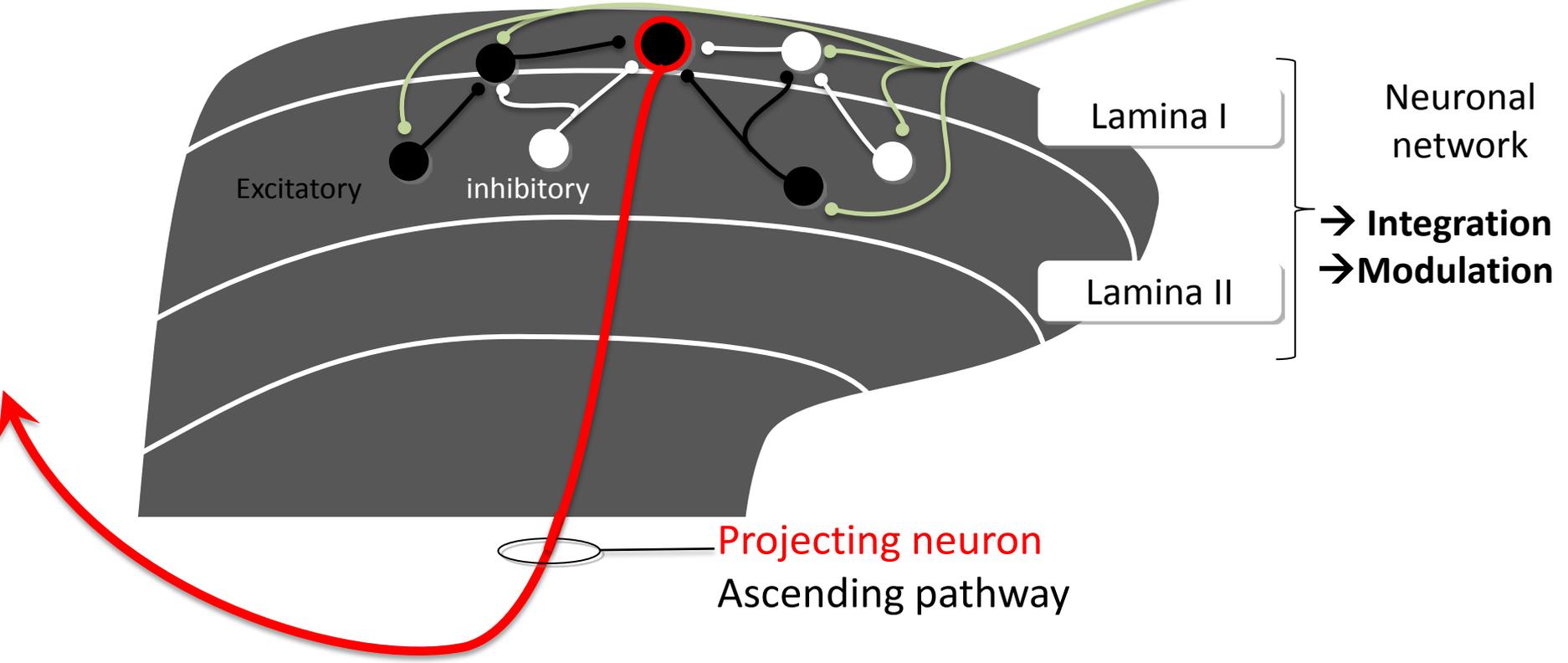
Organization of the somatic sensory system.

# Introduction: Processing nociceptive information



Dorsal Horn

Primary nociceptive afference



Lamina I

Neuronal network

Excitatory

Inhibitory

→ Integration

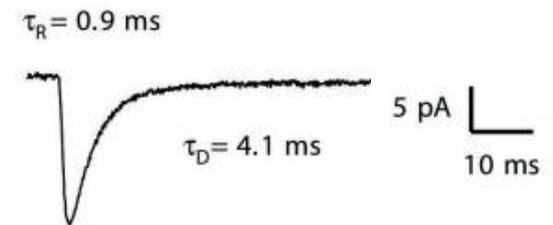
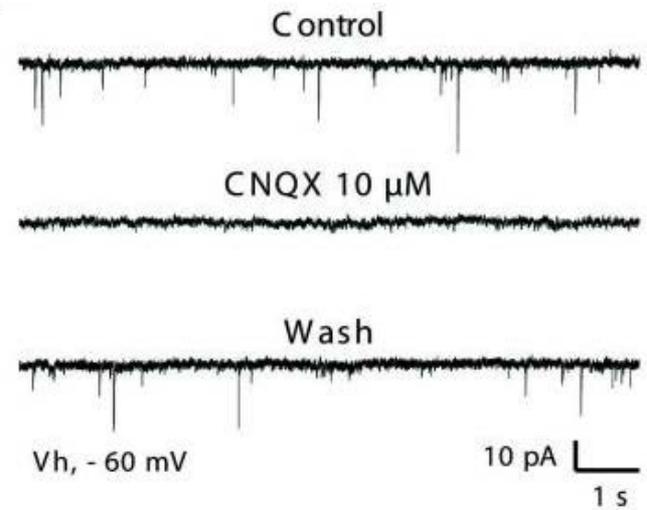
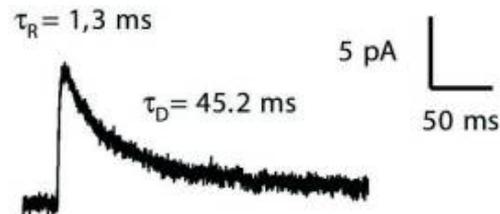
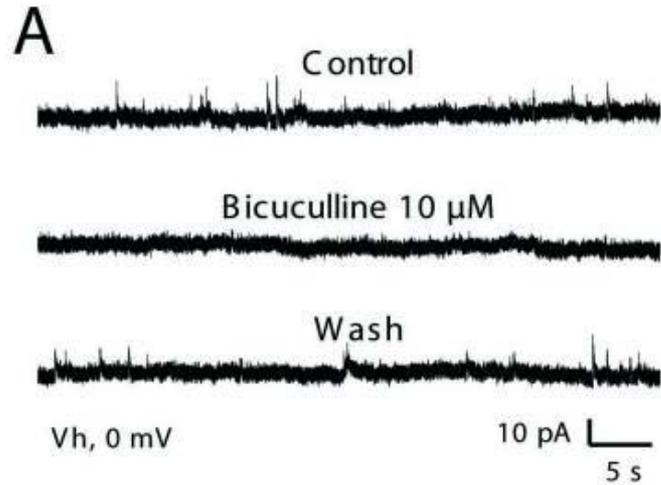
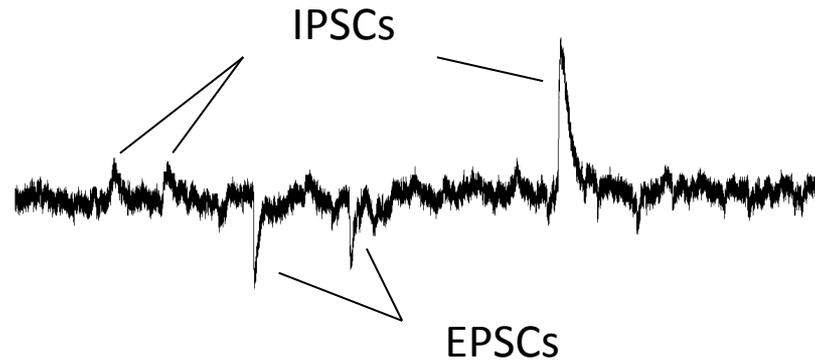
→ Modulation

Lamina II

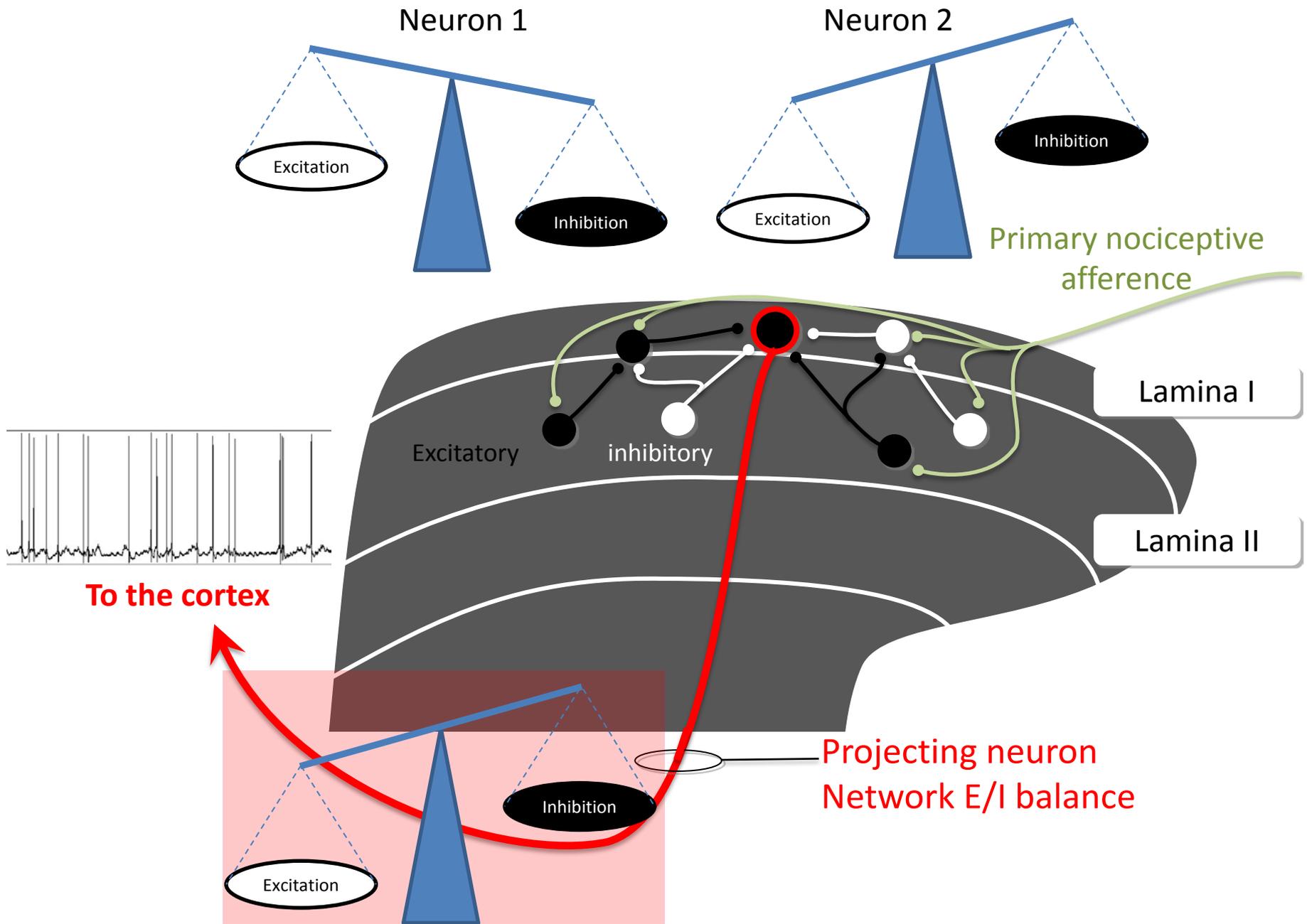
Projecting neuron

Ascending pathway

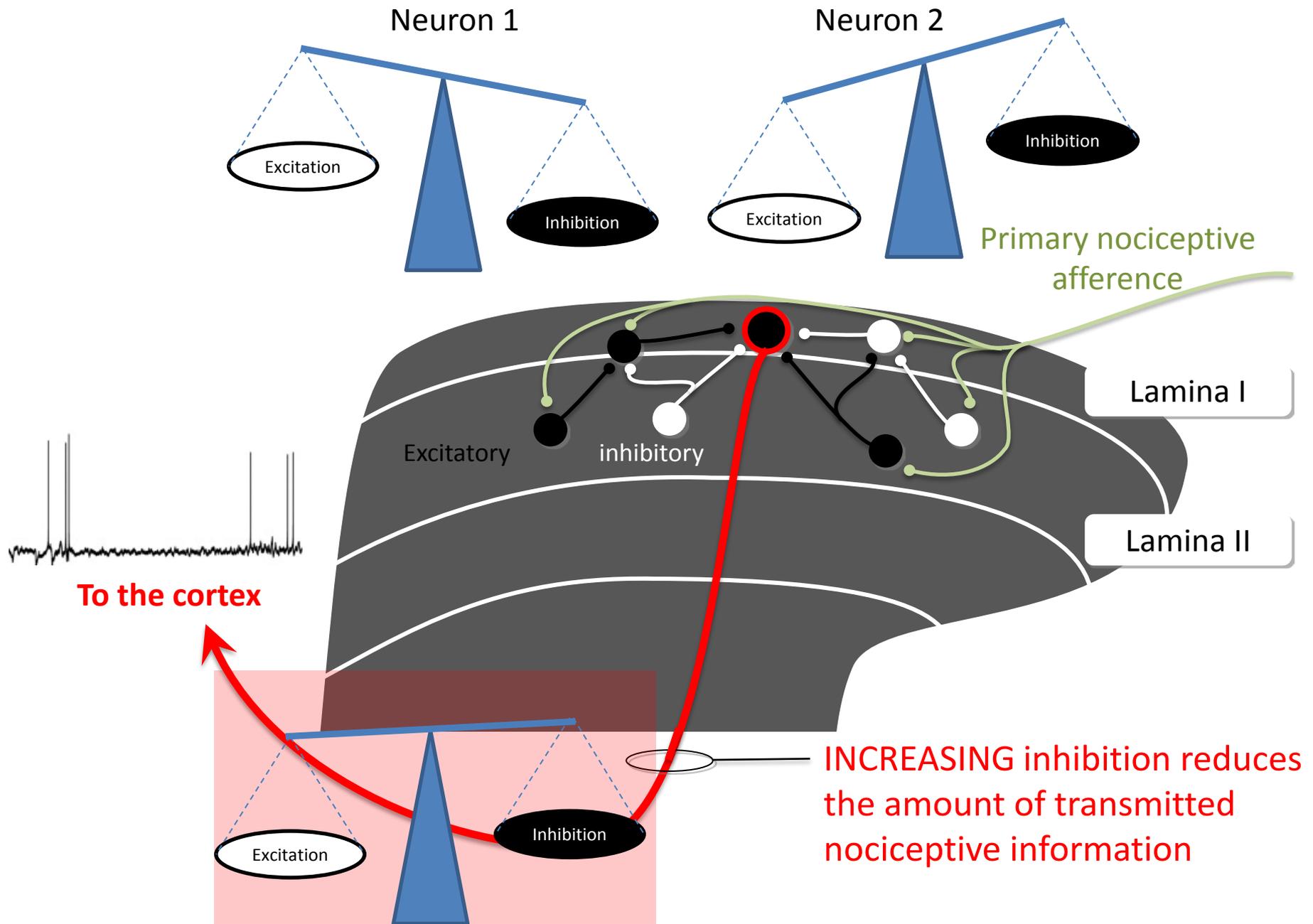
# Introduction: Recording of neuronal network activity (2)



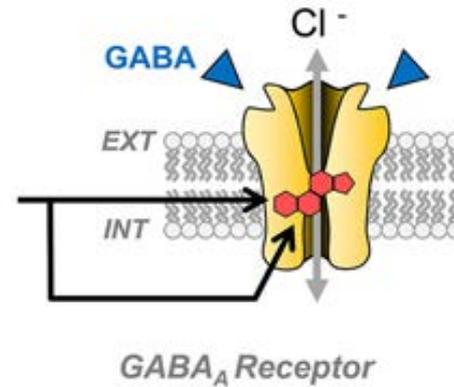
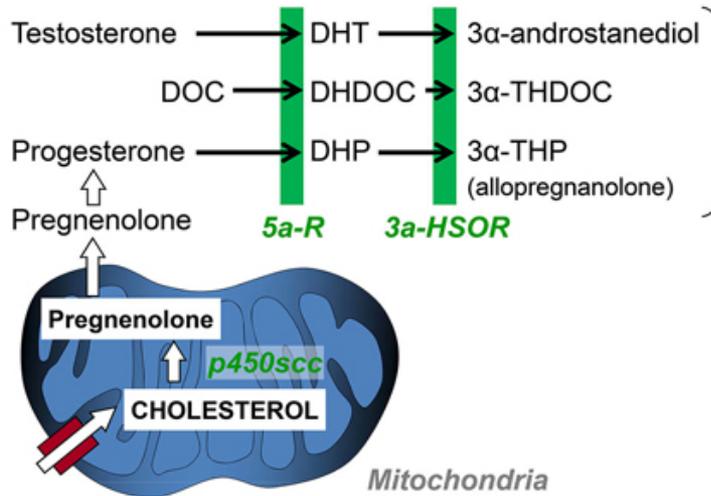
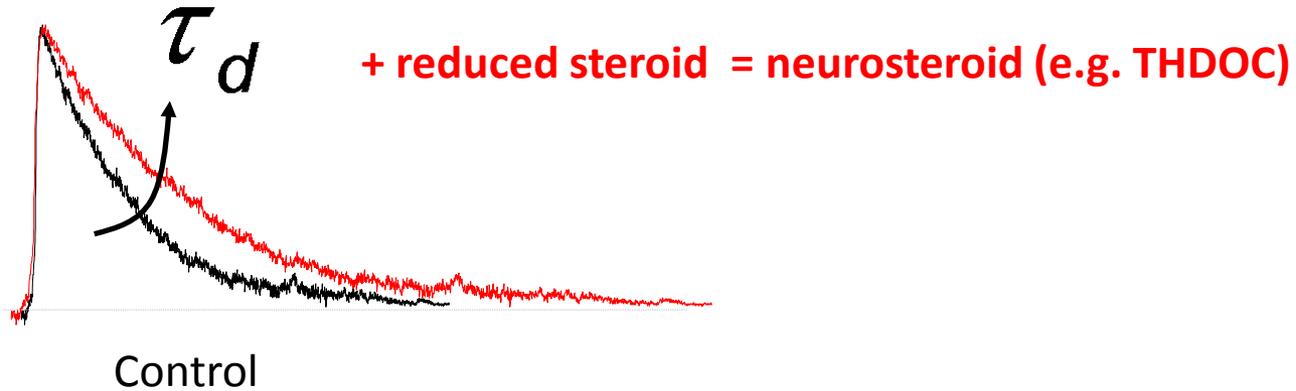
# Introduction: Excitatory/inhibitory balance and network activity



# Introduction: Excitatory/inhibitory balance and network activity



# Introduction: neurosteroides potentiate GABAergic inhibition



## Question ?

Do steroids produced outside of the brain are also able to modulate spinal GABAergic inhibition and therefore decrease pain?

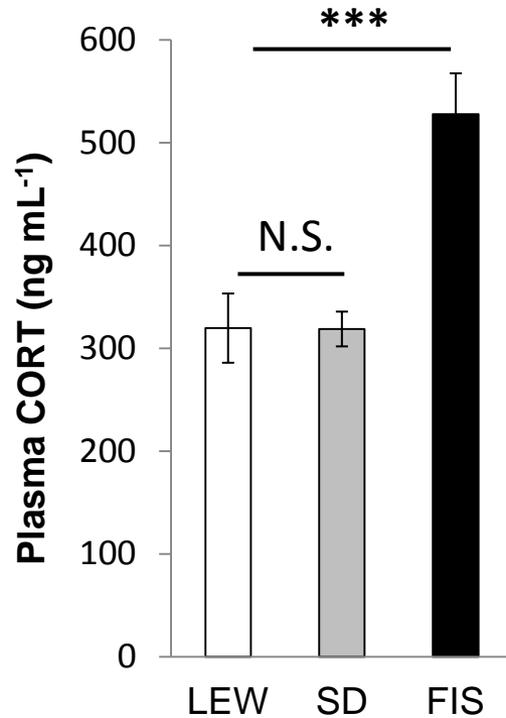
Indeed

a whole class of hormone is composed of non reduced steroid, such as corticosteroid

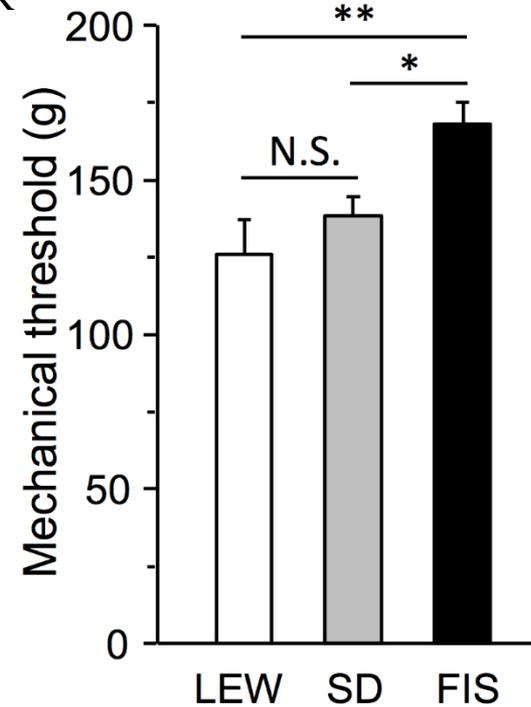
and

we know that the enzymes need to reduce steroids are present in the dorsal horn of the spinal cord.

# Do plasma corticosteroid is able to modulate pain?



(\*\*\* :  $p < 0,001$ ; \*\* :  $p < 0,01$ ; \* :  $p < 0,05$ )

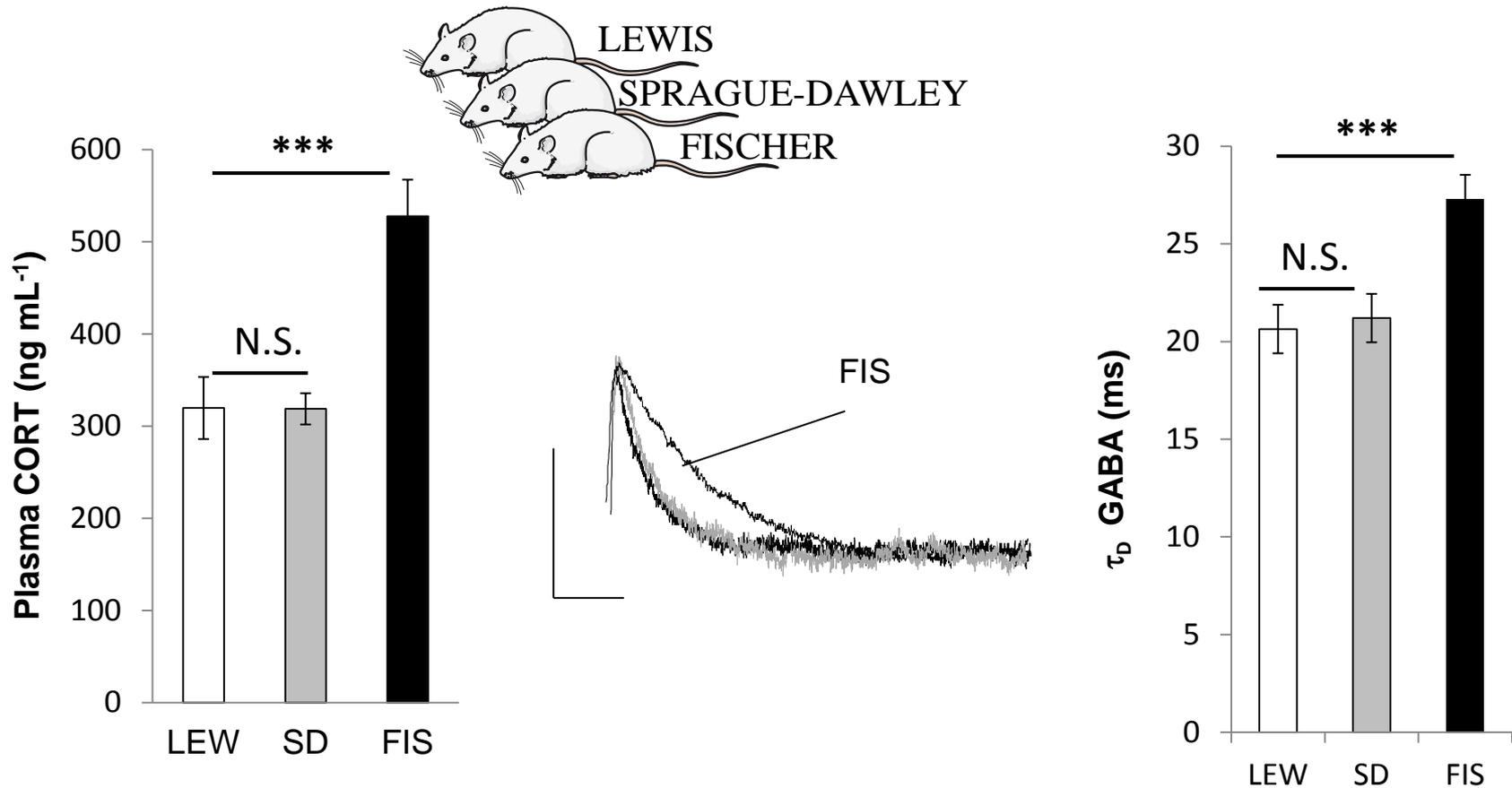


Zell V *et al.* Neurosci Lett. 2014 Aug 22;578:39-43

Rats with higher native level of plasma corticosterone...

... have higher nociceptive threshold.

# Do plasma corticosteroid is able to increase synaptic inhibition?

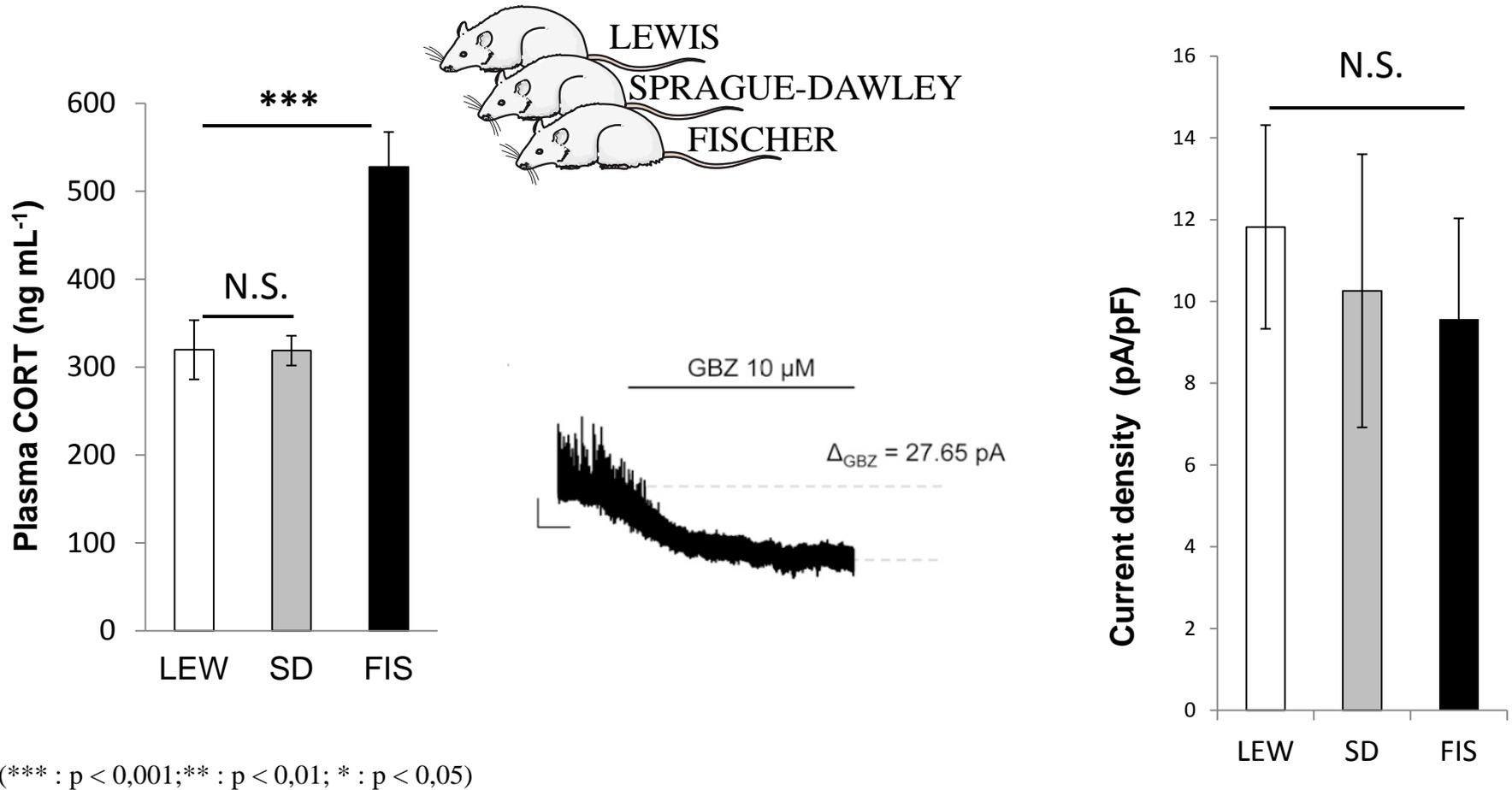


Zell V *et al.* Neurosci Lett. 2014 Aug 22;578:39-43

Rats with higher native level of plasma corticosterone... ..

... have larger GABAergic synaptic inhibition.

# Do plasma corticosteroids alter tonic GABAergic inhibition?



Rats with different native level of plasma corticosterone...

... have a similar tonic GABAergic inhibition.



We have a strong correlation between a level of plasma CORT and

- reduced nociceptive mechanical threshold
- increased synaptic GABAergic inhibition

However, can we demonstrated that CORT is the active molecule that reduces nociceptive mechanical threshold

Indeed

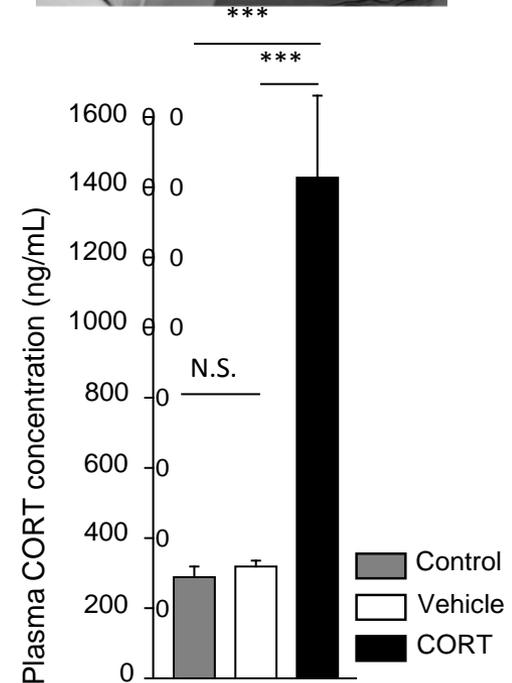
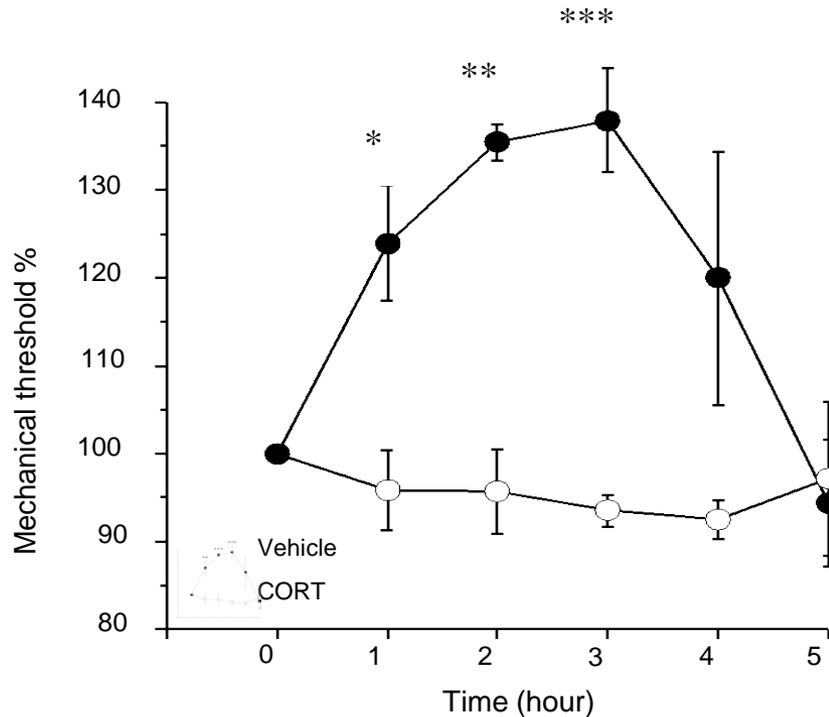
*in vitro* CORT added to a control network does not alter synaptic inhibition.

Moreover

Measuring synaptic activity does not provide a precise estimation the neuronal network activity.

# Does exogenous CORT alter nociceptive threshold?

CORTICOSTERONE

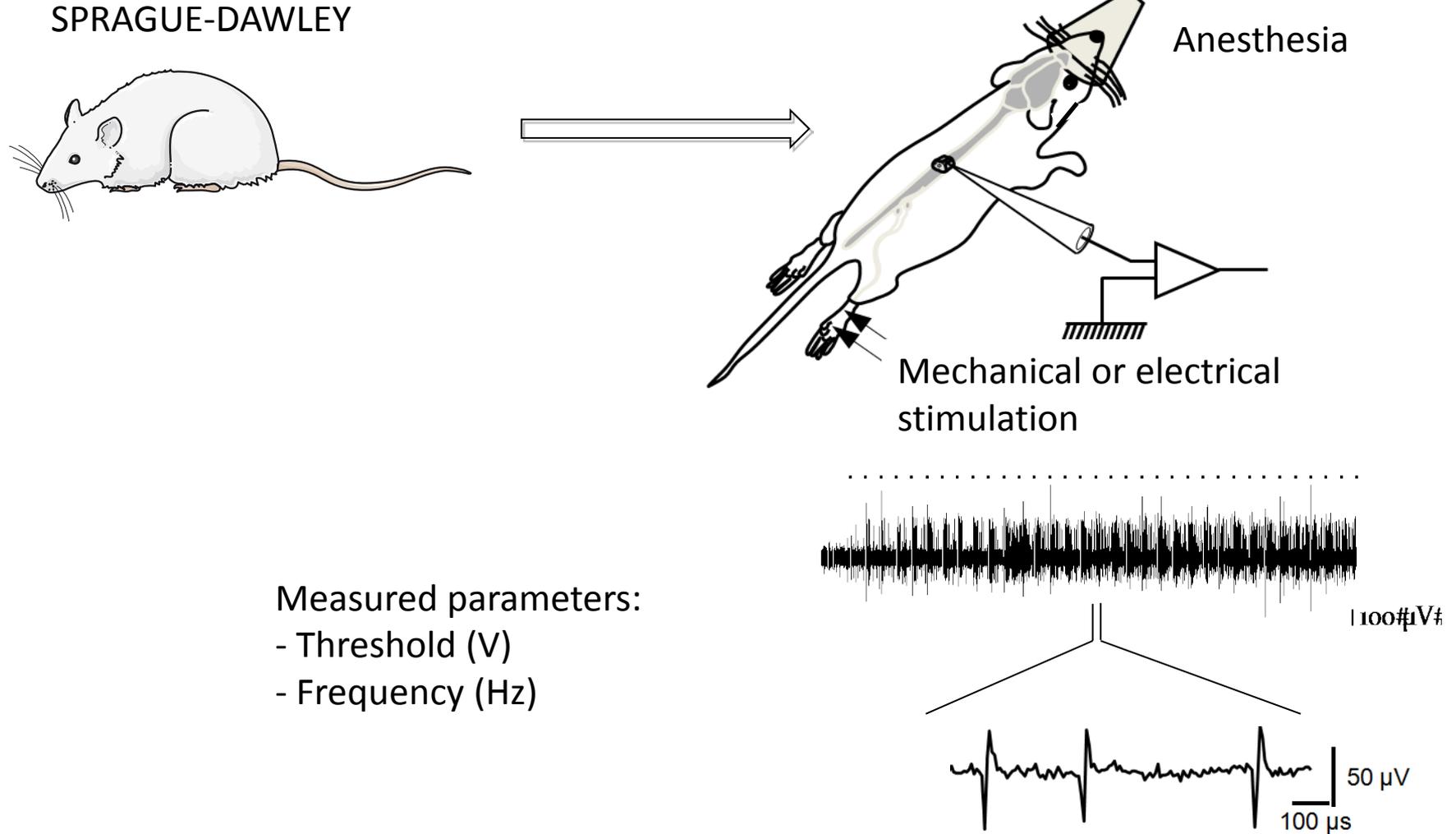


After 2-3 hours, subcutaneously injected CORTICOSTERONE :

- increases mechanical nociceptive threshold
- is detected in the blood.

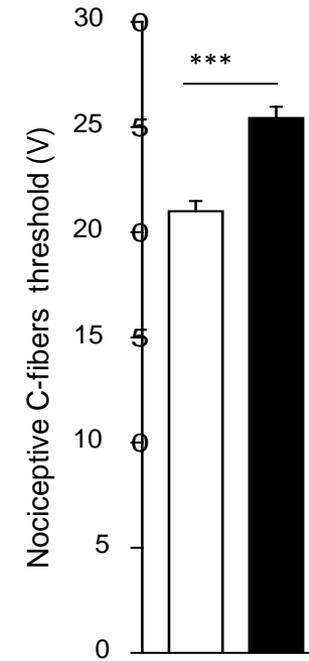
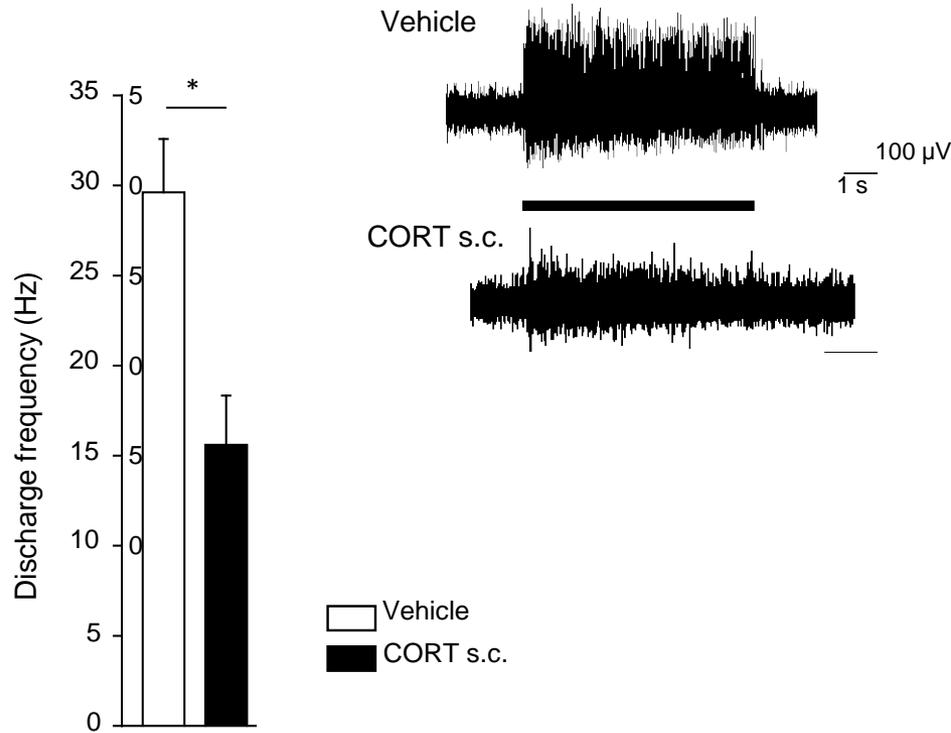


# Does CORT s.c. alter spinal processing of nociceptive input? (1)



*in vivo* extracellular recording of spinal neuron in response to receptive field stimulation provides a overview of the spinal neuronal network activity and of its output

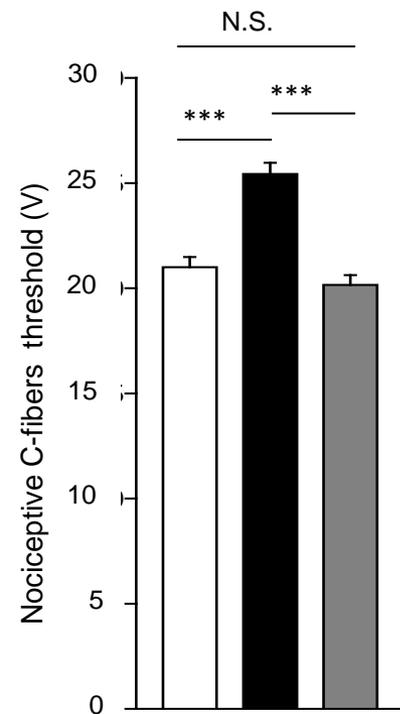
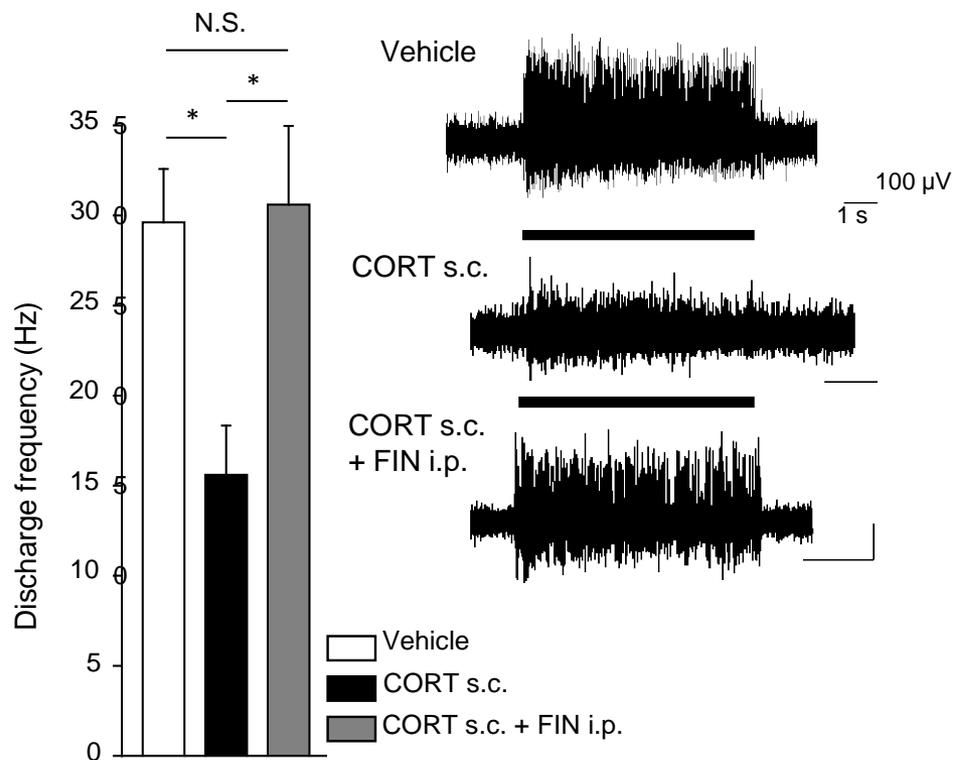
# Does CORT s.c. alter spinal processing of nociceptive input? (2)



Zell *et al.* Eur J Neurosci. 2015 Feb;41(3):390-7

Subcutaneously injected CORT reduces the spinal neuronal network excitability

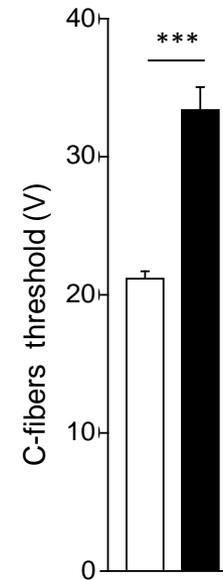
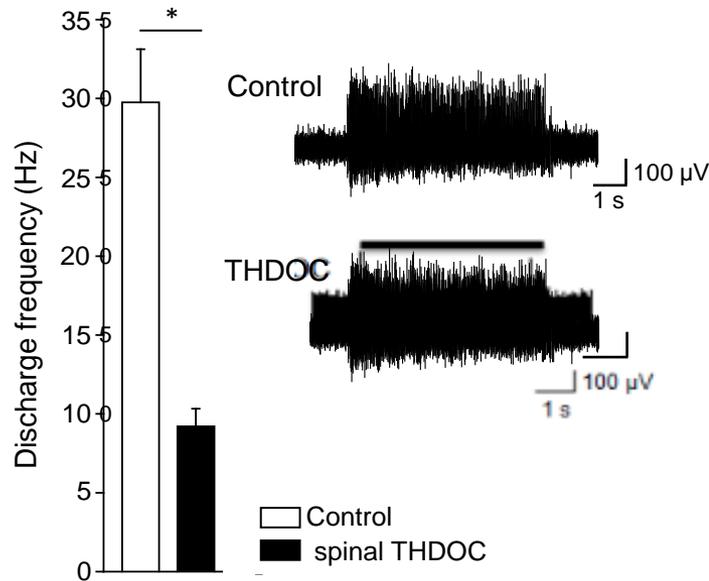
# Does CORT s.c. alter spinal processing of nociceptive input? (3)



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The effect of CORT s.c. is prevented by the blockage of steroid reduction enzyme.  
CORT needs to be converted in reduced steroid to be active.

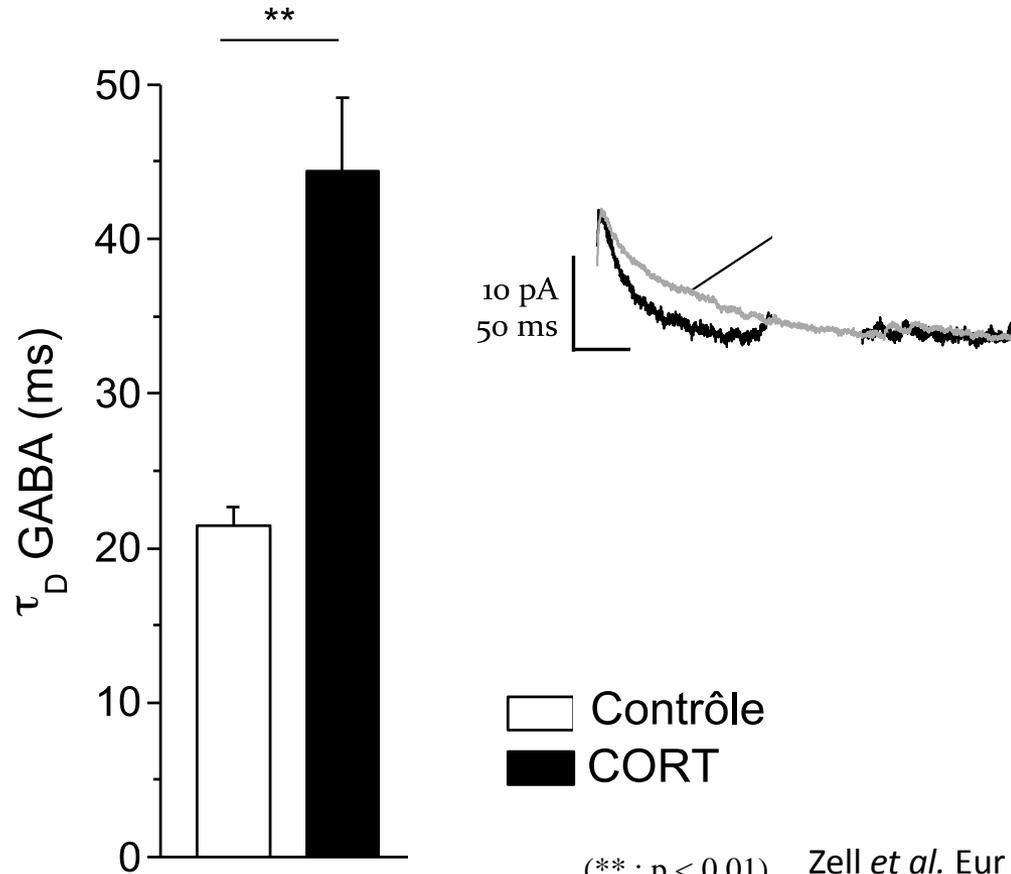
# Where does reduced CORT act?



Zell *et al.* Eur J Neurosci. 2015 Feb;41(3):390-7

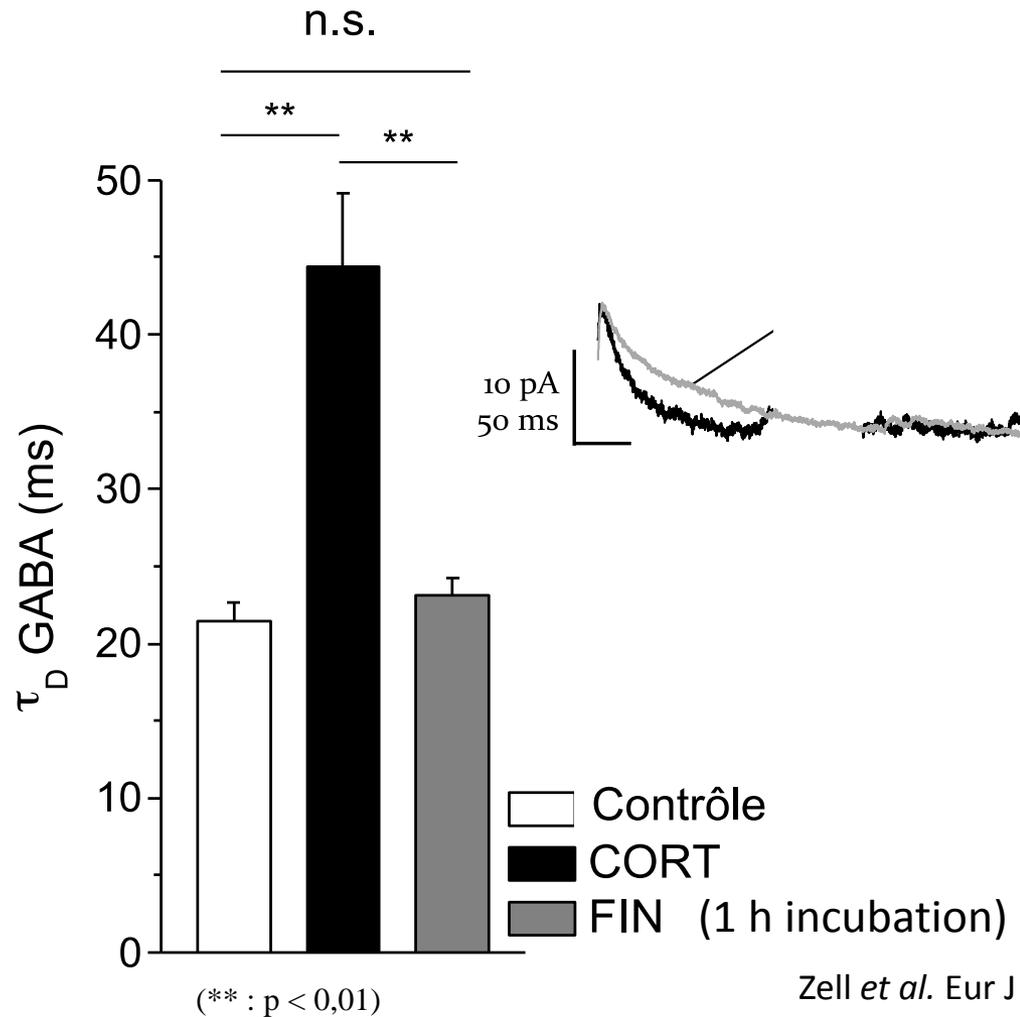
Applying directly on the spinal cord exogenous reduced CORT (THDOC) mimics the action of plasma CORT

# How does reduced CORT act? (1)



Subcutaneously injected CORT increases GABAergic synaptic inhibition

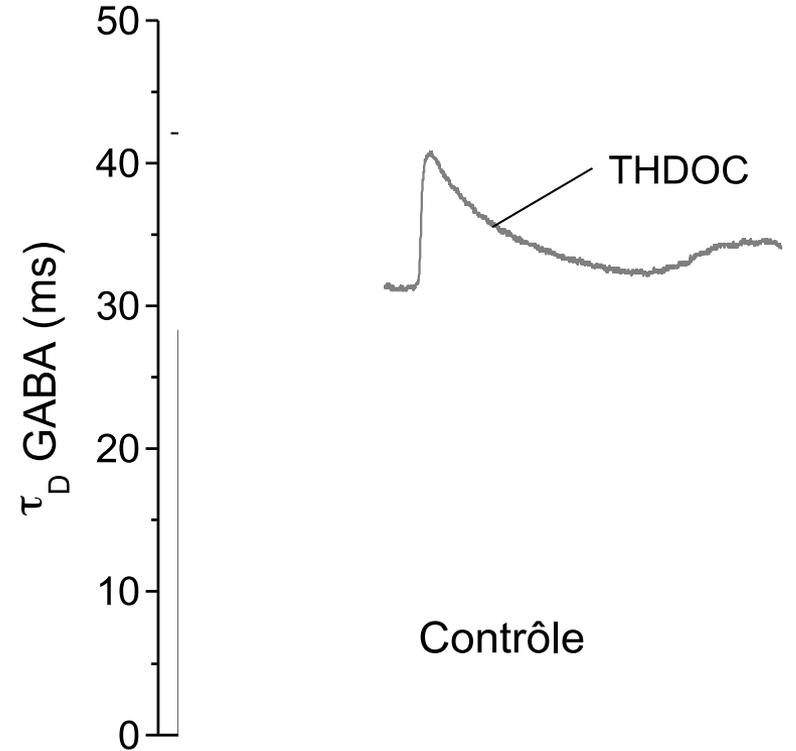
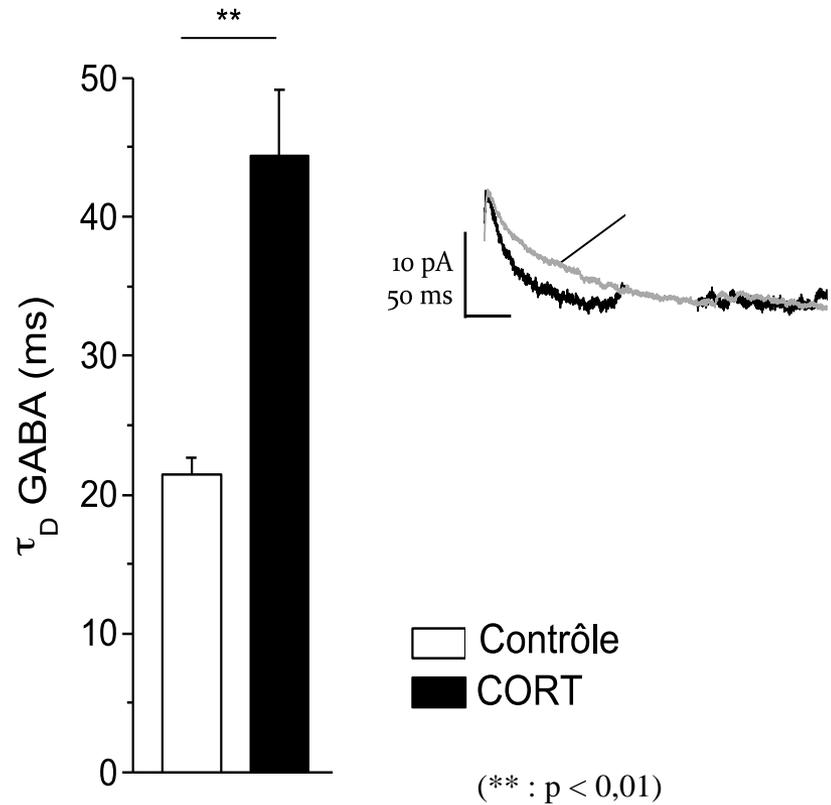
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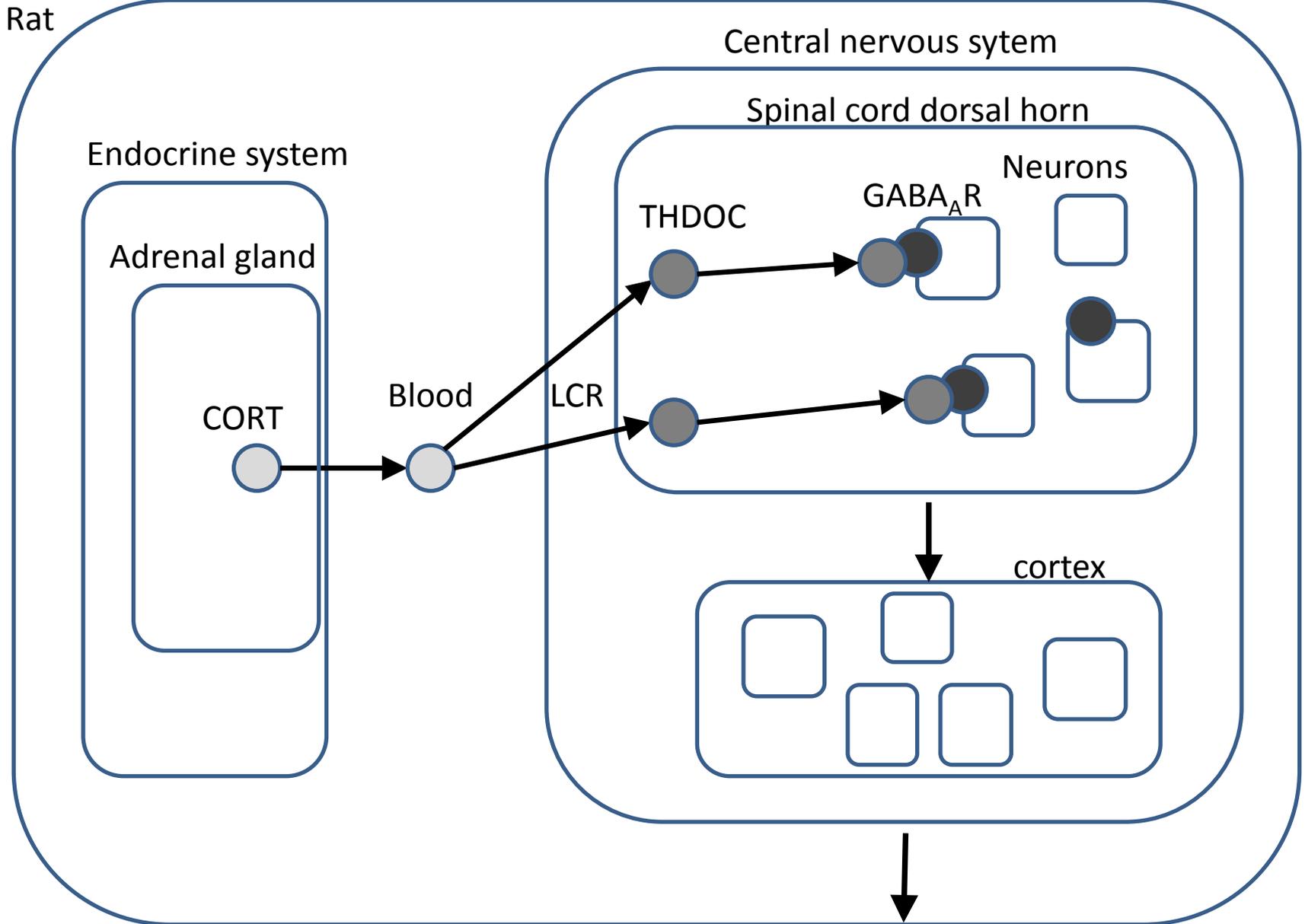
# How does reduced CORT act? (3)



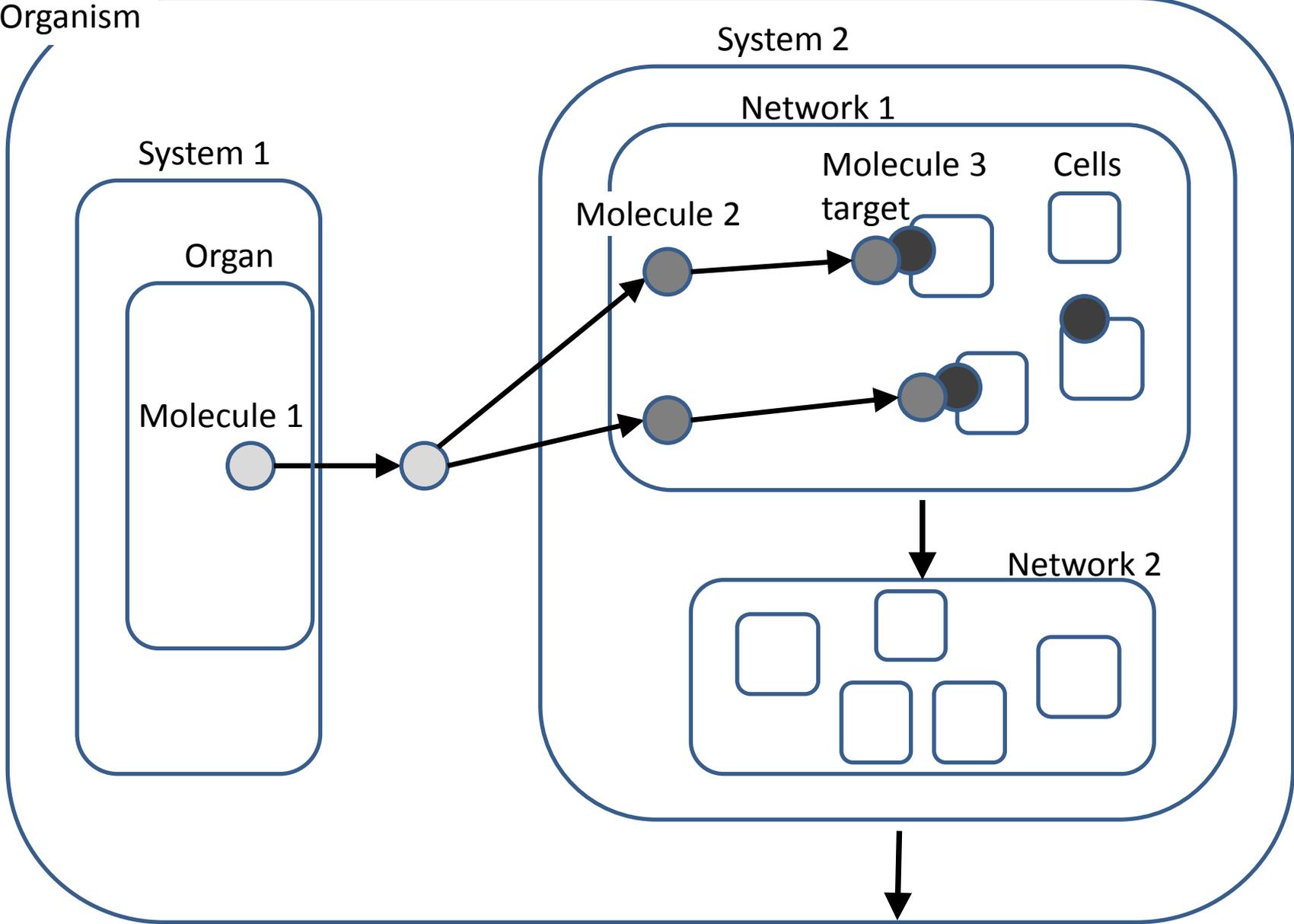
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Applying directly on the spinal cord exogenous reduced CORT (THDOC) mimics the action of plasma CORT

# Plasma CORT modulates pain perception



# A multiscale, multisystem mechanism



## References

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