

# **LDN, Neuroinflammation and Movement Disorders**

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Remission of Complex Regional Pain Syndrome symptoms,  
including Fixed Dystonia

Low-Dose Naltrexone - glial attenuator

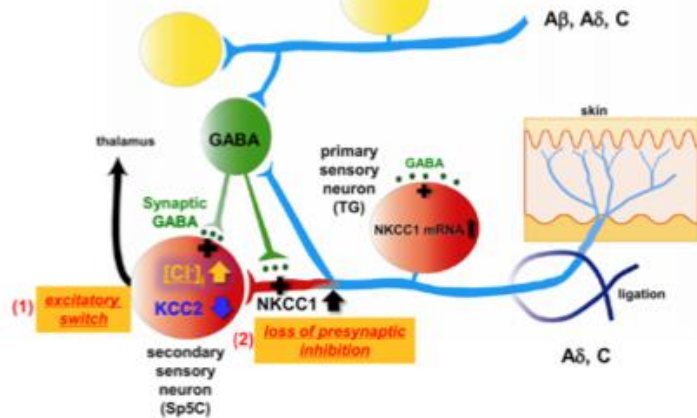
4.5 mg/daily

Pradeep Chopra, MD (Brown University Medical School)

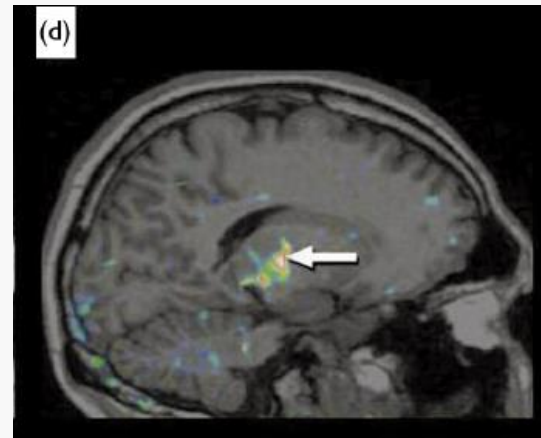
Chopra Cooper (2013)  
J Neuroimmune Pharm

Synaptic Conversion

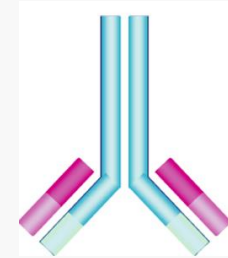
Loss of Pain Gate



Supraspinal Neuroinflammation

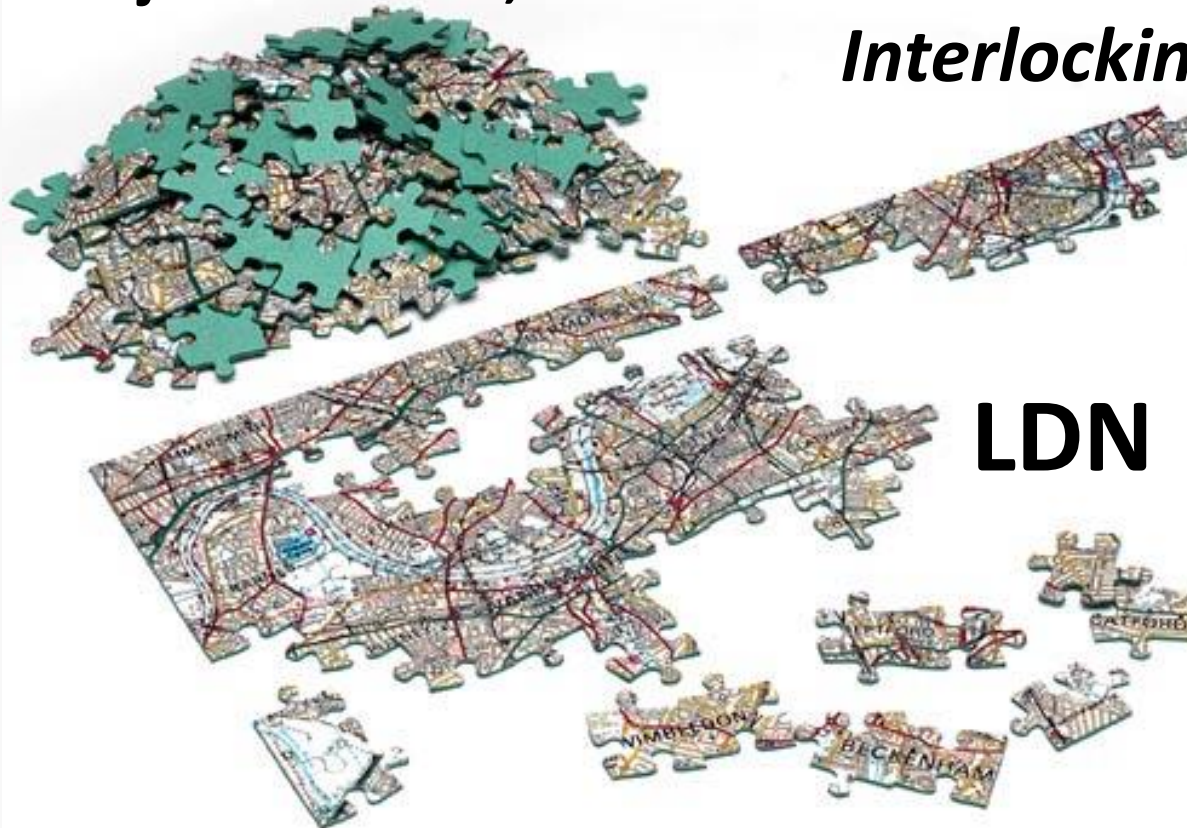


Autoantibodies



Injured Nerves, Activated Glia

*Interlocking Pathologies*



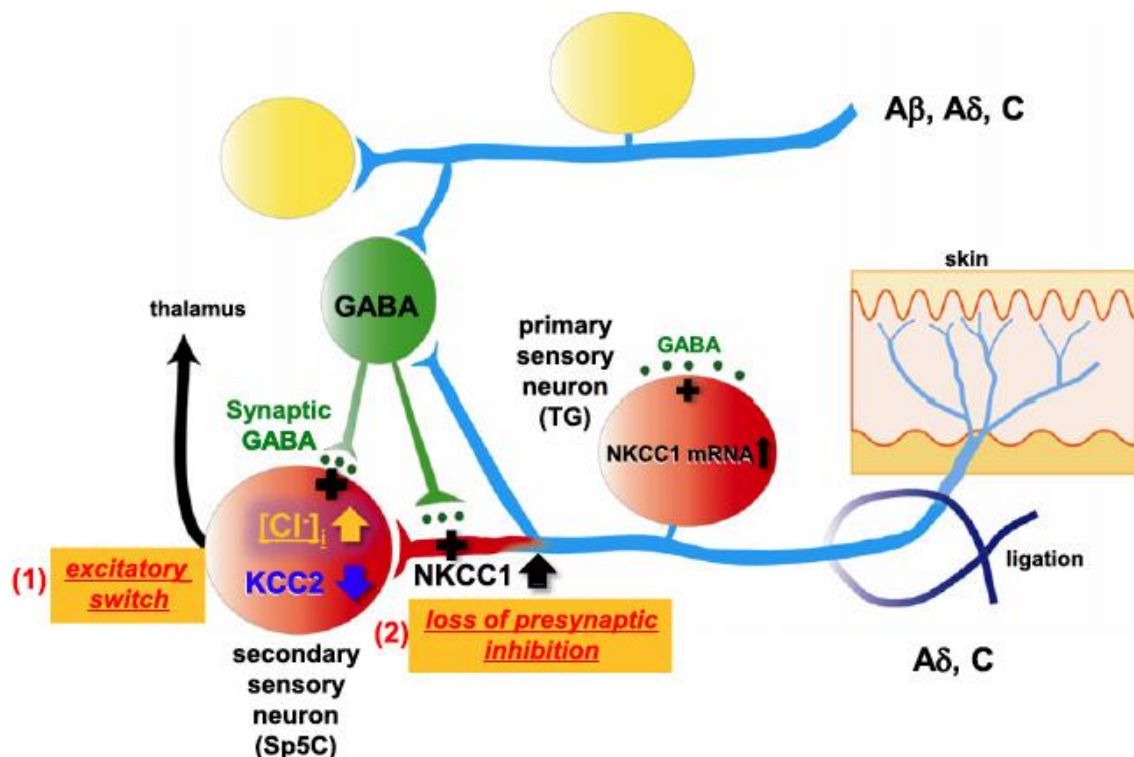
**LDN**

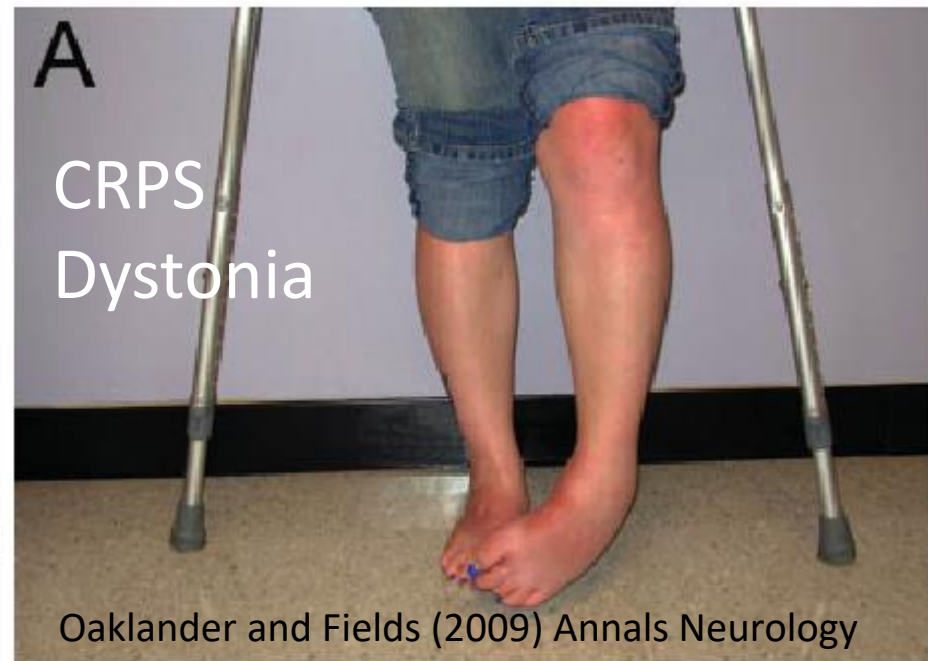
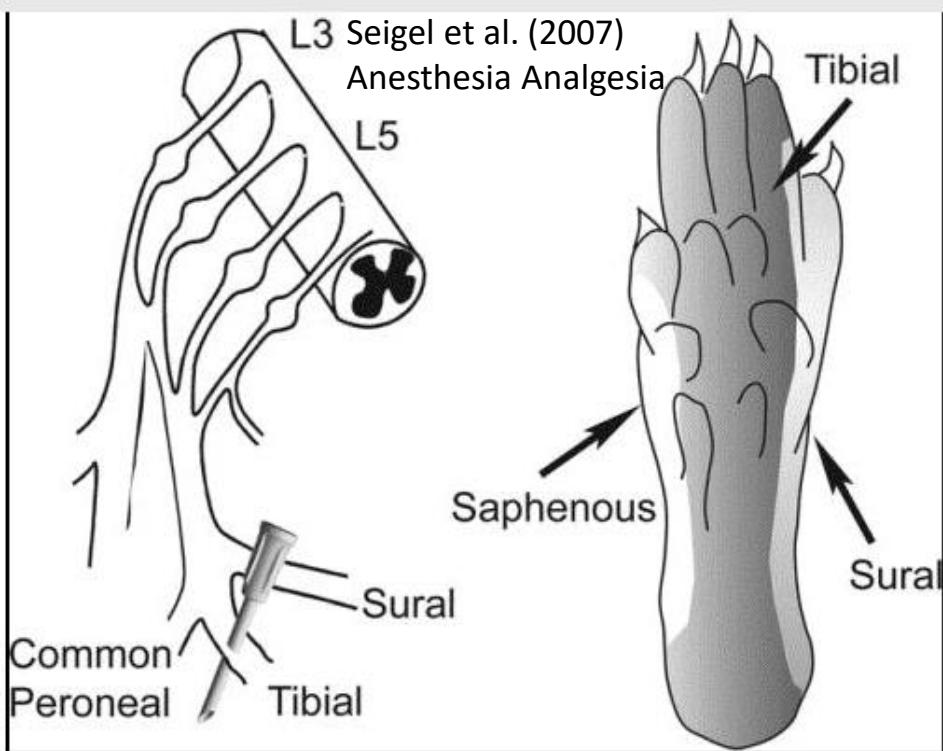




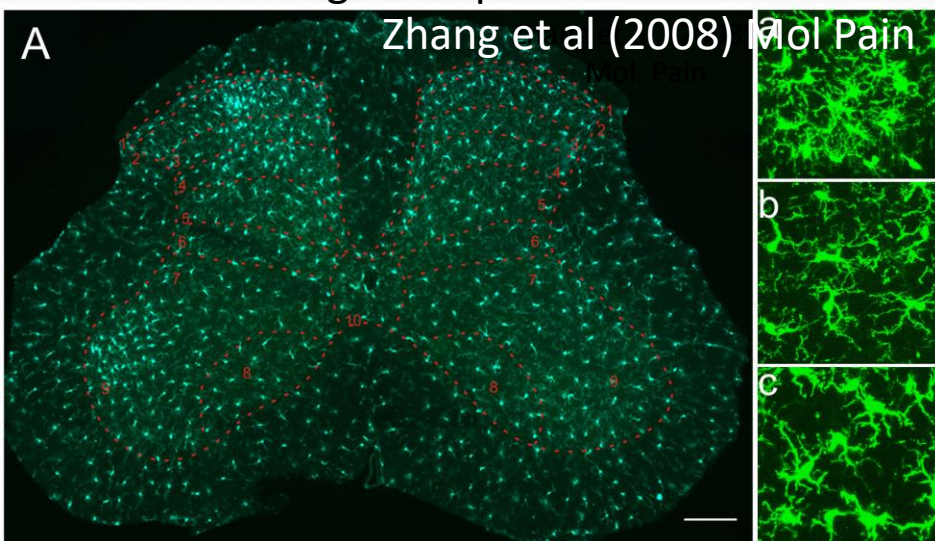
Neuroinflammation can cause Synaptic Conversion, and loss of the spinal pain gate

A Mechanism for Allodynia (extreme tactile pain)

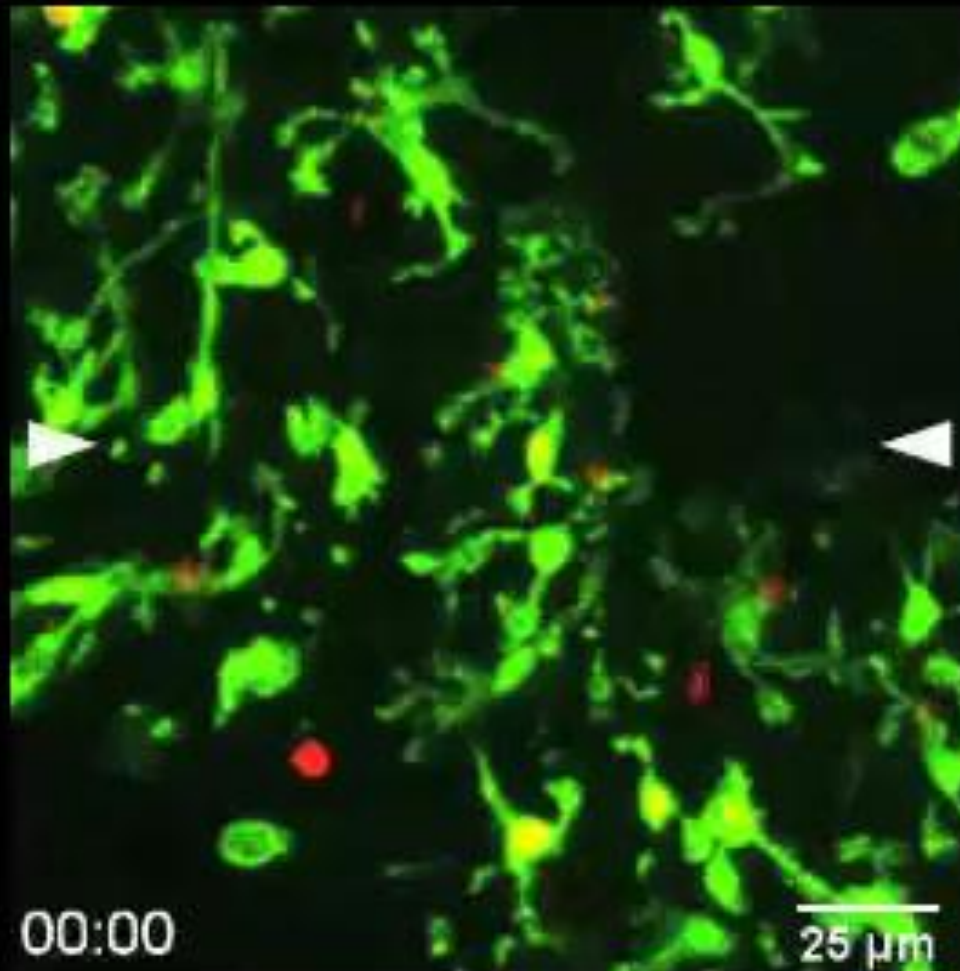




## Activated Microglia in Spinal Cord







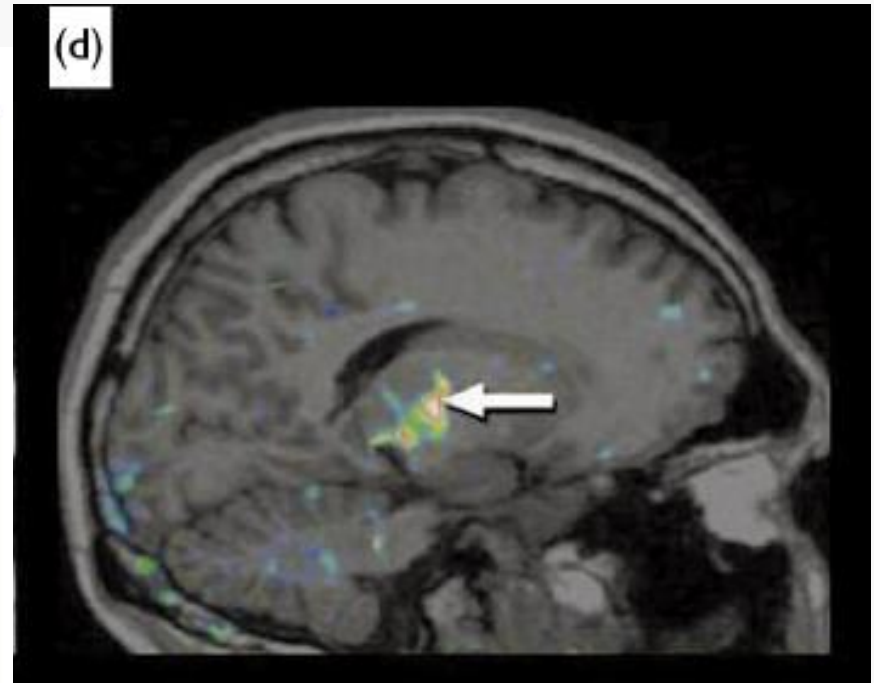
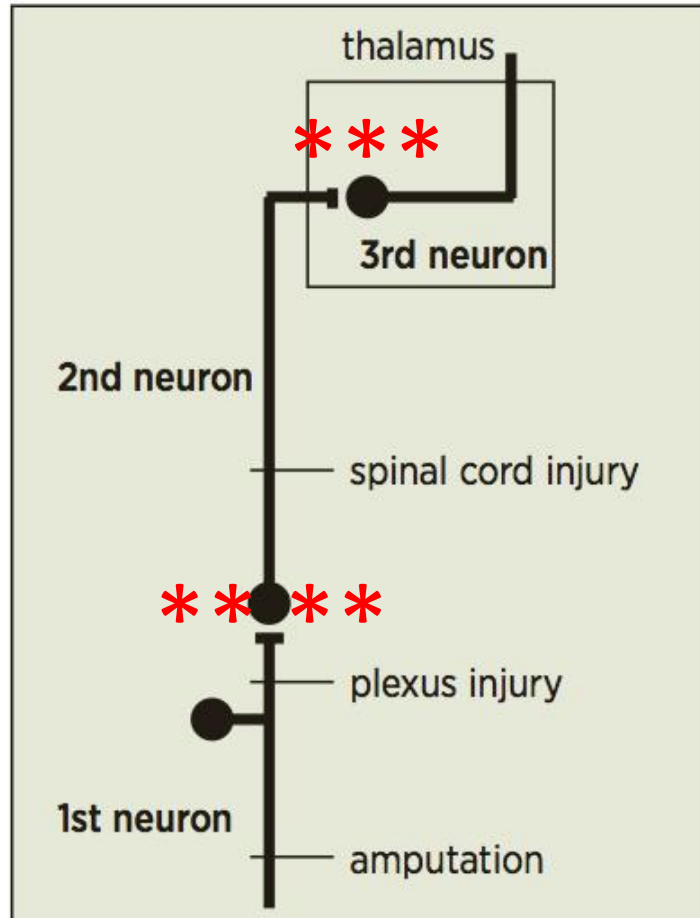
Microglial Activation (Mike Dailey, U. Iowa)

fixed Dystonia

# Inflammation in the Thalamus can Cause Chronic Pain

Banati et al. (2001)

Figure 2A



Remote neuroimmune activation following peripheral nerve injury (Banati et al, NeuroReport (2001)). A. Schematic Diagram: A peripheral nerve injury induces a transsynaptic activation of microglia in the projection area of the second-order neuron. B. Experimental Evidence for the Model: No structural changes can be detected in the brain of a patient with chronic pain, 36 months after amputation of the forearm (volumetric T1-weighted MRI). In contrast, [ $^{11}\text{C}$ ] (R)-PK11195 PET (a marker for activated microglia) superimposed onto the patient's MRI reveals a significant regional increase in [ $^{11}\text{C}$ ] (R)-PK11195 binding, signifying the presence of persistent activated microglial cells in the left ventral posterolateral nucleus of the thalamus (white arrow), contralateral to the peripheral nerve injury (reproduced with permission from Lippincott, Williams & Wilkins, publisher of NeuroReport).

## Thalamocortical radiations

Central sulcus

### Thalamic nuclei

**CM** Centromedian  
**LD** Lateral dorsal  
**LP** Lateral posterior  
**MD** Medial dorsal  
**VA** Ventral anterior  
**VI** Ventral intermedial  
**VL** Ventral lateral  
**VPL** Ventral posterolateral  
**VPM** Ventral posteromedial

From globus pallidus and substantia nigra

Reticular nucleus (*pulled away*)

From cerebellum

Somesthetic from body (spinothalamic tract and medial lemniscus)

Somesthetic from head (trigeminal nerve)

Internal medullary lamina

Intralaminar nuclei

Other medial nuclei

Midline (median) nuclei

Interthalamic adhesion

*F. Netter M.D.*

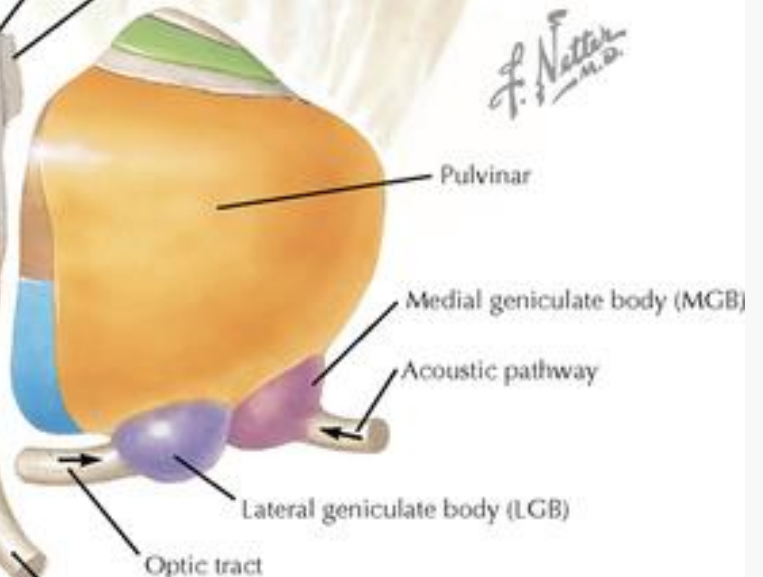
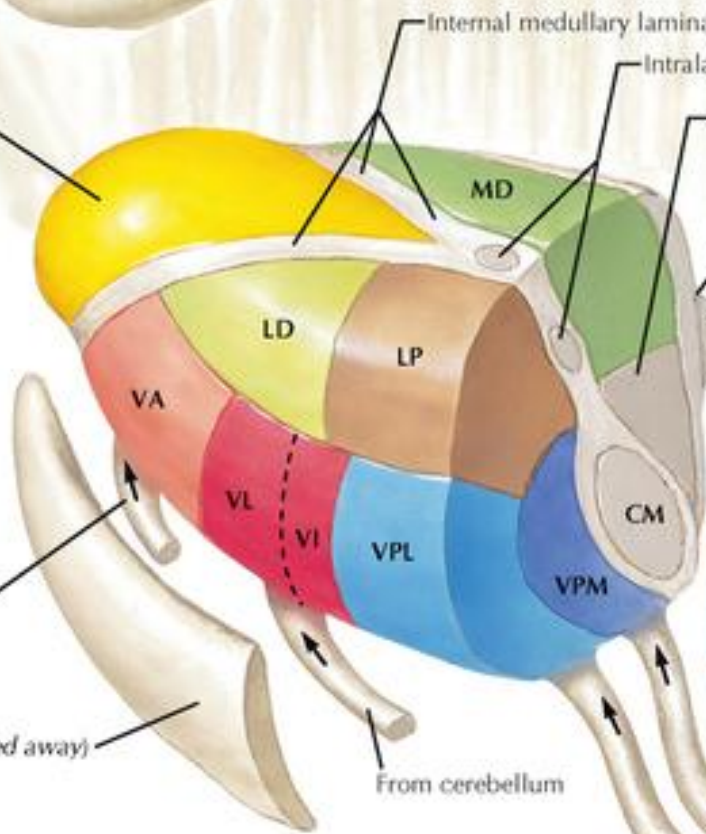
Pulvinar

Medial geniculate body (MGB)

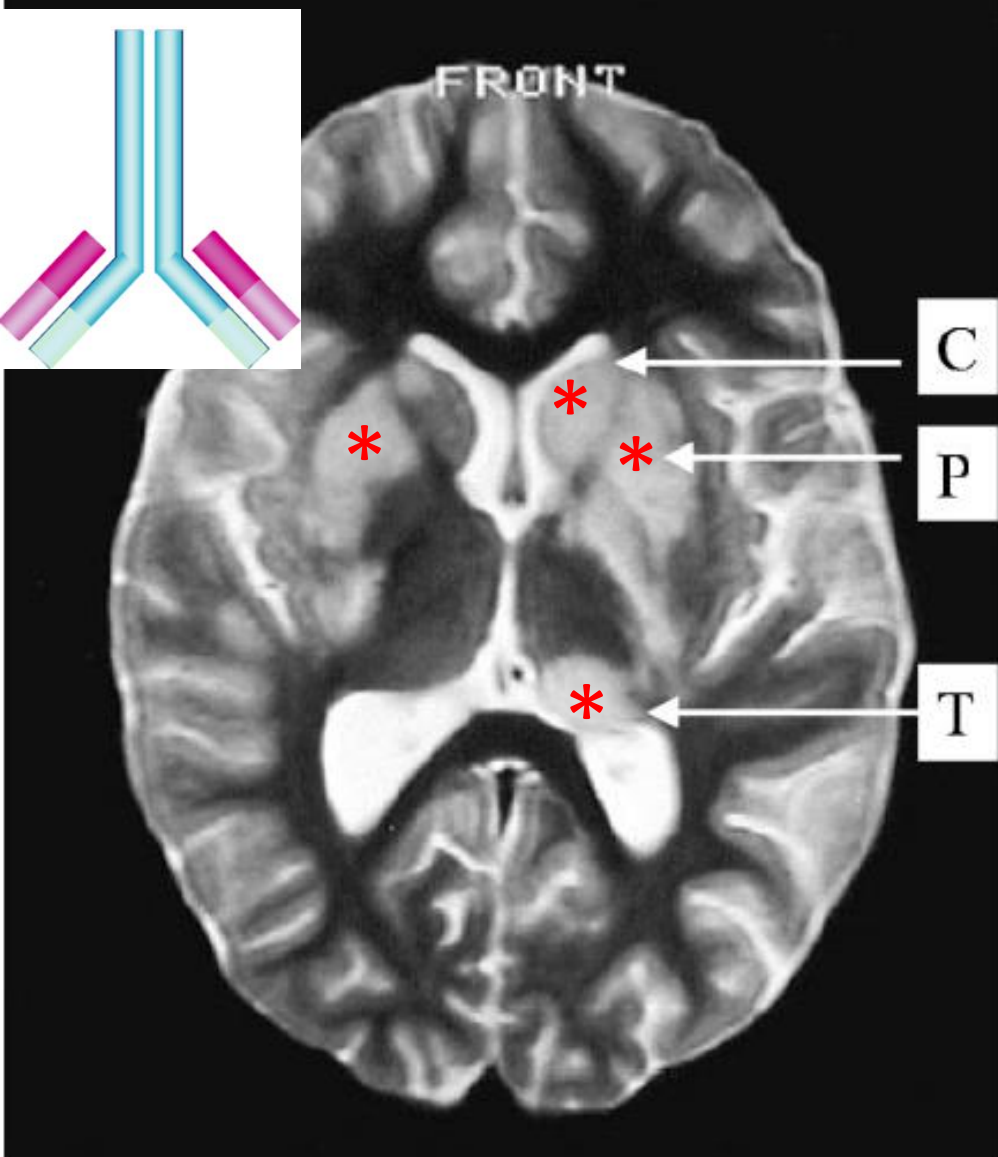
Acoustic pathway

Lateral geniculate body (LGB)

Optic tract







**Figure 1.** Post-streptococcal encephalitis presenting with dystonia and behavioural alteration. MRI brain T2 weighting, demonstrating inflammatory changes in bilateral caudate nuclei (C) bilateral putamen (P) and thalamus (T).



**Autoantibodies**

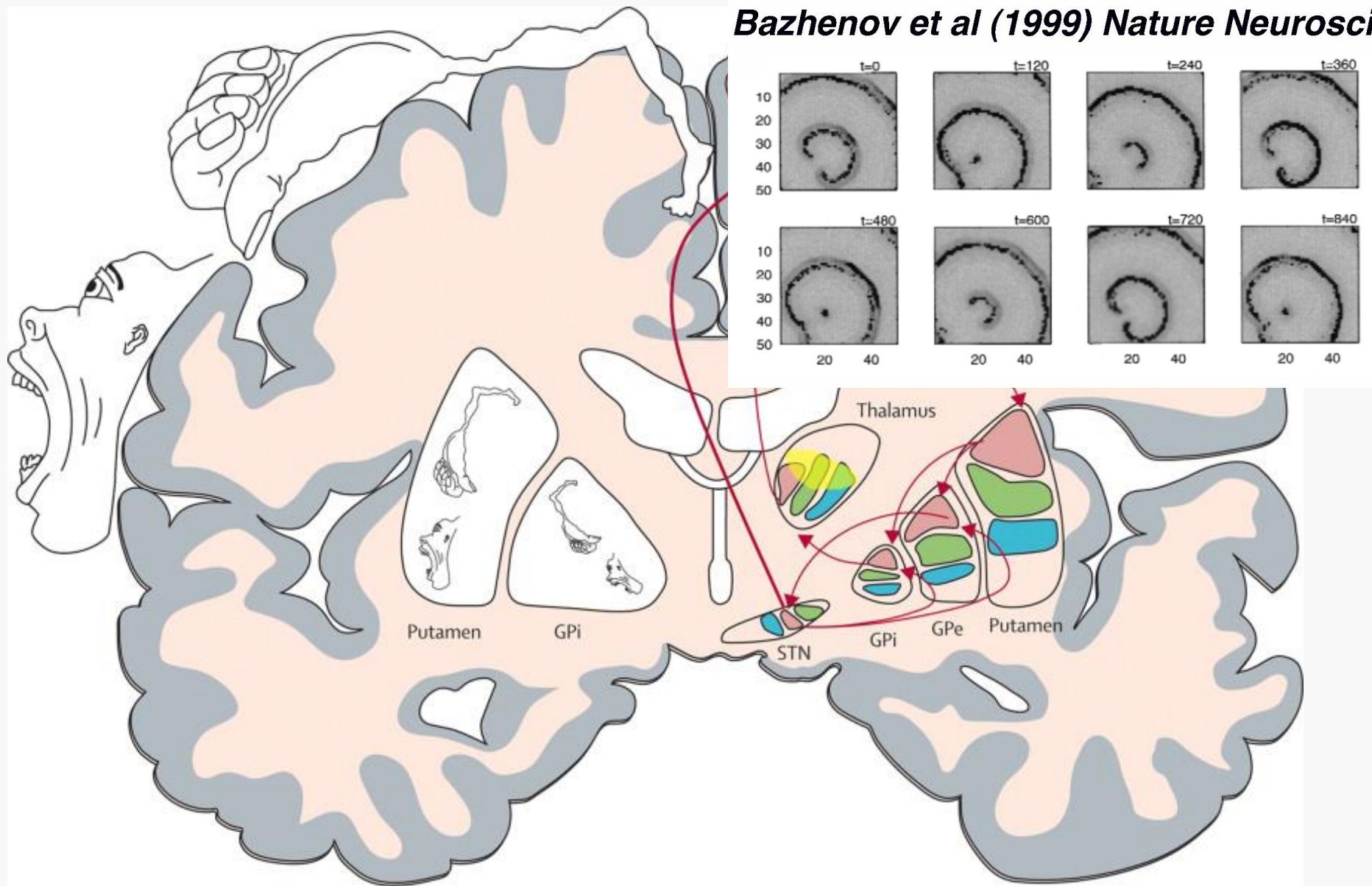
**Inflaming the Brain**

Dale (2003) Q J Med

# A Hemidystonia Responsive to Low-Dose Naltrexone

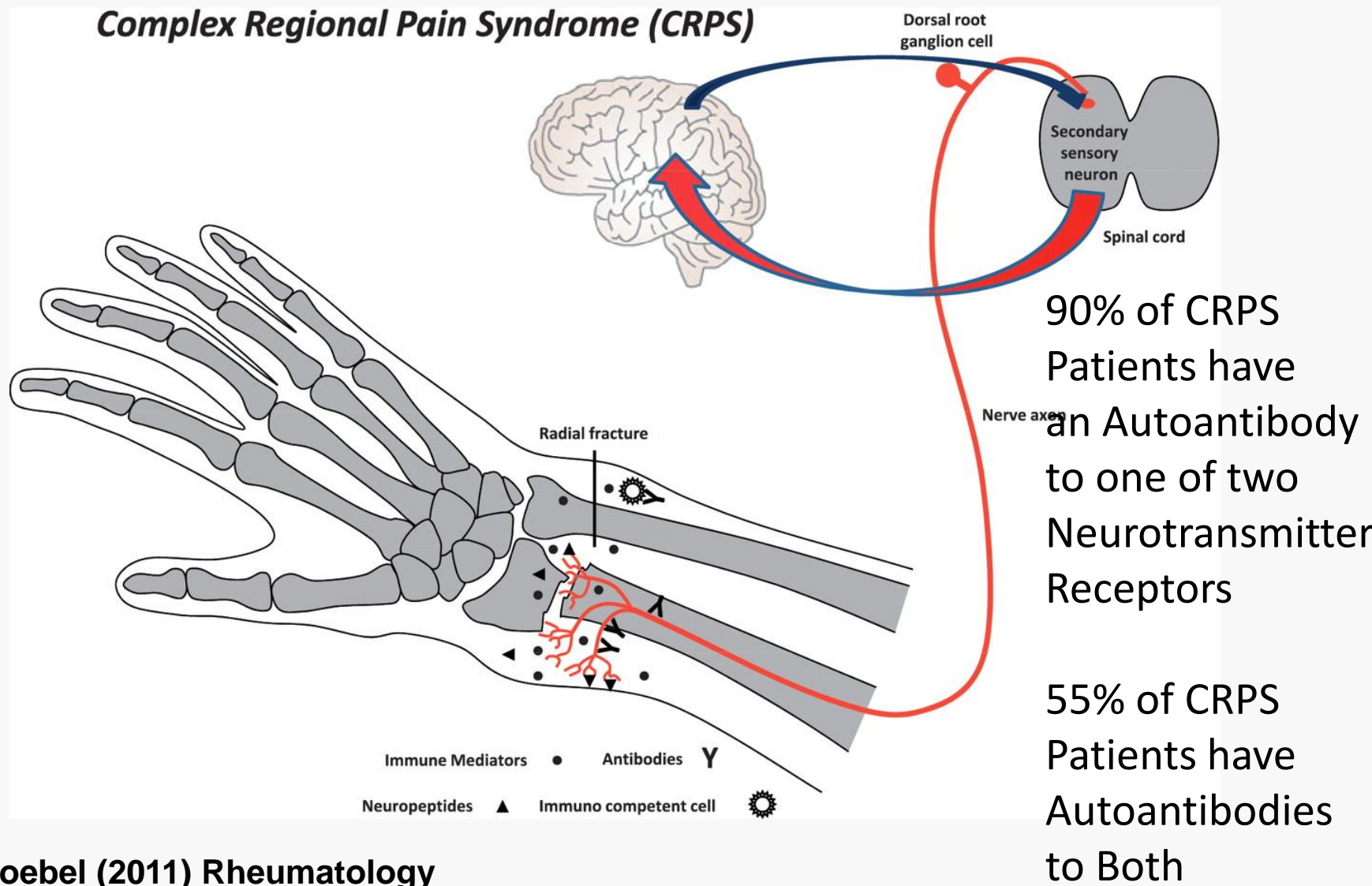






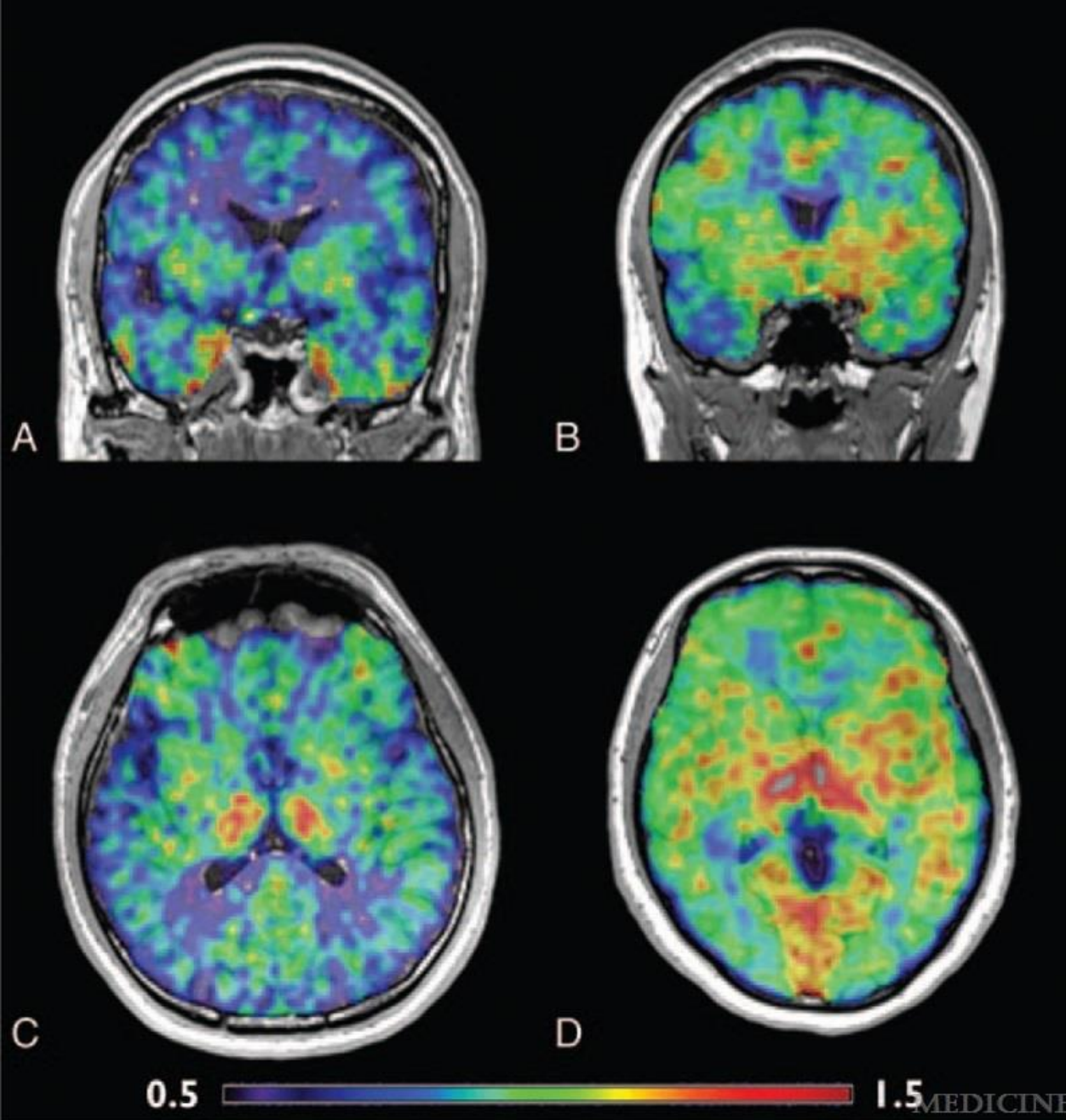


# Conceptual Model of CRPS: An Autoantibody-Mediated Neuroinflammatory Disorder



**Goebel (2011) Rheumatology**

**RHEUMATOLOGY**



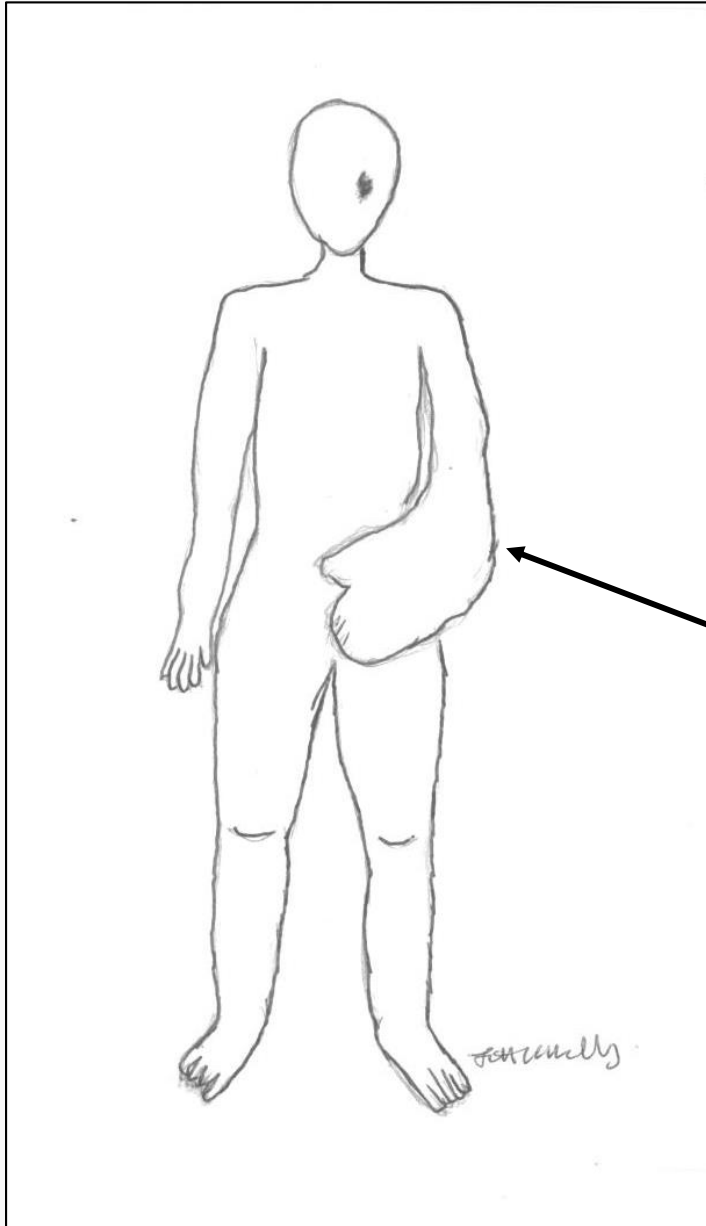
Activated Microglia in  
the Thalami and Basal  
Ganglia of a CRPS Patient  
(panels B and D)

11C-PK11195 PET/MRI  
scan

Jeon et al (2017)  
Medicine

# Altered body perception in a CRPS Patient

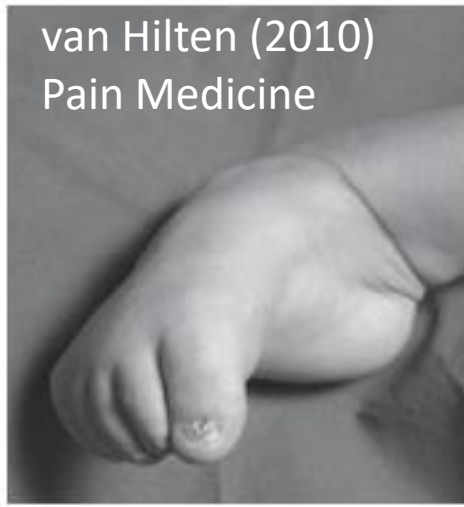
(Candy McCabe, Univ. of the West, UK)







van Hilten (2010)  
Pain Medicine



**Figure 1** Shows examples of upper and lower extremity dystonia in CRPS patients.

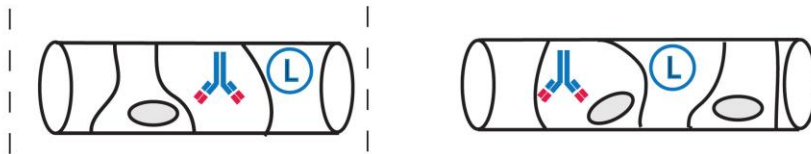
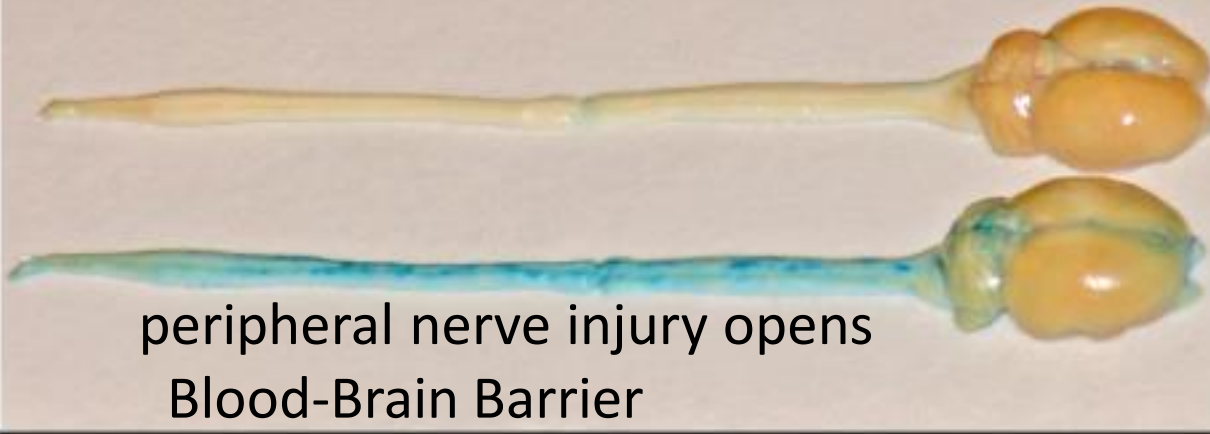


Before Ketamine



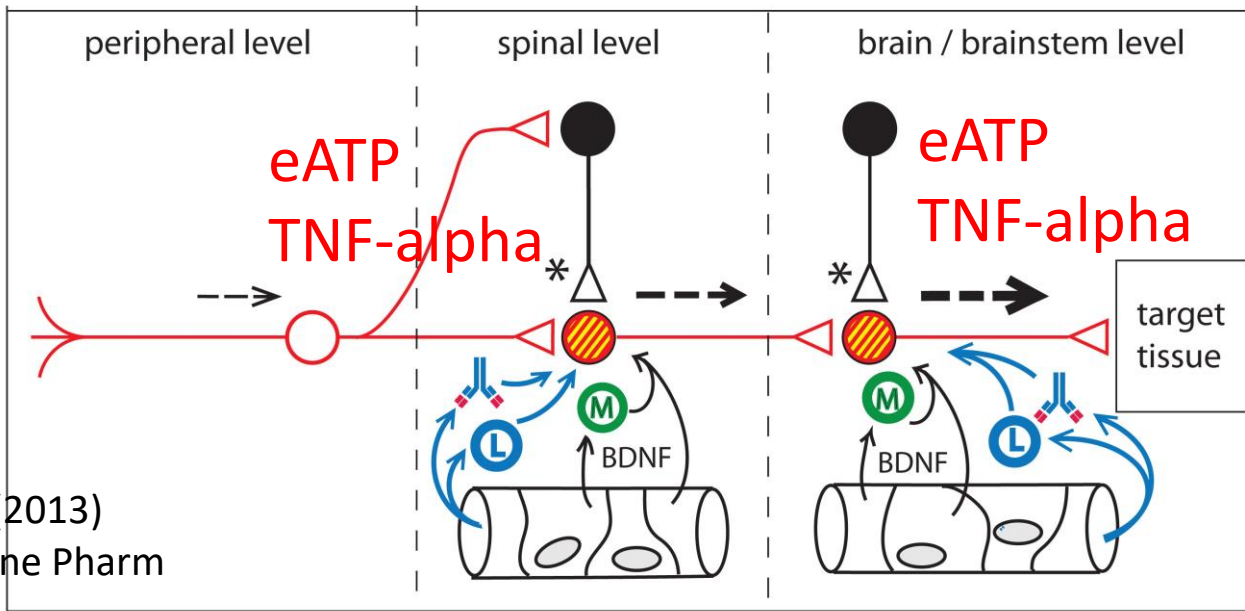
After Ketamine

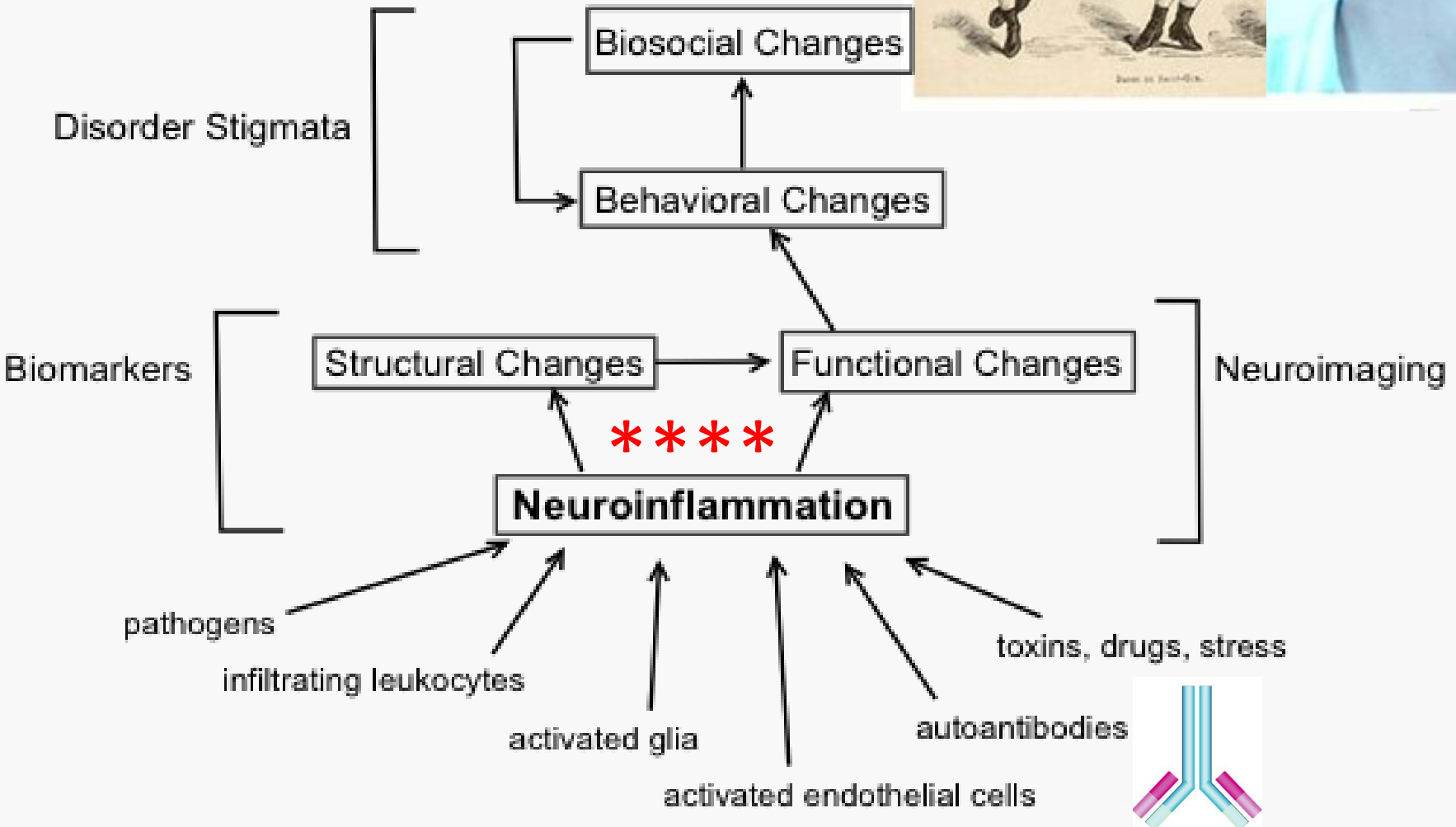
# Beggs et al (2010) Molecular Pain



B

## Low Dose Naltrexone (inhibits TLRs)







# Conclusions

- Neuroinflammation can spread through the neuraxis via axonal projections
  - Autoantibodies can ignite neuroinflammation
  - Fixed dystonic postures can arise in certain neuroinflammatory disorders
- Some of these disorders are responsive to LDN

# A Clinical Lesson at the Salpêtrière

Harris (2005) Arch Gen Psychiatry

*Hysteria has its laws, its determination, precisely like a nervous ailment with a material lesion. Its anatomical lesion still eludes our means of investigation . . .*

Jean-Martin Charcot, 1890<sup>1(p77),2(p208)</sup>



The LDN 2018 Conference Presentation

By

Mark S. Cooper, PhD

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