Complex Regional Pain Syndrome

Aaditya Verma, MSIV

History

- Described by Paul Sudeck over 100 years ago in paper discussing post-traumatic bone atrophy

- Publications have used over 72 names for syndrome
  - Reflex sympathetic dystrophy, causalgia, Sudeck's atrophy, transient osteoporosis, algodystrophy, etc

- 1993 in Orlando: International Association for the Study of Pain agreed on CRPS

What is CRPS?

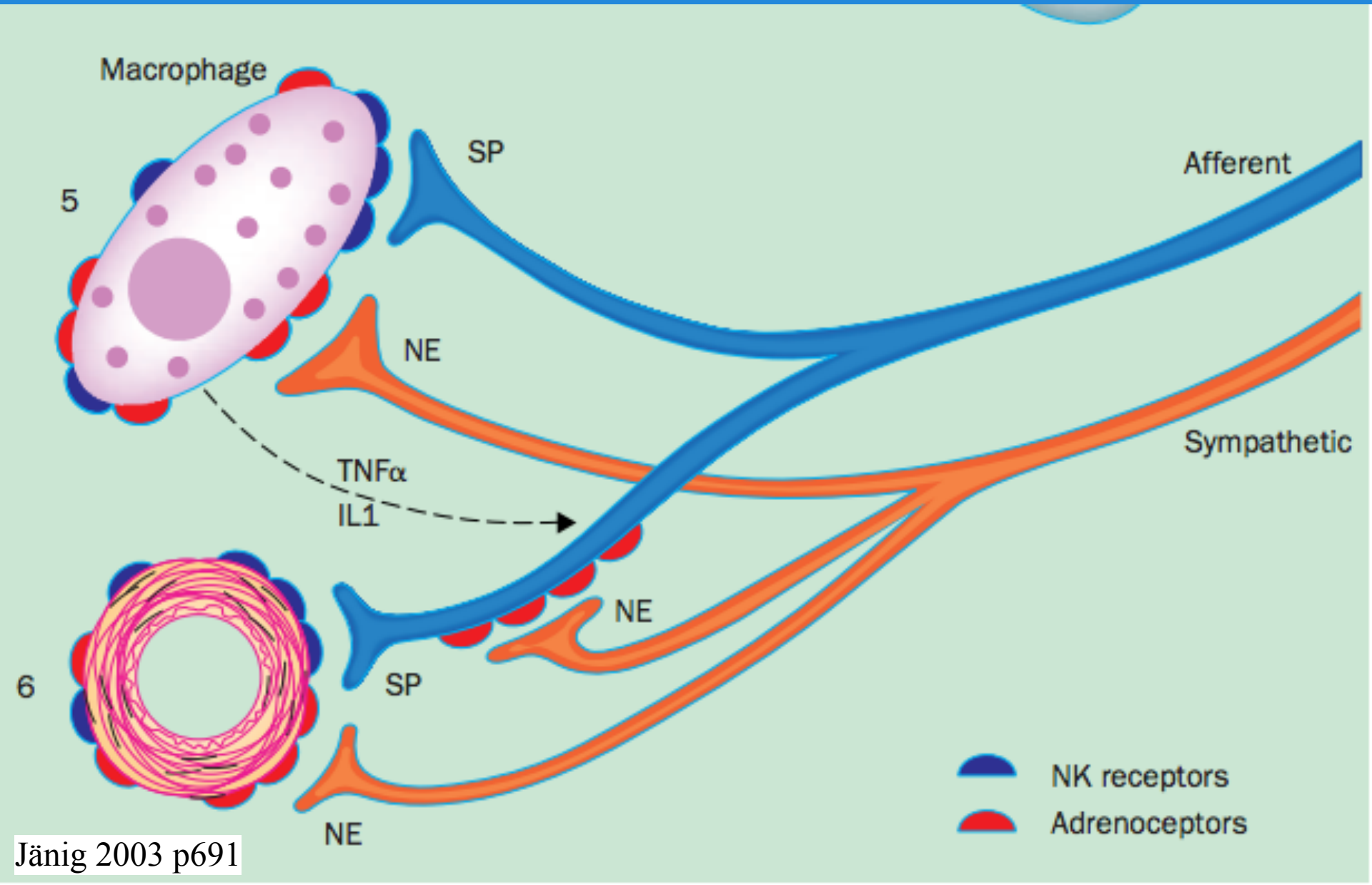
- Painful conditions following trauma
  - Out of proportion to Inciting trauma
- Conditions include edema, hyperalgesia, allodynia, movement disorders, vasomotor and sudomotor dysfunction, trophic skin changes
- Classified as neuropathic pain
  - CRPS I: no specific nerve lesion but from pathology that affects nervous system
  - CRPS II: distinct nerve lesion present
  - Symptoms of CRPS do not occur in distribution of one nerve

Pathophysiology

- Subject of debate
- Neurogenic inflammation
- Sympathetic, central, peripheral nervous dysfunction

Neurogenic Inflammation

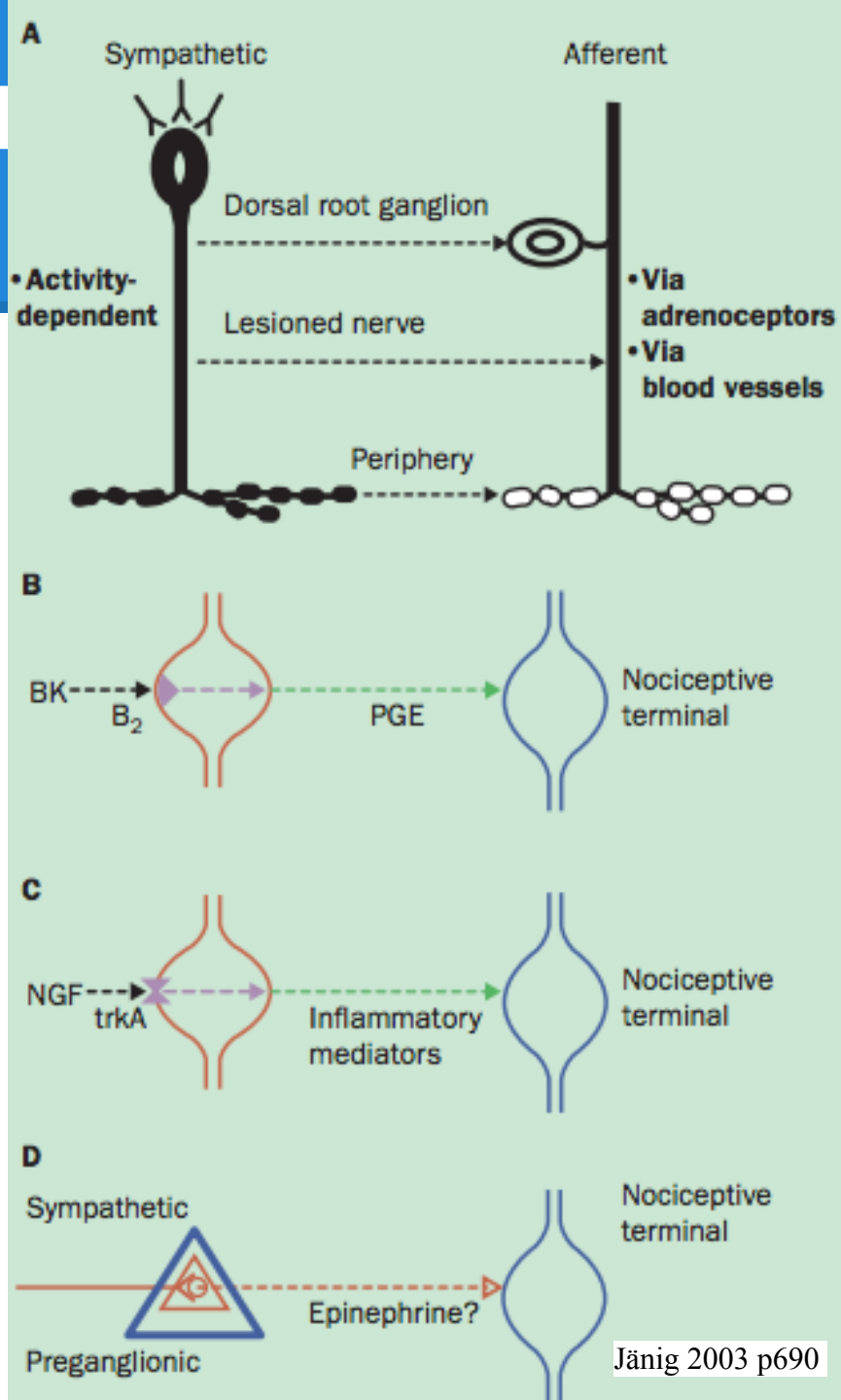
- Inciting event activates and sensitizes primary afferent fibers
  - Neuropeptide (substance P) released
- Stimulates inflammatory cells to release cytokines
  - Further stimulation of primary afferents
- Primary afferents release vasoactive compounds in addition to neuropeptides
  - Vasodilation and plasma protein extravasation
  - Humans do not have enough substance P to induce plasma protein extravasation, yet CRPS patients have significant amounts



Jänig 2003 p691

Sympathetic Mediated Pain

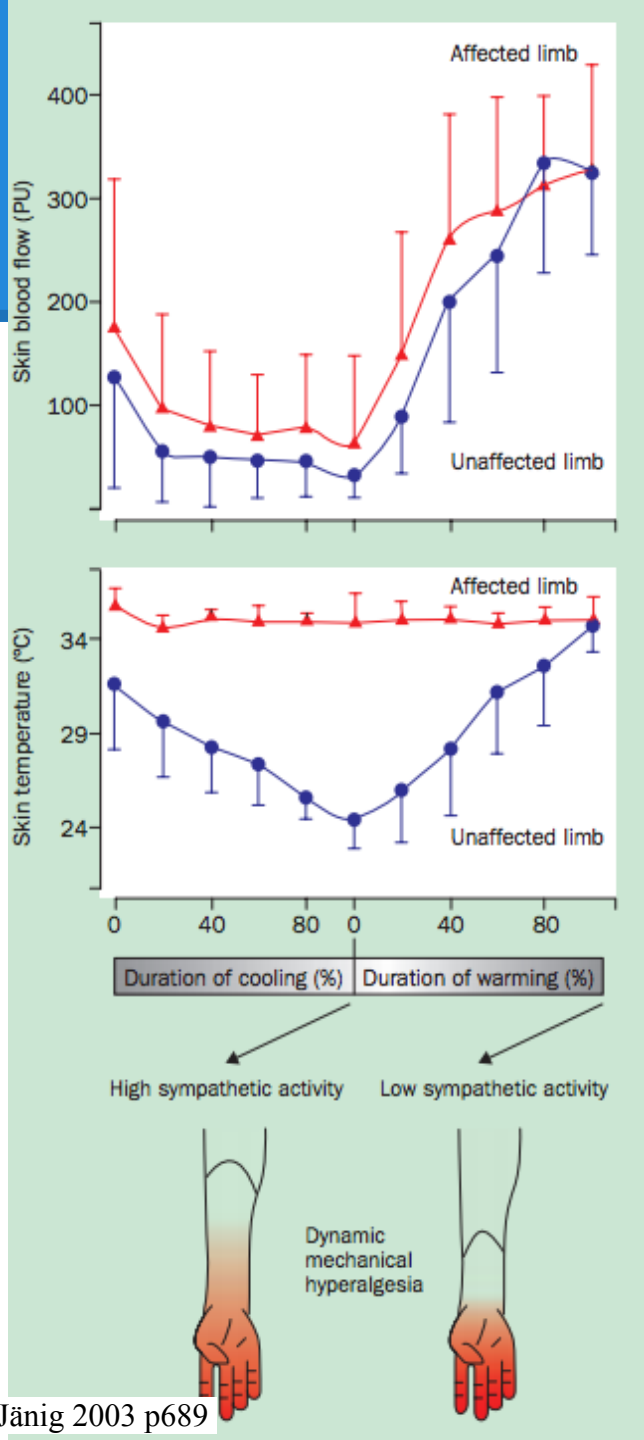
- Coupling of sympathetic nerves to primary afferent fibers
  - CRPS II: lesioned fibers sensitized to catecholamines
- Partial relief from sympathetic blockade
  - Indirect and direct
- SMP only exists in a subset of CRPS patients



Jänig 2003 p690

Sympathetic Dysfunction

- Sympathetic stimulation can increase pain in affected limb
- Sudomotor and vasomotor dysregulation
- Increased α-adrenergic receptors in skin but decreased serum catecholamine levels
- Postulated trophic effects on tissues



Jänig 2003 p689

Central Dysfunction

- Magnetoencephalography and functional MRI show altered somatosensory representation of affected limb
- Cortical reorganization of motor units correlates with motor dysfunction
- Sensitization of spinal neurons to continuous nociception
- CNS dysregulation of SNS
  - Unilateral sympathetic nerve block improves b/l sx
  - Skin temperature differences in CRPS I patients
  - Simultaneous decreased vasoconstriction and increased sudomotor activity

Diagnostic Criteria

IASP Criteria

- Preceding noxious event
- Spontaneous disproportionate pain or hyperalgesia not confined to one nerve's distribution
- Edematous, vasomotor, sudomotor abnormalities, motor symptoms trophic changes on affected limb
- Other possible diagnoses excluded

Diagnostic Criteria

Budapest

- Ongoing pain that is out of proportion to any inciting event
- Report sx in three categories
  - Sensory: hyperesthesia/allodynia
  - Vasomotor: either skin temperature asymmetry, skin color changes, or skin color asymmetry
  - Sudomotor/edematous: edema, sweating, or sweating asymmetry
  - Motor/trophic: ROM decrease, tremor, weakness, dystonia, trophic changes in hair/nail/skin
- Have signs in two categories
- Other causes excluded

Diagnostic Studies

- Autonomic testing
  - Increased resting sweat output
  - Quantitative sudomotor axon reflex test
    - Measures resting skin temp, resting sweat output, and stimulated sweat output
    - When both are abnormal: Sn 94% Sp 98%
  - Should be used only if diagnosis is doubtful
- Bone scintigraphy
  - Decreased perfusion of affected areas after symptom onset
  - Delayed scintigraphy shows increased uptake after six weeks symptom duration

Diagnostic Studies

- Radiograph
  - Osteopenia
  - Joint and bone destruction
    - CT shows "swiss cheese"
  - Proliferative bone formation
  - Subchondral degeneration
  - Useful in stage III
- MRI
  - Edema
  - Skin thickening
  - Contrast enhancement of tissue
  - Muscle atrophy

Inciting Events

- 40% of cases due to soft tissue trauma
- 25% due to fracture
- MI-25%
- CVA-3%
  - Found in 12-20% of hemiplegics
- No precipitating trauma in 35% of cases
- Emotional disturbance at onset of CRPS
- MI and hemiplegia CRPS incidence decreased with arm stretching and ambulation in pts with prolonged IV use

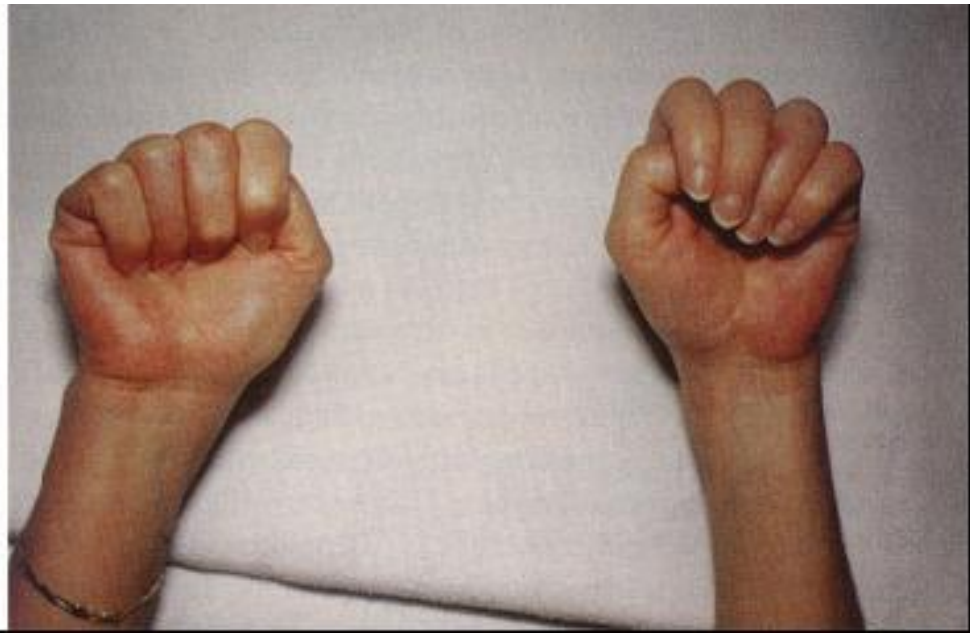
Disease Course

- Stage I: acute
  - Allodynia/hyperalgesia
  - Vasomotor dysfunction
  - Sudomotor dysfunction and edematous changes
  - Normal/patchy demineralization
- Stage II: dystrophic
  - Development of motor disturbances and muscle wasting
  - Progression of edema
    - Thickened skin and articular tissue
    - Brawny skin

Disease Course

- Stage III: atrophic
  - Severe motion restriction
  - Contractures
  - Waxy skin changes
  - Brittle nails
  - Bone demineralization


Salahadin 2012



Schott 2007

Management

Prevention

- Mobilization reduces CRPS in stroke, MI, prolonged IV use

- Vitamin C after upper extremity fracture

Management

- Conservative
  - Physical therapy
    - Graded motor imagery with imagined hand movements and mirror therapy for UE
  - Psychological support
    - CRPS>2 months
    - No response to treatment
    - Comorbid psych disorders

- Pharmacotherapy
  - Tailor to prominent symptoms

Anti inflammatory

- NSAIDs considered inferior to calcitonin in scintigraphic results
- Free radical scavengers
  - Topical DMSO-50% and oral N-acetylcysteine effective in CRPS I
- Bisphosphonates more effective than calcitonin in bone turnover reduction
- Glucocorticoids
  - Prednisone taper caused 75% clinical improvement in RCT

Analgesics

- No studies of acetaminophen in CRPS
- Slow release morphine ineffective
- Carbamazepine
- Gabapentin works on subpopulation
- IV ketamine efficacious in 1 retrospective and 2 double blind RCT
- TCAs
  - No studies on efficacy

Vasodilators

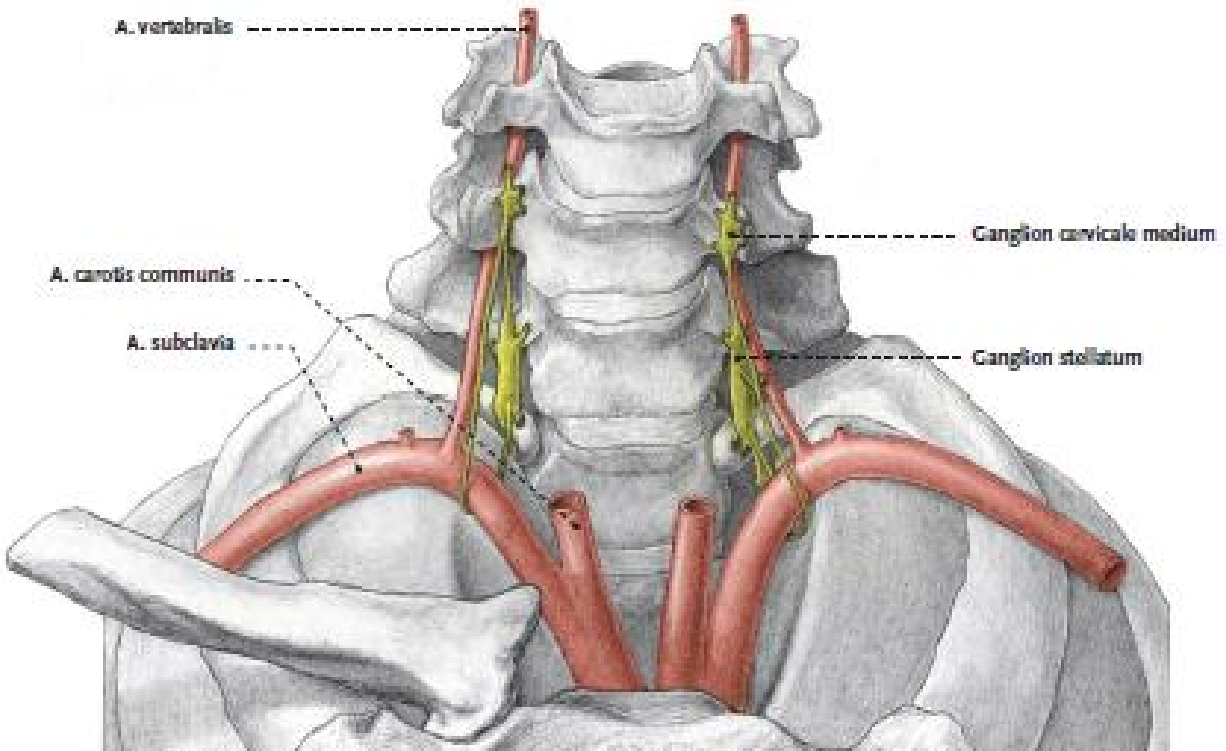
- α-blockers
- Calcium channel blockers

Spasmolytic

- Oral benzos
- Baclofen
- Both are effective in dystonia, tremor, and myoclonus

Stellate Ganglion Block

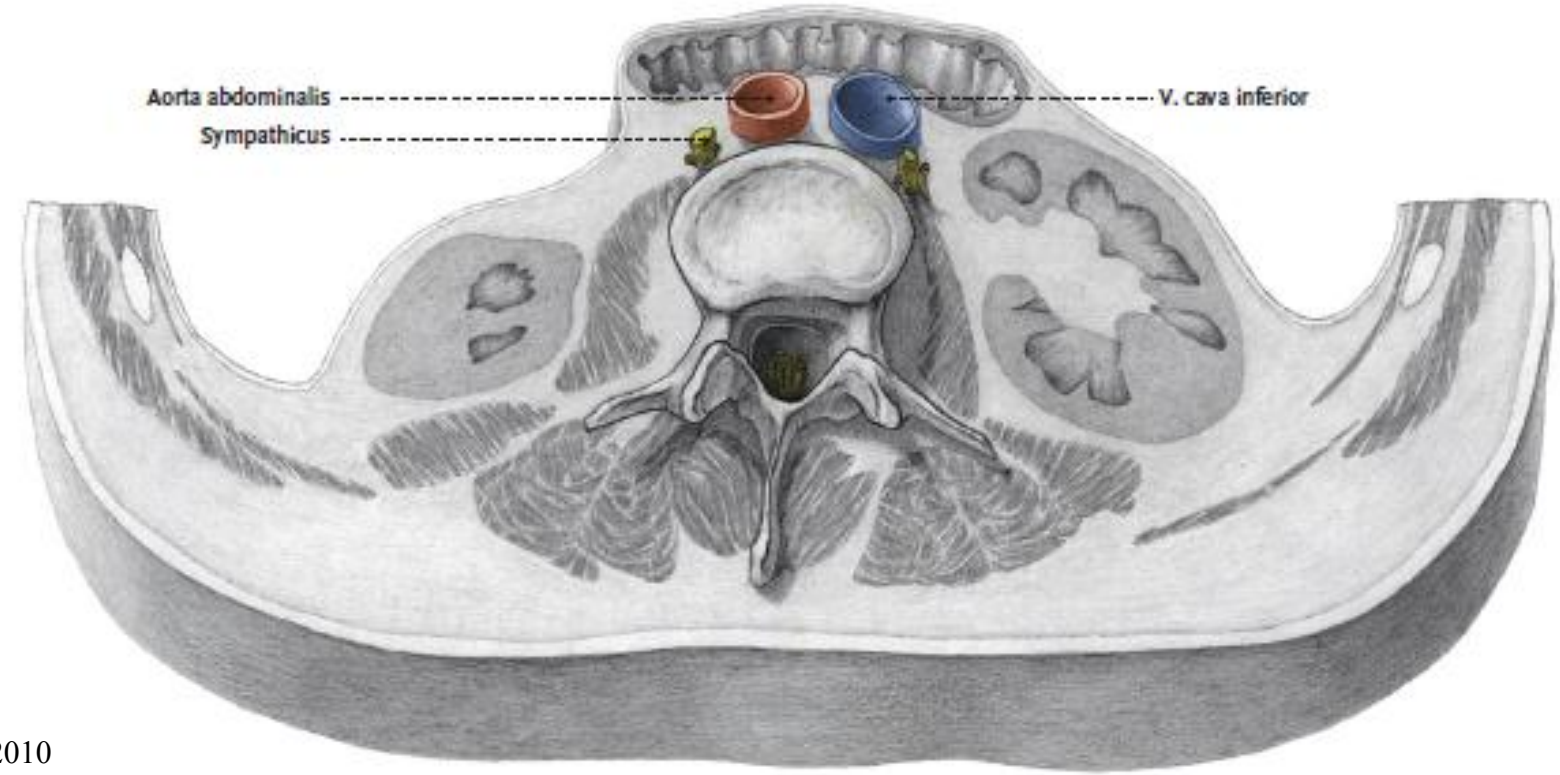
- Performed for UE CRPS
- Sends sympathetic afferents to truncus cervicalis and brachial plexus



Van Eijs 2010

Lumbar Sympathetic Block

- Performed at L2-L4 for LE CRPS
- Needs to be performed with image guidance



Van Eijs 2010

Other Interventional Therapies

- TENS
  - No conclusive evidence
- Spinal stimulation
  - RCT compared to PT showed increased pain relief 5 years after implantation
- Peripheral nerve stim
  - Effective only if pain is in nerve distribution
- Epidural
  - Bupivicaine+opioid allowed recovery of knee use
  - Clonidine gives short term relief
  - u/l cervical bupivicaine and clonidine: 90% improvement if done within 1 year of onset

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