THE ROLE OF THE DORSAL ROOT GANGLION IN CERVICAL RADICULAR PAIN

PATHOPHYSIOLOGY AND RATIONALE FOR TREATMENT

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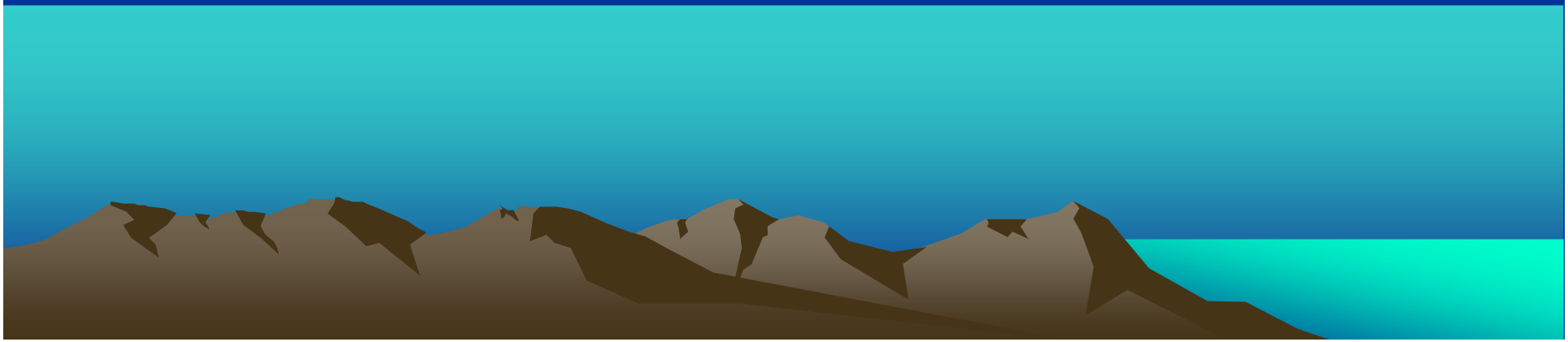
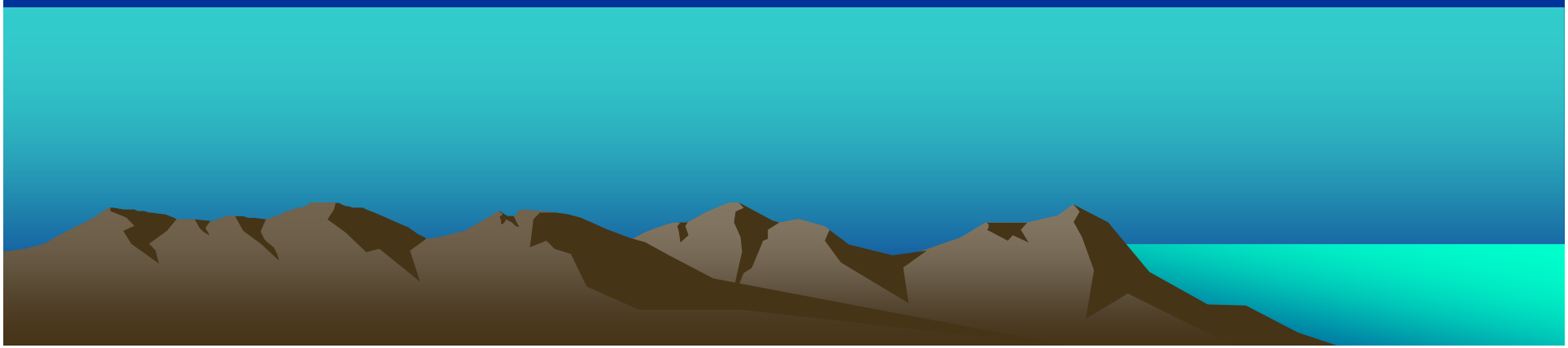


DEFINITION

- Cervical radicular pain is pain perceived in the upper limb that is shooting or electric in quality
- Caused by irritation and/or injury of a cervical spinal nerve
- IASP defines it as pain caused by ectopic activation of nociceptive afferent fibers in a spinal nerve or its roots or other neuropathic mecahnisms

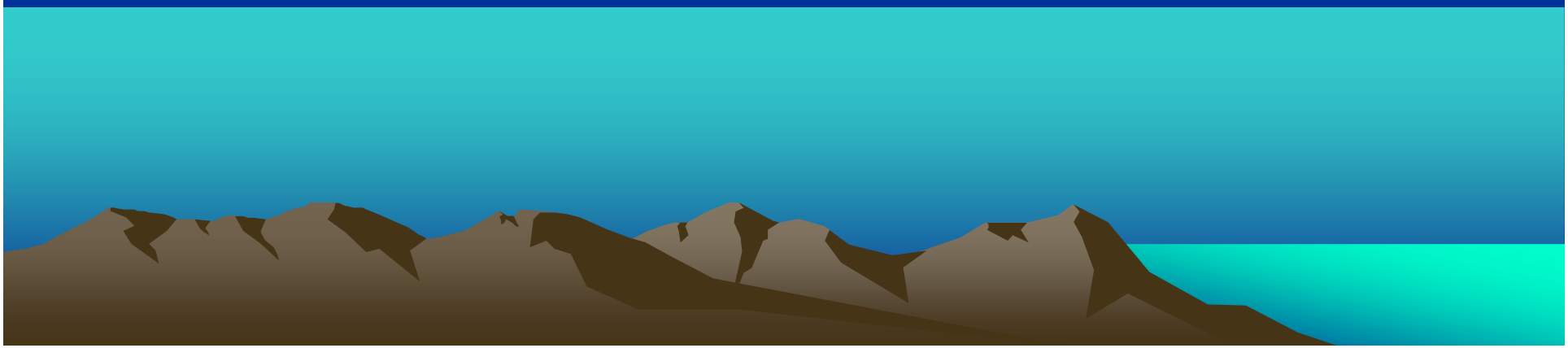
history

- Condition first described in literature vby Parkinson in 1817, as a “rheumatic disease of the deltoid muscle”
- A century later (1914) Dejerine formulated the concept of cervical radiculitis



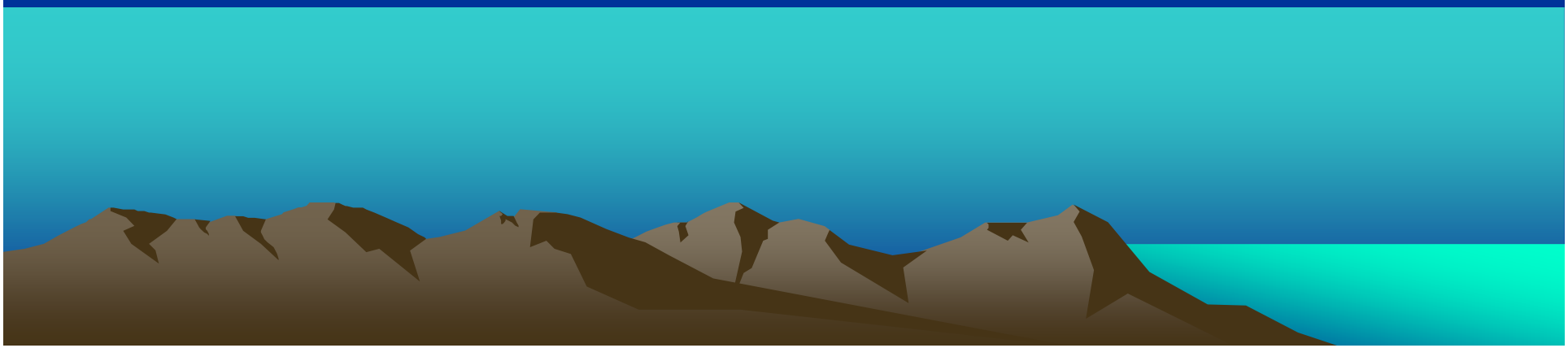
radiculopathy

- Distinguished from radicular pain as a condition in which objective loss of sensory and/or motor function is present
- Radicular pain is caused by ectopic impulse generation



Causes

- Narrowing of intervertebral foramen
- Disc herniation
- Radiculitis due to arteritis, infection or inflammatory exudates



Pain distribution

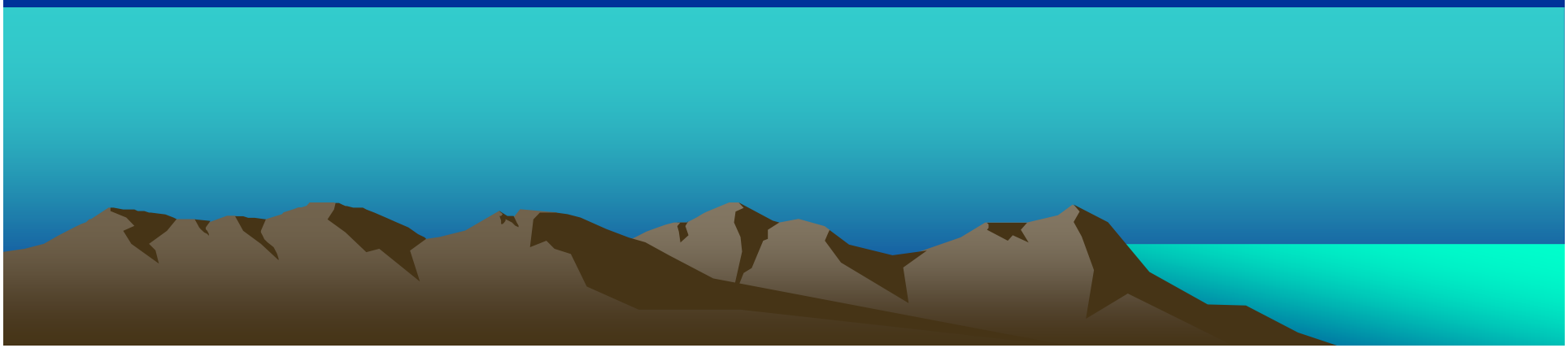
- Bogduk summarised the pain distribution as follows
- C4: restricted to neck and suprascpular regions
- C5: extends into the upper arm
- C6&C7: extends form the neck and shoulder into the forearm and hand

Epidemiology

- Mayo clinic calculated in a popn btn 13 & 91yrs an annual incidence of cervical radiculopathy of 83 per 100,000
- Adjusted figures, males 104/100,000, females 64/100,000
- Highest incidence: age 50-54; 203/100,000
- 15% of pts ,hx of trauma preceded Sx
- 41% had hx of lumbar radiculopathy

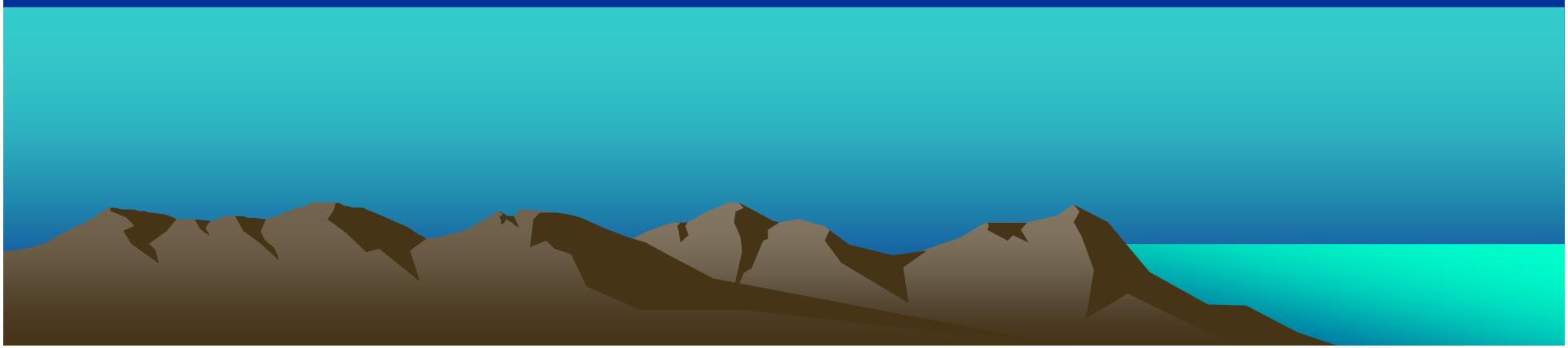
Epidemiology

- C7 was most freq involved level 45-60%
- C6: 20-25%
- C5 &C8 : represent about 10%
- C5 was the most treated level



Diagnosis

- If cerv radic pain is unresolved spontaneously in 3 mths r/o CA, infection, shoulder pathology, etc
- Neuro exam includes strength, sensation and reflexes

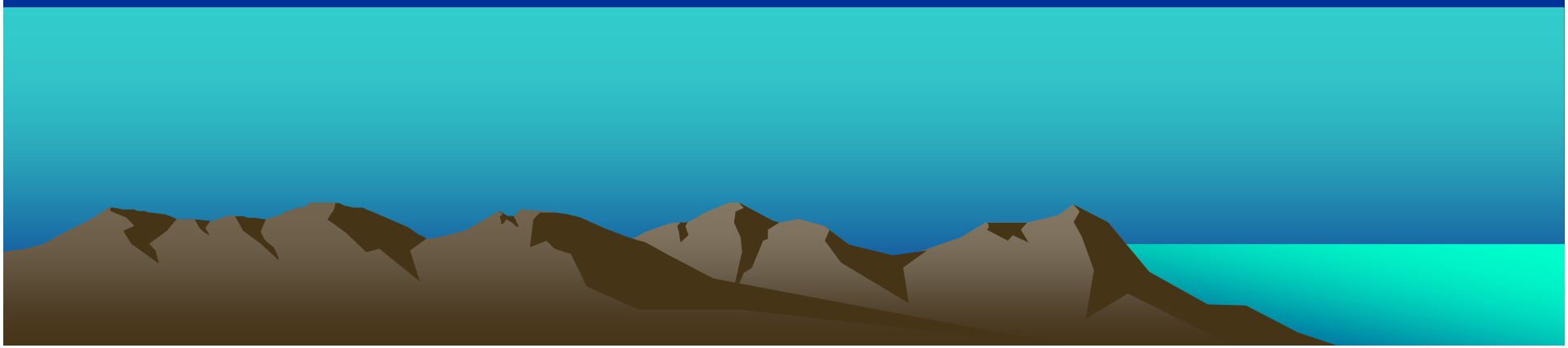


Diagnostic Tests

- Spurlings test: Spine extended with head rotated to affected shoulder while axially loaded. Reproduction of pts shoulder or arm pain is positive.
- Shoulder Abd test: pt lifts hand above head, dissapearance of radicular Sx is positive
- Axial Manual Traction test: Pt in supine position, an axial traction force of 10-15kg is applied decrease of Sx is positive

Diagnostic Tests

- The 3 tests have a high specificity 81-100%
- low Senstivity 26-50%
- Spurlings test validated with EMG showed specificity 93% & sensitivity 30%



Imaging/EDx testing

- MRI modality of choice
- No diagnostic gold standard
- Abnormal MRI ‘s in 19%-28% of asymptomatic pts
- CT good for cortical bone structures
- EMG is the most sensitive method
- SNRB’s can aid in diagnosis

Pathophysiology

- Nucleus pulposus material leaking onto the nerve root
- Compression of the nerve root by anatomic abnormalities
- Either/Or of the above induce; inflammatory reaction, changes in ion channel functioning
- This leads to hyperexcitability & spontaneous activity in the DRG interpreted as pain
- Howe et al in 1977 recognized repetitive firing in the DRG after minimal compression of a normal DRG

Inflammatory Process

- Nuclear Material Exposure to DRG
- Release of Arachidonic Acid, then Cox 1&2 enymes induce the Release of Cytokines, i.e. Prostaglandins(PG), Nerve Growth Factor (NGF), TNF-alpha,Interleukins, MAPK and Brain Derived neurotropic Factor (BDNF)
- NGF and BDNF are key players in the cascade of events in the inflammatory process

Ion Channel Modulation

- Voltage gated Na,K and Ca channels are modified
- Increased Na channel plasticity & gene expression in the DRG after injury.
- K role in ectopic d/c generation not clear, redn in K currents after injury
- Na channel blockes inhibit ectopic d/c
- Ca channel blocklers eg verapamil (L-type) and contoxin (irreversible blocker Ntype) reduced rate of d/c

Spontaneously firing DRG

- Key players are;
- Modulation of ion channels in the DRG
- Increased expression of BDNF shown to directly and rapidly gate Na channels resulting in firing of action potentials.
- In the future, Gene arrays, analyze gene expression, proteomic technologies used to determine genome sequences may help encode proteins involved in radicular pain.

Therapies

- Anti-inflammatory: NSAIDS, corticosteroids, future TNF-a Inhibitors.
- NSAIDS have not been investigated for radicular pain
- Cortocosteroids: Inhibits PLA-2
- IM Vs epidural injections: 68% showed good pain relief in one year in the epidural grp compared to 11% in the IM grp

Evidence for treatment of Cervical Radicular Pain

- Transforaminal ESI(flouro Guided): Vallee Et al; NC prospective. 53% success after 6 mths.
- Transforaminal ESI (CT guided): Cyvetal et al; NC prospective. 60% success after 6 mths.
- RF Cervical DRG (Van Cleef et al PRDB;Sig pain redn at 8mths compared to sham
- RF Cervical DRG Slappendal PRDB; RF40deg Vs 67 deg; sig pain redn in both grps at 3 mths
- Pulsed RF DRG Van Zundert, NCP 72% success at 8 wks, 33% at 1 yr
- Neck Surgery:Parson PR SurgeryVs physio Vs Collar, surgery not more effective as C-collar ot PT at 12 mths

TNF-alpha inhibitors

- TNF alpha inhibitors: may provide pain relief in nucleus pulposus(NP) induced nerve injury.
- Open label trials show systemically injected TNF-I have potential benefit for lumbar radicular pain.
- TNF –I attenuate elevated BDNF levels induced by NP application to nerve root.

Sodium Channel Blockers

- Anticonvulsants: carpamezapine, oxacarbazepine used for central and peripheral neurogenic pain.
- Valproic Acid; not superior to placebo in tx of polyneuropathy.
- Mexilitene: effective in a variety of neuropathic syndromes, however questionable efficacy of oral mexilitene making it difficult to draw conclusions

Future Treatment Modalities

- MAPK pathway: Mast cell stabilizers could potentially ablate some effects of NGF in pain originating from the DRG. Targets specific downstream p38MAPK using tyrosine kinase inhibitors.
- Vanilloid Receptors: resinferatoxin (ultrapotent capsaicin analog) has ben used in pts with hypersenstive lower urinary tract

Future Treatment Modalities

- Long-acting local anesthetics: block Na channel and play a major role in identification of caustive nerve structure.
- Animal experiments with butamben suspension given epidurally to rats with nerve injury induced allodynia indicate that multiple doses were required for several days to give prolonged analgesia.
- Tonicaine was injected intrathecally in rats producing a sensory blockade longer than mercaine. Has a narrow therapeutic index with substantial neurotoxicity in rats that may limit its clinical value. Must be confirmed inhuman subjects

Future Treatment Modalities

- TCA's; mode of action classically attributed to blockade or serotonin and norepinephrine reuptake. Elavil may be a potent blocker of sodium channels.
- Literature shows a possible role of TCA'a as long acting anesthetics
- Prelim studies: Elavil showed no better nerve blockade than local anesthetics

Future Treatment Modalities

- Gene therapy: subcutaneous innoculation of herpes simplex virus vectors can be used to transduce neurons of the dorsal root ganglion to provide therapeutic effect in models of polyneuropathy and chronic regional pain.
- In human trials; direct injection of replication-competent HSV into brain tumors has been safe, and HSV gene transfer by SQ innoculation for the treatment of chronic intractable pain is about to commence

References

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