When The Shark Bites: Central Pain Syndromes

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Disclosure

- Nothing to disclose

Learning Objectives

- Define the major central pain syndromes
- Recognize the pathophysiological differences between them
- Identify the treatment modalities for general central pain syndromes
- Contrast the Syndrome specific treatments
Epidemiology

- No less than 10% of all CNS CVAs develop CPS
- 20%-25% of SCI
- 18% of patients with MS
- 2% of patients with CA
- In the USA, 600,000 patients have CPS
- CP may be complication of neurosurgical procedures:
  - Disc ablation at dorsal levels
  - Tumor excision in parietal lobe, brainstem, and SC
  - Thalamotomies, mesencephalotomies, and cordotomies (pain relieving procedures)

Components of CPS

- Constant spontaneous pain (aching, burning, pricking, lancinating or cramping), dysesthesia, paresthesia or a combination of these
  - Typically more than one form of pain is experienced in 99% of the patients
  - Cord CPS and MS associated CPS are more dysesthetic
- Spontaneous, intermittent, generally lancinating, pain in 10%-20% of cases
- Evoked pain in 2/3 of patients
  - May be only presenting symptom
Common Central Pain Conditions

- Direct brain injury
  - Multiple sclerosis
  - Parkinson’s disease
  - Spinal cord injury
  - Phantom limb pain
  - Poststroke pain syndrome
  - mTBI

Definition

The various definitions of neuropathic pain indicate that there is pain caused by a lesion or disease of the somatosensory nervous system. The most common neuropathies, peripheral neuropathies, are often secondary to peripheral, small nerve fiber damage typically in the distal upper and lower extremities. This is in contrast to the origins of central neuropathic pain.

Multiple Sclerosis (MS)
Brain MRI Scan Showing White Lesions Associated With Multiple Sclerosis

Common Types of Pain

- Pain in MS is very common, with prevalence ranging from 43%-54% (1) to 86% (2)
- These patients have different types of pain (in addition to central pain):
  - Dysesthesias in the extremities
  - Complex regional pain
  - Lhermitte's sign
  - Painful tonic spasms
  - Trigeminal neuralgia (may be forme frust)

www.msaustralia.org.au; Bermejo et al, Revista de neurologia, 2010
Ectopic vs Ephaptic

- Crosstalk

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Pain in MS

- Central neuropathic pain in MS is thought to be secondary to damage to myelinated nerves in the CNS and propagated by two main mechanisms:
  - The generation of ectopic impulses at demyelinated lesions in response to neural damage [3]
  - or secondary to removal of modulation of efferent A-delta and C-fiber pain pathways by interruption of inhibitory impulses from the brain [4]

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Parkinson’s Disease
Respondent Demographic Information

- **Current age**
  - 20-29 2%
  - 30-39 4%
  - 40-49 20%
  - 50-59 32%

- **Years since diagnosis**
  - 0-2 years (newly diagnosed) 19%
  - 3-5 24%
  - 6-10 31%
  - 11-15 10%
  - 16+ 15%

Conducted by: The APDA National Young Onset Center – Spring, 2011

An informal, online survey available to www.youngparkinsons.org website visitors from March-May, 2011, conducted for informational purposes only. If you are experiencing pain with Parkinson’s disease, please consult with your physician.

Parkinson’s Disease

- Parkinson’s disease (PD) is a progressive neurodegenerative disorder that results from depletion of the neurotransmitter dopamine in the brain.
Pain in Parkinson’s Disease

- PD patients report multiple types of pain
  - Attributable to varying peripheral pain mechanisms
  - Role of motor symptoms in causing or increasing pain
  - Role of PD pathophysiology in pain processing
- Treatment of pain in PD is entirely based on empirical data

Pain in Parkinson’s Disease (cont’d)

- The PD patient may experience CNP via stabbing, burning, scalding, or lancinating pain that is unprovoked in unusual locations such as the face, mouth, genitalia, pelvis, anus, or abdomen
Pain in Parkinson’s Disease (cont’d)

- A neurophysiological study of CNP in PD patients was done by Schestatsky et al.
  - Found that while conduction along the peripheral and central pain pathways was normal, with or without primary central pain, there were signs of hyperalgesia.
  - Their patients exhibited a lack of habituation of sympathetic sudomotor responses to repetitive pain stimuli that suggested an abnormal control of pain on the autonomic centers.
- These abnormalities were diminished by L-dopa, which suggested that the dysfunction may occur in dopaminergic centers regulating the autonomic functions and inhibitory modulation of pain inputs.

Schestatsky et al, Neurology, 2007

Pain in Parkinson’s Disease (cont’d)

- It has been shown that the pharmacological, electrical, and surgical manipulation of the substantia nigra and striatum in non-PD patients can affect behavioral and neuronal responses to algetic stimulation:
  - The basal ganglia may be involved in the modulating of nociceptive information (including sensory-discriminative aspects, cognitive and affective aspects of noxious stimuli).

Pain in Parkinson’s Disease (cont’d)

- This modulation most likely occurs within the medial thalamus. It is possible that the structures in the basal ganglia provide a gating mechanism for regulation of nociceptive stimuli to higher motor centers.
- The use of L-dopa or injections of apomorphine may transiently help patients with CNP with PD.
  - Dopaminergically maintained pain

Spinal Cord Injury (SCI)

Causes of SCI

- Pain after SCI is very difficult to treat
- It may involve various aspects of the brain
- These patients may experience central pain beginning within weeks or months after injury
  - It is typically felt at or below the level of SCI in areas where patients have lost some or all of their sensation
  - There may be segmental pain, around the border where patients have normal sensation and loss of feeling secondary to the SCI
SCI (cont’d)

- It can be slightly above or below the level of SCI
  - This usually develops during the first few months after injury
  - Segmental pain may be associated with allodynia and hyperalgesia in the painful region
  - Nerve root entrapment and syringomyelia (a hollow, fluid filled cavity, or syrinx in the spinal cord that commonly expands causing more neurological damage) may also develop

SCI (cont’d)

- Some research shows the development of central sensitization of dorsal horn neurons after spinal cord hemisection
- This would provide a logical mechanism for the development of mechanical and thermal allodynia after SCI

Christensen et al. J Neurotrauma, 1997

SCI (cont’d)

- Recent research takes this hypothesis further
- Dendritic spine remodeling occurs on second-order wide dynamic range neurons and accompanies neuropathic pain after SCI
  - Showing the possibility that a synaptic model of long-term memory storage could explain the persistent nature of neuropathic pain
  - As SCI-induced synaptic potentiation engages a putative spinal memory mechanism

Tan et al. Exp neurol, 2011
SCI (cont’d)

- Still other research demonstrates that chronic pain after SCI appears to be associated with nociceptive primary afferent neurons
  - Which display persistent hyperexcitability and spontaneous activity in their peripheral branches
  - With somata in dorsal root ganglia (DRG) after SCI, suggesting that SCI-induced alterations of primary nociceptors contribute to central sensitization and chronic pain after SCI

SCI (cont’d)

- Gwak et al indicates the SCI induced release of glutamate, proinflammatory cytokines, ATP, reactive oxygen species, and neurotrophic factors trigger activation of postsynaptic neuron and glial cells via their own receptors and channels
  - This contributes to neuronal-neuronal- and neuronal-glial interactions as well as microglial-astrocytic interactions
  - Post SCI, dysfunctional glia, a condition called “gliopathy” is a key contributor to underlying cellular mechanisms contributing to central neuropathic pain

SCI (cont’d)

- Finnerup indicates that chronic pain is present in about 70% of patients with SCI and chronic central neuropathic pain in 30%-50%
  - Her findings include the facts that:
    - Evoked types of pain are more common in SCI patients with central pain
    - Lesions in central grey matter are larger in SCI patients with central pain
    - Some believe that lesions are equally common in SCI patients with and without central pain
  - Difficult to treat

Finnerup, Dan Med Bull, 2009
Phantom Limb Pain (PLP)

In the Amputees With PLP, the Cortical Representation of the Mouth Extends into the Region of the Hand and Arm

![Image of brain diagram showing cortical representation]
PLP

Main Factors Possibly Relevant to the Development of PLP

- Long lasting noxious input to the limb
- Development of a cortical pain memory enhanced excitability
- Amputation
  - Reorganization of the amputation zone
  - In somatosensory cortex
  - Selective loss of C fibers
  - Random input from stump neuroma
  - Abnormal changes in the dorsal root ganglion and dorsal horn
  - Sympathetic activation

Mirror Box Therapy

The principle of mirror therapy [2] is the use of a mirror to create a reflective illusion of an affected limb in order to train the brain into thinking movement has occurred without pain. A mirror box places the affected limb in front of a mirror, making it appear as if the limb is moving. This illusion can help to alter the brain's perception of pain and movement, potentially reducing pain in chronic pain conditions like PLP and CRPS.

Used for PLP and CRPS.
There are still many questions behind the pathophysiology of PLP. One can say it is induced by the elimination or interruption of sensory nerve impulses by destroying or injuring the sensory nerve fibers after amputation or deafferentation. The incidence of PLP posttrauma or peripheral vascular diseases is 60%-80%. Stump pain is seen in over half of the patients with PLP. PLP does not only occur postlimb amputation, but also postmastectomy (phantom breast syndrome) as well as postenucleation of the eye.

Wolff et al, Pain Pract, 2011

PLP (cont'd)

PLP may be at least partly explained by considering mixed signals from the brain and to the brain from the spinal cord. After amputation, there is no input from the former limb, and nerve death follows. The brain may remap the part of the body's sensory circuitry to another part of the body. The information from the expected but now amputated limb is rerouted elsewhere, from a missing foot to a present nose, for example. In that case, when the nose is touched, it may feel to the patient as if the missing foot is also being touched. However, as this is a tangled sensory web, the result can be pain.

Anderson-Barnes et al, Med Hypotheses, 2009

PLP (cont'd)

Aside from pain, after amputation, the majority of patients with amputation either report the feeling of volitional control over their phantom or a phantom limb that is frozen in a specific position. Anderson-Barnes describes "proprioceptive memory" as the memories of the limb's position prior to amputation remain embedded within an individual's subconscious. Pain memories that may be associated with each limb position contribute to PLP as well as to the experience of a fixed or frozen limb.
PLP (cont’d)

- Phantom pain is described as:
  - Burning
  - Tingling
  - Cramping
  - Shocking
  - Paresthetic
- There may be an unpleasant itch to a more severe clenching and squeezing sensations.

PLP (cont’d)

- Both peripheral and central changes take place post amputation:
  - Sympathetic efferents interacting with sensory afferents modulating afferent activity such as spontaneous pain
  - Changes in neural processing are found proximally at the dorsal root ganglion and dorsal horn of the spinal cord
  - Second order neurons that primarily respond to noxious stimuli begin to respond to input from low-threshold mechanoreceptors A-beta fibers that usually carry non-noxious stimuli, induces exaggerated pain and allodynia
  - This induced central sensitization leads to spontaneous PLP as well as touch-evoked PLP and mechanical residual limb allodynia

Central Poststroke Pain (CPSP)

fMRI and Lesion Mapping

In each syndrome, heterogeneous lesions that themselves had little overlap showed significant network overlap in cortical areas previously implicated in symptom expression (P < 10^{-4}). These results suggest that (i) heterogeneous lesions producing similar symptoms share functional connectivity to specific brain regions involved in symptom expression; and (ii) publicly available human connectome data can be used to incorporate these network effects into traditional lesion mapping approaches.

Diffusion Tensor Imaging

This image of a human brain is created through the process of tractography, remodeling the neural tracts in the brain. The different colors indicate the direction of water flow, showing how connections between different brain regions are made.

Diffusion Tensor Imaging (cont’d)

- MCS = minimally conscious state
Diffusion Tensor Imaging (cont’d)

CPSP

- Central poststroke pain (CPSP) was originally thought to be “thalamic” pain, as described by Dejerine and Roussy, although it was described even earlier in 1883.
- Dejerine and Roussy characterized their eponymous thalamic pain syndrome as including:
  - Hemiplegia
  - Hemiataxia
  - Hemisomatognosia
  - Difficulties with both superficial and deep sensation
  - Persistent, paroxysmal, typically intolerable pain
  - Choreoathetoid movements


CPSP (cont’d)

- This syndrome is now known as central poststroke pain syndrome (CPSP).
- The reported incidence of CPSP varies widely from 2% to 8% in stroke patients.
- To 25% in patients with lateral medullary infarctions (Wallenberg’s Syndrome).

CPSP (cont’d)

• CPSP is broadly defined as central neuropathic pain, secondary to lesions or dysfunction in the central nervous system.

• It is typically characterized by constant or intermittent pain and sensory abnormalities, most commonly of thermal sensation.


CPSP (cont’d)

• The pain is typically described as burning, scalding, or freezing and burning.

• Early diagnosis can be difficult, as the patients who develop CPSP may develop the problem long after their CVA, causing misdiagnosis or significant delay prior to treatment.

    - Also, as these patients may have cognitive or speech difficulties, as well as depression, anxiety, and sleep problems, diagnosis may be further complicated.

• They may also develop spontaneous dysesthesias and stimulus-evoked sensory disturbances including dysesthesia, hyperalgia, and allodynia.


CPSP (cont’d)

• The onset of the pain may be immediate or be delayed for months to years.

• In 40% to 60% of CPSP patients, the onset of their centrally related pain poststroke may occur more than one month after the CVA.

• The pain may encompass a large part of the contralateral body, but it may also involve only a small area.

CPSP (cont’d)

- Sensory abnormalities are also associated with CPSP.
  - These may include altered sensory processing: warm and cold stimulation applied to the skin may be perceived as paresthesias or dysesthesias rather than cold or warm.
  - Allodynia is found in 55% to 70% of patients.
  - Hyperalgesia and dysesthesia are also frequently seen.

- Evaluation of the CPSP patient may be more complex than that of the typical pain patient, at least in part for reasons noted above.
  - The pain history must be accompanied by a pain-specific sensory examination, musculoskeletal and myofascial evaluation, and basic psychological evaluation.
  - Specialized sensory testing may also be needed, something that a neurologist can easily learn but may need specialized tools.

- Locations of the lesions inducing the CPSP have been demonstrated to be referable to the spinothalamocortical tract/pathway, typically associated with abnormal evoked sensations in the peripherally affected area.
  - While at least three thalamic regions, which directly or indirectly receive spinothalamic projections, appear to be involved in the development of CPSP:
    - The ventroposterior thalamus including the posteriorly and inferiorly located nuclei bordering on that region.
    - The reticular nucleus.
    - The medial intralaminar region.

- It is the ventroposterior thalamic region that is proposed to be most significantly involved in central pain.
- It should also be noted that cerebrovascular lesions located above the diencephalon, that is, in the parietal lobe, may also induce CPSP.

CPSP (cont’d)

- While damage to the spinothalamocortical pathway appears to be a necessary condition in CPSP, it is thought that the spontaneous pain linked to CPSP is secondary to hyperexcitability or spontaneous discharges in thalamic or cortical neurons that have lost part of their normal input.

Vestergaard et al, Pain, 1995

CPSP (cont’d)

- CPSP is most typically associated with a single lesion, associated with either a focal gray or white matter lesion.
  - The lesion may be at the spinal, brain stem, or cerebral level, but it is always contralateral to the pain of CPSP.
- CPSP is associated with abnormal somatosensory cortex, particularly thalamic and/or pain sensations.
  - Most commonly, a loss of sensation is seen.
  - One may also see an uncontrolled sensation of pain or temperature.
- The pain of CPSP may occasionally involve the contralateral (to the lesion) face, body, and extremities.
  - It may be focal, involving only a hand, part of a hand, or the face.
  - It may be always within the region of somatic motor or sensory impairment.
  - It may begin at the time of the CVA or be delayed for months.

Casey, Pain, 2004

CPSP (cont’d)

- Using quantitatively evaluated sensory testing, it was found that, in CPSP, tactile allodynia occurs in disturbances of thermal/pain pathways that can spare the tactile signaling pathways, and that cold hypoesthesia itself is not necessary or sufficient for cold allodynia.

- Another way of evaluating CPSP using PET scan technology revealed a striking loss of opioid receptor availability widely distributed throughout a great deal of the hemisphere contralateral to the pain (especially in the thalamus, anterior and posterior cingulate cortex, insula, S2, and lateral prefrontal cortex).

Greenspan et al, Pain, 2004; Willoch et al, Pain, 2004
CPSP (cont’d)

- It has previously been pointed out that decreased opioid receptor binding can also indicate the release of endogenous opioids during pain.
- The authors of the previous study found that the location and distribution of the diminished receptor binding was more extensive and showed little overlap as compared to the second group.
- It is thought possible that the loss of opioid receptor availability in CPSP may be secondary to a reduction or down-regulation of opioid receptors, resulting in a reduction of effectiveness of endogenous, opioid-mediated, analgesic mechanisms.

Willoch et al, Pain, 2004; Zubieta et al, Science, 2001

CPSP (cont’d)

- A later study looked at peripheral vs central neuropathic pain.
  - The authors used PET scans to evaluate patients with peripheral (n = 7) and CPSP (n = 8) neuropathic pain patients.
  - They found that in CPSP patients, interhemispheric comparison indicated a significant decrease in opioid binding in the posterior midbrain, medial thalamus, and the insular, temporal, and prefrontal cortices contralateral to the painful side.
  - The patients with peripheral neuropathic pain did not show any lateralized decrease in opioid binding.
  - The authors concluded that decreases in opioid binding were much more extensive than anatomical cortical lesions and were not localized with the lesions: metabolic depression (diaschisis) and/or degeneration of opioid receptor-bearing neurons secondary to central lesions appear to be the likely mechanism.

Maarrawi et al. Pain, 2007

CPSP (cont’d)

- Sympathetic dysfunction has also been felt to play a role in central pain secondary to signs of abnormal sympathetic activity that are secondary to peripheral issues, or CPSP itself:
  - Edema
  - Hyperesthesia
  - Trigeminal nerve changes (thinning)
  - Changes in skin color (violascence)
  - Decreased skin temperature
- Essentially the picture of CRPS!
- It is also noted that some or many of these changes may be secondary to "movement allodynia," which makes the patient keep the affected limb motionless.

Bowsher, Postgrad Med, 1995; Bowsher, J Neurol Neurosurg Psychiatry, 1996; Riddoch, Lancet, 1938
Minor Traumatic Brain Injury (mTBI)

MRI—N and Severe TBI

(A) Pre-injury magnetic resonance image (MRI) approximately 2 years prior to a severe traumatic brain injury (TBI). Note the normal size of the ventricular system and ventricle-to-brain (VBR) ratio (approximately 1.5 with a 0.5 standard deviation).

(B) Day-of-injury initial CT demonstrating brain edema and reduced VBR, which continues to be reflected in (C,D).

(E) Distinct neurodegeneration has occurred by 16 weeks postinjury, reflected as ventricular dilation and increased VBR, with continued neurodegeneration out to 2 years postinjury as seen in (F).

Diffusion Tensor Imaging—mTBI

Structural and functional connectivity in traumatic brain injury ...
mTBI

- It is the patients with mTBI that feel the pain: the worse the TBI, the less pain is noted by patients
- Headaches are present in 59% of brain injury patients, regardless of trauma severity
- According to the International Headache Society III classification, PTHA may present similar to primary headache disorders
  - Migraine
  - Tension-type
  - Cluster headaches
- PTHA usually develops within 7 to 30 days after injury and usually resolves within the expected tissue-healing time of 3 months


mTBI (cont’d)

- Persistence of pain beyond 3 months suggests pain chronicity with underlying peripheral and central sensitization in the trigeminal system
- The average onset time for chronic head and facial pain is about 6 months


mTBI (cont’d)

- The characteristics of chronic pain after TBI resemble those of chronic central pain from other causes, with painful regions exhibiting allodynia, hyperpathia, and wind-up, but not common
- A 1-year follow-up study on combat veterans with TBI revealed that 54% of those continued to experience headaches; the majority of veterans experienced their headache on a daily basis mostly in the frontal area
- In contrast, in a study that examined the TBI in a civilian population, the occipital area was more involved

mTBI (cont’d)

- The quality of HA pain is usually more pricking, throbbing, and pounding, with few complaints of burning pain, which is more frequent in SCI.
- Sensory profiles of patients with PIHPA reveal higher thermal thresholds and lower mechanical pain thresholds in the hands and face suggestive of a central origin of pain.
- Almost all patients with TBI have movement allodynia, which is not common after SCI.


mTBI (cont’d)

- TBI can directly lead to headaches or can worsen preexisting headaches.
- The literature is scarce on studies that evaluate measures of pain intensity or pain-related behavior among patients with cognitive deficits from moderate to severe TBI. The author’s experience showed that patients with moderate to severe cognitive deficits complained less of pain (of course a number of TBI were in a vegetative state).
- Similarly, no studies compared patients with blast-related headache to patients with other types of headache, or assessed treatments for blast-related headache.


Treatment of Central Pain Syndromes
Basic Treatment

- The pharmacological treatment of CRPS can be broken into several treatment management groups:
  - First-line management includes:
    - TCAs
    - Gabapentin
    - Lamotrigine
    - Topical lidocaine
    - May consider STN DBS or DBS for MCI
  - Second-line management involves the addition of:
    - Other ACMs
    - Other ADMs
  - Third-line management uses extended release opioids and other medications
    - Opioid analgesics (ER) or tramadol along with the first-line medications
    - Anticonvulsants
    - Intrathecal baclofen
    - IV lidocaine

Jay et al, Dis of Month, 2015; Dworkin et al, Pain 2007

Treatment

- CFS: “Cancer of the spirit” with continuous decrement in QOL
- If oral medications do not help within 6 months, neurostimulation should be utilized
  - Extradural cortical stimulation (ECS) of the primary motor or sensory cortex contralateral to pain
  - Deep brain stimulation (DBS) has not borne out its usefulness
  - Spinal cord stimulation (SCS) may be helpful for at least a year, but may lose effect after that time period
- Intrathecal baclofen with clonidine
- Neuroablation, results poor, uses positive, small percutaneous lesion deep in corona radiate/internal capsule to interrupt descending arm of the corticospinal loop


Treatment (cont’d)

- The most common first-line drug is amitriptyline
  - Other drugs including opioids treated as second or third line
- Amitriptyline is thought to be helpful, secondary to its reuptake of norepinephrine and serotonin
  - In a controlled trial of amitriptyline and carbamazepine, only patients on amitriptyline reached a statistically significant reduction compared to placebo
  - Patients on carbamazepine did not but had “some pain relief” and more side effects

### Treatment (cont’d)

- Anticonvulsants including lamotrigine and gabapentin have been reported to provide pain relief with better safety than carbamazepine and phenytoin.
  - In spite of the articles suggesting lamotrigine provided good relief of CPSP, a Cochrane review found that lamotrigine had only limited evidence that it would be useful, and it was, in fact, unlikely to be of benefit for the treatment of neuropathic pain.


- The author was introduced to “Sweet’s Cocktail” during training, which has a very narrow therapeutic index.
  - Amitriptyline 75 mg QHS and Stelazine 1 mg TID
  - While the author never been able to find a quotation related to Dr. Sweet, Duthie published on this combination.
  - A number of patients who were intractable to “typical medications” received relief with this drug combination, although the possible side effects of a phenothiazine must be constantly looked for.
  - Phenothiazines have been used to treat pain for decades.
  - Recent work on atypical antipsychotics for pain.


- Other antidepressants and anticonvulsants have also been tried in the treatment of CPSP, but none has become a primary or gold-standard treatment.
  - The closest is pregabalin.

Treatment (cont’d)

- Carbamazepine is useful for lancinating pain
- Mexiletine is useful for thalamic pain (central pain syndrome)
- NSAIs are also useful, and the author will combine with ACMs prior to XR opioids
- Intravenous lidocaine appeared to be helpful in patients with CPSP
- Intravenous naloxone was not helpful in CPSP
- Intrathecal baclofen, an agonist of GABA-B receptors, did provide relief for CPSP patients


Treatment (cont’d)

- Stimulation of the primary motor cortex for intractable deafferentation pain, as well as central stroke pain, has been used successfully
  - The mechanism of pain relief by this form of electrical stimulation of MI is uncertain
  - However, motor cortex stimulation is felt to be the treatment of choice in poststroke pain, thalamic pain, or anesthesia dolorosa of the face


Treatment (cont’d)

- Repetitive transcranial magnetic stimulation of the primary motor cortex has also been used successfully
  - As long as the postcentral gyrus (MI) is stimulated
  - Another group found this modality to give good but transient relief

Hirayama et al. Pain, 2006; Lefaucheur et al, J Neurol Neurosurg Psychiatry, 2004
Treatment (cont’d)

Other treatments include:

– Surgical interventions including (discussed earlier)
  – Cordotomy
  – Dorsal root entry zone (DREZ) lesions
  – Thalamotomy
  – Cortical and subcortical ablation


Treatment (cont’d)

An important evidence based medicine treatment guideline, was published in 2007 by Dworkin et al.

These EBM guidelines for the pharmacological management of neuropathic pain insisted that first line medications would include:

– Tricyclic antidepressants (TCAs)
– Selective serotonin and norepinephrine reuptake inhibitors (SSRIs)
– Calcium channel alpha 2-delta ligands
– Topical lidocaine

Dworkin et al, Pain, 2007

Treatment (cont’d)

Second line medications included (per Dr. Dworkin):

– Opioid analgesics
  – Tramal

Third-line medications included:

– Other anticonvulsants
– Other antidepressants
– NMDA antagonists
– Topical capsaicin

The author typically considers IR opioids while titrating ACOMs/ADMs, if the patient is doing physical therapy and needs help re: MM/Skel issues

ER opioids third-line, essentially a “Hail Mary” pass (see next slide)
CPSP and Opioids

- Recall that, as noted, there is a paucity of mu opioid receptors in the brain contralateral to the CPSP
- Therefore, to expect opioids to work is fairly incredible—They won’t

Polypharmacy

- Polypharmacy is mandatory
  — But physicians must understand all aspects of all drugs used
  — Particularly if used together (as would be appropriate)

Treatment in SCI: For Gliopathy

- Minocycline—for glial cell hyperactivity
  — 100 mgs Q 12 hours in the adult
  — May also try for CRPS
Sleep and Anxiety

- Medications for sleep: would suggest the use of TCAs (in patients who can take them... be careful of the anticholinergic AEs)
- Antianxiety drugs: not good medicine to mix a benzodiazepine with an opiate

Treatment

- Treatment of these very difficult cases involves more than just a medication:
  - a full out bio-psycho-social intervention is most helpful, and was best found in the interdisciplinary pain center, now extremely hard to find.
  - While medication choices depend on knowledge, experience, and competence, the use of psychological services (such as cognitive behavioral therapy) as well as true rehabilitation is what will truly help the patient with central neuropathic pain

Questions?