Pain Management after Spinal Cord Injury

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Introduction

- Definitions
- Anatomy
- Pathophysiology
- Taxonomy
  - Diagnosis
  - Treatment
- Practical Applications
Objectives

- Review anatomy and pathophysiology of pain
- Discuss pain taxonomy relevant to treatment intervention strategies
- Provide a stepwise approach to managing SCI Pain
Definitions

- **Pain**: Unpleasant sensory & emotional experience associated with actual or potential tissue damage
- **Nociceptive**: Pain in which normal nerves transmit information to the CNS about trauma to tissues
- **Neuropathic**: Pain in which there are structural &/or functional nervous system adaptations due to injury
  - **Alldynia**: Pain due to a stimulus which does not normally provoke pain
  - **Causalgia**: Burning pain, alldynia & hyperpathia, vasomotor & sudomotor dysfunction after traumatic nerve lesion
  - **Central Pain**: Initiated or caused by a 1° lesion in CNS
  - **Dysesthesis**: An unpleasant abnormal sensation, whether spontaneous or evoked
  - **Hyperesthesia**: Increased sensitivity to stimulation, excluding the special senses
  - **Hyperpathic**: Painful syndrome characterized by an abnormally painful reaction to a stimulus, especially a repetitive stimulus
  - **Neuralgia**: Pain in the distribution of a nerve or nerves
  - **Paresthesia**: An abnormal sensation, whether spontaneous or evoked
Central Nervous System

**Autonomic Nervous System**
- **Parasympathetic** (Cranial Nerves)
  - Heart
  - Gastrointestinal
- **Sympathetic** (Thoracolumbar)
  - Cardiovascular
  - Lungs
  - Gastrointestinal
  - (Ad)Renal
  - Sweat Glands
- **Parasympathetic** (Sacral)
  - Bowel
  - Bladder

**Somatic Nervous System**
- C3-C5  Diaphragm
- C5    Elbow Flexors
- C6    Wrist Extensors
- C7    Elbow Extensors
- C8    Finger Flexors
- T1    Finger Abductors
- T2-T8 Intercostals
  - Paraspinals
- T7-T12 Abdominals
- L2    Hip Flexors
- L3    Knee Extensors
- L4    Ankle Dorsiflexors
- L5    Toe Extensors
- S1    Ankle Plantarflexors
Cellular Components of CNS

- Nerve Cells (1)
  - Conduct electrical impulses
- Glial Cells (9X > Neurons)
  - Support, Nourish & Insulate (Protect) Neurons, but do not conduct nerve impulses
  - Types include:
    - Oligodendrocytes (2): CNS Myelin
    - Astrocytes (5): Nutritive Function
    - Ependymal Cells (6): CNS lining
    - Microglia (7): Phagocytic
    - *Schwann Cells: PNS Myelin
      - Not usually found in CNS
Neural Tracts of Spinal Cord

- Fasciculus Semimarginalis
- Fasciculus Gracilis
- Fasciculus Cuneatus
- Fasciculus Dorsolateralis
- Posterior Spino-Cerebellar Tract
- Lateral Spino-Thalamic Tract
- Anterior Spino-Cerebellar Tract
- Spino-Olivary Tract
- Spinotectal Tract
- Anterior Spinthalamic Tract
- Anterior Corticospinal Tract
- Tectospinal Tract
- Ventral Reticulospinal Tract
- Lateral Reticulospinal Tract
- Rubrospinal Tract
- Lateral Corticospinal Tract
- Fasciculus Interfascicularis
Conduction through Spinal Cord

- **Descending Tracts**
  - Lateral Corticospinal
  - Anterior Corticospinal
  - Vestibulospinal
  - Rubrospinal
  - Pontine/Medullary
  - Reticulospinal

- **Ascending Tracts**
  - Spinothalamic
  - Spinoreticular
  - Dorsal Columns

- **Peripheral Nervous System**
  - Afferent (Sensory) Neurons
  - Efferent (Motor) Neurons

- **Interneurons**
  - Facilitatory
  - Inhibitory
Ascending Tracts

- Spinothalamic
  - LT, PP, and Temperature
- Spinoreticular
  - Deep Pain
- Dorsal Columns
  - Proprioception, Vibration, and Light Touch
Decussation of Pathways

- **Pain-Temp** (Spinothalamic)
- **Pos-Vibration** (Post Columns) (Med Lemniscus)
- **Light Touch** (Med Lemniscus) (Spinothalamic)
- **Unconscious Proprioception** (Spinocerebellar)
- **Voluntary Motor** (Corticospinal)
Pain Pathways
Neural Pain Transmission

- **Primary Afferents:** Peripheral organ to dorsal columns of spinal cord
  - **A-beta (Non-nociceptive)**
    - Respond to low-intensity, non-painful, proprioceptive-vibratory & light touch stimuli
    - Thick myelin, large diameter, & fast conducting
  - **A-delta (Nociceptive)**
    - Respond to well-localized sharp pain & assist with pain withdrawal
      - Thermal, Mechanical, Chemical
    - Thin myelin, moderate diameter, & moderately fast conducting
  - **C (Nociceptive)**
    - Respond to variety of noxious stimuli & transmit poorly localized, dull pain
      - Thermal, Mechanical, Chemical
    - Unmyelinated, small diameter, slow conducting

- **Secondary Afferents:** Dorsal Columns to Thalamus & Brain Stem (Reticular)
- **Tertiary Afferents:** Thalamus to Somatosensory Cortex
### Pain-Mediating Neurotransmitters

- **A. Primary Afferents**
  - Transmitters: Glutamate & Aspartate
  - Modulators: Substance P, Calcitonin Gene-related peptide, Vasoactive Intestinal Polypeptide (VIP), Neuropeptide Y (NP-Y)

- **B. Descending Inputs**
  - Transmitters: Glutamate, Ach, Serotonin, Norepi, Dopamine
  - Modulators: Somatostatin, Substance P, Endorphins

- **C. Local Circuit Interneurons**
  - Transmitters: Glutamate, Aspartate, Glycine, GABA, Ach
  - Modulators: Somatostatin, Substance P, Enkephalin, VIP, NP-Y

- **D. Non-specific Targets**
  - Ion Channels (Na⁺, K⁺, Ca⁺⁺, Cl⁻): e.g., NAᵥ1.7 Channel
  - Second Messengers

- **E. Trans-synaptic Signals**
  - Nitric Oxide, Carbon Monoxide, Prostaglandins

- **Other Factors**
  - Neurotrophins
  - Canabinoids
Mechanisms for SCI Neuropathic Pain

- Structural Reorganization of spinal cord and thalamus
  - Brain involvement implied by ineffectiveness of cordectomy
  - Hyperactivity & spontaneous activity noted in deafferentation models
  - Disinhibition or imbalance of spinal pathways
  - Intraspinal sprouting
  - Possible blood brain barrier / CSF abnormalities

- Neurochemical changes
  - Excitatory amino acids (EAA) released after SCI (e.g. glutamate) that contribute to hyperexcitability
  - Inflammatory products
  - Sympathetic Influence
Barriers to SCI Repair

- **Structural Inhibition**
  - Glial Scarring
    - Cell membrane lipid peroxidation
    - Superoxide/Nitric Oxide radicals
  - Lack of Directional Guidance
    - Chemotaxis
    - Structural/Electrical Bridges
- **Bridging the gap**
  - Schwann Cells or Stem Cells
- **Biochemical Inhibition**
  - Nogo proteins from Oligodendrocytes
  - Myelin-associated glycoprotein (MAG)
  - Tumor necrosis factor-α (TNF-α)
  - Nuclear factor kappa B (NF-κB)
- **Growth Factors: Timing & Concentration**
  - Nerve Growth Factor (NGF)
  - Brain-derived neurotrophic factor (BDNF)
  - Glial-derived neurotrophic factor (GDNF)
  - Fibroblast growth factor (FGF-2)
  - cAMP: Regeneration cue
Chemokines in Neuropathic Pain

## Treatment Options

- **Non-Pharmacological**
  - Biomechanical
  - Modalities
  - Psychotherapy

- **Pharmacological**
  - Anti-inflammatory
  - Opioids
  - Antidepressants
  - Anticonvulsants
  - Local Anesthetics
  - Antispasticity

- **Interventional / Surgical**
  - Injections
  - Decompression
  - Ablation (e.g. DREZ Procedure)
  - Dorsal Column Stimulator

<table>
<thead>
<tr>
<th>Mechanisms</th>
<th>Therapeutic options</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Central sensitization</td>
<td>Ca(^2+) channel antagonists, NMDA receptor antagonists, Glutamate antagonists</td>
</tr>
<tr>
<td>B. Reduced inhibition</td>
<td>Central α-receptor agonists, NE reuptake inhibition, Serotonin reuptake inhibition, GABA agonists, TENS, SCS, Opioids</td>
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<td>C. Sympathetic activation</td>
<td>Central α-receptor agonists, Peripheral α-receptor antagonists, Sympathetic nerve blocks, Systemic sympatholytics</td>
</tr>
<tr>
<td>D. Peripheral sensitization</td>
<td>Na(^+) channel antagonists, Ca(^2+) channel antagonists</td>
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Pain Taxonomy in SCI

- Pain above Level of Injury
  - Nociceptive
  - Neuropathic
- Pain @ Level of Injury
  - Nociceptive
  - Neuropathic
- Pain below Level of Injury
  - Nociceptive
  - Neuropathic

2006 Pain Taxonomy for SCI

- Nociceptive
  - Musculoskeletal
  - Visceral
- Neuropathic
  - Above LOI
  - At LOI
  - Below LOI

## 2011 Pain Taxonomy in SCI

<table>
<thead>
<tr>
<th>Tier 1: Pain Type</th>
<th>Tier 2: Pain Subtype</th>
<th>Tier 3: Pain Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nociceptive</td>
<td>Musculoskeletal</td>
<td>E.g. Glenohumeral OA</td>
</tr>
<tr>
<td>Neuropathic</td>
<td>Visceral</td>
<td>E.g. MI, appendicitis</td>
</tr>
<tr>
<td>Other Pain</td>
<td>Other</td>
<td>E.g. AD / Migraine HA</td>
</tr>
<tr>
<td>Unknown Pain</td>
<td>At SCI Level</td>
<td>E.g. Root compression</td>
</tr>
<tr>
<td></td>
<td>Below SCI Level</td>
<td>E.g. Cord ischemia</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>E.g. CTS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E.g. Fibromyalgia, CRPS 1 or 2, Trig. Neuralgia</td>
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<td>?</td>
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</tbody>
</table>

Rx of Pain in SCI

Treatment of Pain

- Assessment
- Identify Pain Type
- Historical Assessment
- Identify Pain Sub-type
- Structural Assessment
- Identify Pathology
- Treat Cause
- Treat Symptoms
System Assessment

- Is pain located in a region of normal sensation?
  - Yes: Noceceptive
  - No: Neuropathic
Site Assessment

- Position-dependent?
  - Activity-related?
  - Somatic-tenderness?
- Viscera-related?
- Above level?
- At level?
- Below level?
Structural Assessment

- Autonomic Signs & Symptoms?
  - Complex Regional Pain Syndrome (CRPS)

- Sensory / Motor deficit on NCS?
  - Peripheral Nerve lesion

- Root compression on imaging studies?
  - Root lesion

- Cystic Cavity on MRI
  - Syringomyelia
Treat Cause

- Sympathetic Blockade
- Functional Rehabilitation
- Surgical Decompression
- Syrinx shunt / detethering
Treat Symptoms

- **First Tier**
  - Sympathetic Blockade (CRPS)
  - Lidocaine Patch (Acute)
  - Gabapentin (Chronic)

- **Second Tier**
  - Tricyclic Antidepressant or Tramadol (Ultram)
  - Combine Gabapentin & TCA

- **Third Tier**
  - Pregabalin
  - Opioids
  - Intrathecal morphine, clonidine or baclofen
  - Non-Pharmacological:
    - TENS, Acupuncture, Dorsal Column Stimulator
    - Dorsal Root End Zone (DREZ) or cordotomy

Pain Above SCI LOI

- Nociceptive
  - Musculoskeletal / Mechanical
  - Visceral
  - Autonomic Dysreflexia (HA)
  - Other
- Neuropathic
  - Compressive Neuropathy
  - Central (Syringomyelia)
  - Other
Nociceptive Pain above SCI

- Musculoskeletal
  - Spine DJD above fusion
  - Rotator Cuff Impingement
  - Epicondylitis
  - DeQuervain’s Tenosynovitis
  - MCP Dysfunction
  - Myofascial Pain
Managing M/S Pain above SCI

- **Prophylaxis**
  - Home Exercise
    - Neck & Scapular Stabilization
    - IR/ER Strengthening
    - Conditioning & Weight Mngmt
  - Optimize ROM, Positioning & Sleep
  - Minimize Noxious Stimuli

- **Treatment**
  - R-I-C-E-D
  - Judicious steroid application
  - Surgical Options

Paralyzed Veterans of America (2005)
Nociceptive Pain above SCI LOI

- Visceral
  - Cardiopulmonary
    - Cardiac Ischemia, Myocardial Infarction
    - Bronchitis, Pleurisy, Tumor, Infection
  - Gastrointestinal
    - Cholecystitis, PUD, Ileus
    - Tumor, Ischemia, Infection
  - Genitourinary
    - Renal/Bladder Calculi, UTI
    - PID, Pregnancy, Tumor, Torsion

- Treat Underlying Cause
Neuropathic Pain Above SCI

- Compressive Neuropathy
  - Ulnar Neuropathy
    - Cubital Tunnel
    - Guyan’s Canal
  - Median Neuropathy
    - Carpal Tunnel Syndrome
  - Radiculopathy

- Central
  - Syringomyelia
    - Abnormal, fluid-filled cavity within the substance of the spinal cord
  - Hematoma
  - Trauma (New)
  - Tumor

- Other (Non-SCI Related)
  - Temporomandibular Joint Dysfunction
  - Temporal Arteritis
Managing Neuropathic Pain above SCI LOI

- Physical Management
  - R-I-C-E
    - Splinting / Cushioning
    - Positioning
    - Neurotension Release
  - Acupuncture
  - Massage
  - TENS

- Pharmacological
  - NSAIDs
  - Tricyclic Antidepressants
  - Anticonvulsants

- Surgical Decompression
Pain @/ Below SCI Level of Injury

- Nociceptive
  - Musculoskeletal / Mechanical
  - Visceral
- Neuropathic
  - Central Pain
  - Radicular
  - Complex Regional Pain Syndrome
- Essential to find underlying cause!
**Autonomic Dysreflexia**

- **Definition:**
  - Massive Sympathetic outflow in response to noxious stimuli below the level of Spinal Cord Injury in complete SCI lesions above T6

- **Complications**
  - CVA
  - Seizures
  - Organ Failure
Splanchnic Vasoconstriction

Bradycardia

Vasodilation

HYPERTENSION!!

Autonomic Dysreflexia

Noxious Stimuli

Splanchnic Vasoconstriction

Bradycardia

Vasodilation

HYPERTENSION!!
Acute Management of AD

- Elevate head
- Loosen tight clothing, leg bags, etc.
- Check bladder, bowel, other sources
- Pharmacological Intervention
Pharmacological Rx of A.D.

- **Immediate/Emergent**
  - Nitropaste 0.5” topically, or
  - NTG 1/150 s.l.
  - Procardia 10 mg p.o./s.l.
  - Clonidine 0.1 to 0.2 mg p.o.
  - Hydralazine - 10 to 20 mg. IM/IV

- **Chronic (Recurrent Episodes)**
  - Dibenzyline 10 mg bid, up to 120 mg/d
  - Prazosin 0.5 -1.0 mg p.o. qd, up to 0.4 mg/kg/d
  - Terazosin 1-5 mg qd, up to 20 mg/d
  - Clonidine 0.2 mg. p.o. b.i.d.
Nociceptive Pain @/Below SCI LOI

- Musculoskeletal / Mechanical
  - Spine &/or Hardware Instability
  - DJD / DDD
  - Muscle Strain / Myofascial Pain
  - Incisional Pain
  - LE Fractures, HO, etc.

- Visceral
  - Cardiopulmonary
    - Myocardial Infarction
    - Pleurisy, Tumor, Infection
  - Gastrointestinal
    - Cholecystitis, PUD, Ileus
    - Tumor, Ischemia, Infection
  - Genitourinary
    - Renal/Bladder Calculi, UTI
    - PID, Pregnancy, Tumor, Torsion
Neuropathic Pain @/Below SCI LOI

- Central
  - Syringomyelia
  - Trauma (New)
  - Tumor
- Radicular: Usually specific root level
- Complex Regional Pain Syndrome
  - Two or more root levels involved
  - Burning pain, hyperalgesia, edema, sudomotor sx including redness, warmth and sweating along root distributions
  - Type I (Reflex Sympathetic Dystrophy)
    - No direct nerve damage identified
  - Type II: Causalgia
    - Direct nerve injury
Managing Neuropathic Pain at or below SCI LOI

- Identify Pathology
- Treat Underlying Cause
  - CRPS: Sympathetic Block
- Pharmacological
  - Oral
    - Tricyclic Antidepressants
      - Amitriptyline
      - Nortriptyline
    - Anticonvulsants
      - Gabapentin
      - Carbamazepine
      - Pregabalin
  - Intravenous
  - Intrathecal
- Surgical Decompression
- Dorsal Column Stimulator
Treatment Options

- **Pharmacological**
  - Anti-inflammatory
  - Opioids
  - Antidepressants
  - Anticonvulsants
  - Local Anesthetics
  - Antispasticity

- **Interventional / Surgical**
  - Injections
  - Decompression
  - Ablation (e.g. DREZ Procedure)
  - Dorsal Column Stimulator

- **Non-Pharmacological**
  - Biomechanical / Physical Modalities
  - Psychotherapy
Pharmacological Rx Plan

**Nociceptive Pain**
- Acetaminophen
- Anti-inflammatory Agents
- Opioids (Acutely)

**Neuropathic Pain**
- First Tier
  - Sympathetic Blockade (CRPS)
  - Lidocaine Patch (Acute)
  - Gabapentin (Chronic)
- Second Tier
  - Tricyclic Antidepressant or Tramadol (Ultram)
  - Combine Gabapentin & TCA
- Third Tier
  - Pregabalin
  - Opioids
  - Intrathecal morphine, clonidine or baclofen
  - Non-Pharmacological:
    - TENS, Acupuncture, Dorsal Column Stimulator
    - Dorsal Root End Zone (DREZ) or cordotomy

Non-Pharmacological Rx

- Physical Management
  - Sleep
  - Exercise & Diet
  - Positioning
  - Acupuncture
  - Massage
  - TENS

- Psychological
  - Cognitive Behavioral Therapy (CBT)
  - Behavioral Activation
  - Relaxation Techniques
  - Hypnosis

- Interventional / Surgical
A Painful close...

"We no other pains endure
Than those that we ourselves procure."

Spencer Dryden
Drummer, Jefferson Airplane
1938-2005