

Pain and Sensory Symptoms: A case based approach

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Objectives

- * Identify types of pain and sensory symptoms typical to patients with MS
- * Review pharmacological and non-pharmacological methods of managing pain
- * Identify factors that contribute to pain response

Why Does it Matter?

- * Pain prevalence reports vary from 29-86% of MS patients^{1,2}
- * More than 50% MS patients find pain to be a problem, and for 10-20% it is a significant problem³
- * Pain is estimated to comprise nearly 30% of all symptomatic treatment⁴
- * Pain can interfere substantially with the ability of patients with MS to work, sleep, maintain relationships and enjoy life⁵

1. Solaro, MD, et al. (2004) The prevalence of pain in multiple sclerosis. *Neurology* 63: 919-921.

2. Betske, AC et al (2004) Pain and sensory complaints in multiple sclerosis. *European Journal of Neurology* 11: 479-482.

3. Schapiro, R (2007) Managing the Symptoms of Multiple Sclerosis

4. Solaro C and Uccelli MM (2011). Management of pain in multiple sclerosis: a pharmacological approach. *Nature Reviews*: 7: 519-527

5. O'Connor AB, Schwid SR, Hermann DN, et al. (2007). Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain*. 137:96-111.

Types of Pain

Pain in MS¹

- * Central Neuropathic Pain: Direct consequence of a demyelinating lesion in the central nervous system
 - ▣ lancinating, pins and needles, burning, electric shock.
Commonly associated with allodynia (painful response to non-painful stimuli) and/or hyperalgesia (increased response to painful stimuli)²
- * Non-neuropathic Pain: Indirect consequence of the disability associated with MS

1. Maloni H. (2012) Pain in Multiple Sclerosis. *Clinical Bulletin*. <http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ClinicalBulletin-Maloni-Pain.pdf>

2. Solaro C and Uccelli MM (2011). Management of pain in multiple sclerosis: a pharmacological approach. *Nature Reviews*: 7: 519-52

Classifications of MS related pain

- * Intermittent Central Neuropathic Pain
- * Continuous Central Neuropathic Pain
 - * Musculoskeletal Pain
 - * Mixed Neuropathic and Non-neuropathic pain

Case Study: Norma

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- * 56-year-old female
- * Diagnosis of RRMS at age 34 with progression since age 48.
- * Presents with minute long episodes of excruciating left jaw pain present for 3 weeks. It is painful to eat, talk, brush her teeth.
- * Evaluated by the dentist, no cause of pain identified.

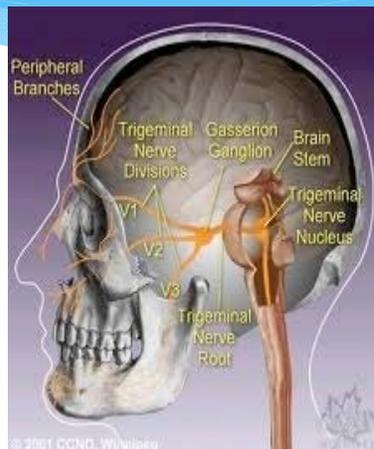
Intermittent Central Neuropathic Pain

- * Neuropathic pain that occurs spontaneously or is paroxysmal
- * Described as shooting, stabbing, shock-like, lancinating, crushing or searing
- * More intense than continuous central neuropathic pain
- * Examples: Trigeminal Neuralgia, Lhermitte's sign

O'Connor AB, Schwid SR, Hermann DN, et al. (2007). Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain*. 137:96-111

Trigeminal Neuralgia

- * Incidence of TN in MS is roughly 20 times the prevalence of the general population¹
- * Prevalence in patients with MS ranges 2-6%^{2,3}
- * Described as a paroxysmal sharp, lancinating pain lasting seconds to minutes affecting one or more branches of the trigeminal nerve²
- * Triggered by facial movement/stimulation talking, chewing, breeze



1. O'Connor AB, Schwid SR, Hermann DN, et al. (2007). Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain*. 137:96-111
 2. Solaro C and Uccelli MM (2011). Management of pain in multiple sclerosis: a pharmacological approach. *Nature Reviews*: 7: 519-52
 3. Nurmikko TJ, Gupta S, MacIver K (2010) Multiple Sclerosis-related central pain disorders. *Curr Pain Headache Rep* 14:189-195.

Trigeminal Neuralgia

- * First line treatment consists of anti-epileptic drugs (AED)
- * Poor tolerability of medications and/or severity of pain necessitates early consideration for neurosurgical consult¹
- * Interventional treatment options:
 - ▣ Percutaneous retrogasserian glycerol rhizotomy
 - ▣ Radiofrequency rhizotomy
 - ▣ Microvascular decompression (reserved for non-responders)

1. Nurmikko TJ, Gupta S, Machver K (2010) Multiple Sclerosis-related central pain disorders. *Curr Pain Headache Rep* 14:189-195

Guiding Principles for Treating Pain

- * Educate patients regarding off label uses of medications
- * Start low, go slow
- * Lower doses of a combination of medications may result in better toleration than high dose of a single agent
- * All AEDs and antidepressants have the potential to increase the risk of suicidal thoughts and behaviors for patients taking them for any reason
- * Consistently assess for benefit and wean appropriately

Anticonvulsants

- * Carbamazepine (Tegretol)
 - ❑ Indications: AED, TN
 - ❑ Side Effects: drowsiness, dizziness, nausea, unsteadiness
 - ❑ Black Box Warning: SJS, TEN, Aplastic Anemia, SI
 - ❑ Monitoring: CBC and CMP at baseline and periodically
 - ❑ Start 100 mg bid. Max dosage 1200 mg/day
 - ❑ Reduces plasma concentrations of oral contraceptives
- * Oxcarbazepine (Trileptal)
 - ❑ Indications: AED
 - ❑ Side Effects: drowsiness, dizziness, nausea, unsteadiness
 - ❑ Monitoring: hyponatremia
 - ▼ Caution with concurrent meds known to decrease Na levels
 - ❑ Start 150 mg bid, increase every 3-7 days. Max dosage 2400 mg/d
 - ❑ Reduces plasma concentrations of oral contraceptives

Anticonvulsants

- * Gabapentin (Neurontin)
 - ❑ Indications: AED and post herpetic neuralgia (PHN)
 - ❑ Side Effects: somnolence, weight gain, dizziness, ataxia, peripheral edema
 - ❑ Caution in renal impairment
 - ❑ ~30% prescriptions for fibromyalgia or chronic neuropathic pain
 - ❑ Initial: 100-300 mg tid, max dosage 3600 mg/day
- * Pregabalin (Lyrica)
 - ❑ FDA indications: AED, neuropathic pain associated with diabetes, fibromyalgia, PHN, and GAD
 - ❑ Similar SE profile to gabapentin
 - ❑ Initial: 50 mg bid, max dosage 600 mg/d

*Moore, RA; Wiffin, PJ; Derry, S; McQuay, JH (2011-03-16). "Gabapentin for chronic neuropathic pain and fibromyalgia in adults.". *Cochran database of systematic reviews (Online)* (3). CD007938.

Anticonvulsants

* Topiramate (Topamax)

- ▣ Indications: Migraine Prophylaxis, AED
- ▣ Side Effects: weight loss, somnolence, psychomotor slowing, paresthesias
 - ▼ Rare: acute myopia and secondary angle closure glaucoma
- ▣ Caution: history of renal calculi, renal or hepatic impairment
- ▣ Monitoring: metabolic acidosis
- ▣ Start 25 mg q hs, can increase by 25 mg weekly. Max dosage 400 mg daily

Norma Continued

- * MRI brain with and without contrast revealed enhancing pontine lesion
- * IVSM 1000 mg x 3 days given
- * Pain reduced from a 10/10 on VAS Pain scale to 5/10
- * Pain reported to be severe enough to merit further treatment
- * Initiated Carbamazepine 200 mg twice daily
- * Depending on benefit and toleration at follow up appointment in 4 weeks, will consider neurosurgery referral.

Other types of Intermittent Neuropathic Nerve Pain

Painful Tonic Spams

- * Paroxysmal abrupt onset attacks of abnormal posture of either arm or leg, typically lasting less than 2 minutes¹
- * Estimated to occur in 11% MS patients^{1,2}
- * Correlates with MRI lesions in the basal ganglia, internal capsule, cerebral peduncle, medulla, and spinal cord³
- * Not always associated with pain³
- * Anecdotal reports of benefit seen with AEDs, baclofen, benzodiazepines²

1. Nurmikko TJ, Gupta S, MacIver K (2010) Multiple Sclerosis-related central pain disorders. *Curr Pain Headache Rep* 14:189-195
2. Solaro C and Uccelli MM (2011). Management of pain in multiple sclerosis: a pharmacological approach. *Nature Reviews*: 7: 519-52
2. O'Connor AB, Schwid SR, Hermann DN, et al. (2007). Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain*. 137:96-111

Lhermitte's Sign

- ▣ Transient, short-lasting sensation related to neck movement, felt in the back of the neck, lower back or in other parts of the body
- ▣ Associated with MRI lesions of the cervical spine^{1,2}
- ▣ Tends to occur during exacerbations
- ▣ 25% patients never reported the symptom¹
- ▣ Symptomatic treatment is not necessary

1. O'Connor AB, Schwid SR, Hermann DN, et al. (2007). Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain*. 137:96-111
2. Nurmikko TJ, Gupta S, MacIver K (2010) Multiple Sclerosis-related central pain disorders. *Curr Pain Headache Rep* 14:189-195

Case Study: Kate

Case Study: Kate

- 32 year old female
- Diagnosis of RRMS 2008
- Initial symptoms consisted of numbness from the waist down
- Residual paresthesias to both feet rated as a 2/10 on the VAS pain scale

Continuous Central Neuropathic Pain

- ❑ Correlates with a CNS lesion/ spinothalamic dysfunction
- ❑ Characterized by abnormal sensations including burning, tingling, aching, itching, band-like, throbbing¹
- ❑ Central neuropathic pain occurs in nearly 50% MS patients²
- ❑ Most common type of pain associated with MS is dysesthetic extremity pain

1. Solaro C and Uccelli MM (2011). Management of pain in multiple sclerosis: a pharmacological approach. *Nature Reviews*: 7: 519-52
2. O'Connor AB, Schwid SR, Hermann DN, et al. (2007). Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain*: 137:96-111

Dysesthetic Extremity Pain

- * Typically bilateral
 - ▣ Affects the legs and feet more often than upper extremities
 - ▣ Usually worse at night
 - ▣ Can be exacerbated by physical activity
- * Symptoms may not be bothersome enough to merit medication
- * Often managed with AEDs and/or certain antidepressants

Back to Kate

- * Kate presents to the office with a significant increase in burning pain to both legs and feet for the past 6 weeks. (VAS 7/10)
- * Neurological exam reveals no changes. She has reduced vibratory sensation and altered temperature sensation to both feet, but these findings are stable.
- * No recent infections, and no symptoms of urinary tract infection.
- * BDI Fast Screen Score is 11 (scores >4 are suggestive of depression).
- * Kate's boyfriend of the past 4 years has broken up with her. She is sleeping poorly, and is stressed at work.

Depression and Pain

- * Pain is associated with depression, anxiety, fatigue.¹
- * Pain is exacerbated by sleep disturbance and spasticity
- * Negative thoughts and catastrophizing pain enhance the intensity of pain ²
- * Pain influences psychological aspects of quality of life resulting in poorer mental health and increased social handicap ¹
- * **Comprehensive management recommended over single-system approach ¹**

1. Solaro C and Uccelli MM (2011). Management of pain in multiple sclerosis: a pharmacological approach. *Nature Reviews*: 7: 519-52
 2. Maloni H. (2012) Pain in Multiple Sclerosis. *Clinical Bulletin*.
<http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf>

Tricyclic Antidepressants

- * Indications: Depression
- * Common side effects include weight gain, sedation, dry mouth, constipation, urinary retention
- * Contraindications: heart block, BPH, use of MAOi
 - ▣ Amitriptyline
 - ∨ Initial 10-25 mg q hs, may increase up to 150 mg/d
Typically most effective, but also has most side effects. Carries potential for cardiac conduction changes, especially with higher doses
 - ∨ Nortriptyline
 - ∨ Desipramine

SNRI

(Selective Norepinephrine Reuptake Inhibitors)

* Venlafaxine

- ❑ Indications: MDD (major depressive disorder)
- ❑ CI: use of MAOi
- ❑ Side effects: nausea, agitation, dry mouth, sweating, may increase blood pressure
- ❑ Start 37.5 mg each morning. Increase by 37.5-75 mg per week. Max dosage 450 mg/d
- ❑ Inhibits NE reuptake at dosages >150 mg/d. Weakly blocks dopamine reuptake at very high doses (above 350 mg/d)

SNRI cont'd

* Duloxetine

- ❑ Indications: MDD, GAD (generalized anxiety disorder), PDPN (painful diabetic peripheral neuropathy), fibromyalgia, chronic OA pain, chronic low back pain
- ❑ Balanced inhibitor of NE and 5-HT reuptake
- ❑ Common side effects: nausea, dry mouth, somnolence, decreased appetite
- ❑ Start 30 mg daily x 7 days then increase to 60 mg daily. Max dosage of 120 mg/day
- ❑ Isolated cases of liver failure have been reported, most cases in patients with history of liver injury, including alcohol abuse

SNRI cont'd

- * Milnacipran
 - ▣ Indications: management of fibromyalgia
 - ▣ MOA: NE and 5-HT reuptake inhibition (3:1 NE to 5-HT)
 - ▣ Side effects: nausea, headache, constipation, dizziness, insomnia, increased heart rate and blood pressure
 - ▣ Dosing: Day 1: 12.5 MG. Day 2-3: 12.5 mg bid. Day 4-7: 25 mg bid. After day 7: 50 mg bid

Kate: Treatment Plan

- * Obtain mental health history.
 - ▣ History of mild depression, treated with sertraline many years ago
- * Discuss management of stressors with Kate
 - ▣ Counseling
 - ▣ Sleep Hygiene
- * Offer medical management with SNRI
- * Follow up in 6 weeks to assess response

Case Study: Pete

Case Study: Pete



- * 48-year-old male
- * Diagnosis of PPMS at age 42
- * Presents with worsening gait and low back pain
- * Reports low back pain as 6/10, worsening to 8/10 with activity

Musculoskeletal Pain¹

- * MS predisposes patients to secondary musculoskeletal pain by causing weakness, muscle spasms, spasticity and reduced mobility
- * Prevalence ranges from 10-16%
- * MS treatments can cause myalgias, osteoporosis resulting in compression fractures, AVN
- * Low back pain can be associated with scoliosis, degenerative joint disease
- * Back pain can be central in origin as well

1. O'Connor AB, Schwid SR, Hermann DN, et al. (2007). Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain*. 137:96-111

Musculoskeletal Pain

- * Management consists of identifying underlying issue
- * Physical Therapy for assessment and management of safety, gait, positioning, seating and effective use of mobility aids
- * Medication management to include NSAIDS, acetaminophen, muscle relaxers

Patients More Likely to Experience Pain¹...

- * Older
- * Longer disease duration
- * Greater disease severity
- * Men and women are equally likely to experience pain, but women tend to have greater severity of pain
- * Progressive forms of MS
- * Co-morbid depression and mental health impairment

1. O'Connor AB, Schwid SR, Hermann DN, et al. (2007). Pain associated with multiple sclerosis: Systematic review and proposed classification. *Pain*. 137:96-111

Exercise

Chronic pain >>>> kinesiophobia >>>> deconditioning >>>> pain when attempt activity >>>> more rest

Breaking this cycle is critical for rehabilitation to take place

Exercise is another way for patients to be active participants in their own care

1. Sullivan AB, Scheman J, Venesy D, and Davin S (2012) The role of exercise and types of exercise in the rehabilitation of chronic pain: specific or nonspecific benefits. *Curr Pain Headache Rep* 16:153-161.

Correlates of Reduced Functioning

- * Catastrophizing cognitions
- * Guarding and resting as coping techniques
- * Belief that one is disabled by pain, that others should be solicitous when one experiences pain, and that pain is an indication of physical damage
- * Solicitous environmental responses to pain behaviors

1. Jensen, MP, Moore MR, Bockow TB, Ehde DM and Engel JM. (2011) Psychosocial Factors and Adjustment to Chronic Pain in Persons with physical disabilities: A systematic review. *Arch Phys Med Rehabil* 92(1):146-160.

Measures to address Reduced Functioning

- * Increase the use of coping strategies such as task persistence, acceptance of disability, behavioral activities, exercise, ignoring pain, and coping self-statements
- * Increase the belief that the patient can control pain and its effects
- * Help the patient seek and obtain more general (non-pain contingent) social support

1. Jensen, MP, Moore MR, Bockow TB, Ehde DM and Engel JM. (2011) Psychosocial Factors and Adjustment to Chronic Pain in Persons with physical disabilities: A systematic review. *Arch Phys Med Rehabil* 92(1):146-160.

Other Measures

Chronic Pain Rehabilitation Program

- * Stretching for spasticity
- * Massage
- * Distraction
- * Acupressure and Acupuncture
- * Cooling
- * Guided imagery

Pete: Assessment

- * Pete denies radicular pain
- * Observation of gait reveals left LE circumduction and mild foot drop
- * Palpation of low back reveals muscle spasm with trigger points to the lumbar paraspinals
- * Pete has a sedentary lifestyle and denies regular exercise or stretching

Pete: Plan

- * Referral to physical therapy to address abnormal gait and lower extremity weakness
- * Referral to orthotist for assistive device evaluation (AFO, E-stim device)
- * Stress importance of home exercise plan once PT has concluded
- * May need to consider anti-spasmodic medications if therapy alone doesn't address low back pain

Mixed Neuropathic and Non neuropathic Pain

- * Headache
 - ▣ More common in patients with MS than in general population
- * Muscle Spasms/Spasticity

A few words on Opioids...

Opioid Therapy

- * Opiates have minimal effect in central MS pain and are not recommended¹
- * In 2007, opioids were associated with more deaths than heroin and cocaine combined²
- * Approximately 1/3 of chronic pain patients may not use prescribed opioids as prescribed or may abuse them³
- * Opioids have become the most commonly prescribed drug category in the US

1. Maloni, H (2012). Clinical Bulletin: Pain in Multiple Sclerosis

2. Grady D, Berkowitz SA, Katz MH. Opioids for Chronic Pain. Arch Intern Med. Volume 171(16), 12 September 2011, p 1426–1427

3. Manchikanti L, Abdi S, Atluri S, et al (2012). American Society of Interventional Pain Physicians (ASIPP) Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain: Part I: Evidence Assessment. *Pain Physician* 15:51-566.

REMS

- * Risk Evaluation and Mitigation Strategy
- * In 2012, The US Food and Drug Administration (FDA) directed makers of all ER/LA opioids to provide free continuing education (CE) to educate prescribers and patients.
 - ▣ Ensure that benefits outweigh risks
 - ▣ Introduces new safety measures to reduce risks and improve safe use of ER/LA opioids while continuing to provide access to these medications for patients.

<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm363722.htm>

Best Practices for use of Opioids¹

- * Opioid treatment agreement
- * Screen for prior or current substance abuse/misuse (alcohol, illicit drugs, heavy tobacco use)
- * Screen for depression
- * Prudent use of random urine drug screening (diversion/non-prescribed drugs)
- * Do not use concomitant sedative-hypnotics or benzos
- * Track pain and function to recognize tolerance and track effectiveness

Franklin, GM. (2014). Opioids for chronic noncancer pain: A position paper of the American Academy of Neurology. *Neurology* 2014;83:1277-1284.

Best Practices for use of Opioids¹

- * Track daily morphine equivalent dosing (MED) using online dosing calculator
- * Seek help if MED reaches 80-120 mg and pain and function have not substantially improved
- * Use the state Prescription Drug Monitoring Program to monitor all sources of controlled substances.

Franklin, GM. (2014). Opioids for chronic noncancer pain: A position paper of the American Academy of Neurology. *Neurology* 2014;83:1277-1284.

Conclusion

- * Pain and sensory symptoms comprise significant amount of symptomatic treatment
- * Multiple modalities exist to assist in the management of pain
- * A comprehensive approach is recommended over single-system approach

Thank you!

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