

# NEURODEGENERATIVE DISEASES: PAIN

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## Disclosures

- There are some brief mentions of off-label use of medications.
- I have no relevant disclosures.



## Introduction

- Neurodegenerative diseases are increasing in frequency
  - Lifespan is longer
  - Longer life is a risk factor for many of these diseases
- Pain is (usually) not the symptom that brings the person to the neurologist, at least at first
  - Might be abnormal movements (i.e. Parkinson disease, Huntington disease)
  - Might be cognitive symptoms (i.e. Alzheimer disease, dementias)
- Despite this, these patients often complain of pain
- These diseases are not often thought of as being painful, so this symptom may be overlooked.



## Pain

- Uncomfortable sensation in the body
- Can range from annoying to debilitating
- Can be consistent or episodic
- Can be localized or generalized
- Chronic pain afflicts an estimated 86 million Americans
- Sometimes called the “fifth vital sign”



## Alzheimer disease

- Pain and Alzheimer prevalence both increase with age
- Difficult to determine pain prevalence because often these patients cannot self report
- Studies using observational tools to assess pain indicate that about 50% of patients with dementia living in nursing homes suffer from pain
- The prevalence correlates with the severity of the disease
- Approximately 94% of patients suffer from persistent pain (>3 months)
- Causes include GU infections, pressure ulcers, skin diseases, and musculoskeletal pathologies



## Alzheimer disease (cont)

- Prevalence rates of dementia patients at home:
  - Varies if study is self-reporting or reporting by caregiver
  - Can differ by over 20%
  - At least 50% of dementia patients in the home seem to have pain
- Pain is prevalent whether the patient lives at home or in a facility



## Pain assessment and pathophysiology

- Self reporting is unreliable
- Behavioral indications of pain are more reliable. Facial expressions of pain in particular are very useful.
- Experience of pain in dementia patients is not diminished and may in fact be enhanced.
- fMRI shows brain activity is preserved, and sometimes elevated, in patients with mild forms of Alzheimer disease.
- In later stages of dementia, the ascending pain pathways may be more severely affected, resulting in reduced pain processing



## Pain management in Alzheimer disease

- Acetaminophen – probably first line agent in nursing homes.
  - One study demonstrated that patients were more active and interactive. Did not reduce agitation. No validated pain assessment scales were used.
  - 39 nursing home patients with advanced AD and degenerative joint diseases were in a randomized crossover trial. DS-DAT (Discomfort scale-Dementia of Alzheimer Type) assessed pain. No differences were found, but the dosage of the analgesic may have been too low.
- Opioids – morphine and oxycodone have been looked at in small studies. With pain scales, no specific differences were found, but there were some differences in subgroup analyses. Need to be careful using these types of medications in this population.



## Pain management in AD – Summary

- There are very few randomized trials.
- Many patients are not assessed using validated scales.
- There is a need for better trials and for better scales.
- The treatment may change depending upon how advanced the dementia is.
- Acetaminophen should probably be used first line, although the data for this is scant.



## Parkinson disease

- Lot of research interest in pain in PD in last fifteen years
- Pain is a known non-motor symptom of PD that can impact greatly on a patient's quality of life
- Definitely higher prevalence than in healthy elderly control subjects
- Not specifically linked to dystonia or rigidity in the disease



## Clinical features of pain in Parkinson disease

- Five different types of pain are recognized
  1. Musculoskeletal
  2. Radicular-neuropathic
  3. Dystonic
  4. Central neuropathic
  5. Akathisia
- Most patients complain of a nociceptive pain, which can be a combination of musculoskeletal and visceral.
  - Musculoskeletal is from abnormal postures from dystonia, rigidity, and akinesia
  - Visceral is the result of abnormal function from the nervous system



## Prevalence of pain in Parkinson disease

- Many studies, ranging from 30% to 80%
- A meta-analysis that used criteria to only include more rigorous studies showed an average prevalence of 67.6%
- Location of the pain varies:
 

Lower limbs – 47.2%	Back 14.3%
Upper limbs – 13.4%	Neck/shoulder region – 12.4%
- Type of pain:
 

Musculoskeletal 46%	Dystonic 19.6%	Radicular 9.1
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- Pain is more prevalent as the disease stage of PD advances



## Treatment of pain in Parkinson disease

- No systematic study on treatment of pain in Parkinson disease
- A review of studies showed
  - 37.6% of patients use non-opioid analgesics
  - 13.5% of patients use opioids
  - 11.8% of patients use anti-depressants and/or anticonvulsants
- Deep brain stimulation (DBS) is used for treatment of PD motor symptoms
  - STN implantation in eight patients showed an increase in the pain threshold when the DBS was switched on as compared to when it was turned off
  - PET investigation revealed that brain activity was reduced related to pain



## Huntington disease

- Study of pain in HD is sparse
- Eight studies representing 1861 patients reported on the prevalence of pain in HD – 41.3%
- There were substantial differences between the studies, however, with the pain prevalence ranging from 10% to 75%
- Studies used different validated scales
- Four of the studies used pain severity as part of prevalence
- Six asked about pain in the last 24 hours, one in the last four weeks, and in one study the time course was unclear



## Huntington disease (cont)

- Pain burden appears to be lower than the general population
- Higher score on depression and anxiety scales, and having comorbid conditions, were associated with an increased severity of pain
- Behavioral disturbances (i.e. irritability) were not associated with an increased severity of pain
- Even though depression is twice as high in HD patients than in general population, the rate of depression seems to be less
  - Anti-depressants and dopamine blockers might have analgesic effect
  - There is also cognitive dysfunction in HD, and these might impact on the patient's ability to communicate about one's pain



## Parkinson-plus disorders: Progressive supranuclear palsy (PSP)

- Disorder that may at first appear to mimic Parkinson disease
- Causes problems with walking, balance, and eye movements
- There are often difficulties with falls and with swallowing
- There can be cognitive problems, particularly impulsiveness and difficulties with reasoning and decision-making
- Currently no treatments
- Much less common than Parkinson disease





## Progressive supranuclear palsy and pain

- One study in the literature of 16 patients
- Appears to be less intense than in patients with Parkinson disease
- Less prevalent than in patients with Parkinson disease
- Cognitive factors in PSP may reduce pain perception
- One patient was on amitriptyline for pain
- Five patients were on regular pain medications, but none were on the typical neuropathic pain medications (i.e. gabapentin, pregabalin)
- Most common location of pain was the lower limbs followed by the arms



## Parkinson-plus disorders: Multiple system atrophy (MSA)

- Formerly called Shy-Drager, striatonigral degeneration, or olivopontocerebellar atrophy – all are pathologically identical
- Similar to PSP, it may appear to mimic PD, at least at first
- There are two subtypes: Parkinsonian and Cerebellar
- Both can have autonomic issues such as neurogenic orthostatic hypotension, incontinence, sweating abnormalities, and sexual dysfunction

### MSA-P

- Rigidity
- Difficulty bending limbs
- Slow movement
- Problems with posture
- Tremors (but rare compared to PD)

### MSA-C

- Impaired movement and coordination
- Dysarthria
- Dysphagia
- Visual disturbances such as double vision



## Multiple system atrophy and pain

- One study in the literature with 21 patients
- Pain intensity and prevalence similar to Parkinson disease
- Neck and shoulders are common location of pain
- Three patients met criteria for neuropathic pain
- Eleven patients were on regular pain medications
- Four patients were on neuropathic pain medications
- Even though dopaminergic medications provide suboptimal benefit at best for MSA patients, 57% reported improvement in pain symptoms



## Summary

- Pain is common in neurodegenerative disorders
- Patients may not mention it
- Patients may not have the capacity to communicate about it
- It is imperative to ask caregivers about this
- For patients who have dementia, one may need to infer based on changes in behaviors
- Optimizing care of the underlying disease can help reduce the prevalence and the intensity of the pain
- More research is needed in pain in neurodegenerative disorders



Thank you!



"Mr. Osborne, may I be excused? My brain is full."

