

Pain and Parkinson's

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Disclosures

- Research support from:
 - National Institute on Aging, National Institute of Neurological Disorders and Stroke, Parkinson's Foundation, CurePSP, private philanthropic support
- Royalties: UpToDate, Inc.
- Editorial Board: American Academy of Neurology Brain & Life

- Relevant to today's talk:

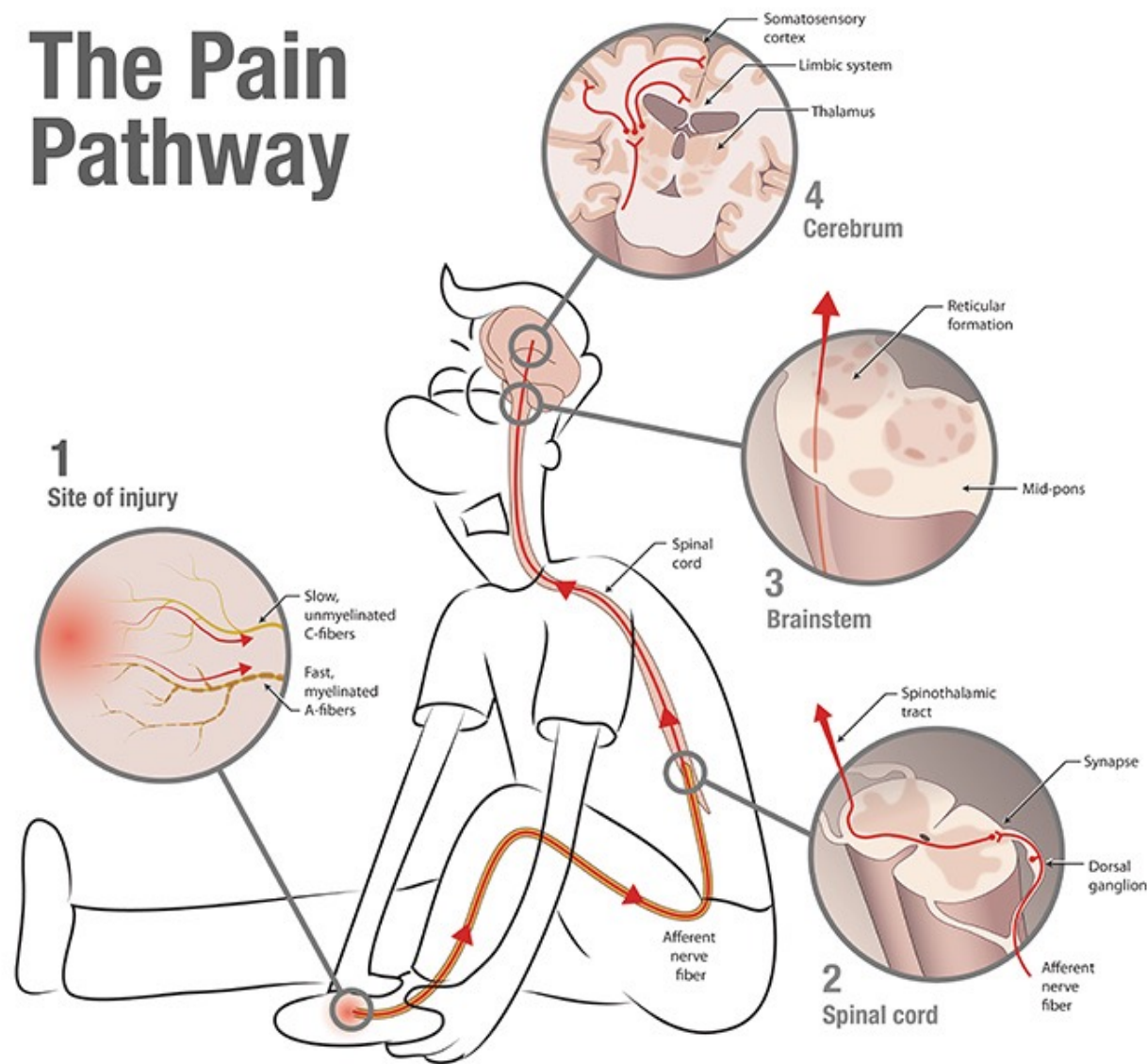


- Some off-label uses of medications described

Objectives

- To understand the prevalence of pain in Parkinson's
- To identify and describe the different types of pain commonly experienced in Parkinson's
- To learn about current treatments for pain in Parkinson's, including pharmacologic and non-pharmacologic options

The Pain Pathway



How Common is Pain in Parkinson's?

- Even Dr. Parkinson recognized it!
- Depending on pain *type*, up to 90% of people with Parkinson's report pain at some point
- Chronic pain is twice as common in Parkinson's
 - Often not discussed

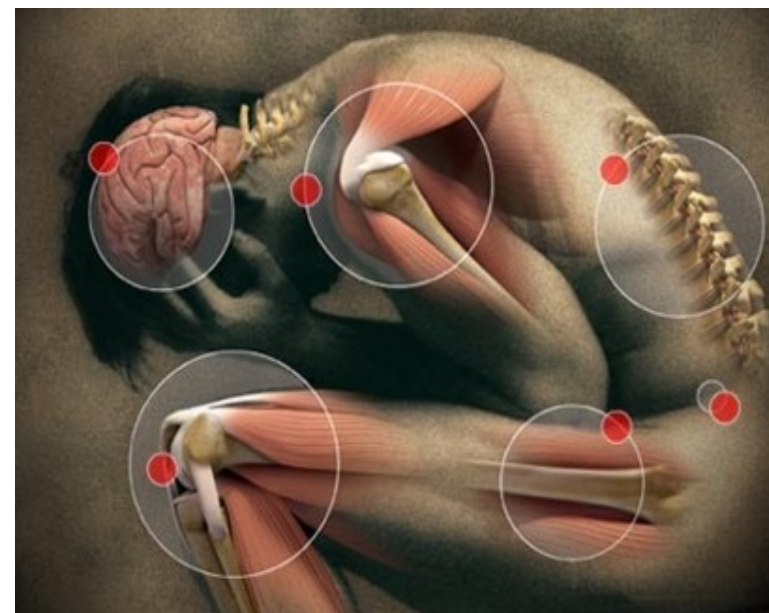


When Do People Experience Pain in Parkinson's?

- In early Parkinson's, pain may be the most bothersome *non-motor* symptom
- In advanced Parkinson's, pain was rated as the sixth most troubling symptom
- Even early in Parkinson's, there are changes in the nerve endings, spinal cord and brainstem pathways that detect and regulate pain

Types of Pain in Parkinson's

- Musculoskeletal pain
- Dystonic pain
- Radicular/neuropathic pain
- Central pain



Musculoskeletal Pain

- **45-75% prevalence**
- Problems in the muscles or bones/skeleton, usually related to rigidity and decreased movement, +/- arthritis
- Muscle cramps, tightness
 - Most often neck, arm, paraspinal, calf muscles
 - May be present for years *before* Parkinson's is diagnosed
- Joint pain
 - Most often **shoulder**, hip, knee, ankle
 - Often unilateral shoulder pain, limited range of motion
 - May be presenting symptom

Dystonic Pain

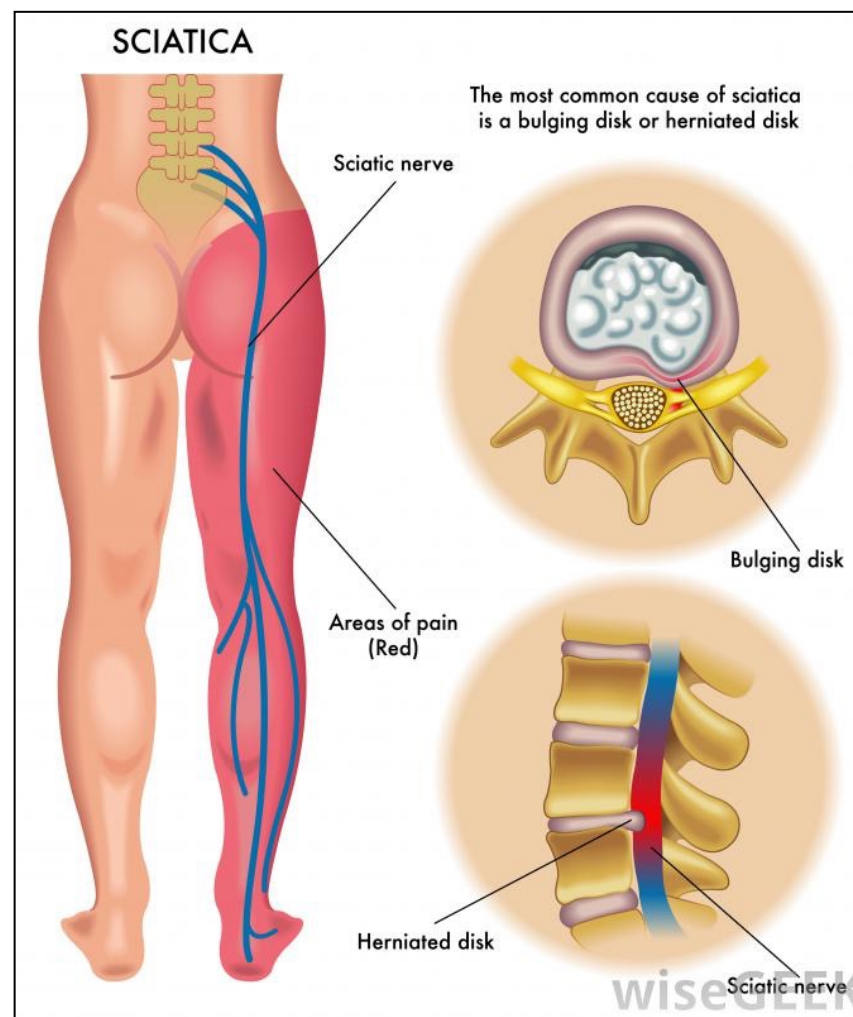
- 8-50% prevalence
- Repetitive, patterned postures of dystonia can cause severe, painful spasms of extremities, face and pharyngeal muscles
 - Paroxysmal; can be spontaneous or triggered by movement
 - Can occur early in Parkinson's unrelated to medications
 - Can occur later in Parkinson's associated with medications

Dystonic Pain

- Foot dystonia (plantar flexion and foot inversion) may occur early and as presenting symptom, particularly early-onset cases, *Parkin* cases
- Dystonia more often as complication of treatment
 - Early morning off-dystonia in 15%, symptom of dopaminergic deficiency
 - Diphasic, peak dose dystonia (most often in neck & face)

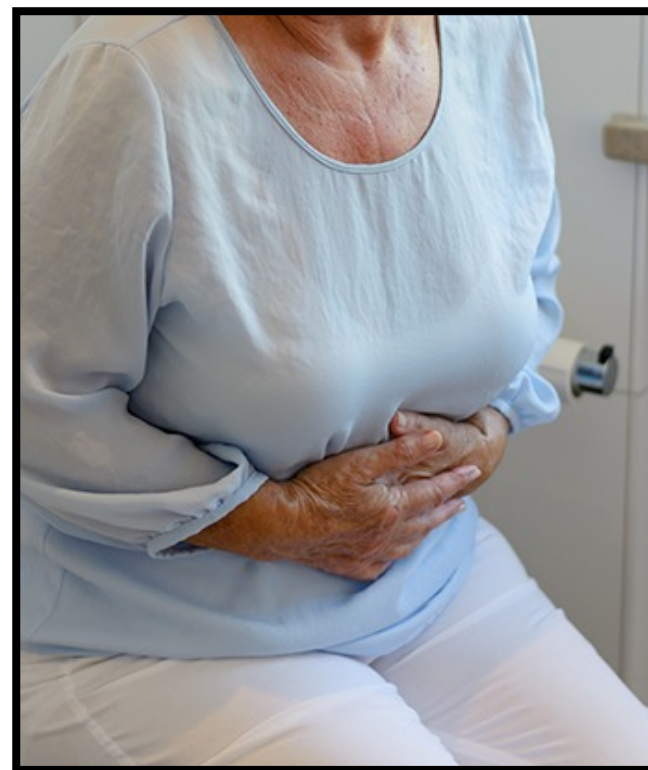
Radicular or Neuropathic Pain

- 5-20% prevalence
- Distribution of one nerve or nerve root
 - Exclude other causes
 - Neurological, electrophysiological and imaging tests may be needed
 - May be due to postural abnormalities or dystonia → discopathy → radiculopathy or mononeuropathy



Central Pain

- 10-12% prevalence
- Poorly localized, vague character, constant pain; not localized to a nerve distribution
 - May have autonomic/visceral character in some people with Parkinson's, with reports of abdominal pain or reflux, dyspnea, or feeling flushed
 - May have oral, genital or rectal pain



Talking with Your Health Care Provider about Pain



Talking with Your Health Care Provider about Pain



- OLD CARTS
 - Onset
 - Location
 - Duration
- Character
- Aggravating and alleviating factors
- Radiation
- Timing
- Severity

HAVE YOU EXPERIENCED ANY OF THE FOLLOWING IN THE LAST MONTH?

	Yes	No
1. Pain around the joints (including pain related to arthritis)	<input type="checkbox"/>	<input type="checkbox"/>
2. Pain related to a specific internal organ (for example, pain around the liver, stomach or bowels)	<input type="checkbox"/>	<input type="checkbox"/>
3. Generalised non-specific pain in your stomach area.....	<input type="checkbox"/>	<input type="checkbox"/>
4. Non-specific pain deep within the body: a generalised constant, dull, aching pain.....	<input type="checkbox"/>	<input type="checkbox"/>
5. Pain related to abnormal involuntary movements (dyskinetic pain)	<input type="checkbox"/>	<input type="checkbox"/>
6. Painful muscle cramps in a specific region during “off” periods (when your medication is not working).....	<input type="checkbox"/>	<input type="checkbox"/>
7. Generalised pain during “off” periods (pain in the whole body or areas that are not affected by muscle cramps).....	<input type="checkbox"/>	<input type="checkbox"/>
8. Pain related to jerking leg movements during the night or an unpleasant burning sensation in the legs which improves with movement (restless legs syndrome)	<input type="checkbox"/>	<input type="checkbox"/>
9. Pain related to difficulties when turning in bed at night	<input type="checkbox"/>	<input type="checkbox"/>
10. Pain when chewing	<input type="checkbox"/>	<input type="checkbox"/>
11. Pain related to grinding teeth during the night	<input type="checkbox"/>	<input type="checkbox"/>
12. Burning sensation in your mouth.....	<input type="checkbox"/>	<input type="checkbox"/>
13. Burning pain in the limbs (often associated with swelling or medication).....	<input type="checkbox"/>	<input type="checkbox"/>
14. Shooting pain/pins and needles down the limbs	<input type="checkbox"/>	<input type="checkbox"/>

Parkinson's Pain Questionnaire

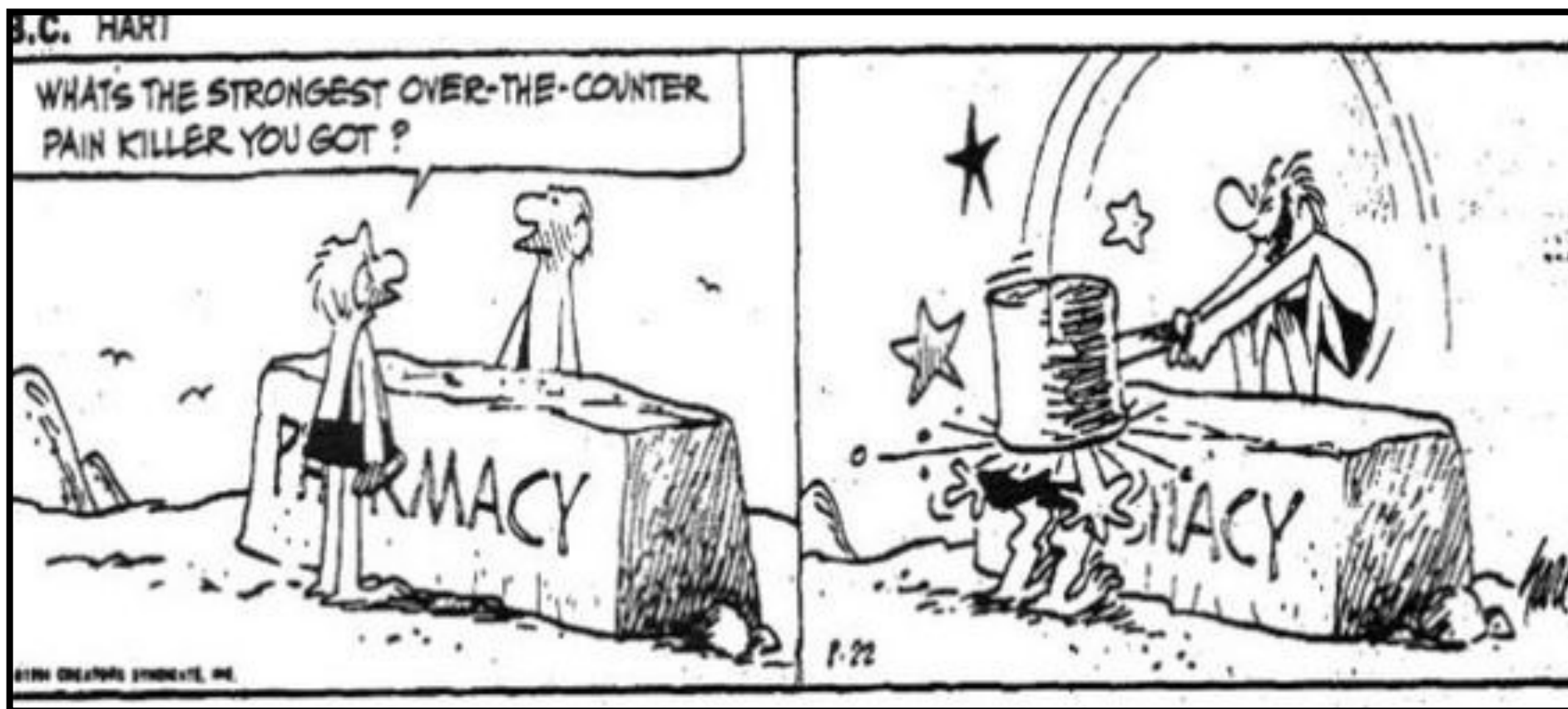
- https://openaccess.sgul.ac.uk/id/eprint/112582/1/First_comprehensive_tool_for_screening_pain.pdf

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Write It Down!

	Meds	Monday	Tuesday	Wednesday
8am	Levodopa	On	<i>Toe curling, pain</i>	On
10am			Took S late	
12pm	Rasagiline			
2pm	Levodopa			
4pm				
6pm			<i>Muscle stiffness</i>	
8pm	Levodopa	<i>Forgot evening dose</i>	On	

Management of Pain in Parkinson's



Management of Pain in Parkinson's

- **Multidisciplinary approach across the Parkinson's spectrum**
- Exercise, physical therapy
 - Maintain range of motion, prevent falls, fractures, contractures
- Interdisciplinary palliative interventions have demonstrated that pain is both common *and* treatable
- Only 3 drugs have been studied for pain in Parkinson's in rigorous randomized controlled trials...and they failed*



Management of Pain in Parkinson's

- **Musculoskeletal Pain:**

- Usually **physical therapy**, +/- medications
- Heat/ice, massage, gentle stretching, topical OTC therapies
- If pain is due mostly to rigidity or bradykinesia: dopaminergic therapy may help
 - Levodopa, dopamine agonists
 - Therapies to extend duration of dopaminergics, including COMT inhibitors (e.g., entacapone) and MAO-B inhibitors (e.g. rasagiline)
 - Safinamide shows possible improvement in use of pain medications
- If rheumatologic or orthopedic: Nonsteroidal anti-inflammatory drugs (such as ibuprofen or naproxen) or other analgesics
- Orthopedic joint surgery if indicated

Management of Pain in Parkinson's

- **Radicular/neuropathic pain:**

- Avoidance of overuse or poor posture – PT & OT
- May require surgery to remove the disc pressing on the nerve
- MANY med options, combination may be most effective:
 - Low-dose antidepressants, including tricyclic antidepressants (e.g., nortriptyline) and selective serotonin-norepinephrine reuptake inhibitors (e.g., duloxetine)
 - Antiepileptics (e.g., gabapentin or pregabalin)
 - Non-steroidal anti-inflammatory drugs (e.g., ibuprofen)
 - Opioid analgesics (e.g., morphine, codeine)

Management of Pain in Parkinson's

- **Dystonic pain:**
 - Manipulation of dopaminergic medications
 - Adjustment of dosage, dosage times, switching to longer acting preparations to reduce dopamine pulsatility
 - **Rotigotine:** improved fluctuation-related and early-morning pain in 2 studies
 - Evaluating and manipulating dietary protein
 - Amantadine for peak-dose dyskinesias
 - Botulinum toxin injections for focal dystonia (striatal toes, dystonic fists)
 - Difficult balance between symptom relief and preserved function
 - DBS to STN and GPi has shown improvement of dystonia, dystonic pain

Management of Pain in Parkinson's

- **Central pain:**
 - Dopaminergic therapy
 - Anti-inflammatory agents
 - Antiepileptics (e.g., carbamazepine, gabapentin)
 - Antidepressants (e.g., tricyclic antidepressants such as nortriptyline)
 - Opiates (e.g., morphine, codeine)
 - Atypical neuroleptics (e.g., clozapine)



Management of Pain in Parkinson's

- **Other contributors:**

- *Depression!!*
- Diabetes
- Osteoporosis
- Rheumatologic disease (e.g., rheumatoid arthritis, psoriatic arthritis, polymyalgia rheumatica)

What about Deep Brain Stimulation?

- Deep Brain Stimulation (DBS) has been studied in relation to pain in multiple studies
 - Most studies, primarily STN DBS, show improvement in pain symptoms with stimulation



What about Alternative Treatments?



What about Medical Marijuana?



Medical Marijuana in Parkinson's

- Aspirin is one chemical
- Marijuana contains at least 60 *active* chemicals, including:
 - THC: tetrahydrocannabinol, psychoactive effects
 - CBD: cannabidiol, potential therapeutic effects
- Receptors for cannabinoids exist throughout the nervous system, especially in the basal ganglia, and have many different effects

Medical Marijuana in Parkinson's

- Survey of 339 people with Parkinson's in Czech Republic:
 - 25% reported using marijuana (not medical); 46% of those people with Parkinson's described some benefit in either tremor, bradykinesia or levodopa-induced dyskinesias
- Small, open-label study (22 people with Parkinson's): subjective improvement in tremor, stiffness, pain and sleep
- 4 controlled clinical studies found NO benefit for motor symptoms and mixed results for dyskinesias and quality of life
 - Most rigorous study of medical marijuana in Parkinson's was for levodopa-induced dyskinesias in 19 people with Parkinson's; insignificant *worsening* of dyskinesias

Medical Marijuana in Parkinson's

- Side effects include: low blood pressure, dizziness, hallucinations, sleepiness, confusion
- Bottom line:
 - Current research suggests that cannabinoids are *probably ineffective* for both levodopa-induced dyskinesias and motor symptoms
 - Further rigorous study of different doses, formulations and target symptoms may reveal specific differences

Summary

- Pain disorders are **common, under-recognized, under-reported, detrimental and manageable** non-motor symptoms of Parkinson's
- **Early, asymmetric stiff or painful shoulder** is a common, often misdiagnosed presenting symptom of Parkinson's
 - Talk with your neurologist/movement disorders specialist *before* you get shoulder surgery!
- Pain categorized as **musculoskeletal, dystonic, neuropathic, or central**, with multiple types present

Summary

- Pain management in Parkinson's requires **attention to timing, quality, and relation to medication doses**
 - **Keep a diary!** Consider using the King's Parkinson's Pain Scale or another standard scale to track symptoms the same way over time
 - **OLD CARTS!** Onset, location, duration, character, aggravating/alleviating factors, radiation, TIMING, severity
- **Multidisciplinary, customized approach** to pain:
 - **Physical therapy and exercise** to improve mobility, prevent contractures, maintain range of motion
 - **Pharmacotherapy tailored to the particular pain type(s)**
 - No proven benefit for medical marijuana or other alternative treatments (yet?)

References

- Boersma I, et al. *Neurol Clin Pract* 2016 Jun;6(3):209-219.
- Cattaneo C, et al. *J Parkinsons Dis* 2016 Oct 11
- Del Sorbo F, et al. *Park and Rel Disord* 2012;18S1:S233-S236
- Fil A, et al. *Park and Rel Disord* 2013;19:285-294
- Geroin C, et al. *Curr Neurol Neurosci Rep* 2016;16:28.
- Ghaffari BD, et al. *Curr Neurol neurosci Rep* 2014 Jun;14(6):451.
- Ha AD, et al. *Mov Disord* 2012;27(4):485-491
- Jarcho JM, et al. *Pain* 2012 April; 153(4)
- Kluger B, et al. *Mov Disord* 2015 Mar; 30(3):313-327.
- Koppel BS, et al. *Neurology* 2014 Apr 29;82(17):1556-1563.
- Martinez-Martin, et al. *Eur J Neurol* 2018;25(10):1255-1261.
- Miyasaki JM, et al. *Parkinsonism Relat Disord* 2012 Dec;18 Suppl 3:S6-9.
- Moreno CB, et al. *Neurologia* 2012;27(8):500-503.
- Rukavina K, et al. *Neuropharmacology* 2022, epub ahead of print.
- Shulman LM, et al. *Mov Disord* 2002 Jul;17(4):799-802.
- Trenkwalder C, et al. *Lancet Neurol* 2015 Dec;14(12):1161-70.
- Truini A, et al. *J Neurol* 2013;260:330-334.

Thank You!



“Art is my therapy for Parkinson’s. Photography takes me on adventures to places where I can observe and experience nature closely. It gives me a way to express myself without words and brings me a joy that comes from sharing my view of the world with others.”

Blue and Gold Morning, Jeanmarie Shelton
PDF Creativity and Parkinson’s Project

Questions and Discussion

