Research on Cannabis and PD: Is there any evidence?

Benzi M. Kluger, MD, MS
Associate Professor of Neurology and Psychiatry
Director Palliative Care Section,
University of Colorado Denver

MOVING FORWARD together

DISCLOSURES

I have no financial disclosures related to the work presented.

However, I do live in Colorado.

MOVING FORWARD together

LEARNING OBJECTIVES

- Define cannabis, cannabinoids and endocannabinoids
- Review the basic science of the potential of cannabinoids to affect Parkinson's and other movement disorders
- Understand the current state of the evidence of cannabinoids as a treatment for Parkinson's
- Know the most common side effects of cannabinoid-based therapies

MOVING FORWARD together

MOVING FORWARD together

OUTLINE

- What is cannabis, cannabinoids and endocannabinoids?
- How does cannabis effect the nervous system?
- Do cannabinoids improve motor or nonmotor symptoms in PD?
- Can cannabinoids slow down the progression of PD?

MOVING FORWARD together

I. WHAT IS CANNABIS, CANNABINOIDS AND ENDOCANNABINOIDS?

MOVING FORWARD together

DEFINITIONS

- Cannabis: Is a genus of flowering plants including sativa, indica and ruderalis
- Cannabinoids: Chemicals that act on cannabinoid receptors in the nervous system and other tissues.
- Synthetic cannabinoids are man-made, phytocannabinoids (now over 100) come from the cannabis plant and endocannabinoids are produced by neurons and other tissues.

MOVING FORWARD together

PHYTOCANNABINOIDS

- D9-tetrahydrocannabinol (THC)
  - Primary psychoactive component of cannabis
  - Higher concentration in Sativa strains
- cannabidiol (CBD)
  - May have more calming effects on the nervous system
  - Significant interest in medical research
  - Higher concentration in indica and ruderalis strains

MOVING FORWARD together

ENDOCANNABINOIDS

- Anandamide
  - name means “bliss”
  - Discovered in 1992
  - May play a role in pain, sleep and other behaviors as well as development
  - Also found in chocolate

MOVING FORWARD together

SYNTHETIC CANNABINOIDS

- Marinol (dronabinol): THC
- Nabilone: Cannabinoid Receptor 1 and 2 agonist
- K2 and Spice
  - Legal alternatives to cannabis
  - Have been associated with adverse health effects and hospitalizations

MOVING FORWARD together

II. HOW DOES CANNABIS EFFECT THE NERVOUS SYSTEM?

MOVING FORWARD together

THE ENDOCANNABINOID SYSTEM

- Cannabinoid Receptor 1 (CB1) and 2 (CB2)
- CB1 primarily in CNS and CB2 in immune system
- Endocannabinoids act on presynaptic neuron to decrease neurotransmitter release at CB1 receptors
- Tend to increase GABA and decrease Glutamate and Dopamine release in the basal ganglia

MOVING FORWARD together

ACTIONS OF CANNABINOIDS

- Agonist, antagonist and partial agonist at CB1 receptors
- Antioxidant and anti-inflammatory effects
- CB2 on microglia
- CB independent effects
  - Other receptors (adenosine A2A)

III A. DO CANNABINOIDS IMPROVE MOTOR SYMPTOMS IN PD?

ANIMAL MODELS

- Published studies generally support motor improvement but effects are mixed as are mechanisms
- CB1 antagonists are most consistently helpful probably through non-dopaminergic mechanisms
- Both CB1 agonists and antagonists have been reported to improve dyskinesias

CLINICAL REPORTS AND TRIALS

- A survey of PD patients (N=339), 25% of respondents reported using cannabis and 46% of these described some benefit; 31% reported improvement of rest tremor, 45% of bradykinesia, and 14% of LID
- In US (N= 207) only 5% reported cannabis use and most reported benefit only for nonmotor symptoms
- All randomized controlled trials to date have been negative

III B. DO CANNABINOIDS IMPROVE NONMOTOR SYMPTOMS IN PD?

CLINICAL REPORTS

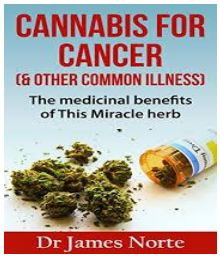
- No randomized controlled trials
- Some case series report benefit for REM Behavior disorder and psychosis
- Colorado experience suggests benefit for appetite, nausea, pain, anxiety and sleep

MOST COMMON SIDE EFFECTS

- Cognitive ("dopey")
- Dizziness
- Low Blood Pressure
- Smoking may increase risk for cancer or other pulmonary issues
- Edibles may have less predictable absorption and dosing

MOVING FORWARD together

IV. CAN CANNABINOIDS SLOW DOWN THE PROGRESSION OF PD?



MOVING FORWARD together

PRECLINICAL MODELS

- Most published studies suggest neuroprotective effect in toxin-based models
- Mechanisms may include anti-inflammatory and microglia effects
- Most studies suggest CB receptors are not involved
- No data in people

MOVING FORWARD together

TAKE HOME MESSAGES

- There are many different psychoactive chemicals in cannabis and products derived from cannabis may vary widely in terms of their benefits and side effects.
- There is currently no conclusive evidence supporting the benefits of cannabis for any aspect of Parkinson's.
- Anecdotal evidence suggests that cannabis may help pain, sleep, appetite, nausea and anxiety.
- Research to date on motor symptoms and dyskinesias in people have been either negative or inconclusive to date.
- Potential side effects include confusion, low blood pressure, falls and pulmonary issues if smoked.

MOVING FORWARD together

QUESTIONS?

MOVING FORWARD together