



Parkinson's Foundation

Marijuana and PD: What Do We Really Know?

Benzi M. Kluger, MD, MS

Associate Professor, Neurology & Psychiatry
University of Colorado Denver

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Better Lives. Together.

I have no financial disclosures related to the work presented.

However, I do live in Colorado.



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





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?



What is cannabis, cannabinoids and endocannabinoids?



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.



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



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



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



How does cannabis effect the nervous system?



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

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)



Do cannabinoids improve motor symptoms in PD?



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

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

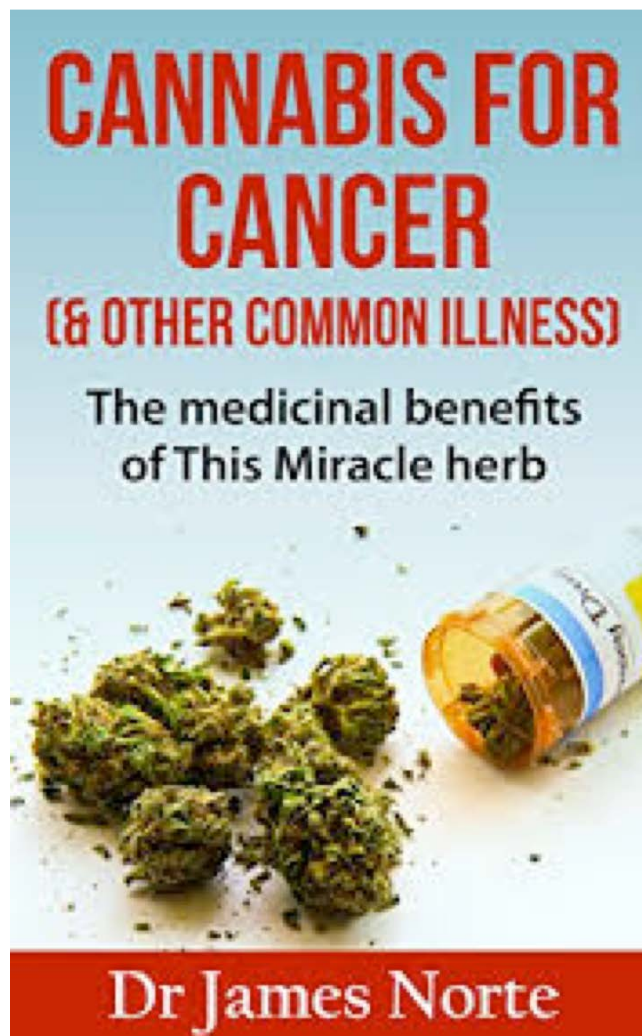
Low Blood Pressure

Smoking may increase risk for cancer or other pulmonary issues

Edibles may have less predictable absorption and dosing



Can cannabinoids slow down the progression of PD?



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



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.





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Monday through Friday
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