

Cannabis and Health

Module 12: Neurocognitive/Brain Disorders Part II

Lecture 5: Cannabis and the Treatment of Parkinson's
Disease and Alzheimer's Disease

Cannabis as Treatment: Parkinson's

- Traditional PD medications (L-dopa) often have side effects when used over the long-term (e.g., dyskinesia)
- Some evidence has implicated the role of the endocannabinoid system in neurodegenerative diseases
 - Leading to hypothesis that cannabinoids may be useful for PD and related conditions
- The NAS committee reviewed the literature on cannabinoids to treat PD symptoms

Cannabis as Treatment: Parkinson's

- The NAS considered two studies on PD
- An RCT (double-blind, placebo-controlled trial; $n = 21$)
 - Administered CBD capsules (75mg, 300mg, or placebo/day).
 - Assessed Dyskinesia (UPDRS) and global functioning (PDQ-39)
 - There was a significant effect on global functioning but not dyskinesia (only in 300 mg/day vs. placebo)
 - Limited by small sample size ($n = 7$ /condition)

Table 2. Variations in the scores of UPDRS, PDQ-39, BDNF levels and NAA/Cr between baseline and final assessment.

	Placebo	CBD 75 mg/day	CBD 300 mg/day	ANOVA (F ; p) or Kruskal-Wallis test (p)
	Variation/Baseline-Final (DP)	Variation/Baseline-Final (DP)	Variation/Baseline-Final (DP)	
UPDRS total on	3.83 (± 6.85)	3.00 (± 5.97)	6.57 (± 5.83)	$F=0.631$; $p=0.544$
PDQ-39 total	6.50 (± 8.48) ^b	10.00 (± 12.15)	25.57 (± 16.30) ^b	$F=4.142$; $p=0.034$

Chagas et al., 2014

Cannabis as Treatment: Parkinson's

- An open-label observational study assessed the effects of smoked cannabis (0.5 g) in 22 patients (*no control*)
 - Assessed dyskinesia (UPDRS), pain, and subjective efficacy
 - Investigators found total motor symptoms improved, as well as specific motor symptoms improved (e.g., tremor, rigidity).
 - There were also subjective effects (pain, sleep)

TABLE 2. Effect of Cannabis on Motor UPDRS Score

	Before Smoking Cannabis	UPDRS	<i>P</i>
		After Smoking Cannabis	
Tremor (items 20–21)	7.55 (4.79)	3.64 (2.8)	0.000
Rigidity (item 22)	7.55 (3.79)	6.48 (3.56)	0.004
Bradykinesia (items 23–27, 30–31)	13.12 (6.88)	8.62 (5.5)	0.000
Posture (items 28–29)	1.90 (1.58)	1.55 (1.1)	0.056

The effect of Cannabis on different categories of the UPDRS.

Cannabis as Treatment: Parkinson's -- Conclusions

- The NAS concluded: “There is insufficient evidence that cannabinoids are an effective treatment for the motor system symptoms associated with Parkinson’s disease or L-dopa induced dyskinesia.”

Cannabis as Treatment: Dementia

- Dementia symptoms cause distress (to patient and caregivers) and may precipitate the patient being placed in institutional care
- Current treatments for dementia target acetylcholine (e.g., cholinesterase inhibitors) and have only modest effects
- Treatments for behavioral disturbances are off-label (antipsychotic medications that sedate)
 - These medications have modest effects to reduce behavioral disturbances but also have substantial adverse effects

Cannabis as Treatment: Dementia

- The disappointing efficacy of dementia treatments has led clinical scientists to look for alternate treatments
- Synaptic transmission is thought to be disordered in dementia and may be related to its symptoms
- CB1r and the endogenous cannabinoid system
 - Thought to be important for regulating synaptic transmission
 - May be neuroprotective
 - Thus, given its potentially neuroprotective and anxiolytic effective, cannabinoids may help treat dementia and/or its behavioral disturbances

Baker et al., 2003; Grundy, 2002

Cannabis as Treatment: Dementia

- The NAS committee identified two good-quality systematic reviews on cannabis and dementia
 - One of these (Krishnan) was a Cochrane review
 - Both reviews identified and reviewed the same two RCTs
- Unfortunately, both identified RCTs were of poor quality
 - A crossover RCT (6-weeks of dronabinol, placebo 2x/day) presented results “in such a way that they could not be abstracted for analysis.”
 - An open-label pilot study evaluated 6 patients with dementia and nighttime agitation, but did not meet review criteria

Cannabis as Treatment: Dementia

- From the primary literature, the NAS committee identified one good-quality RCT ($n = 50$) of varying types of dementia (Alzheimer's, vascular, mixed)
 - Patients were given 1.5mg THC 3x/day for three weeks
 - Patients did not improve in neuropsychiatric symptoms, agitation, quality of life, or activity of daily living (vs. placebo)
- Notably, the study recruited less than half of the planned sample size, but the authors estimated “only a 5% chance that enrolling more participants would have shown a clinically important effect.”

Conclusions

- The two strongest pieces of evidence on dementia and cannabis come from a good-quality Cochrane review and a good-quality RCT
 - Both found no evidence that cannabinoids are effective for dementia
- NAS Conclusion: There is *limited evidence that cannabinoids are ineffective* treatments for improving the symptoms associated with dementia.
 - That is, while evidence is limited, what evidence there is suggests that cannabinoids do not reduce dementia symptoms.
- But what has been done since the NAS report?