Duration of Neurocognitive Impairment With Medical Cannabis Use: A Scoping Review

Lindsay Lo MSc[1], April Christiansen MSc(C)[2], Lauren Eadie MD[3], Caroline MacCallum MD[3,4]

[1]Dalla Lana School of Public Health, University of Toronto, Toronto, ON, [2]Department of Neuroscience, Queen's University, Kingston, ON, [3]Department of Medicine, Faculty of Medicine, University of British Columbia, Vancouver, BC

Background

- The recreational use of cannabis has well-established dose-dependent effects on neurocognitive and psychomotor functioning, but there is little consensus on the degree and duration of impairment typically seen with medical cannabis use. [1,2]
- Distinct differences between medical and recreational use may not allow the same conclusions to be drawn about the presence or extent of impairment in medical cannabis patients
- THC impairment disrupts important cognitive and psychomotor functions needed for safety-sensitive work, including driving motorized vehicles, thus, the need to elucidate safety regulations surrounding THC use for medical cannabis patients is critical.

Study aims

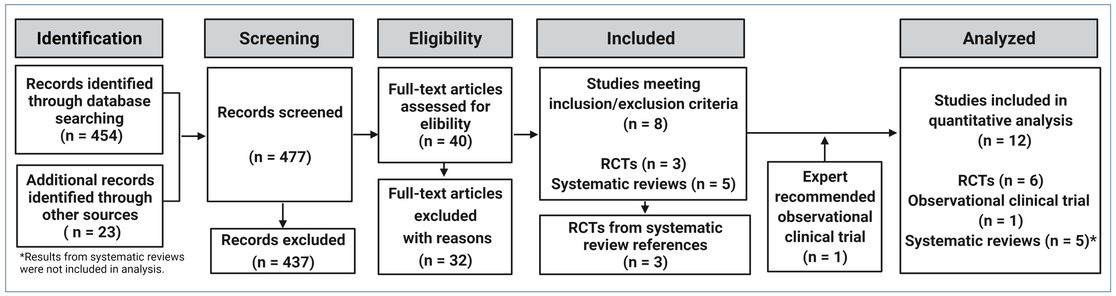
To identify and summarize studies that investigate the duration and degree of acute neurocognitive impairment with medical cannabis use.

Determine	Discover	Compare
What is a reasonable timeline for medical patients to anticipate possible THC-induced impairment.	What standardized objectives were the best at determining THC-induced impairment.	These results to recreational cannabis impairment in literature.

Methods

- **Databases:** Ovid MEDLINE, EMBASE
- **Search terms:** Cannabinoids, dronabinol, marijuana, THC, Sativex, chronic pain, impairment, intoxication, reaction time, coordination, neurocognitive, psychomotor, and their synonyms/variations (available in publication).
- **Inclusion & Exclusion criteria:** See PICOS statement

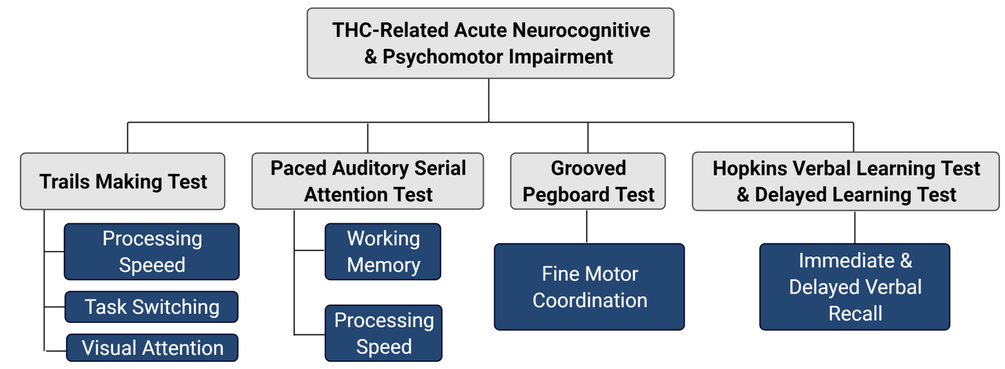
P (Problem, Patient, Population)	Adults living with chronic, non-cancer pain (pain of >3month duration) and/or spasticity.
I (Intervention/ Indicator)	Medical cannabis use or cannabinoid-based medicines.
C (Comparison)	Chronic pain/spasticity controls (without cannabis use). Studies without comparator were included.
O (Outcome of interest)	Duration of acute neurocognitive and psychomotor impairment using objective standardized measures.
S (Study types selected)	Randomized controlled trials and other trials were included.



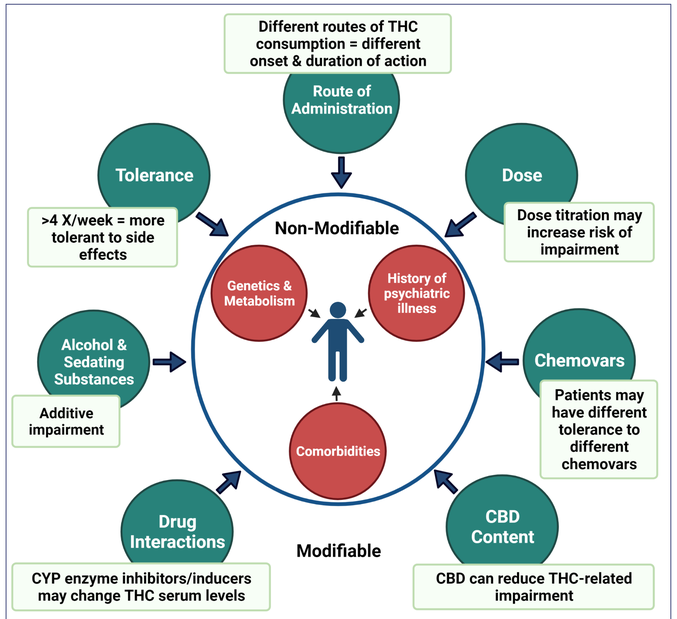
Results

Study	Population	Results
Wallace et al., (2015)[4] Randomized, double-blind, placebo-controlled crossover	Painful Diabetic Neuropathy (n = 16)	Dose-dependent decline in neurocognitive performance with THC exposure. No difference between THC & placebo groups at 240 min (4hr).
Wilsey et al. (2008)[5] Double-blind, placebo - controlled crossover study	Central and Peripheral Neuropathic Pain (n = 38)	Modest decline in cognitive performance with THC use, most significant in the THC group. 76% of participants had cognitive impairment at baseline.
Corey-Bloom et al. (2012)[6] Randomized placebo-controlled trial	Multiple Sclerosis Spasticity (n = 37)	Timed walk: no difference Paced Auditory Serial Attention Test: 4% THC group had worse performance compared to placebo at 45-min.
Notcutt et al. (2004)[7] Prospective, randomized, double-blind, placebo, crossover study	Chronic mostly neuropathic pain (n = 34)	Testing improved after initiation of cannabis-based medicines.
Wilsey et al. (2016)[8] Crossover, randomized, placebo-controlled human laboratory experiment	Patients with refractory neuropathic pain who have disease or injury to their spinal cord (n = 48)	THC showed dose-dependent neurocognitive impairment and resolution 2 hours after inhalation of THC.
Wilsey et al. (2013)[9] Randomized double-blind placebo controlled cross-over trial	Central or peripheral neuropathic pain (Refractory) (n = 39)	THC produced short term neurocognitive impairment. No difference in performance between THC and placebo at 2 h after the last dosing session.
Olla et al. (2019)[10] Observational Clinical Trial	Medical Cannabis Patients (n = 22)	No psychometric evidence for a decline in performance on cognitive testing following THC ingestion compared to normative sample.

- **Neurocognitive assessments post-THC exposure showed no difference between placebo or any THC groups within 4 hours**
- THC impairment was dose-dependent
- Acute impairment was found in the following neurocognitive and psychomotor domains as determined by their respective tests:



Discussion



- Modifiable and non-modifiable factors influence the degree & duration of impairment

Clinical Implications

- Tolerance can be built to the impairing effects of THC using a consistent, low THC dose[3]
- Slow titration method should be used at initiation
  - Utilize CBD dominant or 1:1 THC:CBD chemovars when possible
- Counsel patients on driving or engaging in safety sensitive activities no less than 4 hr (inhaled) or 6 hr (ingested) after cannabis consumption
- Adjust concomitant medications if patient is achieving adequate symptom control with cannabis to decrease risk of drug interactions or compounded sedation

Limitations

- Large heterogeneity in study populations, designs, protocols, objectives measures of impairment
- Only 3/6 studies had baseline cognitive functioning tests for comparison
- Very limited literature on oral THC products
- Relatively small sample sizes → issues in statistical power and strength of conclusions made

References

1. Weil, A. T. (1969). Marihuana. *Science (New York, NY)*, *163*(3872), 1145
2. Eadie, L., Lo, L. A., Christiansen, A., Brubacher, J. R., Barr, A. M., Panenka, W. J., & MacCallum, C. A. (2021). Duration of neurocognitive impairment with medical cannabis use: a scoping review. *Frontiers in psychiatry*, *12*, 286.
3. Grotenhermen, F. (2007). The toxicology of cannabis and cannabis prohibition. *Chemistry & biodiversity*, *4*(8), 1744-1769
4. Wallace, M. S., Marcotte, T. D., Umlauf, A., Gouaux, B., & Atkinson, J. H. (2015). Efficacy of inhaled cannabis on painful diabetic neuropathy. *The Journal of Pain*, *16*(7), 616-627.
5. Wilsey, B., Marcotte, T., Tsodikov, A., Millman, J., Bentley, H., Gouaux, B., & Fishman, S. (2008). A randomized, placebo-controlled, crossover trial of cannabis cigarettes in neuropathic pain. *The Journal of Pain*, *9*(6), 506-521.
6. Corey-Bloom, J., Wolfson, T., Gamst, A., Jin, S., Marcotte, T. D., Bentley, H., & Gouaux, B. (2012). Smoked cannabis for spasticity in multiple sclerosis: a randomized, placebo-controlled trial. *Cmaj*, *184*(10), 1143-1150.
7. Notcutt, W., Price, M., Miller, R., Newport, S., Phillips, C., Simmons, S., & Sansom, C. (2004). Initial experiences with medicinal extracts of cannabis for chronic pain: results from 34 'N of 1'studies. *Anaesthesia*, *59*(5), 440-452.
8. Wilsey, B., Marcotte, T. D., Deutsch, R., Zhao, H., Prasad, H., & Phan, A. (2016). An exploratory human laboratory experiment evaluating vaporized cannabis in the treatment of neuropathic pain from spinal cord injury and disease. *The Journal of Pain*, *17*(9), 982-1000.
9. Wilsey, B., Marcotte, T., Deutsch, R., Gouaux, B., Sakai, S., & Donaghe, H. (2013). Low-dose vaporized cannabis significantly improves neuropathic pain. *The Journal of Pain*, *14*(2), 136-148.
10. Olla, P., Rybalski, N., Hurtubise, J. L., Bartol, S., Foote, R., Cutler, L., ... & Erdozi, L. A. (2019). Short-term effects of cannabis consumption on cognitive performance in medical cannabis patients. *Applied Neuropsychology: Adult*, 1-11.