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

April Christiansen MSc[1], Lauren Eadie MD[2], Lindsay Lo MSc, MPH(C)[3], Carly Pistawka BScH[4], Jeffery Brubacher MD[5], Alasdair Barr PhD[6], Will Panenka MD[7], Caroline MacCallum MD[2]

[1]Centre for Neuroscience Studies, Queen's University, Kingston, ON; [2]Department of Medicine, Faculty of Medicine, University of British Columbia, Vancouver, BC; [3]Dalla Lana School of Public Health, University of Toronto, Toronto, ON; [4]Faculty of Science, University of British Columbia, Vancouver, BC; [5]Department of Emergency Medicine, Faculty of Medicine, University of British Columbia; [6]Department of Anesthesiology, Pharmacology & Therapeutics, Faculty of Medicine, University of British Columbia, Vancouver, BC; [7]Department of Psychiatry, Faculty of Medicine, University of British Columbia, Vancouver, BC

Background

- Recreational cannabis use is associated with acute, dose-dependent impairment in neurocognitive and psychomotor domains required for the execution of safety-sensitive tasks
- There is a limited literature examining the degree and duration of impairment with medical cannabis use
- The magnitude and duration of cannabis impairment in patients using medical cannabis may be exacerbated or mitigated by several modifiable and non-modifiable factors
- Understanding the determinants of these neurocognitive effects in populations using cannabis therapeutically will have a considerable impact on how healthcare providers and policy makers manage and offset potential risks for consumers

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 potential THC-induced impairment?	What measures were the best at determining THC-induced impairment?	How does acute impairment with medical cannabis use compare to that of recreational?

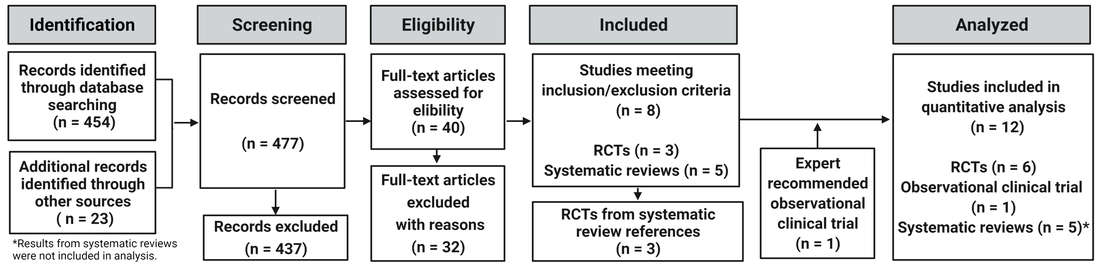
Methods

Databases: Ovid MEDLINE, EMBASE

Search terms: Cannabinoids, dronabinol, marijuana, THC, Sativex, chronic pain, impair, intoxication, reaction time, coordination, neurocognitive, psychomotor, and their synonyms/variations (available in publication)

Inclusion & Exclusion criteria: See PICOS statement

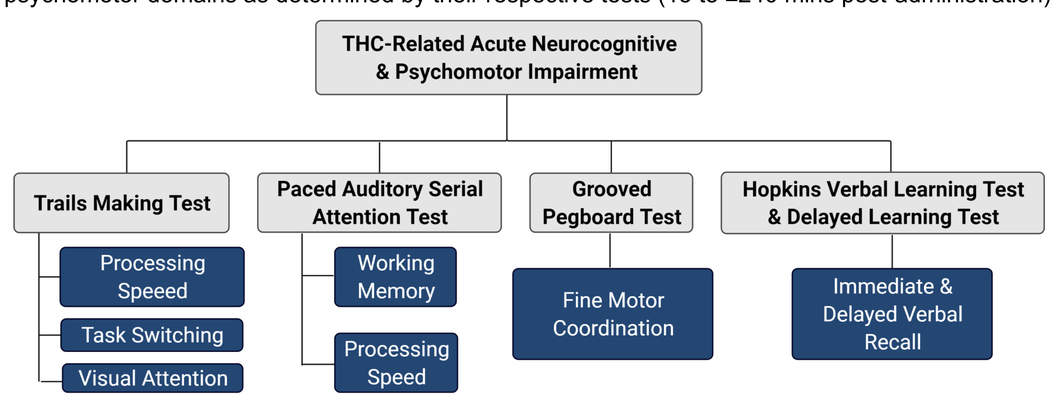
P (Problem, Patient, Population)	Adults living with chronic, non-cancer pain (pain of >3month duration) and/or spasticity.
I (Intervention/ Indicator)	Medical cannabis use or cannabinoid-based medicines.
C (Comparison)	Chronic pain/spasticity controls (without cannabis use). Studies without comparator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



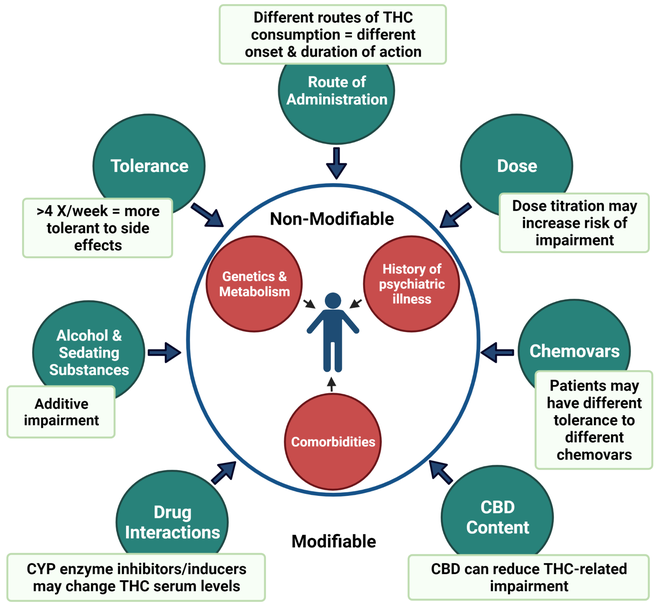
Results

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.

- Cognitive performance declined in a dose-dependent manner with no difference between placebo or any of the THC groups on any neurocognitive measure 4 hours post-THC exposure
- There was variability in the dose-dependent relationship, suggesting there are other important factors contributing to the duration of neurocognitive impairment
- Acute impairment was found to be statistically significant in the following neurocognitive and psychomotor domains as determined by their respective tests (15 to ≤240 mins post-administration):



Discussion



- Cannabis-related impairments in neurocognitive function are time-limited and dependent upon the amount and chemovar used, method of consumption, frequency and length of use.
- Genetics, comorbidities, metabolism and other person-specific factors may influence cannabis-related impairment

Clinical Implications

- Tolerance may 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 and impairment
- Relatively small sample sizes, limiting statistical power and strength of conclusions made

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