

UC San Diego Health

# Role of Cannabis in Essential Tremor

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# Overview

- Review of Tremor symptoms
- Review literature on use of cannabis
- Discuss the status of ongoing cannabis clinical trial for ET

# Types of Tremor

## Ways to Classify Tremors

- **Body part** (head, arms, trunk, legs, voice, etc.)
- **When it occurs** [rest vs. action (postural/kinetic)]
- **Frequency** (fast, medium, slow)
- **Symmetry** (bilateral vs. unilateral)
- **Timing** (constant, intermittent, episodic)

*‘Essential Tremor’ varies by the individual...*

# Causes of Action Tremor

Common

- Enhanced Physiological Tremor
- Essential Tremor
- Parkinson disease
- Functional Tremor
- Dystonic Tremor

- Myoclonus/Asterixis
- Clonus
- Ataxia
- Weakness
- Etc.

Rare

# Treatment Strategies – Therapeutic rationale

- Management of ET depends on disability > severity.
- Treatment can be ‘as needed’ in milder cases that may event-related (going out to dinner or speaking in public) or taken daily when tremors impact activities of daily living.
- Alcohol should not be recommended as a regular therapy for a number of reasons:
  - Tremor suppression is brief
  - Rebound tremors can increase disability
  - Addiction/habitation potential
- You decide whether your tremors are mild, moderate, or severe! (magnitude [of tremor] does not matter)

# Role for Cannabis in ET?

- Anecdotal patient experimentation...maybe
- Pilot data...limited
- Randomized-controlled trials...none

# Literature on use of Cannabis

- Despite anecdotal evidence, small double-blind, controlled trials in multiple sclerosis (Fox 2004) and dystonia (Fox 2002) were negative.
- Oral Cannabidiol (CBD) has received FDA approval for the treatment of seizures associated with Lennox-Gastaut or Dravet syndrome in patients two years of age or older.
- High levels of cannabinoid receptor 1 (CB1) expression in the basal ganglia and cerebellum have been postulated to mediate the potentially beneficial effects of cannabis by inhibiting glutamate release and decreasing reuptake of GABA.
- CB1 blockade has been shown to reduce tremors in rats using a harmaline model of Essential Tremor (Abbassian 2016).

# The road to a well-designed Cannabis Trial

- **Finding a partner:** 1 for 4 on industry partners (3/4 lacked interest in ET or expertise to develop FDA-grade drug)
- **Funding:** Received <\$40k (IETF, Tilray, UCSD CMCR) to run a \$200k+ trial
- **Regulation:** FDA, DEA, Health Canada, UCSD IRB, California Research Advisory Panel
- **Recruitment:** 100's interested, <50 replied to follow up emails, <20 eligible (right diagnosis, willing to participate), <10 participated due to COVID.
- **Using Technology in Future Trials:** COVID has shown how fragile our clinical trial infrastructure is and the need to develop methods for remote assessment.



# Goals of a Cannabis Trial in ET

- Does it work?
- Is it safe?
- What dose is needed for safety/efficacy?
- Does it help everyone?
- How long does it last (how frequently does it need to be dosed)?
- What are the side effects?

# Summary

- Symptoms of tremor are common and sometimes benign.
- Treatment will depend on severity and cause of the tremors
- There is a theoretical rationale for cannabinoids improving essential tremor
- Existing data remains anecdotal
- Coming Soon: Stay tuned to the results of our study!
- **ADVICE TO PATIENTS:** There remains limited information about the regular use of cannabis to treat Essential Tremor. Most importantly, we don't know the dose, side effects, potential interactions and efficacy in an elderly population likely to be on other medications.